

Maternal Dengue and Health Outcomes of Children

Foureaux Koppensteiner , Martin; Menezes, Livia

DOI:

[10.1257/app.20210656](https://doi.org/10.1257/app.20210656)

Document Version

Peer reviewed version

Citation for published version (Harvard):

Foureaux Koppensteiner , M & Menezes, L 2024, 'Maternal Dengue and Health Outcomes of Children', *American Economic Journal: Applied Economics*, vol. 16, no. 2, pp. 530-553.

<https://doi.org/10.1257/app.20210656>

[Link to publication on Research at Birmingham portal](#)

General rights

Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

- Users may freely distribute the URL that is used to identify this publication.
- Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
- User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
- Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

Take down policy

While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact UBIRA@lists.bham.ac.uk providing details and we will remove access to the work immediately and investigate.

Maternal Dengue and Health Outcomes of Children*

Martin Foureaux Koppensteiner[†]

Lívia Menezes[‡]

June 10, 2023

Abstract

We study the effect of maternal dengue infections on birth outcomes using linked administrative records from Brazil estimating maternal fixed-effect specifications. In contrast to previous studies, we find robust evidence for the negative effect of dengue infections on birth weight (BW). The effect is particularly pronounced at lower parts of the BW distribution, with an increase of 15%, 67%, and 133% for low, very low, and extremely low BW, respectively. We also document large increases in children's hospitalizations and medical expenditures for up to three years after birth.

JEL Classification: I15, I18, J13

*We would like to thank Marcus Eder, Claudio Ferraz, Adrienne Lucas, Matthias Parey, James Rockey, Rodrigo Soares, and seminar participants at Birmingham, Leicester, Surrey, the Essen Health Conference, the European Winter Meeting of the Econometric Society, The Royal Economic Society 2022 Conference and the iHEA World Congress Dublin for their very useful comments and suggestions. The usual disclaimer applies. We thank the Brazilian Ministry of Health and the State Secretariat of Health in Minas Gerais for very useful discussions and for help with the data. Foureaux Koppensteiner very gratefully acknowledges financial support received through the Economic and Social Research Council grant ES/N017706/1. The research of this manuscript was conducted under IRB approval from the Research Ethics Committee of the University of Leicester (1666-mk332-economics).

[†]University of Surrey, School of Economics, Guildford, Surrey, GU2 7XH, UK and IZA, Bonn, Germany. Email: m.koppensteiner@surrey.ac.uk

[‡]University of Birmingham, Department of Economics, Birmingham, B15 2TT, UK. Email: l.menezes@bham.ac.uk

1 Introduction

Dengue fever is the most prevalent mosquito-borne disease, which threatens the health of about half of the world’s population (Bhatt et al. (2013)). In 2019, the Americas alone registered more than 3 million cases, contributing to the record high of dengue cases worldwide in the same year (WHO (2020)). While dengue was nearly nonexistent in the 1960s, it has since expanded rapidly and is now endemic in more than 100 countries. Climate change means that more countries outside of the tropics and subtropics have become suitable breeding grounds for the dengue vector, *Aedes* mosquitoes, allowing the disease to expand further geographically—including, for example, in Croatia, France, Portugal, and the southern states of the USA (Colón-González et al. (2021)).

Despite relatively low mortality, dengue has a substantial economic burden, caused by both direct medical costs due to hospitalization and ambulatory treatment and indirect costs due, for example, to work absenteeism and subsequent impacts on productivity (Shepard et al. (2016)). One of the potential externalities of dengue arises from the damaging effect a maternal dengue infection may have on the unborn child’s health. Several viral infections have been shown to affect the development of the baby in utero and to affect the health at birth and later in life, including rubella (Dudgeon (1967)), influenza (Schwandt (2017), Kelly (2011)), and malaria (Barreca (2010)).

Although dengue has been endemic in Brazil for over 20 years and in many countries around the equator, to date, there is no causal evidence of the effect maternal dengue might have on the health of the unborn child and subsequent measures of health. In this paper, we provide the first causal evidence of the effect dengue has on several measures of health at birth as well as on longer-term health outcomes. We leverage unique population-level administrative data linking dengue cases with birth records for mothers with multiple births over time. This allows us to estimate the effect of maternal dengue on birth outcomes by comparing children exposed to dengue in utero with unexposed children, holding maternal characteristics constant. This enables us to overcome the concerns with previous studies based on selected samples of mothers hospitalized with dengue during pregnancy and problems due to selected reporting of dengue infections in epidemiological studies.

Several studies have used hospital records to show that the birth outcomes of mothers hospitalized for dengue are worse, reporting an increase in fetal death. Most of these case reports and retrospective studies are based on small samples of hospitalized mothers and do not account for selection when studying pregnant dengue patients hospitalized for the infection (Adam et al. (2010), Basurko et al. (2009), Chitra and Panicker (2011)). Pouliot et al. (2010) provide an overview of earlier studies, and Paixão et al. (2017) a meta-analysis. Although these studies are limited by their small and highly selected samples and lack of a control group, they allow the in-depth study of cases to provide crucial insights into the potential underlying mechanisms. Chiong Tan et al. (2008), for example, study the relevance of vertical transmission of dengue during pregnancy from the mother to the child by testing for dengue virus in umbilical cord samples and show that, while there is evidence for the transmission of the virus from the mother to the child in utero, the incidence is low.

A second set of—mostly epidemiological—papers uses larger sets of health records linking dengue infections with subsequent birth outcomes. Paixão et al. (2017) investigates stillbirth as a possible consequence of maternal dengue by using stillborn babies and a random sample of live births, identifying for those whether the mother was infected with dengue –during pregnancy. They document an increase in the odds ratio for stillbirth, controlling for maternal age and education. Nascimento et al. (2017) study dengue infections on live birth outcomes and find no effect of maternal dengue on low BW and malformations but find a small positive effect on the risk for preterm birth. Paixão et al. (2019) find that severe dengue hemorrhagic fever, which accounts only for a small fraction of all dengue infections ($<1\%$), mostly for repeat infections with different dengue serotypes, increases the risk for preterm birth and low BW. They find no effect for the vast majority of dengue cases.

These studies provide interesting correlations for the impacts of severe dengue, but either focus on rare cases of severe forms of dengue infections or are limited by potential endogeneity due to selection. For example, for case studies investigating the birth outcomes of mothers hospitalized for dengue, these likely represent a sample of the most severe dengue infections not representative of dengue infections generally, and therefore likely lead to overestimating the effect of dengue on birth outcomes. Previous epidemiological studies linking cohorts of administrative records on dengue infections with birth records do not address selection

into reporting of dengue. If the propensity to get diagnosed with dengue increases with the availability of local health services, the better availability of health services may also directly impact the health of the unborn child, for example, through the more rapid detection of underlying maternal health conditions like pre-eclampsia or gestational diabetes during pregnancy.

Because of the uncertain evidence base and the mixed results from previous studies for regular dengue, dengue is not included in the definition of TORCH infections.¹ This means dengue has to date not been considered as *maternal infection of concern*, leading to the omission of maternal dengue from advice by public health authorities on antenatal management of viral infections during pregnancy (CDC (2021), PAHO (2010)), in contrast, for example, to the viral infection Zika.²

We focus on the southeastern Brazilian state of Minas Gerais, the second most populous state in Brazil. Minas Gerais provides an ideal setting for our study for a number of reasons. First, its large population generates sufficient birth observations to estimate the effect of maternal dengue on relatively rare outcomes, such as low BW classifications and hospitalizations after birth. Second, Minas Gerais has an incidence of dengue infections representative of the average incidence across Brazil, which facilitates our understanding the impact of dengue across Brazil. Third, beyond the dengue incidence, the state of Minas Gerais has a representative nature for all of Brazil, with a mix of urban and rural, rich and poor municipalities that help us to understand dengue in a variety of settings. Lastly, we have access to high-quality linked administrative records for the state, enabling us to provide causal estimates of in-utero maternal dengue infections on the health outcomes of children.

This paper makes two contributions to the literature.

First, we provide causal evidence on the effect of maternal dengue on health at birth using a wide range of outcomes and population-level microdata. Leveraging linked adminis-

¹TORCH infections include a wide range of infections with pathogens including *Toxoplasma gondii*, Zika virus, rubella, cytomegalovirus, and herpes simplex virus, causing infections known to increase the risk of miscarriage, stillbirth, short gestation, and intrauterine growth restriction (Megli and Coyne (2021), Silasi et al. (2015)).

²In 2015, there was a significant outbreak of the previously little-known Zika virus, from the same family of flaviviruses as dengue and also transmitted by *Aedes* mosquitoes in Brazil. Commonly leading only to mild symptoms, the virus was identified as a factor leading to the rare congenital disability microcephaly and other severe congenital brain abnormalities for children of mothers infected during pregnancy. Although the state of Minas Gerais was not heavily affected by the Zika outbreak, we ensure that our estimates are not affected by Zika, for example, through simultaneous infection with dengue and Zika during pregnancy.

trative data for mothers with multiple births, enabling us to estimate maternal fixed-effect specifications, we document the significant detrimental effect of maternal dengue on birth outcomes. We find that in-utero dengue reduces BW by about 27 grams on average. Much of this effect is driven by impacts at the lower end of the BW distribution, with increasing effects relative to the mean further down the BW distribution. While we find that maternal dengue increases the propensity for the newborn to be classified as low BW by 15% compared to the mean incidence and the coefficient being imprecisely measured, we find more pronounced and significant effects for very low and extremely low BW: an increase of 67% and 133%, respectively. The results on BW are matched by effects on gestational length. While we find a small and insignificant negative effect on gestational length, we find a strong positive effect on the risk of very preterm birth (before week 32) of 77%, significant at the 1% level. We provide a battery of robustness checks, such as the inclusion of a number of additional fixed-effects (for neighborhood and hospital) and allowing for neighborhood-specific trends, hospital-specific trends, and an alternative control group definition, using mothers who have been infected with dengue after pregnancy as the control group. We also probe the results further by the inclusion of alternative temperature controls using maximum daily temperature. We also test for the balancing of time-varying maternal characteristics and for changes in location of residence in response to dengue. Lastly, we provide a falsification exercise using trimester leads providing additional credibility to the estimation strategy.

Second, beyond estimating the effect of maternal dengue on health at birth, we study the effect on longer-term measures of child health by linking birth records with mortality and hospitalization records. While we find sizeable positive—but insignificant—effects on a number of measures of child mortality, a rare outcome, we document the lasting effect of maternal dengue on more subtle measures of child health using hospitalization records. We find that maternal dengue during pregnancy increases the risk of hospitalization of children substantially; maternal dengue leads to a 27% increase in hospitalizations over a three-year period after birth. The effects are long-lasting, with the strongest relative effect sizes estimated in the second year after birth, leading to a 76% increase in hospitalizations. We find no evidence for more severe hospitalizations through ICU utilization, and no statistically significant increase in the duration of the hospital stay. Using information on the individual

costs of hospital treatment, we find that maternal dengue substantially increases subsequent medical expenditures related to hospitalization in the first and second year after birth.

2 Background on dengue virus

Dengue is a vector-borne viral infection endemic in as many as 100 countries in the tropics and subtropics that provide a habitat for the female mosquitoes of the genus *Aedes*, which are responsible for the transmission of the dengue virus ([WHO \(2020\)](#)). The virus responsible for dengue belongs to the group of flaviviruses, which also include yellow fever and Zika, both of which are also transmitted by *Aedes* mosquitoes ([Payne \(2017\)](#)). Symptoms of dengue infections range from subclinical states, where individuals without symptoms may not be aware of the disease, to severe flu-like symptoms, including high fever, severe headache, muscle and joint pain, nausea, vomiting, and skin rash lasting for up to one week. There are several serotypes of the virus (DENV-1, DENV-2, DENV-3, and DENV-4) that cause dengue. Infection with one strain is believed to lead to lifelong immunity to the same strain, but only temporal and partial immunity to other serotypes. Subsequent infection with different strains increases the risk of developing severe dengue complications ([Murugesan and Manoharan \(2020\)](#)). The presence of several serotypes complicates the development of effective vaccines, requiring any vaccine to protect from infection against all strains of the virus ([Henein et al. \(2021\)](#)).

There is currently no treatment available, so medication is aimed at lessening the symptoms. While the majority of patients recover without long-term consequences from the illness, in a small number of cases, an infection leads to *severe dengue*. Severe dengue (or *dengue hemorrhagic fever*) is a potentially fatal complication with intense internal bleeding and organ impairment. Severe dengue requires close medical observation to avoid complications and risk of death ([Wilder-Smith et al. \(2019\)](#)). In this paper, we are interested in infection with regular dengue, which accounts for the vast majority of cases. Hence, we drop rare cases of severe dengue.

3 Data sources

Previous work on the health consequences of maternal dengue in the medical literature mostly relies on data from hospitalizations due to dengue in pregnant mothers and subsequent birth outcomes, focusing on dengue infections close to delivery, leading to concerns with selection. Hospitalization records also limit the analysis to a cross-section of infected mothers, where it is difficult to establish a relevant control group and not normally possible to link records for a mother with subsequent births. Furthermore, birth records do not generally permit linking with subsequent health information, such as hospital admissions. Therefore, analyses are limited to studying health at birth. To learn about the causal effect of maternal dengue infections on short- and longer-term health, ideally, such research would require data covering registered dengue infections linked to the universe of birth and hospitalization records.

As dengue infections and some outcomes, such as low BW, are relatively rare events, a large number of observations is required to estimate precise effects. The state of Minas Gerais in Brazil is ideally suited for the analysis of maternal dengue on children’s health outcomes because of the quality of public health records and the sheer number of births (and dengue cases), providing us with a sufficient number of observations to estimate precise effects. For our analysis, we link four sets of administrative data from Minas Gerais using individual identifiers. We link vital statistics on birth and death records, hospitalization records, and records from official dengue notifications. We link multiple births to the same mother for the within-mother analysis using individual identifiers. Lastly, we add data on daily records for average and maximum temperatures and auxiliary data from the Brazilian population census and the census bureau on population estimates. We briefly discuss below each dataset and provide details on the origin of each dataset, the procedure to merge the datasets, and the construction of variables, and we discuss descriptive statistics in Appendix D.

3.1 Birth records

The first dataset contains birth records from vital statistics data collected through the *Live Birth Information System* (Sistema de Informações sobre Nascidos Vivos (SINASC), in Portuguese) (HSMG (2022d)). These records are based on the universe of birth certificates issued in Brazil, whether they were issued in hospitals, birth clinics, or from midwives after home deliveries, accounting for more than 99% of all births (Foureaux Koppensteiner and Manacorda (2016)). For the period between 2011 and 2017, we have information for over 1.6 million births. For our within-mother analysis, we focus on the sample of mothers with multiple singleton births that occur over this seven-year period. We are left with 136,788 mothers and 281,497 births.

3.2 Infant mortality data

The second dataset comes from vital statistics death records from the *Brazilian Mortality Information System* (Sistema de Informações sobre Mortalidade (SIM), in Portuguese) (HSMG (2022c)). This dataset contains information on all natural and non-natural deaths in Brazil, including the precise cause of death and characteristics of the deceased. In case of death occurring up to the age of one, these data also register the characteristics of mothers and birth outcomes, thereby allowing us to link birth records with information on child mortality.

3.3 Hospitalization data

The third dataset comprises hospitalization records from the *Hospital Information System* (Sistema de Informações Hospitalares (SIH), in Portuguese) (HSMG (2022b)). It contains details on all admissions from referrals and self-referrals to hospitals in the public health system (SUS),³ including information on duration, cost and type of hospitalization, and the precise primary causes for hospitalization based on the WHO Classification of Diseases (ICD-10).⁴

³In contrast to the other health records used in the analysis (birth records, dengue, and mortality records), the hospitalization data we have access to only captures cases in the public health system. This means that estimates for hospitalization outcomes may be underestimating the true impact of dengue on the overall hospitalization risk.

⁴Compared to the link between dengue, birth, and mortality, for which we use individual identifiers to link records and for which we virtually link all records, the merge with hospitalization records based on address information of mothers only links

3.4 Dengue data

The final main dataset is based on official notifications of dengue fever cases from the *Notifiable Diseases Information System* (Sistema de Informação de Agravos de Notificação (SINAN), in Portuguese) (HSMG (2022a)). Dengue fever is a notifiable disease, and every known case must be recorded in SINAN. SINAN also collects information on the individual and the infection, including on the date of notification and on the diagnosis, i.e., information on whether the dengue infection was diagnosed by clinical assessment through common symptoms such as fever, headache, nausea, rash, and the Tourniquet-Test, a clinical diagnostic test that determines a patient’s hemorrhagic tendency, a common symptom of dengue, or through serological/virological dengue tests. Over the 2011-2017 period, the monthly average dengue incidence rate in Minas Gerais was 97 cases per 100,000 population, among the highest dengue incidence in the world (Zeng et al. (2021)). In Table 1 we report the incidence of dengue during pregnancy in our sample (0.8%) of pregnancies with a positive dengue diagnosis, meaning that 2,282 dengue infections occur in our estimation sample over the period. Over an equivalent time period of nine months, this makes the propensity to contract dengue in the general population remarkably similar to the incidence among pregnant women.⁵ The incidence of dengue by birth order is 0.006, 0.009, 0.010 and 0.011 for first, second, third and fourth pregnancy, respectively.⁶ In Appendix B, we provide detailed information on the temporal and spatial distribution of the dengue incidence over the period of interest.

3.5 Temperature data

We complement our data with high-frequency temperature measures to use as controls in our regressions. These data come from ERA5 released by the *European Centre for Medium-*

successfully just over 30% of all hospitalization records with birth records, limiting the number of observations we have available for the analysis. This is mostly due to observations with duplicate address information from postcodes being omitted from the sample.

⁵To be able to compare the propensity to contract dengue between the general population and women during pregnancy, we calculate the average risk to contract dengue of the general population over a nine-month period ($(\div 9 * 0.00097 = 0.0087)$).

⁶This increase is almost entirely due to the nature of the dengue variation in combination with the timing of births in the maternal fixed-effects sample. For example, the propensity to be exposed to dengue is well balanced for dengue in the 2013 wave, with a equal split of first (52%) and second pregnancies (48%); the same is not true for exposure during the 2016 wave, which largely affects second and later births, with only 2% first births being exposed, contributing to the higher dengue incidence for higher birth order pregnancies.

Range Weather Forecasts (ECMWF) as part of the *Copernikus Climate Change Services* (ECMWF (2022)). ERA5 provides hourly information on temperatures at 2 m altitudes for a grid with resolution 0.25×0.25 degrees. We create municipality-level averages by using the inverse-distance weighted average of all weather grid points within a 50 km range of the municipality centroid. We create two different measures, daily average temperature and daily maximum temperature to explore in more detail the effect of average versus extreme temperature as control variables. For the controls in our regressions, we create a count of days in 5°C bands of daily average temperature starting with a lower bound of 10°C and ending at the upper bound of 35°C over the duration of 280 days starting with the day of each conception, creating birth record-specific temperature controls for the municipality of residence of the expectant mother. Using 280-day windows ensures that the temperature controls are independent of gestational length. We repeat the exercise for daily maximum temperature as alternative temperature controls.

3.6 Sample restrictions

We restrict the sample to singleton births (97.60%) of mothers between the ages of 13 and 50 at the time of delivery (99.97%) and drop cases where there is information missing regarding the identity of the mother (0.1% of observations). For the maternal fixed-effect estimates, we restrict the sample to mothers with at least two births over the period 2011 to 2017. Table 1 presents summary statistics for all births and for the sample of mothers with at least two births. Overall, the means across the two samples look similar, with only minor differences in birth outcomes across the two samples. Mother characteristics are also similar, with some differences in maternal age, as expected when comparing mothers with more than one child.

One potential concern for the estimates arises from the emergence of the Zika virus in Brazil in 2015-16. The symptoms of the infection with Zika, a virus from the same virus family as dengue, are similar to dengue. The vast majority of Zika cases occurred in the northeast of Brazil, where the virus was first isolated and for the first time associated with an increase of microcephaly cases in newborns in the region, with Minas Gerais being one of the states in Brazil least affected by Zika (Peiter et al. (2020)). Zika infections were included in the compulsory notification system in November 2015 (Lowe et al. (2018)) and

before cases emerged in Minas Gerais. As the number of maternal infections with Zika in our sample is very small, we drop observations with confirmed Zika infection during pregnancy from the sample (18 birth observations due to 8 maternal Zika infections) to avoid the risk of estimates being biased by Zika.⁷

4 Identification Strategy

We aim to estimate the effect a maternal dengue infection has on newborn health. A simple regression of birth outcomes on an indicator of dengue unlikely would yield unbiased estimates for two primary reasons. First, in the given context, there is a risk of omitting relevant control variables from such a regression. For instance, the risk of contracting dengue may be correlated with unobservable mother characteristics, which may have an independent effect on birth outcomes. This might be the case if expectant mothers living in more deprived areas have a higher infection risk, while limited access to or lower quality of prenatal health care in these areas may lead to poorer birth outcomes. Moreover, some blue-collar occupations are reported to have a higher risk for dengue infections, for example, jobs in construction, agriculture, and manual labor. These occupations may nevertheless also directly affect health at birth due to the relatively lower income compared to white-collar jobs (Chen et al. (2016)) or the physical strain during pregnancy (Cellini et al. (2022)). If the lower, unobserved, socioeconomic status of pregnant women has a negative effect on birth outcomes and is positively correlated with the chance for maternal dengue infection, this may lead to overestimating the effect of maternal dengue on health outcomes at birth. Second, the propensity to be diagnosed with dengue may differ across individuals, leading to a selected sample of recorded infections. If, for example, ease of access to medical facilities affects both the propensity to register a dengue infection and to access prenatal care, which may have a positive health effect on the unborn child, this might lead to underestimating the effect of dengue on health at birth. The overall effect of any bias in OLS regressions hence depends on the relative strengths of any of these two sources of bias.

To overcome these endogeneity issues, we leverage mother identifiers in birth records and

⁷The small number of Zika infections in our sample of mothers confirms the very low incidence rate of Zika in Minas Gerais in the period after Zika was first reported in Brazil (0.006% for 2015-2017).

link siblings to the same mother to estimate the effect of dengue on birth outcomes, employing mother fixed-effects to provide causal estimates of maternal dengue on birth outcomes. We estimate the following equation:

$$y_{itm} = \beta_0 + \beta_1 \text{dengue}_{itm} + \gamma_t + \theta_m + X_i' \tau + \mu_{itm} \quad (1)$$

y_{it} is the outcome of interest for each child i , conceived at time t , born to mother m . γ_t denotes month of conception fixed-effects, θ_m is a maternal fixed-effect, while the vector X_i includes characteristics that may vary within each mother over time: age-in-years dummies, dummies for marital status (married, living together, divorced, single, missing), highest education achieved (incomplete primary, complete primary, incomplete secondary, complete secondary, incomplete higher education, complete higher education), occupation codes, number of previous stillbirths, gestation order, and birth interval (time between conceptions). In addition to the time-varying maternal controls, we include temperature controls. High temperatures have been associated with worse birth outcomes in the literature ([Chersich et al. \(2020\)](#)). Temperature may also be an important factor for the reproduction of the dengue vector ([Campbell et al. \(2013\)](#)), but the relationship between temperature and dengue cases appears to be more complex, with dengue incidence exhibiting a strong seasonal pattern, following temperature variation with a lag.⁸ To test whether temperature affects birth outcomes, we include pregnancy-specific temperature controls across all specifications with the full set of maternal controls. μ_{itm} is the error term, and robust standard errors are clustered at the mother level. As gestational length may mechanically affect the propensity to acquire dengue toward the end of pregnancy (i.e., mothers with shorter gestational length have a smaller risk of contracting dengue during pregnancy) we assign dengue infections based on a full-term gestation period of 280 days, hence estimating an intention-to-treat effect using information on the date of conception.

The coefficient of interest β_1 is identified by comparing children of mothers who had contracted dengue during one of the pregnancies with children of the same mother in unexposed pregnancies. Maternal fixed-effects control for unmeasured time-invariant characteristics of

⁸We provide detailed information on the spatial-temporal variation of dengue in Appendix B.

the mother, alleviating concerns regarding the non-random detection of infections or the non-random reporting of dengue infections during pregnancy in SINAN, assuming that the propensity to report a dengue infection does not vary systematically over time, i.e., across pregnancies. We address remaining concerns regarding selective reporting of dengue infections by limiting the control group to mothers infected with dengue after the last pregnancy reported in our data and hence establishing a control group for which we can assume a similar propensity to get infected and to register the infection, as a robustness check.

Furthermore, we also estimate two-way fixed-effects models in which we include neighborhood (*bairro*) fixed-effects⁹ and hospital fixed-effects, clustering standard errors at the bairro and hospital level, respectively. Neighborhood fixed-effects, for example, capture the local transmission risk that may vary by neighborhood or prenatal care received locally. Hospital fixed-effects control for the quality of any specific prenatal care that is provided by the hospital of delivery (for example, during later stages of pregnancy) and quality of delivery services, including elective C-sections, among other hospital-specific factors. In the most satiated specification, we also separately include neighborhood and hospital-specific time trends in addition to the maternal fixed-effects, controlling for any unobserved differential trends of neighborhoods or hospitals.

We also estimate separately the effect a dengue infection has on health at birth for different trimesters. This may provide information about critical periods during pregnancy when a disease is particularly detrimental to the health of the unborn. We do this by splitting the full-term gestation period into three trimesters, with the first and second trimesters lasting 93 days and 94 days assigned to the third trimester.

We use the trimester exposure setup for a falsification exercise, too, where we include trimester leads of dengue infections, i.e., recorded dengue infections of mothers after delivery. The leads should not affect birth outcomes, and their simultaneous inclusion should also not affect the original trimester coefficients.

⁹Bairros have no official administrative function but are stable and, in many cities, well-defined geographic units broadly equivalent to neighborhoods and therefore capture the local residential background. In the case of rural, low-density municipalities, without further division into neighborhoods, the two-way fixed-effects analysis focuses on municipalities as smallest geographic units.

5 Results

5.1 Main results

We first present the effect of dengue infections on BW and BW classifications, estimating Equation 1, focusing on the mother fixed-effects sample, in Panel A of Table 2. We start with *BW* in columns (1) and (2) followed by the BW classifications, where in odd columns we present the coefficients of specifications without controls, and in even those columns with the full set of controls, including the time-varying maternal controls and the temperature controls. A dengue infection during pregnancy reduces BW substantially by between 31 and 27 grams, significant at 1% and 5%, respectively. The inclusion of the additional time-varying mother controls and temperature controls reduces the effect somewhat.¹⁰

The magnitude of the effect is similar to the effects of maternal influenza (Schwandt (2017)), to the (positive) effect of receiving a generous conditional cash transfer in the context of Uruguay (Amarante et al. (2016)), and to the effect of maternal dismissals during pregnancy (Cellini et al. (2022)). The estimated magnitudes are much larger compared to estimates for factors with more subtle or indirect exposure during pregnancy documented in the literature, for example, the effect of rainfall shocks in semiarid regions in Brazil (Rocha and Soares (2015)), of air pollution (Currie et al. (2009)), or of exposure to local violence (Foureaux Koppensteiner and Manacorda (2016)).

Next, we investigate the effect of dengue on BW classifications. We start with low BW, where the dependent variable is an indicator for BW below 2.5kg. We find that dengue infections during pregnancy increase the chance for low BW by 1.1%, compared to the mean prevalence of 7%: a 15% increase, but the estimate is only marginally significant. Even though the effects of maternal dengue on the propensity for the child to be classified as low BW are imprecisely estimated, they possibly point to negative effects of dengue on lower parts of the BW distribution. This is particularly concerning given the substantial negative consequences of low BW on immediate and longer-term outcomes documented in the literature. We investigate this further by estimating the effects on lower BW categories, i.e.

¹⁰We include time-varying mother controls and the temperature controls separately in Appendix F.

children with a BW below 2kg and 1.5kg, commonly referred to as very low and extremely low BW. We present the results in columns (5) - (8) of Table 2. For the specification, including full controls, we find that maternal dengue during pregnancy increases the chance for very low BW by 0.6%, a 67% increase compared to the baseline and by 0.4% for extremely low BW, a 133% increase given a baseline rate of 0.3%, with both coefficients being significant at the 5% level. The inclusion of maternal controls makes little difference to the estimated coefficients, lending additional credibility to the maternal fixed-effects estimates.

These results indicate that, while there are sizable effects of dengue infections on mean BW, dengue seems to have a particularly strong effect at lower parts of the BW distribution, with increasing relative effect sizes for low, very low, and extremely low BW as outcome variables. These effects are concerning, in light of the body of evidence on the long-term consequences of low BW on children’s future health and socioeconomic status as documented in the literature (Black et al. (2007), Figlio et al. (2014)) and the immediate burden on the health system from additional care received by low, very low, and extremely low BW babies, due to those newborns having some of the highest healthcare expenditures of any in-patient population (Almond et al. (2005), Beam et al. (2020)).¹¹

We also estimate the effect separately by trimester and present the coefficients in Table 3. We find that in-utero dengue has a particularly strong negative effect in the third trimester of gestation, with a reduction in BW of between 53 grams and 63 grams (columns (2) and (3)) and an increase in the risk for low BW by just over a third compared to the mean incidence. The coefficients for the first and second trimester are less pronounced and not statistically significant. BW effects are often attributed to either intrauterine growth retardation and/or reduced gestational length and the effects documented for late pregnancy point to a mechanism of maternal dengue through growth retardation (Almond et al. (2005), Kramer (1987) and Foureau Koppensteiner and Manacorda (2016)).

We probe the sensitiveness of the estimates in Table 4.¹² As a first exercise (presented in column (1), we provide OLS estimates of the effect of maternal dengue, using the same

¹¹In Appendix E, we present a heterogeneity analysis using the mother’s age, race, marital status, and education, documenting the heterogeneous impact of maternal dengue across those dimensions, generally demonstrating relatively limited heterogeneity of the effects along with several mother characteristics.

¹²In Appendix F, we also provide and discuss the results from the falsification exercise using leads of the explanatory variables.

sample as for the mother fixed-effects estimates. The effects are negative for BW and positive for the low BW categories, but much smaller and not statistically significant compared to the mother FE estimates, providing a sense for the size and direction of the bias from OLS estimates, with those estimates being considerably biased towards zero. In columns (2), we present our benchmark estimates from our preferred specification using maternal fixed-effects and the full set of controls (as in column (2) of Table 2). We then probe these estimates by including a number of additional fixed-effects and by using an alternative control group.

We start by including neighborhood fixed-effects, which capture any time-invariant characteristics of the neighborhood—for example, differences in infection risks due to differences in either breeding conditions of *Aedes aegypti* based on geographical features or differences in available health services, addressing potential concerns that these vary for mothers who move from one of 14,917 neighborhoods in our sample to another during their pregnancies.¹³ We present the estimates from this two-way fixed-effects model in column (3). Using those additional neighborhood fixed-effects, the coefficient for a dengue infection during pregnancy is slightly larger across all outcomes.¹⁴ In column (4) we additionally include neighborhood-specific linear trends to account for any differential trends in unobserved variables across neighborhoods. The inclusion leads to a slightly more pronounced effect of dengue on BW, with a reduction of 34 grams, significant at 5%, and a small increase in the coefficient for low, and very low BW, but these estimates remain imprecisely estimated. To address any remaining concerns regarding differences in health services available to pregnant women, we alternatively include hospital fixed-effects for the 586 hospitals and health institutions with maternal care units.¹⁵ Hospital fixed-effects capture any potential differences in prenatal care provided by hospitals and/or proxy for any differences in prenatal services local to hospitals, not captured by neighborhood effects, for mothers who give birth to their children in different hospitals. We find that the coefficients are very similar to our benchmark estimates, both for BW and for low BW classifications in column (5), indicating that differences in

¹³In Appendix F, we investigate further whether dengue causes mothers to relocate in response to dengue infections.

¹⁴The effects on low BW classifications are slightly less precise, likely due to the drop in the number of observations. We lose just over 8% of observations, because of single observations in the small neighborhood areas of our maternal fixed-effects sample.

¹⁵In Brazil, the vast majority of births are delivered in hospitals. For our sample, more than 99.8% of children are delivered in hospitals or medical centers.

health services provided locally to the hospital of delivery do not seem to play an important role. Estimates including hospital-specific trends, which may account for, e.g., trends in the quality of the provision of local health services, are virtually identical when compared to results from our benchmark specification.

Overall, the estimates for the different outcomes reveal a striking stability and change very little when adding additional fixed-effects and trends to the maternal fixed-effects specification. This contrasts with the stark differences when comparing the OLS with the maternal fixed-effects estimates, indicating that maternal fixed-effects succeed in dealing with the potential biases from unobservables and selection. In line with this, we also do not see any substantial changes in the R^2 across the different specifications in Table 4.

Finally, as noted earlier, the concern around selection into the dengue sample motivated the use of maternal fixed-effects. While maternal fixed-effects hold constant the propensity to report and register an in-utero dengue infection, in addition to robustness from the two-way fixed-effects specifications, we would like to examine the robustness of our results further and rule out that any remaining heterogeneity across treatment and control, i.e., between mothers who have dengue during one of their pregnancies and those who do not, biases our estimates. In a further robustness check, we restrict the control group to mothers who have contracted dengue after pregnancy, hence making treatment and control more similar, conditioning the control group to having reported a dengue infection. This ensures that the effects are not driven by differential propensity to report a dengue infection during pregnancy. When constructing the control group in this way, we define end of pregnancy as the estimated due date, rather than the actual birth date, taking into account concerns raised by [Matsumoto \(2018\)](#) regarding the definition of such alternative control groups.

We report the coefficient from this exercise—for what we denote *Alternative Control Group*—in columns (7) and (14). Restricting the sample in this way increases the negative effect on BW substantially. Despite the much smaller number of observations, the coefficient is highly significant. The results presented in Table 2 might therefore underestimate the actual impact. We also find that estimates on low BW are accentuated in this exercise and significant at the 1% level. We document a 28% increase in low BW compared to the baseline. Effects for very and extremely low BW are also accentuated, with an increase by

100% and 175% compared to the mean, respectively.

We probe the robustness and sensitiveness of the results further in Appendix F, where we provide additional insights on the effect of the inclusion of temperature controls. We also provide additional analysis on the balancing properties of time-varying maternal characteristics by infection status during pregnancy, and we formally test whether dengue induces changes in the place of residence of mothers. Lastly, we provide additional insights on the heterogeneous effects of the timing of dengue infections in our maternal fixed-effects sample.

5.2 Additional results

5.2.1 Gestational length and other birth outcomes

In this section, we provide estimates on additional birth outcomes. We start with estimates on the effect of dengue in-utero on gestational length (from day of conception) and several binary outcomes denoting early, very early, and extremely early delivery (<259 , <224 and <196 days, or <37 , <32 , and <28 weeks respectively) in columns (1)-(4) of Panel B of Table 2. Dengue infections reduce mean gestation by half a day (-0.5), but the estimates are not significant. While the mean effect is moderate (a reduction by 0.2% compared to mean gestation), the magnitude is comparable to results elsewhere in the literature from in-utero exposure to a variety of shocks, for example, maternal stress (Black et al. (2016), Quintana-Domeque and Ródenas-Serrano (2017)).

Mean gestation as an outcome nevertheless risks overlooking more pronounced effects along the distribution of gestational length. Hence, we also estimate the effect of dengue infections on the above indicators for short gestation. We find a positive but small increase in the probability of short gestation (<37 weeks) of about 0.5%, but the coefficient is not significant. In contrast, we find a positive and strong effect of maternal dengue on very short gestation of one percentage point, a 77% increase compared to the baseline. The estimate for extremely early delivery is relatively large, but insignificant.¹⁶ Taken together the estimates on gestational length indicate, in line with the findings on low BW categorizations,

¹⁶Estimating the effect on gestation separately by trimester in Appendix A, we find that dengue affects gestation primarily towards the end of pregnancy, and we find that third-trimester infections substantially increase the probability of very short gestation by 100% compared to the baseline.

that maternal dengue affects gestation particularly at the lower parts of the distribution of gestational length.

In Panel A, of Table 5, we present coefficients from additional birth outcomes, for which the sign and magnitudes are as expected, even though most estimates are not significant. We find a positive but small and insignificant effect on emergency C-sections and small positive effects for both one- and five-minute APGAR scores, neither of which are statistically significant. In contrast, we document a positive and highly significant effect of maternal dengue on prenatal visits, possibly indicating that infected mothers seek additional prenatal checks. The magnitude of the effect is moderate, however, with about 0.2 additional visits (a 3% increase compared to the baseline). We do not find an effect on the sex ratio at birth, indicating that maternal dengue infections in-utero unlikely lead to an increase in (selective) survival in utero.¹⁷

5.2.2 Mortality

To investigate the effect of maternal dengue on child mortality, we link birth with mortality records to estimate the effect of dengue infections on the subsequent survival of children. We present the effects in Panel B of Table 5. We estimate the effect separately for early neonatal (one week), neonatal (four weeks), 22 weeks, and 52 weeks mortality.¹⁸

Dengue during pregnancy has a positive effect on early neonatal and neonatal mortality rates, but the coefficients, despite being large compared to the mean incidence are imprecisely estimated, probably due to the relatively infrequent occurrence of child mortality. This is confirmed estimating the effect separately by trimester in Appendix A, with none of the trimester coefficients being significant.

¹⁷The sex ratio is often used as a proxy for selective stillbirth in the absence of direct information on stillbirths in response to in-utero shocks, as information on stillbirth and spontaneous abortion is often not available from the data. Female fetuses are considered more robust to such shocks in the biomedical literature, and an effect on the sex ratio may therefore indicate a (sex-specific) effect on survival in utero.

¹⁸More than two-thirds of infant mortality is due to neonatal mortality, with death occurring during the first month, indicating the increased vulnerability of the newborn. Overall, mortality rates are relatively low, with mean neonatal mortality in our sample of 0.5%, compared to a mean of 0.8% for all children born in Brazil (UNICEF (2020)). This difference likely arises from the different compositions of the newborns in our sample, as our sample focuses on singleton births and multiple births to the same mother.

5.2.3 Hospitalization

The focus on mortality as a measure of children’s subsequent health may overlook more subtle effects on children’s health not captured by mortality. For this reason, we next investigate the effect of maternal dengue on several indicators of health from linked hospitalization records. Access to administrative data from hospitals covered by the public health system, SUS, allows us to link birth records with hospital admission records using individual identifiers. We investigate the effect of maternal dengue on hospitalization for up to three years after birth. Table 6 reports the estimates. Making use of the detailed information from the hospitalization records, we look at a number of different outcomes in addition to overall hospitalization, including admittance to intensive care, the length of stay, and the cost of stay. All estimates include the full set of controls as in our preferred maternal fixed-effects specification of column (2) of Table 2.

We find that maternal dengue infections substantially increase the hospitalization risk of children in the three years after birth. We find an increase in overall hospitalizations by 3.2%, significant at the 5% level, a 27% increase compared to the mean incidence. Compared to effect sizes elsewhere in papers with linked hospitalization records, the estimated effect on hospitalization here is relatively large. For example, we find an increase in hospitalization risk ten times the effect of the death of a maternal relative on hospitalization reported in Persson and Rossin-Slater (2018), both relative to the baseline. Unlike their findings, we also find that the effects persist over time, lasting well beyond year one after birth. When estimating the effect separately by year, we document effects well into the second year after births. We document an increase in the risk of hospitalizations by 76%, compared to the 26% increase in the first year, while we find a smaller positive but insignificant effect for third year hospitalizations. The estimates on hospitalization indicate that maternal dengue affects children’s health beyond measures of immediate health at birth, such as BW or low BW categorizations, pointing to possible longer-term damage to affected children’s health.

To understand better whether the increase in hospitalizations is related to known complications from low BW or short gestation, we make use of the information on the precise causes of hospitalization. For example, in the medical literature, a link between preterm delivery

and asthma in children is well established (Been et al. (2014)). To learn about the reasons for hospitalization, we estimated separate regressions on hospitalization by causes, based on causes from ICD-10 (International Statistical Classification of Diseases and Related Health Problems) available from the hospitalization records. Because of the very large number of causes of hospitalization, we focus on groups defined by the different chapters of ICD-10, providing us with a natural grouping of diseases for all chapters making up more than 2% of cases, and group the remainder in ‘Other’. In Figure A5, we present the estimates for hospitalizations by groups of causes of hospitalization. While coefficients for most groups of causes are relatively small and not significant, we find a significant positive and large effect of maternal dengue on hospitalizations due to ‘diseases of the respiratory system’, a finding in line with evidence of the effects of preterm births on lung development and respiratory issues, such as asthma and wheezing (Boyle et al. (2012)).

In addition to hospitalization risk, we are also interested in learning about the severity of admissions. We use information on the type of hospitalization and estimate the effect on admission to (neonatal) intensive care units. In columns (5)-(8), we provide the coefficients for intensive care utilization for the three-year period and separately for neonatal (first four weeks) and first and second years after birth. We find positive coefficients across outcomes—for example, a 23% increase in intensive care admissions overall—but the coefficients are not statistically significant. This is consistent with maternal dengue leading to an increase in hospitalization risk, but not necessarily to more severe hospitalizations.

To further investigate the severity of admissions, we study the effect on the length of hospitalization, reported in columns (1)-(4) of Panel B. We find a positive effect on the duration of hospitalizations of 0.414 days over the three-year period, a 36% increase in the length of hospitalizations. However, the estimate is not statistically significant. Similarly, we find a positive but insignificant effect of 0.2 days for length of hospitalization in the first year. The coefficients for the second and third year of 0.157 and 0.024, a 140% and 45% increase, respectively, are large but not precisely estimated. Alternatively, when estimating the effect on length of hospitalization conditional on admission, we also do not find significant effects (not reported). However, given the relatively small incidence and the sign and magnitude of the effects, we cannot completely rule out that maternal dengue infections may also lead to

more severe hospital episodes.

The increased risk of hospitalization also points to the additional burden of maternal dengue on the health system, with neonatal intensive care for preterm babies associated with what are among the highest daily health expenditures in hospitalizations (Beam et al. (2020)). To investigate the additional economic burden from the effect of hospitalization, we take the information on hospital costs and estimate the effect of maternal dengue on log hospitalization costs. The average cost due to hospitalization in the first year for all newborns is R\$319.01, and the average cost conditional on admission is R\$3,327.95¹⁹ as expected with very substantial variability (s.d.: 9759.79).²⁰ We find a positive and significant effect on log cost of 0.366 over the three-year period, a 44% increase in hospitalization cost due to maternal dengue infections. When estimating the effects separately by year, we find a coefficient of 0.283 and 0.172 for the first and second year after birth, in line with the effects on hospitalization risk, an equivalent increase of 34% and 19%. We do not find an effect for the third year after birth.

Using hospitalization records linked to birth records for three years after birth, the above results indicate that maternal dengue has health consequences for an extended period after birth. These results are therefore important for understanding the potential long-term consequences of poor health at birth, including on health later in life, education and labor market outcomes, and the long-term effects of low BW and short gestation abundantly documented in the literature (for example Black et al. (2007) and Almond and Currie (2011)). The results also point to the immediate costs of maternal dengue due to the utilization of scarce public health resources, with an increase in hospital admissions, in turn leading to the documented substantial increase in the direct cost to the public health system from those hospitalizations.

6 Final Remarks

Maternal dengue was long believed not to pose a risk for the health of unborn children in utero. While there is substantial literature on the short and long-term effects effect of in-

¹⁹Based on the average 2014 R\$-US\$ exchange rate US\$136 and US\$1,418.70, respectively.

²⁰The mean is skewed heavily, indicated by a median of R\$606.43 and the top 1 percentile of R\$54.82.

utero exposure to a range of different health shocks—including to other infectious diseases during pregnancy—there is no causal evidence on the effect of maternal dengue infections on birth outcomes. This is despite dengue being by far the most prevalent mosquito-borne viral disease worldwide, with tens of millions of cases every year. Previous research was based either on small samples from hospitalized pregnant women or epidemiological studies not accounting for selection and leading to inconclusive findings. Much of the medical evidence is also focused on severe dengue infection cases, which make up about less than 0.5% of cases, neglecting the vast majority of dengue infections and hence discounting the negative impact dengue might have for the majority of relatively mild infections.

In this paper, we provide causal evidence on the effect of dengue during pregnancy on the child’s health using linked population-level administrative records from Brazil. Focusing on mothers with multiple births over time, we provide estimates using maternal fixed-effects, and hence holding constant fixed maternal characteristics, including their propensity to contract and report a dengue infection. In addition, we include a variety of time-varying mother characteristics to account for changes in employment status and other personal circumstances over time that may, for example, impact the health of their unborn child directly (for instance, through early maternal inputs).

The results presented here reveal the devastating impact of generally mild maternal dengue infections on newborns’ health, so far undetected in the literature, with immediate consequences for public health systems and potential long-term consequences of low BW and short gestation documented in the literature ([Almond and Currie \(2011\)](#), [Figlio et al. \(2014\)](#)). Given the rapid growth of the dengue virus in Brazil and in many other countries around the tropics, where *Aedes* mosquitoes find a suitable breeding ground, our estimates point to a health risk to date underestimated, putting more than half of the world’s unborn children at risk of lasting damage to their health. With climate change aiding the breeding conditions of dengue vectors in countries previously unaffected by dengue, dengue virus will likely pose a growing risk over the next years and decades to come in countries outside the tropics ([Romanello et al. \(2022\)](#)).

Besides adding to the understanding of the consequences of maternal dengue for children’s health, our findings are important to inform cost-benefit analyses of dengue vaccines and

vector-control programs in Brazil and other countries affected by dengue. For example, the cost of provision of effective insect repellent for expectant low-income mothers (Goldman (2017)) or innovations to reduce the *Aedes* vector prevalence either through the release of transgenic *Aedes* mosquitoes, which reduce reproduction of the vector (Evans et al. (2019)) or the targeted infection of *Aedes* mosquitoes with the *Wolbachia* bacterium reducing dengue pathogen transmission (Hoffmann et al. (2011)), can be assessed based on the estimates on the effect of maternal dengue on low BW, short gestation, and the increase in hospitalizations. A new and more effective generation of dengue vaccines is also on the horizon, providing immunity against the four different serotypes (Rivera et al. (2022)).

The evidence presented here also cautions against ruling out potential negative effects of a variety of other maternal infections during pregnancy, including most recently of COVID-19, before conclusive evidence from adequate data and suitable methods is available. Maternal dengue, too, was long believed not to pose a risk for children in utero.

References

- Adam, Ishag, Ammar M. Jumaa, Hagir M. Elbashir, and Mubarak S. Karsany, “Maternal and perinatal outcomes of dengue in Port Sudan, Eastern Sudan,” *Virology Journal*, 2010, 7, 7–10.
- Almond, Douglas and Janet Currie, “Killing me softly: The fetal origins hypothesis,” *Journal of Economic Perspectives*, 2011, 25 (3), 153–172.
- , Kenneth Chay, and David Lee, “The costs of low birth weight,” *The Quarterly Journal of Economics*, 2005, 120 (3), 1031–1083.
- Amarante, Verónica, Marco Manacorda, Edward Miguel, and Andrea Vigorito, “Do cash transfers improve birth outcomes? Evidence from matched vital statistics, and program and social security data,” *American Economic Journal: Economic Policy*, 2016, 8 (2), 1–43.
- Barreca, Alan I, “The long-term economic impact of in utero and postnatal exposure to Malaria,” *Journal of Human Resources*, 2010, 45 (4), 865–892.
- Basurko, Célia, Gabriel Carles, Mohamed Youssef, and Wael E.L. Guindi, “Maternal and foetal consequences of dengue fever during pregnancy,” *European Journal of Obstetrics and Gynecology and Reproductive Biology*, 2009, 147 (1), 29–32.
- Beam, Andrew L., Inbar Fried, Nathan Palmer, Denis Agniel, Gabriel Brat, Kathe Fox, Isaac Kohane, Anna Sinaiko, John A.F. Zupancic, and Joanne Armstrong, “Estimates of healthcare spending for preterm and low-birthweight infants in a commercially insured population: 2008–2016,” *Journal of Perinatology*, 2020, 40 (7), 1091–1099.
- Been, Jasper V., Marlies J. Lugtenberg, Eline Smets, Constant P. van Schayck, Boris W. Kramer, Monique Mommers, and Aziz Sheikh, “Preterm birth and childhood wheezing disorders: A systematic review and meta-analysis,” *PLoS Medicine*, 2014, 11 (1).
- Bhatt, Samir, Peter W Gething, Oliver J Brady, Jane P Messina, Andrew W Farlow, Catherine L Moyes, John M Drake, John S Brownstein, Anne G Hoen, Osman Sankoh, Monica F Myers, Dylan B George, and Thomas Jaenisch, “The global distribution and burden of dengue,” *Nature*, 2013, 496 (7446), 504–507.
- Black, Sandra E., Paul J. Devereux, and Kjell G. Salvanes, “From the cradle to the labor market? The effect of birth weight on adult outcomes,” *The Quarterly Journal of Economics*, 2007, 122 (1), 409–439.
- , –, and –, “Does grief transfer across generations? Bereavements during pregnancy and child outcomes,” *American Economic Journal: Applied Economics*, 2016, 8 (1), 193–223.

- Boyle, Elaine M., Gry Poulsen, David J. Field, Jennifer J. Kurinczuk, Dieter Wolke, Zarko Alfirovic, and Maria A. Quigley, “Effects of gestational age at birth on health outcomes at 3 and 5 years of age: Population based cohort study,” *BMJ (Online)*, 3 2012, 344 (7848).
- Campbell, Karen M., C. D. Lin, Sapon Iamsirithaworn, and Thomas W. Scott, “The complex relationship between weather and dengue virus transmission in Thailand,” *American Journal of Tropical Medicine and Hygiene*, 2013, 89 (6), 1066–1080.
- CDC, “Preventing Infections Before and During Pregnancy,” *Centers for Disease Control and Prevention Online resource*, <https://www.cdc.gov/pregnancy/infections.html>, date accessed: 07.11.2022, 2021.
- Cellini, Stefano, Livia Menezes, and Martin Foureaux Koppensteiner, “Maternal displacements during pregnancy and the health of newborns,” *SSRN Electronic Journal*, 2022, (15155).
- Chen, Bin, Jun Yang, Lei Luo, Zhicong Yang, and Qiyong Liu, “Who is vulnerable to dengue fever? A community survey of the 2014 outbreak in Guangzhou, China,” *International Journal of Environmental Research and Public Health*, 2016, 13 (7).
- Chersich, Matthew Francis, Minh Duc Pham, Ashtyn Areal, Marjan Mosalam Haghighi, Albert Manyuchi, Callum P. Swift, Bianca Wernecke, Matthew Robinson, Robyn Hetem, Melanie Boeckmann, and Shakoor Hajat, “Associations between high temperatures in pregnancy and risk of preterm birth, low birth weight, and stillbirths: Systematic review and meta-analysis,” *The BMJ*, 2020, 371, 1–13.
- Chitra, T. V. and Seetha Panicker, “Maternal and fetal outcome of dengue fever in pregnancy,” *Journal of Vector Borne Diseases*, 2011, 48 (4), 210–213.
- Colón-González, Felipe J, Maquins Odhiambo Sewe, Adrian M Tompkins, Henrik Sjödin, Alejandro Casallas, Joacim Rocklöv, and Cyril Caminade, “Projecting the risk of mosquito-borne diseases in a warmer and more populated world: a multi-model, multi-scenario intercomparison modelling study,” *Lancet Planetary Health*, 2021, pp. 404–414.
- Currie, Janet, Matthew Neidell, and Johannes F. Schmieder, “Air pollution and infant health: Lessons from New Jersey,” *Journal of Health Economics*, 2009, 28 (3), 688–703.
- Dudgeon, J A, “Maternal rubella and its effect on the foetus,” *Archives of Disease in Childhood*, 1967, (1944), 110–125.
- ECMWF, “ERA5,” *European Centre for Medium-Range Weather Forecasts*, Downloaded from <https://www.ecmwf.int/en/forecasts/dataset/ecmwf-reanalysis-interim>, accessed 14/04/2022, 2022.

- Evans, Benjamin R, Panayiota Kotsakiozi, Andre Luis Costa da Silva, Rafaella Sayuri Ioshino, Luiza Garziera, Michele C Pedrosa, Aldo Malavasi, Jair F Virginio, Margareth L Capurro, and Jeffrey R Powell**, “Transgenic *Aedes aegypti* mosquitoes transfer genes into a natural population,” *Nature Scientific Reports*, 2019, *9* (13047), 1–6.
- Figlio, David, Jonathan Guryan, Krzysztof Karbownik, and Jeffrey Roth**, “The effects of poor neonatal health on children’s cognitive development,” *American Economic Review*, 2014, *104* (12), 3921–3955.
- Goldman, H**, “Insect repellants during pregnancy in the era of the Zika virus,” *Obstetrics and Gynecology*, 2017, *128* (5), 1111–1115.
- Henein, Sandra, Cameron Adams, Matthew Bonaparte, Janice M. Moser, Alina Munteanu, Ralph Baric, and Aravinda M. De Silva**, “Dengue vaccine breakthrough infections reveal properties of neutralizing antibodies linked to protection,” *Journal of Clinical Investigation*, 7 2021, *131* (13).
- Hoffmann, A A, B L Montgomery, J Popovici, P H Johnson, F Muzzi, M Greenfield, M Durkan, Y S Leong, Y Dong, H Cook, J Axford, A G Callahan, N Kenny, C Omodei, E A McGraw, P A Ryan, S A Ritchie, M Turelli, and S L O Neill**, “Successful establishment of *Wolbachia* in *Aedes* populations to suppress dengue transmission,” *Nature*, 2011, *476*, 454–457.
- HSMG**, “Sistema de Informação de Agravos de Notificação,” *Health Secretariat of Minas Gerais, Brazil*, 2022.
- , “Sistema de Informações Hospitalares, Health Secretariat,” *Health Secretariat of Minas Gerais, Brazil*, 2022.
- , “Sistema de Informações sobre Mortalidade,” *Health Secretariat of Minas Gerais, Brazil*, 2022.
- , “Sistema de Informações sobre Nascidos Vivos,” *Health Secretariat of Minas Gerais, Brazil*, 2022.
- Kelly, Elaine**, “The scourge of Asian flu : In utero exposure to pandemic influenza and the development of a cohort of British children,” 2011, *46* (4), 669–694.
- Koppensteiner, Martin Foureaux and Marco Manacorda**, “Violence and birth outcomes: Evidence from homicides in Brazil,” *Journal of Development Economics*, 2016, *119*, 16–33.
- Kramer, Michael**, “Intrauterine growth and gestational duration determinants,” *Pediatrics*, 1987, *80* (4), 502–511.
- Lowe, Rachel, Christovam Barcellos, Patrícia Brasil, Oswaldo G. Cruz, Nildimar Alves Honório, Hannah Kuper, and Marília Sá Carvalho**, “The zika virus epidemic in brazil: From discovery to future implications,” *International Journal of Environmental Research and Public Health*, 1 2018, *15* (1).

- Matsumoto, Brett**, “Family ruptures, stress, and the mental health of the next generation: Comment,” *American Economic Review*, 2018, *108* (4-5), 1253–1255.
- Megli, Christina J. and Carolyn B. Coyne**, “Infections at the maternal–fetal interface: an overview of pathogenesis and defence,” *Nature Reviews Microbiology*, 2021, *0123456789*.
- Murugesan, Amudhan and Mythreyee Manoharan**, *Emerging and reemerging viral pathogens, chapter 16: Dengue virus*, Elsevier, 2020.
- Nascimento, Laura B, Cláudio M Siqueira, Giovanini E Coelho, and João B Siqueira Jr**, “Symptomatic dengue infection during pregnancy and livebirth outcomes in Brazil , 2007 – 13: a retrospective observational cohort study,” *Lancet Infectious Diseases*, 2017, *17*, 949–956.
- PAHO**, “Infecções Perinatais transmitidas de mãe para filho durante a gravidez,” *Pan American Health Organization: CLAP/SMR*, 2010, *1567* (03), 58.
- Paixão, Enny S, Conceição N Costa, Maria Glória Teixeira, Katie Harron, Marcia Furquim De Almeida, and Mauricio L Barreto**, “Symptomatic dengue infection during pregnancy and the risk of stillbirth in Brazil , 2006 – 12: a matched case-control study,” *The Lancet Infectious Diseases*, 2017, *17* (9), 957–964.
- Paixão, Enny S., Oona M. Campbell, Maria Gloria Teixeira, Maria C.N. Costa, Katie Harron, Mauricio L. Barreto, Maira B. Leal, Marcia F. Almeida, and Laura C. Rodrigues**, “Dengue during pregnancy and live birth outcomes: A cohort of linked data from Brazil,” *BMJ Open*, 2019, *9* (7), 1–8.
- Payne, Susan**, *Viruses: From Understanding to Investigation*, Academic Press, 2017.
- Peiter, Paulo Cesar, Rafael Dos Santos Pereira, Martha Cristina Nunes Moreira, Marcos Nascimento, Maria De Fatima Lobato Tavares, Vivian Da Cruz Franco, Jose Joaquin Carvajal Cortes, Daniel De Souza Campos, and Christovam Barcellos**, “Zika epidemic and microcephaly in Brazil: Challenges for access to health care and promotion in three epidemic areas,” *PLoS ONE*, 7 2020, *15* (7 July).
- Persson, Petra and Maya Rossin-Slater**, “Family ruptures, stress, and the mental health of the next generation,” *American Economic Review*, 2018, *108* (4-5), 1214–1252.
- Pouliot, Sawyer, Xu Xiong, Emily Harville, Valerie Paz-Soldan, Kay Tomashek, Gerard Breart, and Pierre Buekens**, “Maternal dengue and pregnancy outcomes: a systematic review,” *Obstetrical and Gynecological Survey*, 2010, *65* (2), 107–118.
- Quintana-Domeque, Climent and Pedro Ródenas-Serrano**, “The hidden costs of terrorism: The effects on health at birth,” *Journal of Health Economics*, 12 2017, *56*, 47–60.
- Rivera, Luis, Shibadas Biswal, Xavier Sáez-llorens, Humberto Reynales, Eduardo López-medina, Charissa Borja-tabora, and Lulu Bravo**, “Three-year efficacy and safety of Takeda’ s dengue vaccine candidate (TAK-003),” *Clinical Infectious Diseases*, 2022, *7*, 107–117.

- Rocha, Rudi and Rodrigo R. Soares**, “Water Scarcity and Birth Outcomes in the Brazilian Semiarid,” *Journal of Development Economics*, 2015, 112, 72–91.
- Romanello et al.**, “The 2022 Report of The Lancet Countdown on Health and Climate Change: compounding health crises,” *Lancet*, 2022, 6736 (22).
- Schwandt, Hannes**, “The lasting legacy of seasonal influenza: In-utero exposure and labor market outcomes,” *SSRN Electronic Journal*, 2017, (10589).
- Shepard, Donald S, Eduardo A Undurraga, Yara A Halasa, and Jeff D Stanaway**, “The global economic burden of dengue: a systematic analysis,” *Lancet Infectious Diseases*, 2016, 16, 935–941.
- Silasi, Michelle, Ingrid Cardenas, Ja Young Kwon, Karen Racicot, Paula Aldo, and Gil Mor**, “Viral infections during pregnancy,” *American Journal of Reproductive Immunology*, 2015, 73 (3), 199–213.
- Tan, Peng Chiong, Geetha Rajasingam, Shamala Devi, and Siti Zawiah Omar**, “Dengue infection in pregnancy,” *Obstetrics and Gynecology*, 2008, 111 (5), 1111–1117.
- UNICEF**, *Levels and Trends in Child Mortality*, New York: UNICEF, 2020.
- WHO**, “Dengue fact sheet,” <https://www.who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue>, date accessed: 07.11.2022, 2020.
- Wilder-Smith, A, O Eng-Eong, O Horstick, and B Wills**, “Dengue,” *Lancet*, 2019, 393 (10169), 350–363.
- Zeng, Zhilin, Juan Zhan, Liyuan Chen, Huilong Chen, and Sheng Cheng**, “Global, regional, and national dengue burden from 1990 to 2017: A systematic analysis based on the global burden of disease study 2017,” *EClinicalMedicine*, 2021, 32, 100712.

Table 1: Descriptive Statistics

	All mothers		Maternal FE	
	Mean	Std.Dev.	Mean	Std.Dev.
<i>Birth outcomes</i>				
Birth weight	3160.583	511.191	3174.865	501.506
Low birth weight	0.080	0.271	0.073	0.260
Very low birth weight	0.010	0.100	0.009	0.094
Extremely low birth weight	0.004	0.059	0.003	0.057
1st minute APGAR	8.414	1.219	8.448	1.184
5th minute APGAR	9.380	0.825	9.381	0.821
<i>Newborn characteristics</i>				
Female	0.488	0.500	0.482	0.500
<i>Pregnancy and delivery characteristics</i>				
Prenatal visits	8.043	2.565	7.671	2.668
Gestation days	269.727	14.431	269.854	14.433
Gestation days < 259	0.103	0.304	0.103	0.303
Gestation days < 224	0.013	0.112	0.013	0.111
Gestation days < 196	0.003	0.054	0.003	0.055
C-section	0.427	0.495	0.471	0.499
Emergency C-section	0.200	0.400	0.180	0.384
<i>Mothers characteristics</i>				
Age	26.851	6.612	25.205	6.030
20 or less	0.203	0.402	0.255	0.436
21 to 35	0.688	0.463	0.685	0.464
36 and beyond	0.109	0.312	0.060	0.237
White	0.361	0.480	0.342	0.474
Black	0.082	0.275	0.092	0.289
Asian	0.007	0.081	0.007	0.082
Mixed	0.548	0.498	0.557	0.497
Indigenous	0.002	0.045	0.002	0.047
Single	0.395	0.489	0.430	0.495
Married	0.445	0.497	0.414	0.492
Widowed	0.003	0.051	0.002	0.042
Separated divorced	0.016	0.125	0.011	0.103
Stable union	0.142	0.349	0.144	0.351
Low education	0.791	0.406	0.804	0.397
High education	0.190	0.392	0.184	0.387
Dengue during pregnancy	0.007	0.086	0.008	0.090
Observations	1578599		281497	

Table 2: Effect of Dengue on Birth Outcomes

<i>Panel A - Birth Weight (BW)</i>								
	<i>BW</i>		<i>Low BW</i>		<i>Very Low BW</i>		<i>Extremely Low BW</i>	
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
<i>Dengue (pregnancy)</i>	-31.328 (11.416)***	-27.480 (11.306)**	0.013 (0.007)*	0.011 (0.007)*	0.006 (0.003)**	0.006 (0.003)**	0.004 (0.002)**	0.004 (0.002)**
Mean dep. var.	3,174.865	3,174.865	0.073	0.073	0.009	0.009	0.003	0.003
Mothers	136,788	136,788	136,788	136,788	136,788	136,788	136,788	136,788
Observations	281,497	281,497	281,497	281,497	281,497	281,497	281,497	281,497
Controls	No	Yes	No	Yes	No	Yes	No	Yes

<i>Panel B - Gestational Length</i>								
	<i>Gestation (days)</i>		<i>Gestation (<259 days)</i>		<i>Gestation (<224 days)</i>		<i>Gestation (<196 days)</i>	
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
<i>Dengue (pregnancy)</i>	-0.500 (0.407)	-0.474 (0.401)	0.005 (0.008)	0.005 (0.008)	0.011 (0.004)***	0.010 (0.004)***	0.002 (0.002)	0.002 (0.002)
Mean dep. var.	269.854	269.854	0.103	0.103	0.013	0.013	0.003	0.003
Mothers	136,788	136,788	136,788	136,788	136,788	136,788	136,788	136,788
Observations	281,497	281,497	281,497	281,497	281,497	281,497	281,497	281,497
Controls	No	Yes	No	Yes	No	Yes	No	Yes

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$. Robust standard errors are clustered at the mother level in parentheses.

Note: The analysis includes mothers over the period between 2011 and 2017. *BW* is reported in grams. *Low BW*, *Very Low BW* and *Extremely Low BW* are dummies indicating newborns up to 2,500, 1,500 and 1,000 grams, respectively. *Gestation* is reported in days. Columns 3-4, 5-6, and 7-8 in *Panel B* are dummies for early, very early and extremely early delivery, respectively. Explanatory variable *Dengue(pregnancy)* indicates whether the mother had dengue during pregnancy. All regressions include month of conception fixed-effects and maternal fixed-effects. Controls include dummies for maternal age, and dummies for marital status (married, living together, divorced, single, missing), highest education achieved (incomplete primary, complete primary, incomplete secondary, complete secondary, incomplete higher education, complete higher education), occupation codes, number of previous stillbirths, gestation order and birth interval (time between conceptions), number of days during pregnancy with average temperature between 10-15°C, 15-20°C, 20-25°C, 25-30°C and 30-35°C.

Table 3: Effect of Dengue on Birth Outcomes by Trimester

	<i>BW</i>		<i>Low BW</i>		<i>Very Low BW</i>		<i>Extremely Low BW</i>	
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
<i>Dengue</i> (1st trimester)	-24.116 (19.605)	-18.880 (19.368)	0.020 (0.012)	0.017 (0.012)	0.007 (0.005)	0.006 (0.005)	0.004 (0.003)	0.004 (0.003)
<i>Dengue</i> (2nd trimester)	-20.978 (20.148)	-13.202 (19.870)	-0.005 (0.012)	-0.008 (0.012)	0.008 (0.005)	0.007 (0.005)	0.007 (0.003)**	0.006 (0.003)*
<i>Dengue</i> (3rd trimester)	-50.811 (19.315)***	-52.846 (19.265)***	0.025 (0.011)**	0.027 (0.011)**	0.003 (0.005)	0.003 (0.005)	0.002 (0.004)	0.002 (0.004)
Mean dep. var.	3,174.865	3,174.865	0.073	0.073	0.009	0.009	0.003	0.003
Mothers	136,788	136,788	136,788	136,788	136,788	136,788	136,788	136,788
Observations	281,497	281,497	281,497	281,497	281,497	281,497	281,497	281,497
Controls	No	Yes	No	Yes	No	Yes	No	Yes

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$. Robust standard errors are clustered at the neighborhood level for the OLS regressions and the regressions with neighborhood fixed-effects, at the hospital level for the regressions with hospital fixed-effects and at the mother level for the remaining specifications.

Note: The analysis includes mothers over the period between 2011 and 2017. *BW* is reported in grams. *Low BW*, *Very Low BW* and *Extremely Low BW* are dummies indicating newborns up to 2,500, 1,500 and 1,000 grams, respectively. Explanatory variables *Dengue (1st trimester)*, *Dengue (2nd trimester)* and *Dengue (3rd trimester)* indicate mothers who had during the corresponding trimester of their pregnancy. The trimester coefficients are jointly estimated for each column. For a detailed list of controls, see Table 2 note.

Table 4: Effect of Dengue on Birth Outcomes - Sensitivity Analysis

	<i>BW</i>						
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
<i>Dengue</i> (<i>pregnancy</i>)	-8.657 (11.003)	-27.480 (11.306)**	-30.186 (15.001)**	-33.981 (16.687)**	-26.548 (12.569)**	-27.666 (12.438)**	-50.063 (14.202)***
Mean dep. var.	3,174.865	3,174.865	3,176.916	3,176.916	3,174.948	3,174.948	3,166.955
R^2	0.019	0.705	0.737	0.770	0.711	0.713	0.731
	<i>Low BW</i>						
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
<i>Dengue</i> (<i>pregnancy</i>)	0.002 (0.006)	0.011 (0.007)*	0.013 (0.009)	0.014 (0.010)	0.011 (0.007)	0.011 (0.008)	0.021 (0.009)**
Mean dep. var.	0.073	0.073	0.072	0.072	0.073	0.073	0.075
R^2	0.008	0.590	0.635	0.679	0.598	0.599	0.614
	<i>Very Low BW</i>						
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
<i>Dengue</i> (<i>pregnancy</i>)	0.003 (0.002)	0.006 (0.003)**	0.007 (0.004)*	0.008 (0.005)	0.005 (0.003)*	0.006 (0.003)*	0.009 (0.004)**
Mean dep. var.	0.009	0.009	0.009	0.009	0.009	0.009	0.009
R^2	0.003	0.533	0.582	0.632	0.539	0.541	0.566
	<i>Extremely Low BW</i>						
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
<i>Dengue</i> (<i>pregnancy</i>)	0.003 (0.002)*	0.004 (0.002)**	0.005 (0.003)*	0.005 (0.003)*	0.004 (0.003)	0.004 (0.003)	0.007 (0.002)***
Mean dep. var.	0.003	0.003	0.003	0.003	0.003	0.003	0.004
R^2	0.002	0.514	0.563	0.618	0.518	0.519	0.557
Clusters	28,480	136,788	14,917	14,917	586	586	5,049
Observations	281,497	281,497	257,203	257,203	281,153	281,153	10,389
Mother FE	No	Yes	Yes	Yes	Yes	Yes	Yes
Time FE	No	Yes	Yes	Yes	Yes	Yes	Yes
Neighborhood FE	No	No	Yes	Yes	No	No	No
Neighborhood Linear Trends	No	No	No	Yes	No	No	No
Hospital FE	No	No	No	No	Yes	Yes	No
Hospital Linear Trends	No	No	No	No	No	Yes	No
Controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Alternative Control Group	No	No	No	No	No	No	Yes

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$. Robust standard errors are clustered at the neighborhood level for the OLS regressions and the regressions with neighborhood fixed-effects, at the hospital level for the regressions with hospital fixed-effects and at the mother level for the remaining specifications.

Note: The analysis includes mothers over the period between 2011 and 2017. *BW* is reported in grams. *Low BW*, *Very Low BW* and *Extremely Low BW* are dummies indicating newborns up to 2,500, 1,500 and 1,000 grams, respectively. Explanatory variable *Dengue(pregnancy)* indicates whether the mother had dengue during pregnancy. For a detailed list of controls, see Table 2 note. *Alternative Control Group* limits the control group to mothers infected with dengue after pregnancy.

Table 5: Effect of Dengue on Additional Outcomes

<i>Panel A - Additional Outcomes</i>					
	<i>Emergency C-section</i>	<i>APGAR (1st minute)</i>	<i>APGAR (5th minute)</i>	<i>Prenatal visits</i>	<i>Female</i>
	(1)	(2)	(3)	(4)	(5)
<i>Dengue (pregnancy)</i>	0.008 (0.009)	−0.019 (0.036)	−0.015 (0.023)	0.209 (0.063)***	0.016 (0.015)
Mean dep. var.	0.180	8.448	9.381	7.671	0.482
Mothers	136,788	131,140	131,290	134,101	136,742
Observations	281,497	269,676	270,003	275,754	281,403
Controls	Yes	Yes	Yes	Yes	Yes

<i>Panel B - Mortality</i>				
	<i>Mortality (1 week)</i>	<i>Mortality (4 weeks)</i>	<i>Mortality (22 weeks)</i>	<i>Mortality (1 year)</i>
	(1)	(2)	(3)	(4)
<i>Dengue (pregnancy)</i>	0.003 (0.002)	0.002 (0.002)	0.002 (0.003)	0.001 (0.003)
Mean dep. var.	0.004	0.005	0.006	0.007
Mothers	136,788	136,788	136,788	136,788
Observations	281,497	281,497	281,497	281,497
Controls	Yes	Yes	Yes	Yes

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$. Robust standard errors are clustered at the mother level in parentheses.

Note: The analysis includes mothers over the period between 2011 and 2017. *Emergency C-section* is a dummy indicating if the C-section happened after labor began. Explanatory variable *Dengue(pregnancy)* indicates whether the mother had dengue during pregnancy. All regressions include month of conception fixed-effects and maternal fixed-effects and the full set of controls (for a detailed list of controls, see Table 2 note).

Table 6: Effect of Dengue on Hospitalization

<i>Panel A</i>								
	<i>Hospitalization</i>				<i>Intensive Care Unit</i>			
	(1) <i>Total</i>	(2) <i>1st year</i>	(3) <i>2nd year</i>	(4) <i>3rd year</i>	(5) <i>Total</i>	(6) <i>Neonatal</i>	(7) <i>1st year</i>	(8) <i>2nd year</i>
<i>Dengue (pregnancy)</i>	0.032 (0.013)**	0.025 (0.012)**	0.016 (0.006)**	0.001 (0.004)	0.005 (0.006)	0.007 (0.006)	0.004 (0.006)	0.001 (0.001)
Mean dep. var.	0.117	0.096	0.021	0.011	0.022	0.017	0.021	0.001
Mothers	67,962	67,962	67,962	67,962	67,962	67,962	67,962	67,962
Observations	138,751	138,751	138,751	138,751	138,751	138,751	138,751	138,751

<i>Panel B</i>								
	<i>Length of Stay</i>				<i>Cost</i>			
	(1) <i>Total</i>	(2) <i>1st year</i>	(3) <i>2nd year</i>	(4) <i>3rd year</i>	(5) <i>Total</i>	(6) <i>1st year</i>	(7) <i>2nd year</i>	(8) <i>3rd year</i>
<i>Dengue (pregnancy)</i>	0.414 (0.316)	0.234 (0.276)	0.157 (0.112)	0.024 (0.019)	0.366 (0.150)**	0.283 (0.142)**	0.172 (0.070)**	0.011 (0.041)
Mean dep. var.	1.161	0.996	0.112	0.053	352.877	319.011	22.610	11.277
Mothers	67,962	67,962	67,962	67,962	67,962	67,962	67,962	67,962
Observations	138,751	138,751	138,751	138,751	138,751	138,751	138,751	138,751

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$. Robust standard errors are clustered at the mother level in parentheses.

Note: The analysis includes mothers over the period between 2011 and 2017. *Hospitalization* are dummies indicating whether the infant was hospitalized in the first three years of life. *Length of Stay* is the number of days in hospital. *Intensive Care Unit* are dummies indicating whether the infant used ICU. *Cost* is the logarithm of the cost of the hospitalization. Explanatory variable *Dengue(pregnancy)* indicates whether the mother had Dengue during pregnancy. All regressions include month of conception fixed-effects and maternal fixed-effects and the full set of controls (for a detailed list of controls, see Table 2 note).

Online appendix to accompany
Maternal Dengue and Health Outcomes of Children
Martin Foureaux Koppensteiner and Livia Menezes

Appendix A Additional Tables and Figures

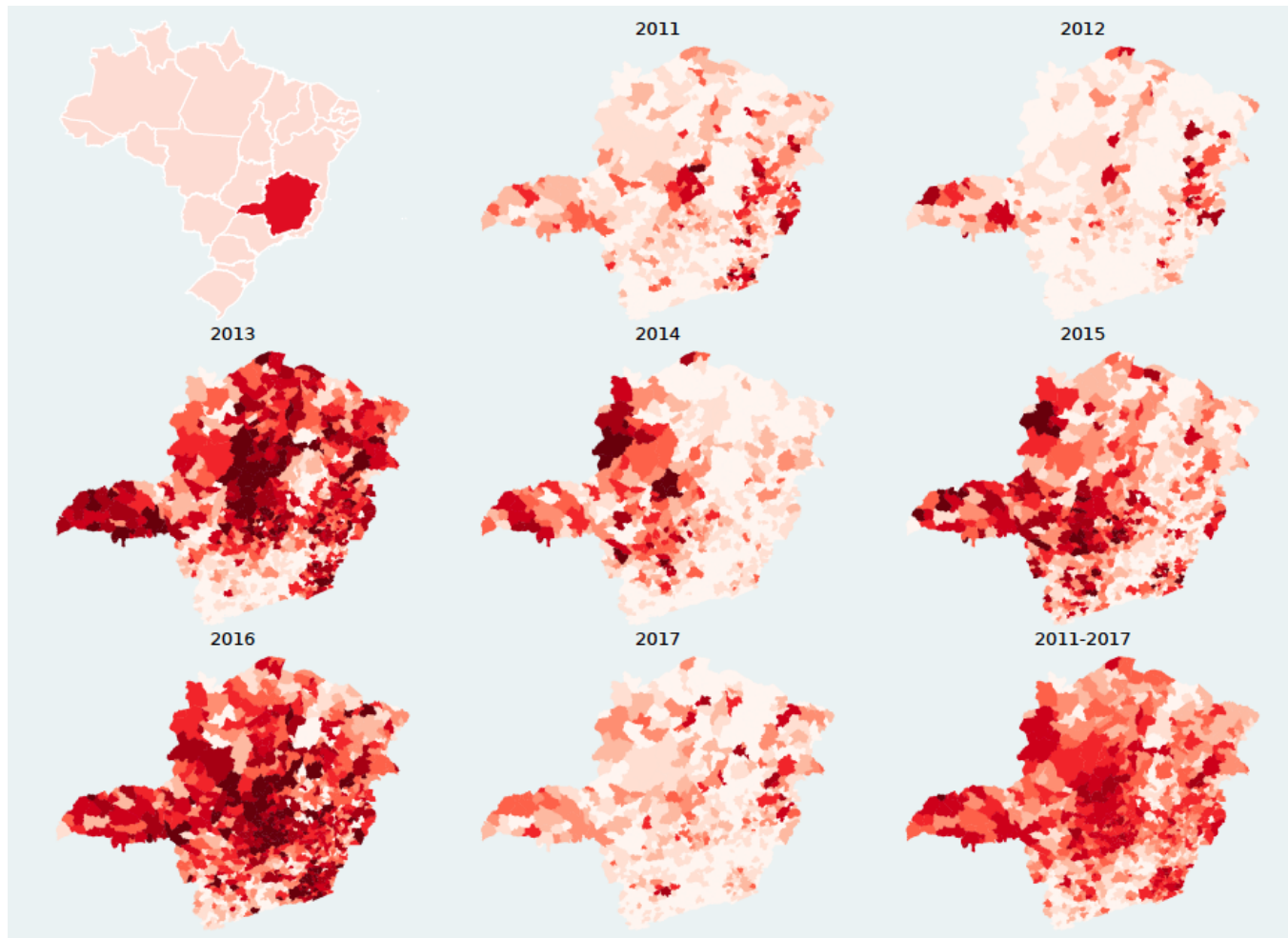


Figure A1: Spacial Distribution of Dengue Cases in the State of Minas Gerais, Brazil

Note: To compare the incident across years, we normalize the shading using the year with the highest cases in 2016. This means that the same shading of red across different years indicates the same dengue incident rate.

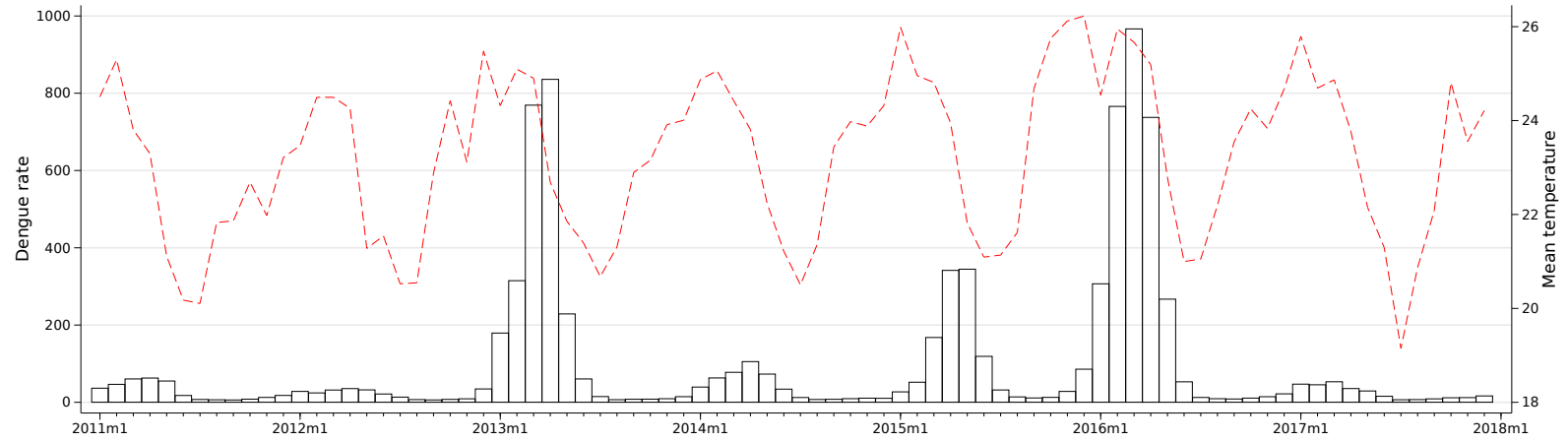


Figure A2: Monthly Dengue Rate and Average Temperature from 2011 to 2017 in Minas Gerais

Note: The dashed red line depicts mean monthly temperature. The bars depict mean monthly dengue rates per 1,000 population.

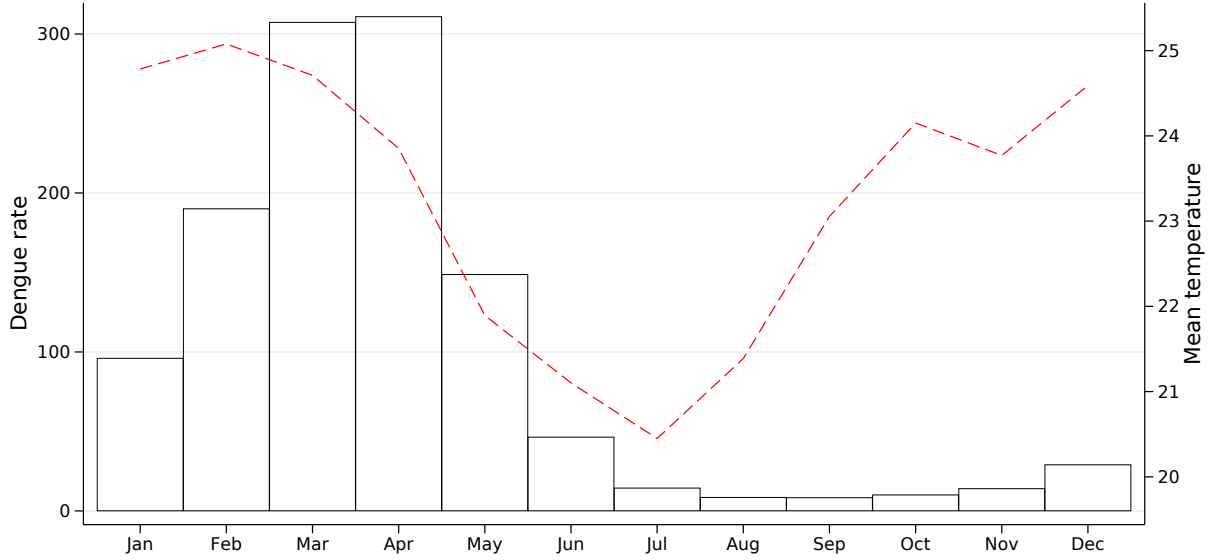


Figure A3: Dengue Rate and Average Temperature by Calendar Month

Note: The dashed red line depicts mean monthly temperature. The bars depict mean monthly dengue rates per 1,000 population.

Table A1: Effect of Dengue on Gestational Length by trimester

	<i>Gestation (days)</i>	<i>Gestation (<259 days)</i>	<i>Gestation (<224 days)</i>	<i>Gestation (<196 days)</i>
	(1)	(2)	(3)	(4)
<i>Dengue (1st trimester)</i>	−0.012 (0.650)	−0.006 (0.014)	0.007 (0.006)	0.005 (0.003)
<i>Dengue (2nd trimester)</i>	−0.870 (0.691)	0.003 (0.013)	0.010 (0.007)	0.001 (0.004)
<i>Dengue (3rd trimester)</i>	−0.555 (0.749)	0.021 (0.015)	0.014 (0.006)**	−0.000 (0.004)
Mean dep. var.	269.854	0.103	0.013	0.003
Mothers	136,788	136,788	136,788	136,788
Observations	281,497	281,497	281,497	281,497

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$. Robust standard errors are clustered at the mother level in parentheses.

Note: The analysis includes mothers over the period between 2011 and 2017. *Gestation* is reported in days. Columns 2, 3, and 4 are dummies for early, very early, and extremely early delivery, respectively. Explanatory variables *Dengue (1st trimester)*, *Dengue (2nd trimester)* and *Dengue (3rd trimester)* indicate the trimester of pregnancy the mother was infected with dengue. All regressions include month of conception fixed-effects and maternal fixed-effects and the full set of controls (for a detailed list of controls, see Table 2 note).

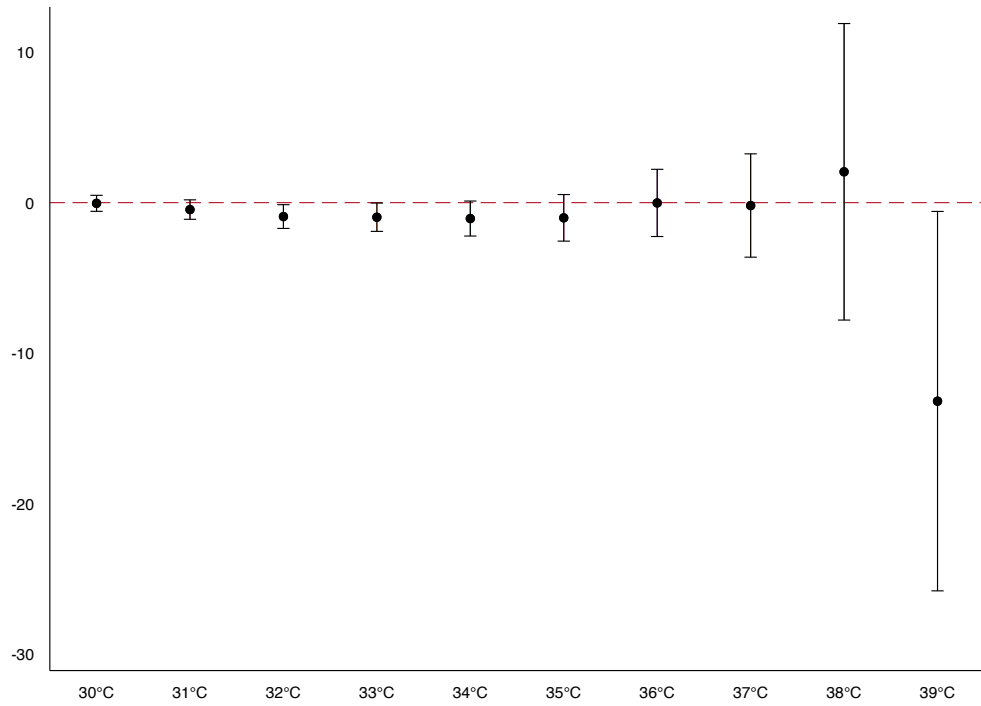


Figure A4: Effect of Temperature on Dengue Rate

Note: Dependent variable is monthly dengue rate at the municipality level. Explanatory variables are the number of days in a month with maximum temperature higher than or equal to 30°C, 31°C,..., 39°C. All regressions include month and municipality fixed-effects.

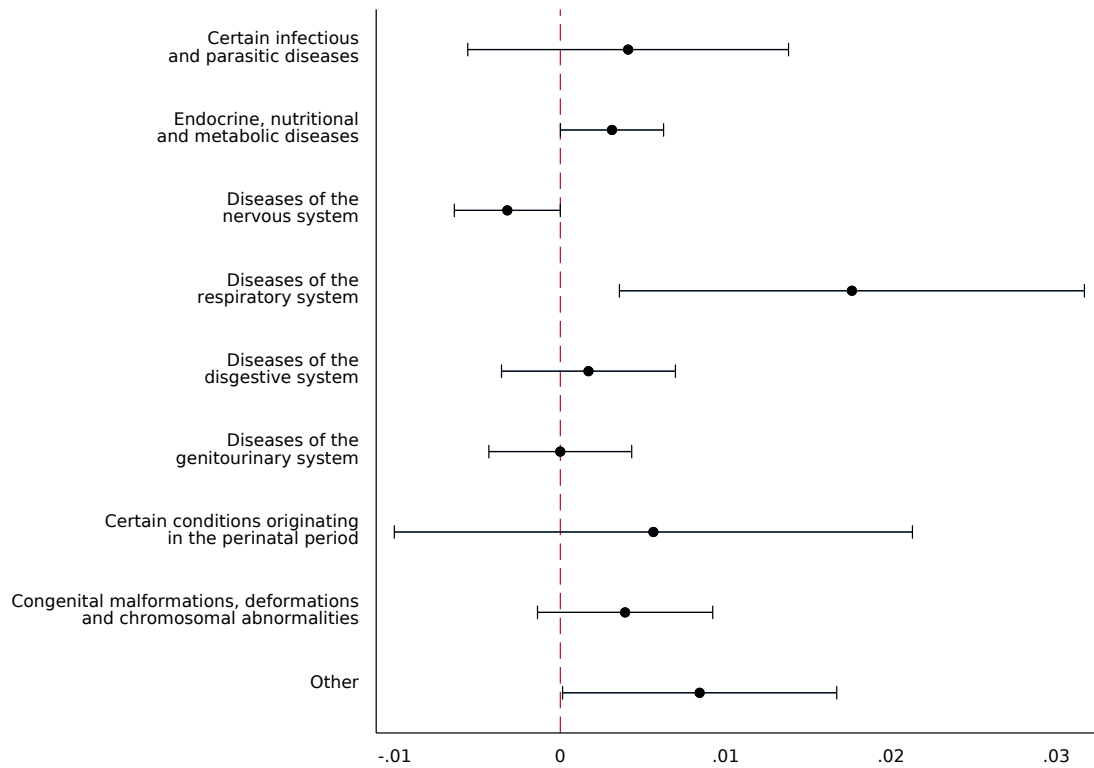


Figure A5: Effect of Dengue on Hospitalization by Cause of Hospitalization

Note: Causes of hospitalization follow the International Statistical Classification of Diseases and Related Health Problems (ICD-10). We report the coefficients for the most common reasons for hospitalization (more than 2% incidence in our sample). The remaining causes are grouped in the category “Other”.

Table A2: Effect of Dengue on Additional Outcomes by trimester

	<i>Emergency C-section</i>	<i>APGAR (1st minute)</i>	<i>APGAR (5th minute)</i>	<i>Prenatal visits</i>	<i>Female</i>	<i>Mortality (1 week)</i>	<i>Mortality (4 weeks)</i>	<i>Mortality (22 weeks)</i>	<i>Mortality (1 year)</i>
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
<i>Dengue (1st trimester)</i>	0.011 (0.015)	−0.031 (0.061)	−0.042 (0.036)	0.265 (0.106)**	−0.005 (0.025)	0.006 (0.004)	0.003 (0.004)	0.001 (0.005)	0.001 (0.005)
<i>Dengue (2nd trimester)</i>	0.005 (0.016)	−0.025 (0.063)	−0.034 (0.038)	0.261 (0.109)**	0.045 (0.025)*	0.002 (0.003)	0.001 (0.003)	0.000 (0.003)	−0.001 (0.004)
<i>Dengue (3rd trimester)</i>	0.008 (0.017)	0.002 (0.066)	0.035 (0.045)	0.087 (0.114)	0.009 (0.026)	0.001 (0.004)	0.002 (0.005)	0.004 (0.005)	0.002 (0.006)
Mean dep. var.	0.180	8.448	9.381	7.671	0.482	0.004	0.005	0.006	0.007
Mothers	136,788	131,140	131,290	134,101	136,742	136,788	136,788	136,788	136,788
Observations	281,497	269,676	270,003	275,754	281,403	281,497	281,497	281,497	281,497

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$. Robust standard errors are clustered at the mother level in parentheses.

Note: The analysis includes mothers over the period between 2011 and 2017. *Emergency C-section* is a dummy indicating if the C-section happened after labor began. Explanatory variables *Dengue (1st trimester)*, *Dengue (2nd trimester)* and *Dengue (3rd trimester)* indicate the trimester of pregnancy the mother was infected with dengue. All regressions include month of conception fixed-effects and maternal fixed-effects and the full set of controls (for a detailed list of controls, see Table 2 note).

Appendix B The Temporal and Spatial Distribution of Dengue Cases

There is substantial temporal and geographic variation in the cases of dengue in Brazil. In Figure A1, we display dengue cases across municipalities in the state of Minas Gerais for each year in our sample and aggregated for the entire period. Municipalities with darker shades of red have higher dengue incident rates. Two features stand out. First, there is substantial variation in dengue cases across space and time, indicating clusters of local outbreaks in different years. Second, there is substantial variation in the overall incidence rate year-by-year, indicated by darker shades in 2013 and 2016 compared to all other years. In Figure A2 we document the temporal variation in dengue. The figure confirms two large dengue outbreaks in 2013 and 2016, with a smaller outbreak in 2015, and years of relative calm in between.¹ The figure also reveals strong seasonality in dengue cases, roughly in line with lagged seasonal temperature variation. Seasonality is even more evident in Figure A3, where we plot dengue rates by calendar month over our sample period. Dengue cases peak in March and April and reach lows during the months of July to November.² We provide additional information on the evolution of the dengue virus in Brazil before the sample period in the following Appendix section C.

¹This is closely matched in our maternal fixed-effects estimation sample with a peak in infections in 2013 and 2016, accounting for 73% of all infections. This is also virtually identical to the infection rates for all mothers, with 73% occurring in these two years.

²Seasonal patterns are confirmed for many other countries suffering from dengue, for example, Thailand (Polwiang (2020)) and Bangladesh (Hossain et al. (2022)).

Appendix C Evolution of Dengue Virus in Brazil

Before the 1970s, the dengue virus was endemic only in a very small number of countries and with a small number of overall infections. Since then, dengue has expanded very rapidly and is now endemic in more than 100 countries, with an estimated half a billion infections every year on average and putting half of today’s world population at risk of disease (Bhatt et al. (2013), Brady et al. (2012)). In Brazil, dengue has been endemic since the 1990s—after a decades-long absence—with an increase in the prevalence and substantial temporal (including seasonal) and spatial variation in the incidence from year to year and across Brazilian municipalities (Andrioli et al. (2020)).

The rapid global expansion of dengue was driven by a combination of increasing human mobility through improved transport links and increased population density and urbanization, as well as inadequate urban infrastructure (Wilder-Smith et al. (2019)). These are also the reasons for dengue spreading rapidly in Brazil starting in the 1990s and dengue now being hyper-endemic, resulting in the co-circulation of the four serotypes (Conrado Guerra Nunes et al. (2019)). Dengue is on the list of compulsory notifiable diseases in Brazil, and there is an efficient reporting system in place. To limit the spread of *Aedes* mosquitoes, Brazil is operating one of the largest dengue vector control programs in the world, with mixed success (Augusto et al. (2016), Araújo et al. (2015)). Vector control strategies are based on a combination of community mobilization to reduce breeding opportunities for mosquitoes³ and the widespread application of insecticides.

While dengue fever has a relatively low mortality rate compared to other tropical infectious diseases, in particular yellow fever and malaria, severe dengue has an elevated risk of mortality of approximately 4% (Andrioli et al. (2020)). There are currently four distinct serotypes of the virus in circulation that differ genetically and serologically. Primary infection with one serotype is believed to lead to lifelong immunity to the same serotype but not to other serotypes. Secondary infection with a different serotype is, on the contrary, associated with an increased risk of developing severe dengue. This is suspected to be caused by

³This includes disposing of manmade habitats that can hold water in private households, applying insecticides to outdoor water storage containers, and improving waste collection, among other activities (Eisen et al. (2009)).

a complex immune response and the mixture of neutralizing and binding antibodies, where neutralizing antibodies are serotype-specific, but binding antibodies are not (Murugesan and Manoharan (2020)).⁴

After many years of research and testing, in 2015, the first dengue vaccine was licensed and received regulatory approval in Brazil and 19 other countries. Despite evidence on the cost-effectiveness for Brazil (Shim (2017)), uptake has been relatively slow. This is possibly due to the low mortality of dengue and some uncertainty on the safety related to the excess risk of developing severe dengue in seronegative vaccine recipients (Sridhar et al. (2018)). Besides vaccines and traditional vector control activities, there are promising advances in modeling the dengue vectors to reduce the spread of dengue through genetic engineering and allowing the mosquitoes to develop immunity to the virus (Buchman et al. (2019)) or by infecting the mosquitoes with a bacterium which can prevent the dengue virus from replicating (Frentiu et al. (2014)).

⁴This feature of the immune response also provides for an extra obstacle in the development of a dengue vaccine, as a successful vaccine candidate needs to give immunity to all prevalent dengue serotypes (Payne (2017); Wilder-Smith et al. (2019)).

Appendix D Data sources and descriptive statistics

D.1 Birth records

The birth records from SINASC data collect detailed information on newborn and mother characteristics and the mode of delivery. Newborn characteristics include BW, 1st and 5th minute APGAR scores, and sex. Mother characteristics include age, previous live births and stillbirths, occupation, marital status, and education. Information on the pregnancy and delivery includes the number of prenatal visits, type of delivery (vaginal vs. C-section), and information on whether the C-section was planned or due to an emergency.

We present summary statistics for the entire sample of singleton births and the within-mother sample in Table 1. Mean BW in our sample is 3,160 grams, and the incidence of low BW ($<2,500$ grams), very low BW ($<2,000$ grams), and extremely low BW ($<1,500$ grams) is 8%, 1% and 0.4%, respectively.⁵ Mean gestational length is 270 days (just over 38 weeks), and the fraction of pregnancies with very preterm delivery (<32 weeks) is 1.3%.⁶ In addition to information on health outcomes of live births, SINASC data also contain information on pregnancy and delivery. Prenatal visits are free in the public health system, and antenatal care is generally of high quality in Brazil (Victora et al. (2011)). On average, women have around eight prenatal care visits.⁷ 42.7% of deliveries were through C-section, and about 20% were initiated after labor began, thus defined as emergency C-section.⁸

Table 1 also presents the summary characteristics of the mothers. Their mean age is 27 years; 20% of mothers are 20 or younger. More than 50% of mothers declare themselves mixed race, 36% are white, and 8% are black. Detailed information on the marital status of the mother is also provided. 39% are single, 44% are married, and 14% are in a stable union. As to their educational background, 19% have high education.

The birth and pregnancy characteristics of the maternal fixed-effects sample we use for the main analysis are very similar to the whole sample. As the within-mother sample is derived

⁵These figures are similar to recent US data on singleton births, with an incident of 6.60 and 1.09% for the fraction of low and very low BW deliveries, respectively (Martin et al. (2019)).

⁶We calculate gestational length by using the information on the date of conception and date of delivery.

⁷These include extensive screening for risk factors, including diabetes, pre-eclampsia, and underlying infections, plus ultrasound scans of the fetus.

⁸Brazil has well-documented high rates of planned Caesarean section delivery (Barros et al. (1991), Rudey et al. (2020)).

from mothers with at least two births over the period, this excludes first-time mothers with at most one child and mothers with multiple births but outside the period from 2011 to 2017. Mother characteristics are also largely very similar, in particular with respect to predetermined characteristics such as educational background and self-declared skin color.

D.2 Infant and child mortality

For any death occurring during the first year of life, SIM data is linked to the birth records from SINASC. We calculate any child death for different periods after births and record early neonatal (1 week), neonatal (4 weeks), 22 weeks and 52 weeks mortality. 0.38% of live-born children die within a week, making up about half of all infant deaths (0.71% of live births).

D.3 Hospitalization

We link birth records with subsequent hospitalizations three years after birth and distinguish between regular admission to hospital and admission to intensive care units (including neonatal intensive care for the first month after birth). For the merge, we use the information on the newborns' date of birth, sex, and address at the time of delivery, limiting the fraction of successfully linked hospitalization records compared to the link between dengue and birth records. The incidence of hospital admission in the first year after birth is just under 10% and drops to 2 and 1% in the second and third years. Neonatal ICU admissions account for about 18% of all hospital admissions in the first year. A unique feature of the hospitalization records is that it includes information on the primary cause of hospitalization (using the ICD-10 classification), length of hospital stay and each hospital admission cost. The average hospital stay in the first year is just over 10 days, with an average price of R\$3,327.95. There is a substantial variation in the hospitalization costs, with the highest observed costs over R\$269,488, with a median of R\$606.43.

D.4 Dengue

We link dengue infections to mothers using individual identifiers. This has the advantage of being able to link mothers to dengue infections during pregnancy and infections that

occur with women who gave birth twice over our period but contracted dengue outside of pregnancy. We focus on ‘classic’ dengue and drop cases of ‘severe’ dengue from our sample.⁹ Severe dengue is rare (0.22%) and unsurprisingly, due to its severity, may affect the unborn children of mothers suffering from its complications.

In this paper, we are interested in the effect *classic* dengue, comprising the vast majority of dengue cases, has on the health of unborn children. We hence remove a small number of cases clinically identified with symptoms of severe dengue (0.22%), mostly with hemorrhagic complications. An infection of a particular dengue serotype leads to individuals being immune to the same strain but increases the risk for complications when infected with different dengue serotypes, potentially leading to changes in the behavior of expectant mothers with the knowledge of a previous infection.

We also link the birth records with another notifiable disease, Zika virus. Zika is in the same family as the dengue virus and was first identified in the northeast of Brazil in 2015. From the end of 2015, every laboratory-confirmed Zika infection was included in the *Notifiable Diseases Information System*, collecting the same information as for dengue infections. Because of the risk of microcephaly in children born to mothers infected with Zika during pregnancy, the outbreak received considerable attention from health authorities in Brazil and beyond. While the spread of Zika was largely concentrated in the northeast region of Brazil, which accounted for 61.1% of cases, the number of cases in Minas Gerais, the Brazilian state for which we have data, saw only a very small number of Zika cases (and cases of microcephaly) in comparison. In our sample, 8 cases of Zika during pregnancy occurred. We removed these mother observations from our estimation sample.

D.5 Temperature data

The temperature data ERA5 from ECMWF consists of reanalysis data combining past observations with models to generate consistent time series of temperature variables at a 0.25×0.25 degrees grid. We follow the literature to assign a weighted average temperature to each of the 843 municipalities by using an inverse-distance weighted average of all weather grid points

⁹Severe dengue is associated with any number of complications linked with severe bleeding, organ impairment, and/or plasma leakage and can have life-threatening consequences. Severe dengue has been associated with repeat infection by other dengue serotypes after the initial infection.

within a 50 km range of the municipality centroid (Rocha and Soares (2015)). Figure A2 depicts the daily average temperature over time for the period 2011 to 2017. Mean daily temperature over this period is 23.2°C with a minimum of 11.6°C and a maximum average temperature of 33.5°C. The highest maximum daily temperature recorded in the data is 40.7°C. While less pronounced due to the proximity to the equator, there is still considerable variability over the year, as can be seen in Figure A3, with the highest average temperatures in February and the lowest in July.

Appendix E Heterogeneous effects

To learn whether the effect of maternal dengue may differ by mother characteristics, we split the sample of mothers using information on their age, race, marital status, and education. For time-varying characteristics (age, marital status, and education) we use their values at the first pregnancy we observe to split the sample. We report the results from this exercise in Table E3. First, we look at three age groups of mothers separately, where we define those age groups so that all birth observations for each mother meet the age criteria. This means that for the first group, we look at estimates for mothers 20 years and younger at last observed birth; for the second group we use mothers with all births between ages 21 and 35; and for the last group we use mothers older than 35 for the first observed birth.¹⁰ We find that the effect of dengue infections during pregnancy is more pronounced for younger mothers, with the strongest effect for mothers aged 20 and under (-56 grams), but given the smaller sample, the coefficient is only marginally significant. This may either indicate a medical vulnerability of younger mothers in line with findings in the medical literature on the higher rate of low BW births among this age group and/or age being a proxy for socioeconomic background, with younger mothers being over represented with regard to a more deprived economic status. The effect for mothers above the age of 35 is very close to zero and insignificant. We find a similar picture for low BW. The effects for the older age groups are smaller. We find a similar pattern for the low BW classifications, with the most pronounced effects for low BW and extremely low BW for the group of younger mothers. When splitting the sample by mothers'

¹⁰This means we lose a small number of observations, where mothers have births falling outside these age ranges.

self-declared color of skin, we find slightly more pronounced effects for non-white mothers, both for BW and for low BW. We do not find any systematic differences by marital status, with coefficients being very close for married and unmarried mothers. Finally, we split the sample by mothers' education. We find stronger but insignificant effects on BW for mothers with higher levels of education but more pronounced effects on low BW for mothers with lower levels of education, possibly indicating diverging effects by educational background at different parts of the distribution. Given the much-reduced sample sizes, the estimates are nevertheless imprecise.

Table E3: Heterogeneity Analysis

<i>Panel A - Birth Weight</i>									
	<i>Mother's age</i>			<i>Mother's race</i>		<i>Mother's marital status</i>		<i>Mother's education</i>	
	<i>20 or less</i>	<i>21 to 35</i>	<i>36 and beyond</i>	<i>White</i>	<i>Non-white</i>	<i>Married</i>	<i>Not married</i>	<i>Low</i>	<i>High</i>
	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>
	−55.971 (29.159)*	−14.833 (14.797)	−28.329 (76.582)	−22.042 (27.533)	−35.627 (15.074)**	−25.525 (18.142)	−24.377 (17.162)	−26.600 (12.307)**	−43.630 (35.144)
Mean dep. var.	3,113.303	3,194.305	3,214.501	3,177.668	3,172.161	3,197.004	3,146.790	3,169.481	3,198.518
Mothers	22,419	77,887	4,119	33,215	71,642	62,879	46,434	105,581	22,421
Observations	46,054	158,651	8,286	67,491	147,691	127,733	95,955	218,054	45,313
<i>Panel B - Low Birth Weight</i>									
	<i>Mother's age</i>			<i>Mother's race</i>		<i>Mother's marital status</i>		<i>Mother's education</i>	
	<i>20 or less</i>	<i>21 to 35</i>	<i>36 and beyond</i>	<i>White</i>	<i>Non-white</i>	<i>Married</i>	<i>Not married</i>	<i>Low</i>	<i>High</i>
	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>
	0.036 (0.019)*	0.010 (0.009)	−0.031 (0.046)	0.021 (0.016)	0.022 (0.009)**	0.006 (0.011)	0.020 (0.011)*	0.014 (0.007)*	0.000 (0.022)
Mean dep. var.	0.089	0.068	0.069	0.068	0.076	0.065	0.083	0.076	0.061
Mothers	22,419	77,887	4,119	33,215	71,642	62,879	46,434	105,581	22,421
Observations	46,054	158,651	8,286	67,491	147,691	127,733	95,955	218,054	45,313
<i>Panel C - Very Low Birth Weight</i>									
	<i>Mother's age</i>			<i>Mother's race</i>		<i>Mother's marital status</i>		<i>Mother's education</i>	
	<i>20 or less</i>	<i>21 to 35</i>	<i>36 and beyond</i>	<i>White</i>	<i>Non-white</i>	<i>Married</i>	<i>Not married</i>	<i>Low</i>	<i>High</i>
	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>
	0.003 (0.008)	0.005 (0.003)	−0.019 (0.019)	0.015 (0.007)**	0.005 (0.004)	0.005 (0.004)	0.004 (0.004)	0.006 (0.003)*	0.013 (0.008)
Mean dep. var.	0.010	0.008	0.011	0.008	0.009	0.008	0.010	0.009	0.008
Mothers	22,419	77,887	4,119	33,215	71,642	62,879	46,434	105,581	22,421
Observations	46,054	158,651	8,286	67,491	147,691	127,733	95,955	218,054	45,313
<i>Panel D - Extremely Low Birth Weight</i>									
	<i>Mother's age</i>			<i>Mother's race</i>		<i>Mother's marital status</i>		<i>Mother's education</i>	
	<i>20 or less</i>	<i>21 to 35</i>	<i>36 and beyond</i>	<i>White</i>	<i>Non-white</i>	<i>Married</i>	<i>Not married</i>	<i>Low</i>	<i>High</i>
	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>	<i>Dengue (pregnancy)</i>
	0.005 (0.006)	0.004 (0.002)*	−0.021 (0.019)	0.004 (0.005)	0.004 (0.003)	0.002 (0.003)	0.003 (0.003)	0.003 (0.002)	0.010 (0.006)
Mean dep. var.	0.003	0.003	0.004	0.003	0.003	0.003	0.004	0.003	0.003
Mothers	22,419	77,887	4,119	33,215	71,642	62,879	46,434	105,581	22,421
Observations	46,054	158,651	8,286	67,491	147,691	127,733	95,955	218,054	45,313

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$. Robust standard errors are clustered at the mother level in parentheses.

Note: The analysis includes mothers over the period between 2011 and 2017. Explanatory variable *Dengue(pregnancy)* indicates whether the mother had dengue during pregnancy. All regressions include month of conception fixed-effects and maternal fixed-effects and the full set of controls (for a detailed list of controls, see Table 2 note).

Appendix F Additional analysis

In this appendix, we systematically probe the main estimates further in addition to the sensitiveness checks provided in Section 5. We also test sensitivity to additional sample restrictions, provide a falsification exercise for the main results, and discuss robustness of the hospitalization results in line with the sensitivity analysis of the main outcomes.

F.1 Temperature controls

We start by providing insights on the sensitiveness of the main estimates to the inclusion of temperature controls. In Table 2, we include temperature controls together with other controls not meaningfully affecting our estimates. In Table F4, we further test the effects temperature controls have on the main estimates. To disentangle the effect of temperature and maternal controls, we separately enter maternal controls in columns (2) and (6). We find that maternal controls reduce the coefficients for BW and the low BW classification slightly, without impacting the overall significance of the estimates. However, the inclusion of the temperature controls in columns (3) and (7) reduces only the BW estimates minimally, without any further change on the coefficients for very low and extremely low BW. Furthermore, we show additional robustness to the choice of temperature controls. In columns (4) and (8), we include alternatively maximum daily temperatures as controls rather than average daily temperature. In line with the average temperature controls, we calculate the number of days in bands of 5°C for each pregnancy, starting with the due date and ending with the predicted due date for 280 days of a full-term pregnancy. The inclusion of maximum daily temperature controls leaves the coefficients unchanged, both in terms of magnitude and precision.

Table F4: Effect of Dengue on Birth Outcomes - Additional Temperature Controls

	<i>BW</i>				<i>Low BW</i>			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
<i>Dengue</i> (<i>pregnancy</i>)	-31.328 (11.416)***	-27.413 (11.307)**	-27.480 (11.306)**	-27.481 (11.306)**	0.013 (0.007)*	0.011 (0.007)*	0.011 (0.007)*	0.011 (0.007)*
Mean dep. var.	3,174.865	3,174.865	3,174.865	3,174.865	0.073	0.073	0.073	0.073
Mothers	136,788	136,788	136,788	136,788	136,788	136,788	136,788	136,788
Observations	281,497	281,497	281,497	281,497	281,497	281,497	281,497	281,497
	<i>Very Low BW</i>				<i>Extremely Low BW</i>			
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
<i>Dengue</i> (<i>pregnancy</i>)	0.006 (0.003)**	0.006 (0.003)**	0.006 (0.003)**	0.006 (0.003)**	0.004 (0.002)**	0.004 (0.002)**	0.004 (0.002)**	0.004 (0.002)**
Mean dep. var.	0.009	0.009	0.009	0.009	0.003	0.003	0.003	0.003
Mothers	136,788	136,788	136,788	136,788	136,788	136,788	136,788	136,788
Observations	281,497	281,497	281,497	281,497	281,497	281,497	281,497	281,497
Maternal Controls	No	Yes	Yes	Yes	No	Yes	Yes	Yes
Temperature (average) Controls	No	No	Yes	No	No	No	Yes	No
Temperature (maximum) Controls	No	No	No	Yes	No	No	No	Yes

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$. Robust standard errors are clustered at the mother level in parentheses.

Note: The analysis includes mothers over the period between 2011 and 2017. *BW* is reported in grams. *Low BW*, *Very Low BW* and *Extremely Low BW* are dummies indicating newborns up to 2,500, 1,500 and 1,000 grams, respectively. Explanatory variable *Dengue(pregnancy)* indicates whether the mother had dengue during pregnancy. All regressions include month of conception fixed-effects and maternal fixed-effects. Maternal controls include dummies for maternal age, and dummies for marital status (married, living together, divorced, single, missing), highest education achieved (incomplete primary, complete primary, incomplete secondary, complete secondary, incomplete higher education, complete higher education), occupation codes, number of previous stillbirths, birth order and birth interval (time between conceptions). Temperature (average) controls are variables measuring the number of days during pregnancy with average temperature between 10-15°C, 15-20°C, 20-25°C, 25-30°C and 30-35°C. Temperature (maximum) controls are variables measuring the number of days during pregnancy with maximum temperature between 10-15°C, 15-20°C, 20-25°C, 25-30°C, 30-35°C, 35-40°C and 40-45°C.

F.2 Balancing property of time-varying maternal characteristics and location choice

Our mother fixed-effects estimation strategy deals with any time-invariant maternal characteristics by holding these characteristics constant across the multiple pregnancies observed for the mothers. To also account for remaining time-varying characteristics of the mother and pregnancy that may affect birth outcomes, we add time-varying controls across all estimates, including controls for maternal age, and occupation, and dummies for marital status, highest education achieved, the number of previous stillbirths, birth order, and time between conceptions.¹¹ To understand whether the time-varying characteristics of mothers are linked to dengue, we test directly whether dengue is related to those characteristics. We provide the results in Table F5 focusing on the time-varying maternal characteristics proxying for socioeconomic status, including maternal age, marital status, education, and occupation. We dichotomize these characteristics for ease of interpretation. Using our preferred specification, including the remaining controls, we find that dengue as a predictor has no effect on those maternal characteristics; the coefficients are small and not statistically significant, providing further credibility to our estimation strategy.

Table F5: Time Varying Maternal Characteristics as Outcomes

	<i>Mother's age</i>			<i>Mother's marital status</i>	<i>Mother's education</i>	<i>Mother's occupation</i>
	<i>20 or less</i>	<i>21 to 35</i>	<i>36 and beyond</i>	<i>Married</i>	<i>High</i>	<i>High-skilled</i>
<i>Dengue</i> <i>(pregnancy)</i>	−0.014 (0.008)	0.016 (0.010)	−0.002 (0.004)	−0.011 (0.009)	0.002 (0.004)	0.017 (0.020)
Mean dep. var.	0.255	0.685	0.060	0.558	0.184	0.486
Mothers	136,788	136,788	136,788	134,606	132,957	24,302
Observations	281,497	281,497	281,497	276,934	273,519	49,062

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$. Robust standard errors are clustered at the mother level in parentheses.

Note: The analysis includes mothers over the period between 2011 and 2017. All regressions include month of conception fixed-effects and maternal fixed-effects and the full set of (remaining) controls (for a detailed list of controls, see Table 2 note).

In addition to time-varying maternal socio-economic characteristics, we also investigate

¹¹In detail, we look at the following outcomes: age (20 or less, 21 to 35, 36 and beyond), marital status, high education (where the variable takes a value of 1 for higher education and zero otherwise), high-skilled occupation (with the dummy taking a value of 1 for occupations including high-skilled white collar and high-skilled blue-collar occupations based on the detailed Brazilian Classification of Occupations. We focus on skill levels of occupations based on ISCO-88 definitions by ILO, which we map to the Brazilian occupations).

whether dengue leads to changes in the location of the residence of the mother. In Table F6 we provide the coefficients from estimates of dengue (during the first pregnancy) on different definitions of ‘relocation’ outcomes.¹²

Table F6: Effect of Dengue on Relocation

	<i>Relocation 1</i>	<i>Relocation 2</i>	<i>Relocation 3</i>	<i>Relocation 4</i>	<i>Relocation 5</i>	<i>Relocation 6</i>
	(1)	(2)	(3)	(4)	(5)	(6)
<i>Dengue</i> (<i>pregnancy</i>)	0.016 (0.014)	0.005 (0.005)	0.001 (0.005)	−0.001 (0.007)	−0.004 (0.008)	−0.011 (0.021)
Mean dep. var.	0.064	0.009	0.007	0.011	0.014	0.279
Mothers	91,436	91,436	91,436	91,436	91,436	91,436
Observations	182,872	182,872	182,872	182,872	182,872	182,872

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$. Robust standard errors are clustered at the mother level in parentheses.

Note: The analysis includes mothers over the period between 2011 and 2017. All regressions include month of conception fixed-effects and maternal fixed-effects and the full set of controls (for a detailed list of controls, see Table 2 note).

First, in column (1), the outcome variable takes a value of 1 if the mother changes place of residence from one municipality during the first pregnancy to another municipality of residence in the subsequent pregnancy. From column (2) to column (5), we look at selective changes in municipality of residence, with the outcome taking a value of 1 for moving to a relatively richer municipality (where relatively rich municipalities are municipalities with a per-capita income above the median (R\$ 466.8)) in column (2), a value of 1 for moving from a municipality with a high share of population with low income to a municipality with a low share of low income individuals (where “high” municipalities have a fraction of individuals with low income greater than the median value 40.75 and “low” municipalities with a fraction smaller than or equal to the median) in column (3), a value of 1 for relocation from an urban to a rural municipality (where we use the official definition of the Brazilian statistical bureau (IBGE) or urban and rural municipalities) in column (4) and a value of 1 for relocation from a municipality with a large population to a municipality with relatively small population (where we consider municipalities with a population of more than 100,000 as “high” population municipalities), and zero otherwise across those definitions. Lastly, as relocation decisions may be more subtle than moving from one municipality to another, we also use as an outcome whether mothers change their neighborhood in response to dengue, providing a

¹²Because we rely on the location information from the birth records (location of residence during pregnancy), we need to restrict the analysis to dengue infections during the first pregnancy, as we do not have information on the residence after the last observed pregnancy in the data.

much more localized relocation variable, particularly for large urban municipalities (column 6). We find that none of the coefficients for relocation are significant, with coefficients being close to zero across the different outcomes, a result that is probably unsurprising given the distribution of dengue across space and time depicted in the maps in Figure A1.

F.3 Timing of dengue infection

In this section, we investigate heterogeneous effects by the timing of dengue infections over multiple pregnancies. For this purpose, we estimate separately the effect of dengue infections in the first pregnancy versus in the last pregnancy in our data. We present the results in Table F7, where in columns (1)-(4) we present the results for first pregnancy infections (and drop observations with dengue infections in subsequent pregnancies) and in columns (6)-(10) for dengue infections during the last observed pregnancy in our sample. We find a moderately larger effect on BW for dengue infections during the first pregnancy compared to the last pregnancy.¹³ In contrast, we find a positive effect on the propensity for low BW for infections in the last pregnancy, but not in the first pregnancy, whereas the effects for very and extremely low BW are once more accentuated for infections during first pregnancy, although the estimates are not statistically significant. In contrast, the effects on gestation appear to be slightly more accentuated for infections during the last pregnancy, possibly pointing to some competing mechanism at work here. Splitting the sample by the timing of infections nevertheless reduces the available variation in each exercise, and the coefficients are less precise, with the estimates on very and extremely low BW not being significant. The more pronounced effects for infections during first pregnancy are in line with findings in the medical literature that point to first pregnancies being linked to lower BW.

¹³Although the estimated effect size is smaller for the last pregnancies, these are estimated with more precision. This is due to the fact that we have a larger number of dengue infections in the later pregnancies. We discuss the reasons for this in the data section on dengue.

Table F7: Effect of Dengue on Birth Outcomes by Gestation

<i>Panel A - Birth Weight</i>								
	<i>First pregnancy</i>				<i>Last pregnancy in the data</i>			
	(1) <i>BW</i>	(2) <i>Low BW</i>	(3) <i>Very Low BW</i>	(4) <i>Extremely Low BW</i>	(5) <i>BW</i>	(6) <i>Low BW</i>	(7) <i>Very Low BW</i>	(8) <i>Extremely Low BW</i>
<i>Dengue (pregnancy)</i>	−38.925 (22.816)*	−0.017 (0.015)	0.008 (0.006)	0.007 (0.005)	−29.965 (14.419)**	0.019 (0.008)**	0.004 (0.004)	0.004 (0.002)*
Mean dep. var.	3,174.689	0.073	0.009	0.003	3,174.932	0.073	0.009	0.003
Mothers	135,229	135,229	135,229	135,229	136,024	136,024	136,024	136,024
Observations	278,202	278,202	278,202	278,202	279,849	279,849	279,849	279,849

<i>Panel B - Gestation</i>								
	<i>First pregnancy</i>				<i>Last pregnancy in the data</i>			
	(1) <i>Gestation (days)</i>	(2) <i>Gestation (<259 days)</i>	(3) <i>Gestation (<224 days)</i>	(4) <i>Gestation (<196 days)</i>	(5) <i>Gestation (days)</i>	(6) <i>Gestation (<259 days)</i>	(7) <i>Gestation (<224 days)</i>	(8) <i>Gestation (<196 days)</i>
<i>Dengue (pregnancy)</i>	0.331 (0.865)	−0.005 (0.017)	0.011 (0.009)	0.005 (0.004)	−0.765 (0.510)	0.010 (0.010)	0.008 (0.004)*	0.001 (0.003)
Mean dep. var.	269.849	0.103	0.013	0.003	269.855	0.102	0.012	0.003
Mothers	135,229	135,229	135,229	135,229	136,024	136,024	136,024	136,024
Observations	278,202	278,202	278,202	278,202	279,849	279,849	279,849	279,849

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$. Robust standard errors are clustered at the mother level in parentheses.

Note: The analysis includes mothers over the period between 2011 and 2017. *First pregnancy* refers to mothers who had dengue in the first pregnancy and *Last pregnancy in the data* refers to mothers who had dengue in the last pregnancy observed in the data. All regressions include month of conception fixed-effects and maternal fixed-effects and the full set of controls (for a detailed list of controls, see Table 2 note).

F.4 Falsification exercise

We also engage in a falsification exercise, using the information on the timing of reported dengue infections. Mechanically, dengue infections after birth cannot affect birth outcomes. We test this by estimating lead variables of infections by trimester using our preferred maternal fixed-effects specification for the significant results of BW, very and extremely low BW, and very preterm birth of Table 2. We display the results in Figure F6, where we plot the point estimates for the three trimesters of pregnancy and three trimesters post-birth.¹⁴ Confirming the results in Table 4, we find a significant decrease in BW for third-trimester infections and smaller negative but insignificant effects for the first and second trimesters, as well as a significant positive effect for very preterm births for third-trimester infections. The graph also displays the coefficient for three trimesters post-birth. As expected, all lead coefficients are small and not significant, lending additional credibility to our identification strategy.

¹⁴We follow the literature and construct trimesters, during pregnancy and post pregnancy, from conception date irrespective of gestational length (Quintana-Domeque and Ródenas-Serrano (2017)). We construct the lead variables in analogue to the trimester variables, based on equal-sized trimesters continuing the trimester variables based on conception date.

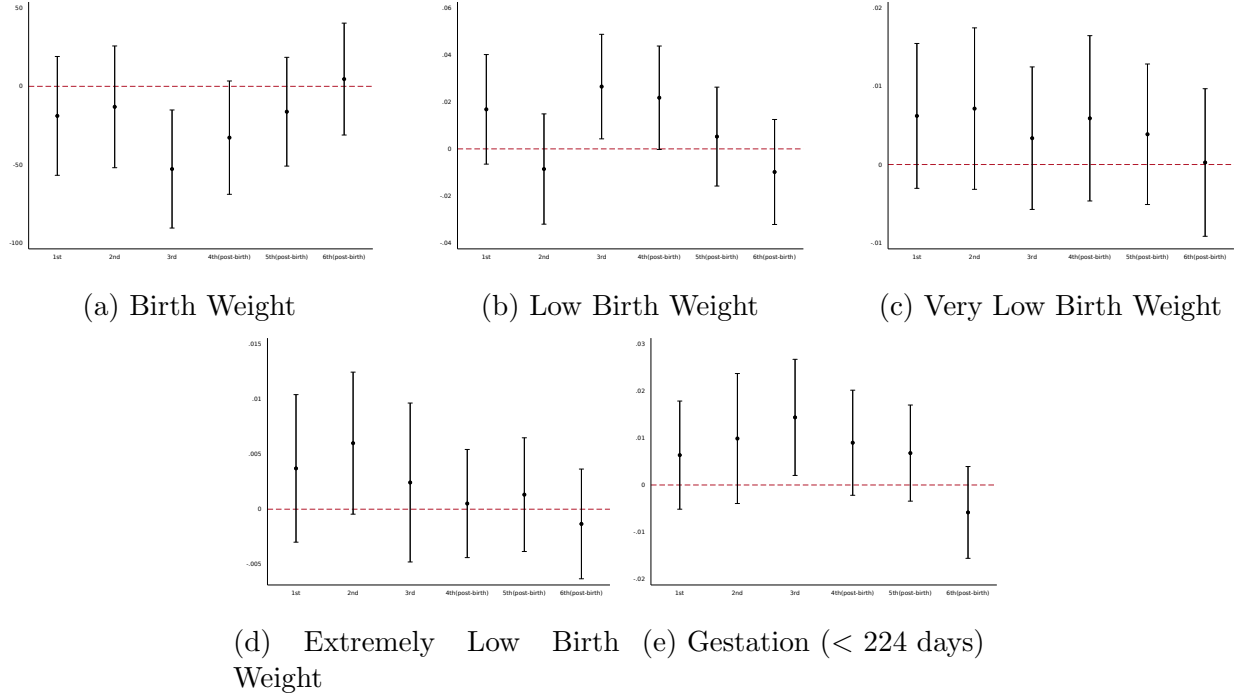


Figure F6: Effect of Dengue on Birth Weight and Very Preterm Birth

Note: We report graphs only for the significant results in Table 2.

F.5 Sensitiveness of effects on hospitalization

In Table F8, we provide the sensitiveness analysis for the significant hospitalization outcomes in analogue to the exercise for the main estimates on BW and gestation for different combinations of fixed-effects and the alternative control group. Across specifications, the coefficients for hospitalization are very stable, but we lose significance when including neighborhood fixed-effects and neighborhood linear trends. This is possibly due to the smaller number of observations when including the neighborhood fixed-effects.¹⁵ In particular, the estimates are very similar when including hospital fixed-effects and hospital linear trends (columns (5) and (6), compared to our benchmark specification. In line with the effects on BW, we also find a slightly accentuated effect for hospitalizations when using the alternative control group. The pattern for hospitalization cost is very similar, with very stable coefficients across specifications and the slightly larger effect when using the alternative control group.

¹⁵We lose observations as we drop singleton observations in these specifications due to small geographic expansion of neighborhoods with small populations in combination with the mother fixed-effects.

Table F8: Effect of Dengue on Hospitalization - Sensitiveness Analysis

	<i>Hospitalization</i>						
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
<i>Dengue</i> (<i>pregnancy</i>)	0.034 (0.011)***	0.032 (0.013)**	0.027 (0.020)	0.027 (0.023)	0.030 (0.017)*	0.029 (0.017)*	0.040 (0.017)**
Mean dep. var.	0.117	0.117	0.115	0.115	0.117	0.117	0.145
Clusters	18,303	67,962	9,578	9,578	522	522	2,516
Observations	138,751	138,751	123,428	123,428	138,515	138,515	5,138
R^2	0.029	0.560	0.625	0.696	0.568	0.574	0.611
	<i>Cost</i>						
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
<i>Dengue</i> (<i>pregnancy</i>)	0.396 (0.125)***	0.366 (0.150)**	0.316 (0.223)	0.322 (0.256)	0.339 (0.192)*	0.331 (0.194)*	0.471 (0.191)**
Mean dep. var.	352.877	352.877	338.974	338.974	352.264	352.264	428.410
Clusters	18,303	67,962	9,578	9,578	522	522	2,516
Observations	138,751	138,751	123,428	123,428	138,515	138,515	5,138
R^2	0.029	0.562	0.626	0.697	0.570	0.575	0.615
Mother FE	No	Yes	Yes	Yes	Yes	Yes	Yes
Time FE	No	Yes	Yes	Yes	Yes	Yes	Yes
Neighborhood FE	No	No	Yes	Yes	No	No	No
Neighborhood Linear Trends	No	No	No	Yes	No	No	No
Hospital FE	No	No	No	No	Yes	Yes	No
Hospital Linear Trends	No	No	No	No	No	Yes	No
Controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Alternative Control Group	No	No	No	No	No	No	Yes

* $p < 0.1$, ** $p < 0.05$, *** $p < 0.01$. Robust standard errors are clustered at the neighborhood level the regressions with neighborhood fixed-effects, at the hospital level for the regressions with hospital fixed-effects and at the mother level for the remaining specifications.

Note: The analysis includes mothers over the period between 2011 and 2017. *Hospitalization* is a dummy indicating whether the infant was hospitalized in the first three years of life. *Cost* is the logarithm of the cost of the hospitalization. Explanatory variable *Dengue(pregnancy)* indicates whether the mother had dengue during pregnancy. For a detailed list of controls, see Table 2 note. *Alternative Control Group* limits the control group to mothers infected with dengue after pregnancy.

References

- Andrioli, Denise Catarina, Maria Assunta Busato, and Junir Antonio Lutinski, "Spatial and temporal distribution of dengue in Brazil, 1990 - 2017," *PLoS ONE*, 2020, *15* (2), 1–13.
- Araújo, Helena R.C., Danilo O. Carvalho, Rafaella S. Ioshino, André L. Costa da Silva, and Margareth L. Capurro, "Aedes aegypti control strategies in Brazil: Incorporation of new technologies to overcome the persistence of dengue epidemics," *Insects*, 2015, *6* (2), 576–594.
- Barros, F., C. Victoria, J. Vaughan, and M. Huttly, "Epidemic of caesarean sections in Brazil," *Lancet*, 1991, *338* (8760), 167–169.
- Bhatt, Samir, Peter W Gething, Oliver J Brady, Jane P Messina, Andrew W Farlow, Catherine L Moyes, John M Drake, John S Brownstein, Anne G Hoen, Osman Sankoh, Monica F Myers, Dylan B George, and Thomas Jaenisch, "The global distribution and burden of dengue," *Nature*, 2013, *496* (7446), 504–507.
- Brady, Oliver J., Peter W. Gething, Samir Bhatt, Jane P. Messina, John S. Brownstein, Anne G. Hoen, Catherine L. Moyes, Andrew W. Farlow, Thomas W. Scott, and Simon I. Hay, "Refining the global spatial limits of dengue virus transmission by evidence-based consensus," *PLoS Neglected Tropical Diseases*, 2012, *6* (8).
- Buchman, Anna, Stephanie Gamez, Ming Li, Igor Antoshechkin, Shin-Hang Lee, Shin-Wei Wang, Chun-Hong Chen, Melissa J. Klein, Jean-Bernard Duchemin, James E. Crowe, Prasad N. Paradkar, and Omar Akbari, "Broad dengue neutralization in mosquitoes expressing an engineered antibody," *PLOS Pathogens*, 2019, *16* (1), 1–20.
- da Silva Augusto, Lia Giraldo, Aline M Gurgel, Francisco A Lacaz Gabriel Parra-Henao André M Costa Finn Diderichsen, and Solange L Santos Raguel M Rigotto Rubens Nodari, "Aedes aegypti control in Brazil," *Lancet*, 2016, pp. 2–3.
- Eisen, Lars, Barry J. Beaty, Amy C. Morrison, and Thomas W. Scott, "Proactive vector control strategies and improved monitoring and evaluation practices for dengue prevention," *Journal of Medical Entomology*, 2009, *46* (6), 1245–1255.
- Frentiu, Francesca D., Tasnim Zakir, Thomas Walker, Jean Popovici, Alyssa T. Pyke, Andrew van den Hurk, Elizabeth A. McGraw, and Scott L. O'Neill, "Limited dengue virus replication in field-collected Aedes aegypti mosquitoes infected with Wolbachia," *PLoS Neglected Tropical Diseases*, 2014, *8* (2), 1–10.
- Hossain, Mohammad Sorowar, Robed Amin, and Abdullah Al Mosabbir, "COVID-19 onslaught is masking the 2021 dengue outbreak in Dhaka, Bangladesh," *PLoS Neglected Tropical Diseases*, 1 2022, *16* (1).

- Martin, Joyce A., Brady E. Hamilton, Michelle J.K. Osterman, and Anne K. Driscoll**, “Births: Final data for 2018,” *National Vital Statistics Reports*, 2019, 68 (13), 1980–2018.
- Murugesan, Amudhan and Mythreyee Manoharan**, *Emerging and reemerging viral pathogens, chapter 16: Dengue virus*, Elsevier, 2020.
- Nunes, Priscila Conrado Guerra, Regina Paiva Daumas, Juan Camilo Sánchez-Arcila, and Maria Rita Ribeiro Nogueira**, “30 years of fatal dengue cases in Brazil: a review,” *BMC Public Health*, 2019, 19 (329), 1–11.
- Payne, Susan**, *Viruses: From Understanding to Investigation*, Academic Press, 2017.
- Polwiang, Sittisede**, “The time series seasonal patterns of dengue fever and associated weather variables in Bangkok (2003-2017),” *BMC Infectious Diseases*, 3 2020, 20 (1).
- Quintana-Domeque, Climent and Pedro Ródenas-Serrano**, “The hidden costs of terrorism: The effects on health at birth,” *Journal of Health Economics*, 12 2017, 56, 47–60.
- Rocha, Rudi and Rodrigo R. Soares**, “Water Scarcity and Birth Outcomes in the Brazilian Semiarid,” *Journal of Development Economics*, 2015, 112, 72–91.
- Rudey, Edson Luciano, Maria do Carmo Leal, and Guilhermina Rego**, “Cesarean section rates in Brazil: Trend analysis using the Robson classification system,” *Medicine*, 2020, 99 (17), e19880.
- Shim, Eunha**, “Cost-effectiveness of dengue vaccination programs in Brazil,” *American Journal of Tropical Medicine and Hygiene*, 2017, 96 (5), 1227–1234.
- Sridhar, Saranya, Alexander Luedtke, Edith Langevin, Ming Zhu, Matthew Bonaparte, Tiffany Machabert, Stephen Savarino, Betzana Zambrano, Annick Moureau, Alena Khromava, Zoe Moodie, Ted Westling, Cesar Mascareñas, Carina Frago, Margarita Cortés, Danaya Chansinghakul, Fernando Noriega, Alain Bouckenoghe, Josh Chen, Su Peing Ng, Peter B. Gilbert, Sanjay Gurunathan, and Carlos A. DiazGranados**, “Effect of dengue serostatus on dengue vaccine safety and efficacy,” *New England Journal of Medicine*, 2018, 379 (4), 327–340.
- Victora, Cesar G., Estela M.I. Aquino, Maria Do Carmo Leal, Carlos Augusto Monteiro, Fernando C. Barros, and Celia L. Szwarcwald**, “Maternal and child health in Brazil: Progress and challenges,” *The Lancet*, 2011, 377 (9780), 1863–1876.
- Wilder-Smith, A, O Eng-Eong, O Horstick, and B Wills**, “Dengue,” *Lancet*, 2019, 393 (10169), 350–363.