Perinatal Outcomes in Brazil:
The Impact of Time, Region, and Income Level on Stillbirth and Neonatal Mortality
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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ABSTRACT

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Abstract

Background: Neonatal mortality and stillbirth remain prominent global health issues. The majority of these perinatal losses occur in low- and middle-income countries and are related to lack of quality care around delivery. Brazil transitioned from a lower-middle income country to an upper-middle income country in 2006 and has over 95% of its births occurring within the health system.

Methods: We conducted a longitudinal, ecological cohort study based on publicly available data from the Brazilian Ministry of Health's data repository on live births and deaths. Data was analyzed at the municipality level from 2000 to 2019. Records from the Atlas of Human Development in Brazil were then used to associate each region with a World Bank income classification.

Results: National neonatal mortality rate decreased from 21.2 in 2000 to 12.4 in 2019. Stillbirth rate decreased from 12.0 to 10.2 over this time. Rates were lower when infants born before 28 weeks gestation were excluded. For infants born between 22- and 27-weeks' gestation, worsening perinatal outcomes were seen after 2012. Municipalities with higher wealth status have lower stillbirth and neonatal mortality rates across all years of the study.

Conclusion: Brazil has made significant progress in neonatal mortality and stillbirth rates from 2000 to 2019, yet inequity in perinatal outcomes remains across the country and is correlated with economic status. Nationally, ongoing improvement is needed for infants below 28 weeks gestation and closer exploration is needed into why there are increasing rates of negative perinatal outcomes amongst infants 22-27 weeks gestation.

Dedication

To my family: My husband Longxiu, my son Leander, and my mother Judy.

For your endless love, support, and encouragement.

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Thank you to my mentors, Dr. Catherine Staton and Dr. Joao Vissoci, who supported my work and career development in the field of neonatal global health. I will be forever grateful for your guidance in research and in life. Thank you to Thiago Rocha and Lincoln Silva for their assistance and instruction in data analysis and use of the Brazilian healthcare databases, and to the rest of the GEMINI Center on your constant support and partnership. Thank you to Dr. Alexandre Filho, who welcomed me into the world of studying health outcomes in Brazil via large data, and to Dr. Mary Story for serving on my thesis committee and sharing her valuable insights in global health.

Thank you to all my professors at the Duke Global Health Institute, from whom I learned how to approach global health through the lenses of clinical medicine, public health, research, and health policy. Equally, I would like to thank my classmates, who brought with them a wealth of personal and professional experience that shaped our learning environment for two years. Our cohort was talented, kind, and resilient. I look forward to continuing to work together to tackle the many global health challenges that face our generation.

Finally, thank you to my friends and family who have supported me throughout all my years of study, including this master's program. Without your constant support I would never have made it this far. Thank you.

1. Introduction

Over 2.4 million neonatal deaths occur each year.[1] The vast majority of these deaths occur in low- and middle-income countries (LMICs),[2,3] and an estimated two-thirds of global newborn deaths can be attributed to a lack of quality care in the perinatal period.[4] Additionally, more than 2.6 million stillbirths occur each year, with 98% occurring in LMICs.[5] Over the past two decades, there has been an increased global focus on pediatric and newborn outcomes, fueled in part by the World Health Organization's (WHO) Millennium Development Goals and subsequent Sustainable Development Goals.[1] While the global community achieved a remarkable reduction in overall child mortality, decreasing from 90 deaths per 1000 live births in 1990 to 43 deaths per 1000 live births in 2015,[6] improvement in neonatal mortality has been less robust. Neonatal mortality now makes up 48% percent of under-5 deaths and remains a key global target for maternal-child health improvements.[1] Stillbirth was not explicitly listed in the MDG goals, and studies on the regional prevalence of stillbirth in LMICs are rare. Stillbirth has been described as one of the "most shamefully neglected areas of public health",[7] and there have been global calls for increased investment in stillbirth research.[8] Together, neonatal mortality and stillbirth represent key global targets for improving maternal-child health outcomes.

1.1 Global Action Against Stillbirth and Neonatal Mortality

In 2014, the WHO released the Every Newborn Action Plan, which set a target of 12 or fewer neonatal deaths per 1000 live births and 12 or fewer stillbirths per 1000 total births in all countries by 2030.[9] While most high-income countries already have perinatal loss rates well below these thresholds, estimates show that many LMICs are unlikely to achieve these outcome goals within this decade. As of 2019, 65% of countries reported neonatal mortality rates at 12 or lower, with 2030 predictions estimating only a moderate increase to 68% of countries achieving this global target.[1] Similarly, we see most high-income and upper middle-income countries already below the 12 stillbirths or less per 1000 total births goal.[2]

Two key challenges exist with the data reporting on neonatal death and stillbirth. First, national level data masks intra-country variation in outcomes. Second, the countries with highest rates of perinatal loss have limited data systems for documenting and reporting deaths, and there is concern about underreporting of stillbirth rates.[5,10] Stillbirth and neonatal mortality both serve as indicators to reflect the quality of the health system. Often these outcomes are interrelated, as obstetrical interventions to prevent stillbirth may increase medically indicated preterm deliveries,[11] and an increase in live preterm deliveries may increase the rate of neonatal mortality in regions lacking the resources to appropriately support these premature infants.

Globally, an estimated 10.6% of infants are born preterm, below 37 weeks gestation, with only four percent of preterm birth occurring before 28 weeks.[12] Preterm infants who are liveborn often need invasive respiratory support, intravenous nutrition, and other forms of medical assistance to survive outside of the womb. In high-income countries, we have seen an increase in preterm survival in recent decades, owing in large part to active resuscitation by medical teams at gestational ages that are considered "periviable".[13] Currently, over 90% of babies born before 28 weeks in high-income countries survive. In contrast, less than 10% of babies below 28 weeks gestation survive in low-income settings, a finding known as the "90:10 survival gap"[14] and a contributing factor to disparate neonatal survival rates in high vs low- and middle-income regions. In past decades, this 28-week threshold was often used when collecting and reporting neonatal mortality rates,[14] but given increasing survival trends below this point, few countries are now applying this threshold for reporting[15] and many nations are now tracking outcomes on all births for infants with signs of life at delivery. This expanded data tracking includes the reporting of stillbirth and neonatal mortality rates for "extremely preterm infants", or those born before 28 weeks gestation.

1.2 Perinatal Outcomes in Brazil

Brazil is an upper middle-income country, as defined by the World Bank Group,[16] and has been since 2006. Prior to this time, however, it was a lower-middle income country and ranked among the worst performing countries in terms of perinatal mortality rates. With progressive improvement in perinatal outcomes at a national level, as of 2015 Brazil no longer ranks amongst the top 10 countries for neonatal mortality or stillbirth.[10] As of 2020, Brazil reported a national neonatal mortality rate of 8 per 1000 live births[3] and, as of 2019, a stillbirth rate of 7.5 per 1000 total births for infants delivered at or after 28 weeks gestation.[17] Across Brazil, over 95% of deliveries occur within the formal health sector,[18] with both live birth and stillbirth data recorded in national databases. These databases, the Live birth Information System[19] and Mortality Information System[20], have been used for over two decades to compile and examine population-level health data in Brazil. Such near-universal data recording allows for thorough tracking of perinatal outcomes, such as stillbirth and neonatal mortality, over time and across municipalities.

A key contributing factor to the improved health outcomes in Brazil, and the ability for Brazil to reliably track these outcomes over time, is the development of the Unified Health System (Sistema Unico de Saude (SUS)) and concurrent efforts by the Brazilian Ministry of Health to accurately measure birth and death outcomes. In 1988, the Brazilian Constitution defined health as a universal right. Two years later, the SUS was launched in attempt to provide unified health coverage in Brazil.[21] The SUS has been widely recognized as a positive example of health system reform in Latin America,[22] and has contributed to the democratization of Brazil.[23] An important feature of the 1988 constitution was that it mandated states to take responsibility of providing healthcare to the people. As part of this decentralization process, Brazilian municipalities were tasked with creating a local health department, which was responsible for co-financing health programs and ensuring that health-care services were delivered.[21]

Geographic variation in health outcomes across Brazil are well described, including for neonatal mortality and stillbirth.[24-27] Complimentary work has demonstrated regional gaps in the health system's capacity for care in specialties such as pediatric surgery,[28,29] and pediatric primary care,[30] and noted an ongoing need for specialty care in many regions of Brazil. Several studies have analyzed factors associated with preterm birth in Brazil including sociodemographic factors and the availability of perinatal care.[31-33] Such regional variation has been linked with differences in population demographics and health services resources. At the same time, gaps have been noted between regional studies and data from the national live birth information system.[34] The regional variation in perinatal outcomes and the concerns about data consistency between studies has fueled the need for an updated in-depth analysis of birth outcomes in Brazil. Additionally, the demographic and socioeconomic diversity across Brazil raises questions about disparities within reported national perinatal outcome rates.

In this study we report trends in the national and regional prevalence of stillbirth and neonatal mortality in Brazil, covering the years 2000 to 2019, and describe these critical perinatal outcomes in the context of regional variations in available economic resources to support health.

2. Methods

In part 1 of this study, we conducted a repeated cross-sectional ecological cohort study based on publicly available and regularly collected data from within the Brazilian healthcare system. Specifically, we used data from the Brazilian Ministry of Health's data repository[35] on deaths[20] and live births[19]. These vital statistics are collected by the State Health Secretariats, reported to the Ministry of Health, and are subject to quality review before being made public. Data was analyzed at the municipality level and was collected between 2000 and 2019. Stillbirths, live births, and subsequent neonatal deaths were recorded.

In part 2 of this study, we used records from the publicly available Atlas of Human Development in Brazil[36], from the United Nations Development Program, addressing municipal and state wealth status across Brazil, from 2002 to 2019. We associated each region with the associated world bank classification of lower income, lower-middle income, upper-middle income, and high-income from the relevant year, following the World Bank Atlas Method.[37]

2.1 Setting and Population

This study pertained to all live born and stillborn infants delivered at a health facility in Brazil from 2000 – 2019.

Brazil is the largest country in South America, and the fifth most populous in the world[38] at approximately 216 million people.[39] It is divided into five main geographic regions: North, Northeast, Midwest, Southeast, and South. Nationally, over 3/4 of individuals live in an urban environment. Population and wealth are not distributed equally between the 5 major regions. For example, the Southeast region, which includes the wealthy states of Rio de Janeiro and São Paulo, covers just 11% of Brazil's territory but accounts for 43% of the population and 56% of its gross domestic product (GDP).[23]

As of 2019, neonatal disorders ranked 13 in terms of causes of death across Brazil.[40] The fertility rate has declined over recent decades and sits at 1.8 births per woman.[41]

2.2 Procedures

Data were extracted from three publicly available data sets: the Brazilian Ministry of Health's data repository[35] on deaths[20] and live births[19] for health outcome data and the Atlas of Human Development in Brazil[36] for wealth status by municipality and state. For health data, records with missing gestational age or birth outcome were excluded. The national datasets categorized births into six gestational age categories: <22 weeks, 22-27 weeks, 28-31 weeks, 32-36 weeks, 37-41 weeks, and ≥ 42 weeks gestation. We therefore utilized these same gestational age categories throughout our analysis.

Using the Atlas of Human Development in Brazil[36] to determine municipal and state Gross Domestic Product (GDP) levels for each year, geographic regions were categorized as "high-income", "upper middle-income", "lower middle-income", and “low-income”, based on World Bank Group Classifications. Geographic regions were reclassified each year.

Ethical approval was not obtained for this study as data was derived from freely available public sources. No patient identifiers were retained in the data sets that could identify an individual person.

2.3 Measures

This study focused on three measures: Stillbirth rates and neonatal mortality rates were clinical measures, and wealth status was an economic demographic measure.

2.3.1 Live Birth

A live birth was defined as any infant born with signs of life at delivery. Live birth status was determined from the SINASC database.

2.3.2 Stillbirth

Stillbirth was defined as any infant born without signs of life at delivery, including heart rate or respiratory effort. Stillbirth status was determined from the SIM database.

While the WHO’s international comparison definition of stillbirth is limited to infants born weighing 1000g or more or at 28 weeks of gestation or later, we use the term to reflect any stillborn infant whose death was recorded in the SIM database. This includes infants born before 28 weeks gestation, in line with international trends in stillbirth reporting.[15,42]

2.3.3 Stillbirth Rate

Stillbirth Rate is defined as the number of stillbirths in a given region of interest divided by the total number of births within that same region of a defined time period.

2.3.4 Neonatal Mortality

Neonatal Mortality was defined as death of an infant that was born alive, with the death occurring within 28 days of birth. Neonatal Mortality status was determined from the SIM database.

2.3.5 Neonatal Mortality Rate

Neonatal Mortality Rate is defined as the number of neonatal deaths in a given region of interest divided by the total number of live births within that same region of a defined time period.

2.3.6 Municipal or State Wealth Status

Geographic regions (municipality and state) were categorized as “high-income”, “upper middle-income”, “lower middle-income”, and “low-income”, based on World Bank Group Classifications. Please see Appendix B for a historic breakdown of Gross National Income cutoffs from the World Bank Group.

2.4 Analysis

Birth and death data for this study were extracted from publicly available sources. Data was then input, cleaned, and analyzed with R studio version 4.2. The SIM and SINASC databases are maintained, and quality controlled, by the Brazilian Ministry of Health. Variables analyzed included: live births (count), stillbirths (count), neonatal death (count), gestational age, sex, region of birth, state of birth, municipality of birth, number of infants delivered per pregnancy, and mode of delivery. Data was aggregated by year, from 2000-2019.

Wealth status of Brazilian state and municipal districts was extracted from the Atlas of Human Development in Brazil before being input into R. Geographic mapping of municipal wealth status (low-income, lower-middle income, upper-middle income, and high-income) was done in R Studio. Variables analyzed included: region, state, municipality, and Gross Domestic Product (GDP). GDP was then used to associate each municipality with a World Bank income designation. Next, we used the Atlas Methodology,[37] as used by the World Bank, adapted to the Brazilian municipality GDP data. This methodology extracts an income value for the a given location (countries in the World Bank approximation) by extrapolating the GNI into the population. We used this approach to approximate our municipalities classification, using the GDP as the proxy for are resources development, instead of the GNI.

Focused analysis of state wealth status and perinatal outcomes was done at 4 time points: 2002, 2006, 20012, and 2019. The first and last timepoints represent the earliest and most recent years for which we had complete perinatal outcome and state economic status data. The year 2006 was chosen as a time point preceding the 2008 global financial crisis. Lastly, 2012 was selected as a time following this recession but preceding a subsequent period of financial and political instability in Brazil that is most reported as starting in 2014.[43]

Data for all portions of this study were extracted in March 2021. Records within SIM and SINASC that had incomplete gestational age or perinatal outcome data were excluded. These records were not factored into percentage calculations and were treated as not contributing to the dataset.

3. Results

A total of 60.4 million records were retrieved from the health databases for the years 2000-2019, from which 59.5 million records had non-missing data and were included in subsequent analysis. From this, there were 58.2 million live births, 588,198 stillbirths, and 694,973 neonatal deaths. Over 98% percent of recorded live births represent singleton deliveries. The greatest number of births occurred between 37- and 41-weeks' gestation for live births (**Figure 1)** and between 32- and 36 weeks gestation for stillbirths. For liveborn infants, 8.7% were born preterm, or before 37 weeks gestation, with less than half a percent of births occurring before 28 weeks.

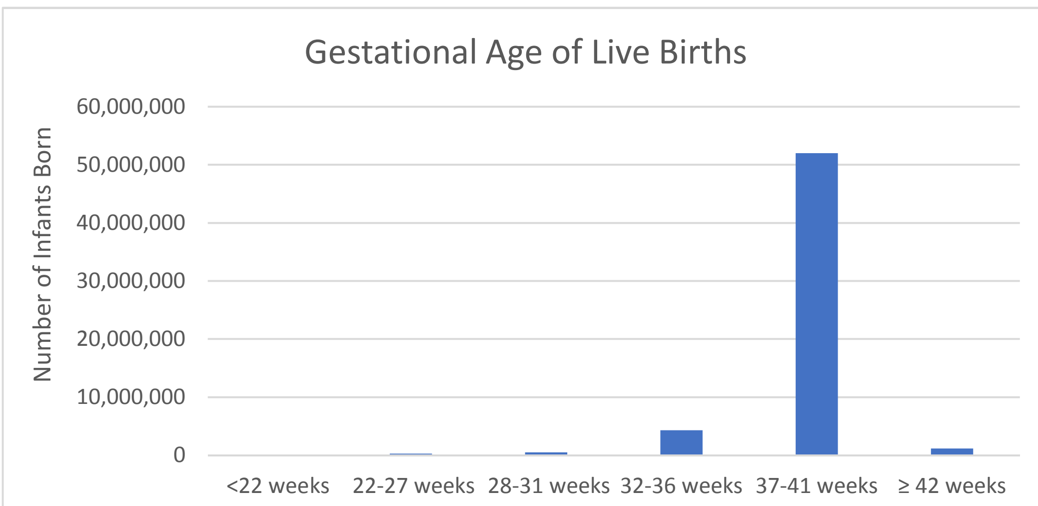

Figure 1: Gestational Age of Live Births in Brazil. Data from SINASC 2000-2019.

For stillborn infants, preterm birth rates are higher with 73.4 percent of stillbirths occurring before 37 weeks gestation and 29.7 before 28 weeks (**Figure 2)**. Similarly, 63.6% of neonatal deaths occurred preterm with 25.7% occurring before 28 weeks gestation. Infants born before 22 weeks gestation made up 0.05% of recorded live births, 6.7% of recorded stillbirths, and 4.42% of recorded neonatal deaths.

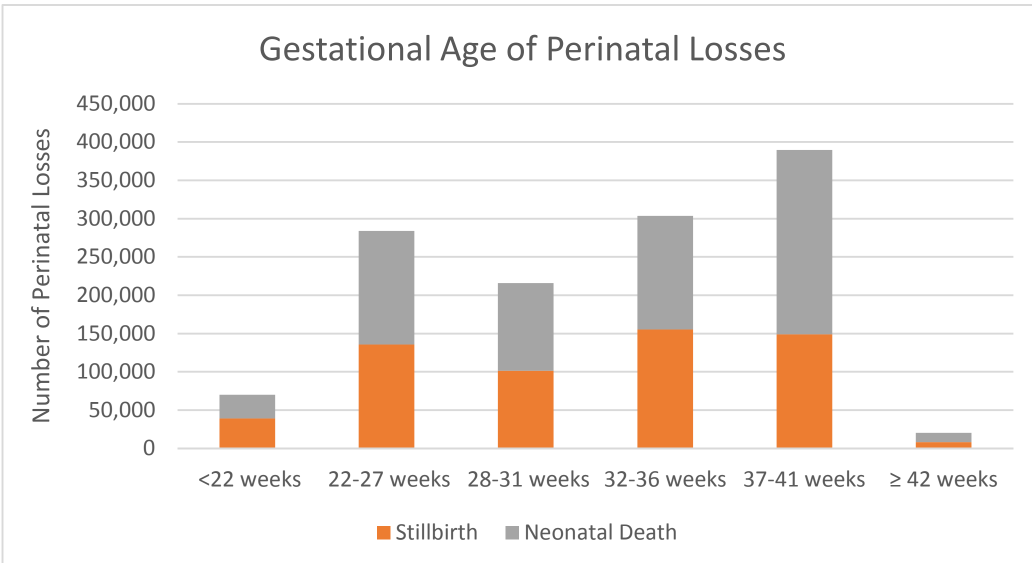

Figure 2: Gestational Age of Perinatal Losses in Brazil. Data from SIM 2000-2019.

Just over half of liveborn infants, 50.9%, were delivered vaginally. A greater number, 71.4%, of stillbirths were delivered vaginally. See **Table 1** for additional delivery parameters.

Table 1: Health Demographics from SIM and SINASC Databases

Demographics		Livebirth		Stillbirth		Neonatal Mortality	
		n	%	n	%	n	%
Gestational Age	<22 weeks	28,106	0.05	39,202	6.66	30,697	4.42
	22-27 weeks	245,339	0.42	135,627	23.06	148,184	21.32
	28-31 weeks	501,440	0.86	101,347	17.23	114,579	16.49
	32-36 weeks	4,305,581	7.40	155,286	26.40	148,355	21.35
	37-41 weeks	52,001,024	89.32	148,788	25.30	240,739	34.64
	≥ 42 weeks	1,135,473	1.95	7,948	1.35	12,419	1.79
	Ignored	1,055,880		69,386		212,477	
Number of Infants	Singleton	58,002,240	98.03	569,934	94.43	666,931	90.86
	Twins	1,126,948	1.90	32,151	5.33	62,590	8.53
	Higher Order Multiples	38,759	0.07	1,483	0.25	4,476	0.61
	Ignored	104,896		53,556		173,451	
Delivery Mode	Vaginal	30,097,998	50.89	425,480	71.38	426,105	58.56
	C-Section	29,048,318	49.11	170,575	28.62	301,594	41.44
	Ignored	126,527		60,557		179,749	
Region	Centro Oeste (Center West)	4,623,460	7.80	45,717	6.96	67,098	7.39
	Nordeste (Northeast)	17,359,649	29.29	223,746	34.06	311,662	34.34
	Norte (North)	6,224,396	10.50	71,294	10.85	113,055	12.46
	Sudeste (Southeast)	23,242,157	39.21	245,478	37.37	317,009	34.93
	Sul (South)	7,823,181	13.20	70,619	10.75	98624	10.87

3.1 *Time Trends in Perinatal Outcomes*

Time trends since 2000 show decreasing neonatal mortality and stillbirth across gestational ages (**Figure 3)**. National neonatal mortality rate (NMR), or deaths per 1000 live births, across all ages decreased from 21.2 in 2000 to 12.4 in 2019. For infants delivered after 28 weeks, Brazil has met the WHO target of an NMR below 12 since 2000, with the NMR further improving from 10.4 in 2000 to 7.3 in 2019. The most rapid improvements in this gestational age group were seen between 2009 and 2011, with the NMR falling from 9.7 to 7.6 deaths per 1000 live births over this two-year period.

Neonatal mortality for live born infants born between 22- and 27-weeks gestational age is higher throughout the study period for all regions. The national NMR in 2000 was 669.9 and peaked at 757.4 in 2005. Similar to gestationally older infants, more premature infants saw a sharp decline in mortality rates around 2010, with the NMR falling from 645.8 in 2010 to 478.9 in 2012. Since 2013, however, there has been a steady rise in the NMR in this age range with a 2019 NMR of 575.2, nationally.

Stillbirth trends parallel neonatal mortality trends across gestational age groups. In 2000 the stillbirth rate (SBR), or stillbirths per 1000 total births, nationally was 12.0. This value decreased steadily to 10.2 in 2019. For stillbirths at 28 weeks gestation or later, the SBR decreased from 7.1 to 6.5 over this same time period. Greater change in SBR was seen in the 22-27 weeks gestational age cohort. In 2019 the national SBR was 780.4, decreasing steadily until 2010 where it reached a value of 587.9. Similar to NMR, the SBR then declined sharply and reached a nadir at 368.6 in 2013. Since 2013, the SBR in this extremely preterm population has increased across Brazil and reached a value of 471.6 in 2019.

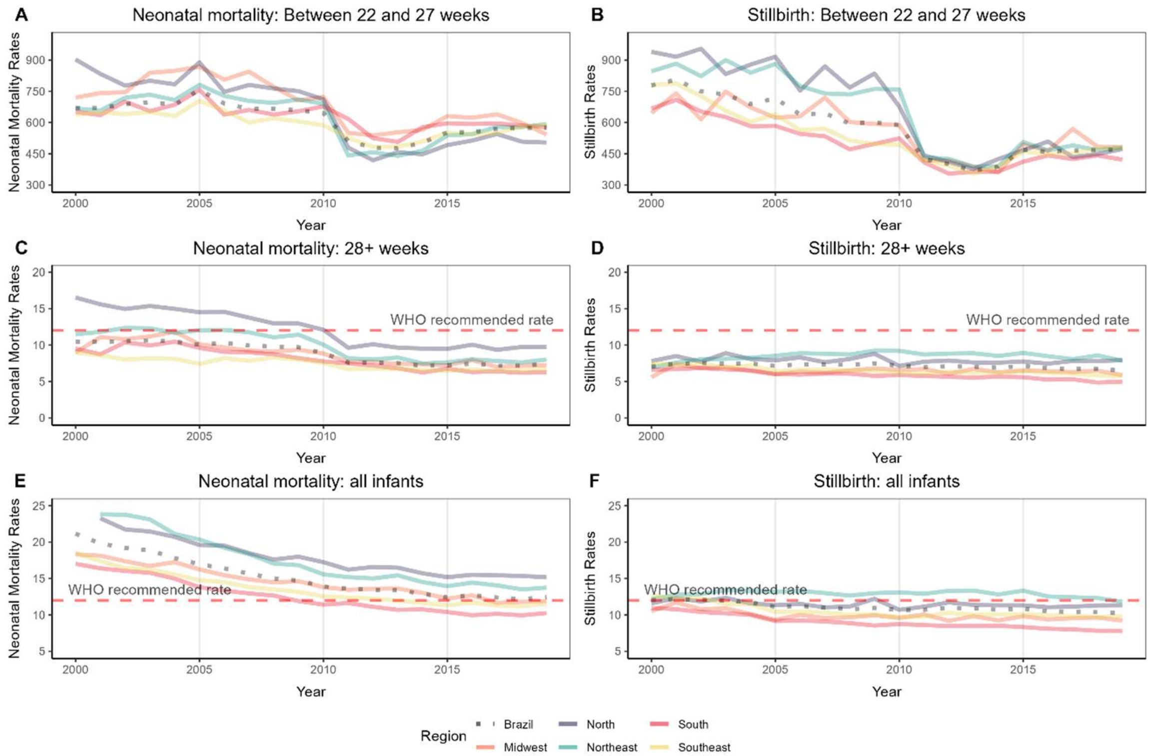

Figure 3: Time Trends in Neonatal Mortality and Stillbirth Across Brazil by Gestational Age

There have also been changes in the relative prevalence of stillbirth and neonatal mortality over time. For infants over 28 weeks gestation, in 2000, 11.86 percent of municipalities had a higher stillbirth rate than a neonatal mortality rate. In 2019, 16.62 percent of municipalities have stillbirth rates that exceed neonatal mortality rates. When we incorporate infants all infants in the data set, including those below 28 weeks gestation, we see 15.63% municipalities in 2000 and 20.19% in 2019 with higher stillbirth rates than neonatal mortality rates.

3.2 Impact of Regional Wealth Status on Perinatal Outcomes

National variation in negative perinatal outcomes exist and parallel regional wealth inequality, with the North and Northeast regions reporting 2019 NMRs of 15.2 and 13.7, compared to 11.9 in the Midwest, 11.6 in the Southwest, and 10.3 in the South. Similarly, the North and Northeast had the highest SBRs in 2019, 11.3 and 11.8, respectively while the South reported the lowest SBR at 7.8.

In 2002 Brazil had 5,543 unique municipalities. In 2019, this had increased to 5,570. When these municipalities were categorized individually as "high-income", "upper middle-income", "lower middle-income", and "low-income", we can see disparate outcomes based on wealth status both within and between regions. In 2002, 0.305 percent of municipalities were high-income, 3.66% upper-middle income, and 47.6% lower-middle income, and 48.3% lower-income. In 2019, this distribution shifted to 7.85% high-income, 47.1% upper-middle income, and 45.0% lower-middle income with no lower-income municipalities remaining (**Table 2**). At a population level, this represents 22.81% of Brazilians living in a high-income municipality, 54.32% in an upper middle-income municipality, and 22.86% in a lower middle-income municipality in 2019.

Table 2: Change in Wealth Status by Region Across Brazil

Income Class	Year	Regions (n)	States (n)	Municipalities (n)	Percent of Population (%)
Lower	2002	5	3	2,689	25.85
	2019	0	0	0	0
Lower-Middle	2002	1	23	2,650	56.60
	2019	1	2	2,508	22.86
Upper Middle	2002	1	1	204	17.16
	2019	5	23	2,625	54.32
High	2002	0	0	0	0
	2019	2	2	437	22.82

The North and Northeast regions consistently contained the municipalities with the lowest income strata throughout the study period, while the South and Southeast regions had the higher income strata municipalities. The Midwest region showed less change during the study period and retained the highest prevalence of high-income municipalities from 2002 to 2019 (**Figure 4).**

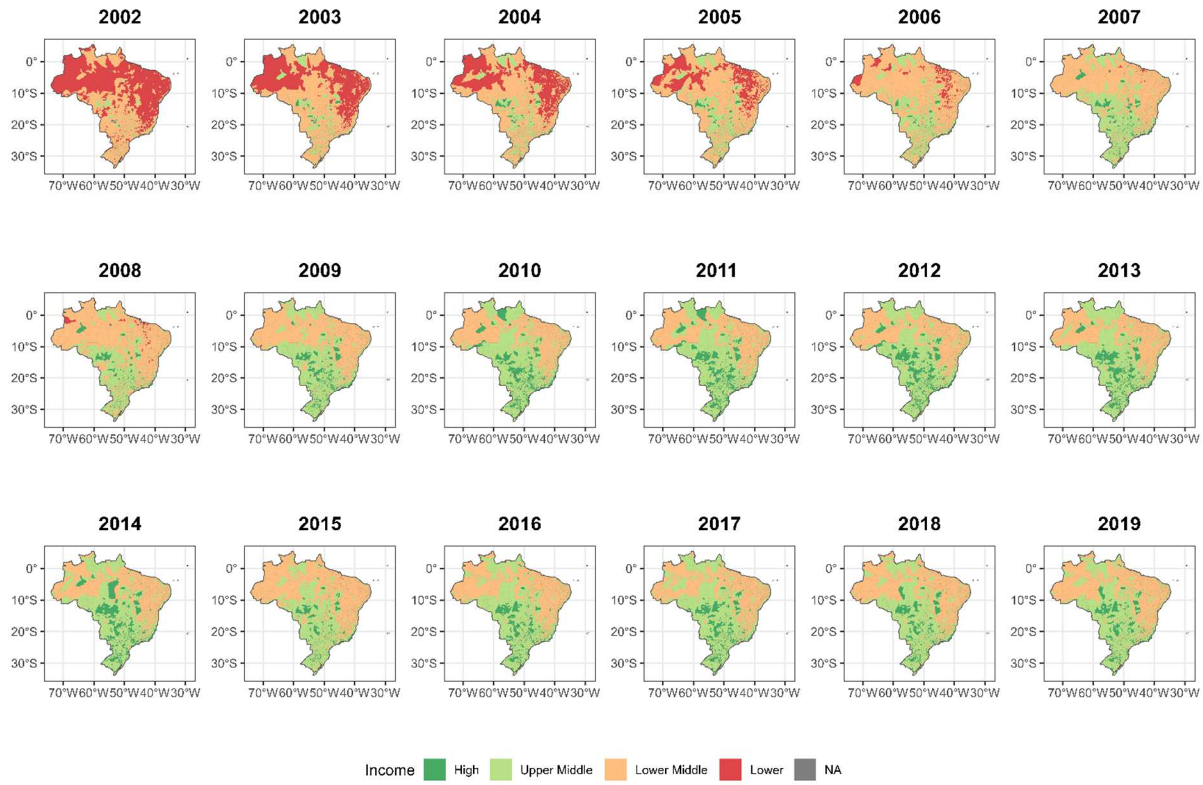

Figure 4: Change in Wealth Status by Municipality Across Brazil 2002-2019

Negative perinatal outcome rates also varied by income status of a region. Looking across all gestational age ranges, in 2002 the neonatal mortality rate in high-income municipalities was 13.44 deaths per 1000 live births. This is compared to 15.15 in upper-middle municipalities, 18.58 in lower-middle municipalities, and 22.80 in lower income municipalities. In 2019 we see this distribution shift to a rate of 10.86 in high-income municipalities, 12.21 in upper-middle municipalities, 14.37 in lower-middle income municipalities (**Figure 5**).

The trend for stillbirth mirrors that of neonatal mortality. In 2002, the stillbirth rate in high-income municipalities was 9.46 per 1000 total births. This is compared to 11.02 in upper-middle income municipalities, 12.24 in lower-middle income municipalities, and 12.33 in lower income municipalities. In 2019 the stillbirth rates were 9.06 in high-income municipalities, 9.60 in upper-middle municipalities, and 12.68 in lower-middle municipalities.

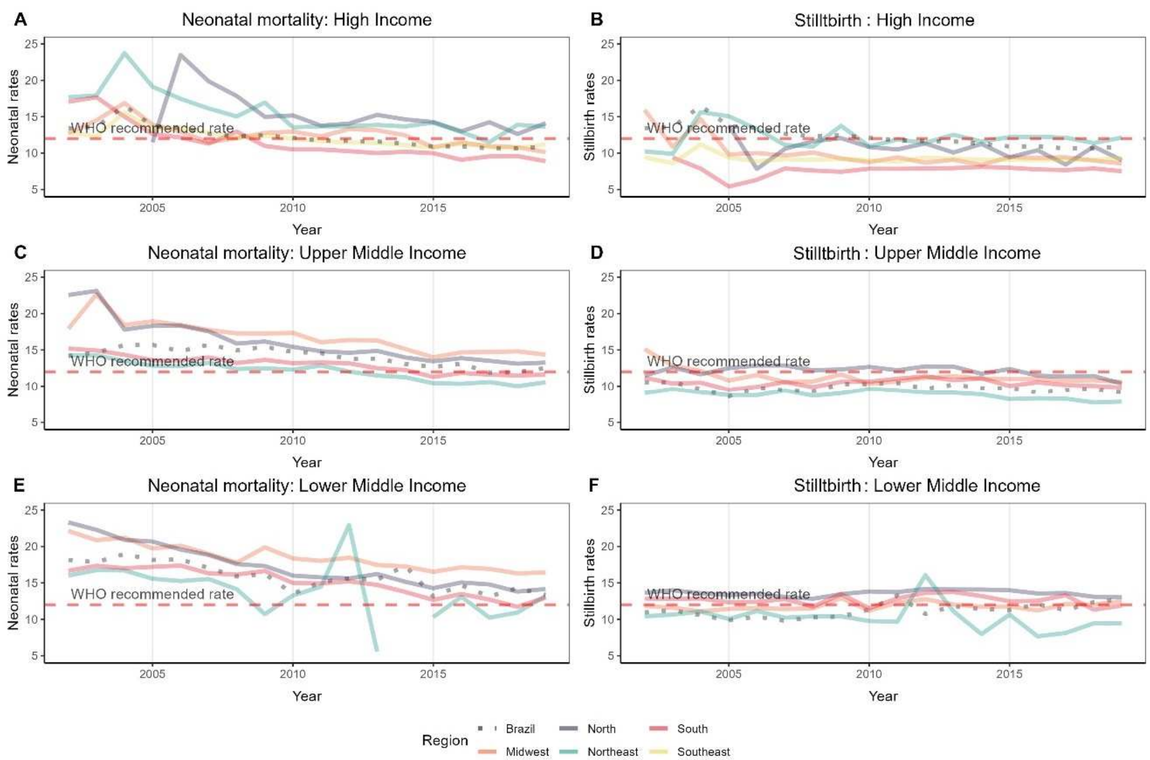

Figure 5: Time Trends in Neonatal Mortality and Stillbirth across Brazil by Regional Income Status

Wealth status at the state and municipality level was also correlated with their progress over time in improving stillbirth rates and neonatal mortality rates. **Figure 6** shows the progression of the 26 states in Brazil towards improved perinatal outcomes and their respective income-status classification at 4 time points: 2002, 2006, 2012, and 2019. Data here includes all analyzed births from the SIM and SINASC databases, including births below 28 weeks gestation. In 2002, all states had neonatal mortality rates greater than 12 deaths per 1000 live births. There were no high-income states and only one upper-middle income state. In 2019, there are two lower-middle income states, which are amongst the five worse states in terms of neonatal mortality and stillbirth. The two high-income states are amongst the five best states for perinatal outcomes.

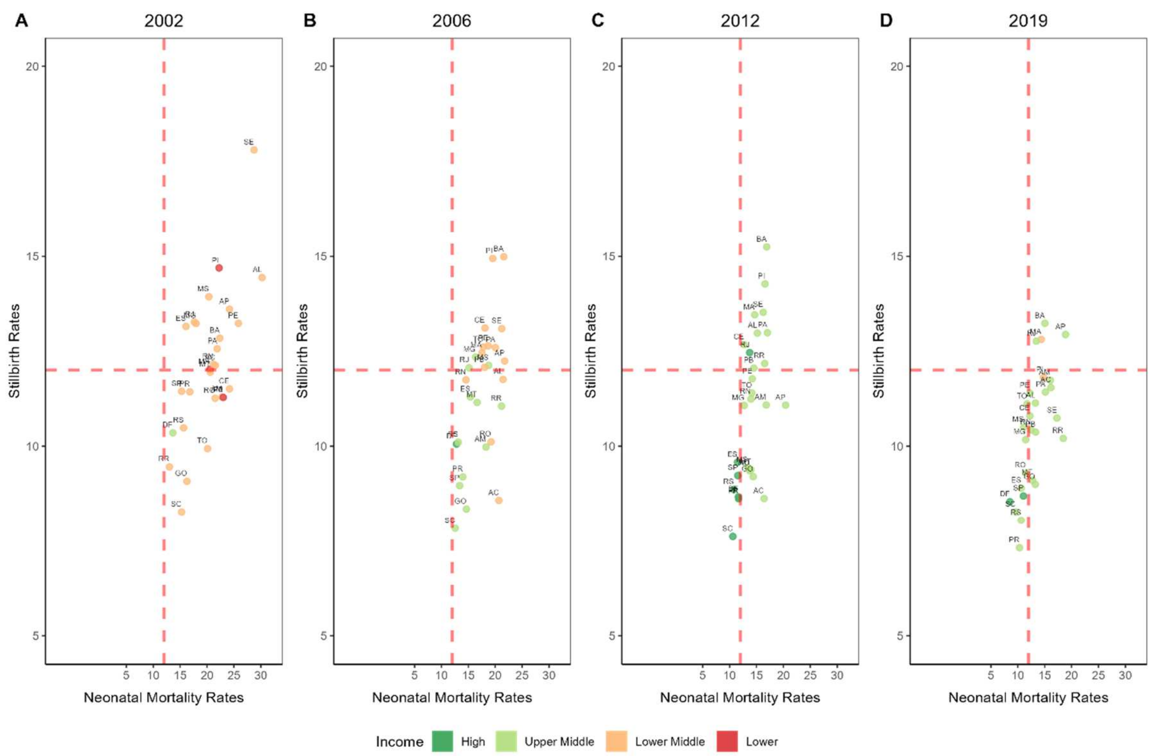

Figure 6: Changes in Perinatal Outcomes by State Wealth Status in Brazil. Red dashed lines correspond to the *Every Newborn Action Plan* targets of 12 neonatal deaths per 1000 live births and 12 stillbirths per 1000 total births. Data obtained from the SIM database from 2000-2019.

The rates seen across geographic regions in Brazil represent a difference in medians 9 of neonatal deaths per 1000 live births and 3 stillbirths per 1000 total births between high-income and lower-middle income municipalities in 2002 ($p < 0.01$ for NMR and $p = 0.6$ for stillbirth). In 2019, the differences in the medians of neonatal deaths and stillbirths per 1000 total births in high-income and lower-middle income regions were 4 and 4, respectively ($p < 0.01$ for NMR and SBR).

Looking across all infants included in this data set, we see an overall neonatal mortality rate of 11.63 in high-income municipalities compared to 17.29 in lower-middle and 22.24 in low-income municipalities (**Table 3**). Therefore, from 2002 to 2019 in Brazil, the odds of having a neonatal death in a lower middle-income municipality was 1.50 [1.46, 1.54] that of in an upper-middle income municipality and 1.69 [1.45, 1.99] that of in a high-income municipality. For stillbirth we see a rate of 9.08 for high-income regions compared to 12.71 for lower-middle and 12.64 for low-income municipalities. As with NMR, comparing the risk of stillbirth in lower-middle income regions to upper-middle and high-income municipalities, we see odds of 1.11 [1.08, 1.15] and 1.30[1.08, 1.57], respectively.

	Municipal Wealth Classification	Gestational Age		
		<28 Weeks	≥ 28 Weeks	All Infants
Neonatal Mortality Rate	High-Income	614.49	6.93	11.63
	Upper-Middle Income	660.66	7.97	13.62
	Lower-Middle Income	671.51	10.42	17.29
	Low Income	675.60	13.11	22.24
	National Average	654.71	8.90	15.31
Stillbirth Rate	High-Income	508.23	5.63	9.08
	Upper-Middle Income	595.04	6.76	10.45
	Lower-Middle Income	740.27	8.46	12.71
	Low Income	900.68	8.56	12.64
	National Average	639.99	7.13	11.07

Table 3: Neonatal Mortality and Stillbirth Rate by Gestational Age and Municipal Income Strata (2002-2019)

Looking just at the current state of perinatal outcomes in Brazil, data from 2019 shows that regardless of gestational age, the odds of having a neonatal death in a lower-middle income municipality is 1.17 [1.14, 1.20] that of in an upper-middle income municipality and 1.32 [1.28, 1.36] that of in a high-income municipality. For stillbirth there is even a greater difference, with odds of 1.32 [1.28, 1.35] and 1.40[1.35, 1.44], respectively in the same period. Considering only the extremely preterm infants, or those born below 28 weeks gestation, we see less of a difference. In 2019 the odds of having a neonatal death in a lower-middle income municipality was 1.00 [0.94, 1.06] that of in an upper-middle income municipality and 1.06 [0.98, 1.14] that of in a high-income municipality. For stillbirth these odds were 1.13 [1.06, 1.20] and 1.09[1.01, 1.17], respectively.

4. Discussion

This study described time trends in neonatal mortality and stillbirth from 2000-2019 across Brazil and evaluated the impact of regional wealth disparity on these negative perinatal health outcomes. We used large-scale, publicly available data to quantify and trend these outcomes, subdivided by gestational age category. We found improving neonatal and stillbirth rates, nationally and at the sub-national level when examining all births and the subset of births occurring at 28 weeks gestation or later. For infants delivered at or after 28 weeks gestation, Brazil has met the targets laid out in the World Health Organization's *Every Newborn Action Plan* since 2000 for both neonatal mortality and stillbirth. For stillbirth, all regions have reported rates below 12 stillbirths per 1000 total births throughout the study time period. For neonatal mortality, the North consistently had the highest rates of neonatal mortality and reached the WHO goal of 12 neonatal deaths per 1000 live births in 2010. When we extracted data specific to infants born between 22- and 27-weeks' gestation, however, a new trend emerged. For both neonatal mortality and stillbirth, we see a steady improvement in outcomes from 2000 to 2010, followed by a much more rapid and significant improvement over the following 3 years. Following the nadirs of 2012 for NMR and 2013 for SBR, however, there is a steady increase in rates of negative perinatal outcomes across all regions and at a national level.

Our geographic stratification of outcomes by local wealth status showed both improving economic status across Brazil at the state level and improving perinatal outcomes over time. Disparities in outcomes were evident, however, across the timespan analyzed. In 2002, the two lower-income states are amongst the worst performing states in terms of perinatal outcomes whereas in 2019 the two high-income states are amongst the best performing states.

This study mirrors past studies in by demonstrating both the overall progress made in health outcomes across Brazil in the past two decades as well as the ongoing health inequities that plague the nation. Our study adds to the literature on Brazilian healthcare by amplifying recognition of the worsening trend in perinatal outcomes experienced by extremely preterm infants, or those born before 28 weeks gestation.

There is a bulk of literature exploring perinatal outcomes in Brazil. One large systematic review on fetal deaths, including stillbirths in Brazil from 2003 to 2013 found a reduction in fetal mortality over that time period.[44] A similar study from 1996 to 2012 cited a decrease in national SBR from 13.4 to 10.0.[27] For NMRs, a study from 2007 to 2017 noted a 2.15% reduction in NMR nationally per year.[45] Work from São Paulo state addressing neonatal mortality due to perinatal asphyxia also noted differing time-trends based on gestational age, with a reduction in mortality in 2008 for infants 32-31 weeks gestation, in 2009 for those 28-31 weeks, and in 2011 for the extremely preterm population.[46] Additionally, in São Paulo from 2004 to 2013, researchers noted lower rates of improvement in neonatal mortality for infants below 32 weeks gestation compared to older infants.[47] While these, and similar, studies parallel our findings in terms of overall improving perinatal outcomes over time, to our knowledge, ours is the first study to report a focused analysis of NMR and SBR for extremely preterm infants across Brazil.

Survival of extremely preterm infants, those born before 28 weeks gestation, is increasing globally.[48-51]. Survival at this young age has been found to be directly linked to active provision of care at the time of delivery[13] and therefore is associated with having sufficient health resources at the delivering institution to support the complex needs of an extremely preterm infant.[52] Indeed, infants born below 28 weeks gestation who do not receive adequate support at delivery and in the neonatal period are unlikely to survive.[5] One 2015 study of Neonatal Resuscitation Providers in Brazil noted that 81% of respondents were likely to initiate resuscitation, including intubation, in infants below 25 weeks gestation,[53] highlighting the potential for significant variation in resuscitation practices across the country. Antenatal management can also impact perinatal outcomes. Administration of steroids to a mother at risk of preterm delivery has been shown to improve fetal lung maturity and increase the odds of survival.[54] In 2000, the Ministry of Health guidelines for high risk pregnancies recommended giving antenatal steroids to women at risk for delivery at 28-34 weeks gestation,[55] whereas by 2010 the guidelines were revised to anticipated deliveries between 24-34 weeks gestation.[56]

The inequity in health resources across Brazil has been previously reported, with the North and Northeast regions cited as having the worst health infrastructure.[57] Additionally, work looking at access to emergent and intensive care across Brazil noted that 12% of the population was more than 120km away from a health facility with a neonatal intensive care unit (NICU)[58] and therefore disadvantaged when it comes to access to quality neonatal care. The seminal 2014 "Birth in Brazil" paper also addressed this issue, noting that 50% of babies weighing less that 1500g died if delivered in hospitals without a neonatal intensive care unit.[57]

Our approach to correlating wealth status with perinatal outcomes is novel in that we assigned each state and municipality an income class. Prior work from Brazil has noted both that region is a stronger predictor of stillbirth than individual socioeconomic level,[24] and that relative socio-economic inequalities continue to be strongly correlated with gaps in stillbirth and neonatal mortality rates.[26] Since healthcare in Brazil is governed and administered at the state and municipal, rather than regional, level, looking at the wealth status of these smaller geographic regions and the impact on perinatal outcomes is important. Our analysis filled this gap by demonstrating that, across all gestational ages, the historic and current SBR and NMRs are better for high-income municipalities compared to their poorer neighboring municipalities. This is further supported by our focused 2019 analysis where we showed the statistically significantly higher rates of neonatal mortality and stillbirth in the lower-income municipalities. Interestingly, when looking at the extremely preterm neonatal population, the protective effect of being born in a wealthier municipality had less of an effect or was eliminated.

Changes in national health policies over the study period likely had an effect on the outcomes described in this paper. In 2000, Brazil introduced the "National Program for the Humanization of Pregnancy and Childbirth", followed by the "Pact for the Reduction of Maternal and Newborn Mortality" in 2004, the creation of local committees to prevent infant mortality in 2005, and the "Pact for Life" in 2006.[46,59] These efforts were followed by the development of the "Stork Network" in 2011, which emphasized creating a stronger network of health facilities and improving transport capabilities to higher levels of care when needed.[60]

Our finding that stillbirth and neonatal mortality outcomes amongst the extremely preterm population have been worsening since 2013 echo's findings in other work that tie negative changes in health to changes in health and social policy since that time. In 2014 Brazil experienced its worst recession on record, and in 2015 austerity policies introduced by the government led to major cuts in public investment to health.[43] Next, in 2016 a constitutional amendment limited federal expenditure on health for the next 20 years. More recently, public support programs such as *Bolsa Familia*, a national conditional cash transfer program, have been discontinued. *Bolsa Familia* participation was linked with a reduction in child mortality, with a greater association for preterm infants and children living in municipalities in the lowest income quintile.[61]

Unfortunately, while Brazil had been closing the gap on key health indicators, such as infant mortality, between wealthier and poorer municipalities, targeted projections incorporating the 2018 austerity measures put in place across Brazil forecast a re-worsening of regional infant mortality inequities.[21,62] Other projections looking at the future of Brazil and the SUS' ability to care for the health of the Brazilian people show a deterioration in the government's ability to provide care, including newborn care, as funding is limited. This projected deterioration was more pronounced in smaller munisipalities,[21] underscoring the impact of pre-existing geographic inequalities and the importance of looking at health outcomes at the municipal level. Our finding that perinatal outcomes remain worse in states classified as lower-middle income, as compared to national averages, supports this concern about a persistent care gap amongst the wealthiest and poorest regions across Brazil.

While the SUS in Brazil undoubtedly ushered in a new wave of access to healthcare following its initiation in 1990, its ability to care for the modern Brazilian population is unclear. User satisfaction of the program waned in the early 2010s,[21] and the regionalization of care and financing set up in the SUS has been criticized as reproducing geographic inequities across Brazil.[63] Since 2015, public health expenditure in Brazil has declined and millions of people have lost private health coverage,[64] putting more pressure on this public health system. Recent health policy changes and austerity measures put into place to curb increases in health financing have the potential to further worsen health inequities, especially amongst vulnerable populations.

4.1 Study strengths and limitations

This study had several key strengths. First, it utilized the vast and comprehensive SIM and SINASC databases from Brazil, which capture over 95% of births and birth outcomes across Brazil. This allows for powerful national comparisons of outcomes over time and across regions. Second, this study leveraged publicly available economic data, via the Atlas of Human Development in Brazil, to draw connections between perinatal outcomes and health-economic factors.

This study is not without limitations. First, despite its comprehensive nature, there are still unrecorded births and deaths across Brazil that were not captured in the utilized databases. Similarly, there is global concern about under reporting of births and deaths, including stillbirths, in extremely preterm infants.[65,66] While the data collection mechanisms within Brazil strive to incorporate infants of all gestational ages, it remains possible that extremely preterm infants are underrepresented in the dataset. Additionally, about 1.5% of available records were excluded prior to analysis due to missing data on gestational age or perinatal outcome. It is not clear if these missing records unequally represent infants from any specific gestational age, regional, or wealth demographic that would impact the calculated results. Second, the SIM and SINASC databases are not linked at a patient level, making it impossible to draw more complex inferences about predictors of preterm birth and stillbirth based on patient-level data. Third, there was a change in data reporting that took place between 2010 and 2011, wherein providers had to input a precise gestational age rather than selecting from one of several gestational age categories. It is possible that the increase precision of this approach led to more accurate reporting amongst younger gestational age infants and contributed to the sharp decline in negative perinatal outcomes seen after 2010. Next, wealth inequality exists even within a given municipality and municipal level outcome data may not reflect the lived experience of many families within that location. Lastly, this analysis does not incorporate health systems factors or regional variations in health policy that could impact access to care or care delivery, nor does it address changes in clinical practice guidelines that may have influenced care delivery during the study period.

4.2 Implications for Policy and Practice

This study underscores the importance of implementing health policies that addresses both neonatal mortality and stillbirth rates across all gestational ages. Stillbirth rates reflect maternal health status, access to care, and care quality. Neonatal mortality, similarly, reflects adequate delivery room care and pediatric management following birth. Such care is dependent upon skilled clinicians and access to sufficient resources. Health policies that prioritize health access, resource availability, and medical training across all regions are Brazil are essential.

The worsening neonatal mortality and stillbirth rates amongst extremely preterm infants is also a key health policy issue. The value of a newborn's life is not defined by their gestational age, and it is the responsibility of Brazil's healthcare system to strive to improve access to life sustaining care to extremely preterm infants and minimize the inter-municipality disparity in survival of these infants. Better quality healthcare care, especially during labor and the neonatal period, are key public policy issues to reduce both geographic and gestational age inequities in Brazil.

Lastly, our findings remind clinicians, researchers, and policy makers that we cannot allow national-level improvements in outcomes to overshadow inequities at the local level. Policy changes and health interventions must target the most in-need populations so that perinatal outcomes across Brazil can once again be on a trajectory of improvement.

4.3 Implications for Further Research

Further work in this space should explore the intersection of personal socio-economic factors and municipal wealth status on perinatal outcomes. Similarly, looking at the role of health infrastructure on health outcomes, especially amongst extremely preterm infants or other vulnerable populations, will be critical. Specifically, future work should explore the impact of access to neonatal intensive care units, staffing of delivery hospitals, and transport availability on perinatal outcomes. Lastly, we know there has been an increase in preterm birth over the past 20 years, so additional analysis looking at the impact of preterm birth on stillbirth and neonatal mortality in municipalities of different wealth status could be performed.

Beyond Brazil, our work emphasizes the importance of looking at smaller-scale wealth status when comparing negative health outcomes across a population rather than relying on national or regional trends. Lastly, researchers looking at global trends in the perinatal space should ensure a thorough analysis of sub-populations such as extremely preterm infants in order to better identify and understand changes in health outcomes.

5. Conclusion

Brazil has made significant progress in neonatal mortality and stillbirth rates from 2000 to 2019, yet inequity in perinatal outcomes remains across the country. This inequity is correlated with local economic status, with the poorest states and municipalities of Brazil experiencing the highest rates of perinatal loss. Nationally, ongoing improvement is needed for infants below 28 weeks gestation and closer exploration is needed into why there are increasing rates of negative perinatal outcomes amongst infants 22-27 weeks gestation. Targeted health policy and interventions are needed to address these geographic and gestational disparities in perinatal health outcomes.

Appendix A

Figure A.1: Map of Brazil

Source:
https://commons.wikimedia.org/wiki/File:Brazil,_administrative_divisions_(states)_-_en_-_colored.svg

Appendix B

Bank's fiscal year:	**FY90**	**FY91**	**FY92**	**FY93**	**FY94**	**FY95**	**FY96**
Data for calendar year :	**1988**	**1989**	**1990**	**1991**	**1992**	**1993**	**1994**
Low income (L)	<= 545	<= 580	<= 610	<= 635	<= 675	<= 695	<= 725
Lower middle income (LM)	546-2,200	581-2,335	611-2,465	636-2,555	676-2,695	696-2,785	726-2,895
Upper middle income (UM)	2,201-6,000	2,336-6,000	2,466-7,620	2,556-7,910	2,696-8,355	2,786-8,625	2,896-8,955
High income (H)	> 6,000	> 6,000	> 7,620	> 7,910	> 8,355	> 8,625	> 8,955
Brazil	LM	UM	UM	UM	UM	UM	UM
Bank's fiscal year:	**FY97**	**FY98**	**FY99**	**FY00**	**FY01**		
Data for calendar year :	**1995**	**1996**	**1997**	**1998**	**1999**		
Low income (L)	<= 765	<= 785	<= 785	<= 760	<= 755		
Lower middle income (LM)	766-3,035	786-3,115	786-3,125	761-3,030	756-2,995		
Upper middle income (UM)	3,036-9,385	3,116-9,645	3,126- 9,655	3,031-9,360	2,996-9,265		
High income (H)	> 9,385	> 9,645	> 9,655	> 9,360	> 9,265		
Brazil	UM	UM	UM	UM	UM		
Bank's fiscal year:	**FY02**	**FY03**	**FY04**	**FY05**	**FY06**		
Data for calendar year :	**2000**	**2001**	**2002**	**2003**	**2004**		
Low income (L)	<= 755	<= 745	<= 735	<= 765	<= 825		
Lower middle income (LM)	756-2,995	746-2,975	736-2,935	766-3,035	826-3,255		
Upper middle income (UM)	2,996-9,265	2,976-9,205	2,936-9,075	3,036-9,385	3,256-10,065		
High income (H)	> 9,265	> 9,205	> 9,075	> 9,385	> 10,065		
Brazil	UM	UM	LM	LM	LM		
Bank's fiscal year:	**FY07**	**FY08**	**FY09**	**FY10**	**FY11**		
Data for calendar year :	**2005**	**2006**	**2007**	**2008**	**2009**		
Low income (L)	<= 875	<= 905	<= 935	<= 975	<= 995		
Lower middle income (LM)	876-3,465	906-3,595	936-3,705	976-3,855	996-3,945		
Upper middle income (UM)	3,466-10,725	3,596-11,115	3,706-11,455	3,856-11,905	3,946-12,195		
High income (H)	> 10,725	> 11,115	> 11,455	> 11,905	> 12,195		
Brazil	LM	UM	UM	UM	UM		
Bank's fiscal year:	**FY12**	**FY13**	**FY14**	**FY15**	**FY16**		
Data for calendar year :	**2010**	**2011**	**2012**	**2013**	**2014**		
Low income (L)	<= 1,005	<= 1,025	<= 1,035	<= 1,045	<= 1,045		
Lower middle income (LM)	1,006-3,975	1,026-4,035	1,036-4,085	1,046-4,125	1,046-4,125		
Upper middle income (UM)	3,976-12,275	4,036-12,475	4,086-12,615	4,126-12,745	4,126-12,735		
High income (H)	> 12,275	> 12,475	> 12,615	> 12,745	> 12,735		
Brazil	UM	UM	UM	UM	UM		
Bank's fiscal year:	**FY17**	**FY18**	**FY19**	**FY20**	**FY21**	**FY22**	**FY23**
Data for calendar year :	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**
Low income (L)	<= 1,025	<= 1,005	<= 995	<= 1,025	<= 1,035	<= 1,045	<= 1,085
Lower middle income (LM)	1,026-4,035	1,006-3,955	996-3,895	1,026-3,995	1,036 - 4,045	1,046 - 4,095	1,086 - 4,255
Upper middle income (UM)	4,036-12,475	3,956-12,235	3,896-12,055	3,996-12,375	4,046 - 12,535	4,096 - 12,695	4,256 - 13,205
High income (H)	> 12,475	> 12,235	> 12,055	> 12,375	> 12,535	> 12,695	> 13,205
Brazil	UM	UM	UM	UM	UM	UM	UM

Figure B.1: Historic World Bank Lending Group Classifications: 1988-2021

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