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Maternal Dengue and Health Outcomes of Children[†]

By Martin Foureaux Koppensteiner and Lívia Menezes*

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 percent, 67 percent, and 133 percent 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* I12, I18, J13, J16, O15)

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

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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) investigate 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 (less than 1 percent), 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 preeclampsia 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 a 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 administrative 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 percent 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 percent

[1] TORCH 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 2022; Silasi et al. 2015).

[2] In 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.

and 133 percent, 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 percent, significant at the 1 percent 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 percent 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 percent 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.

I. 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 includes 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.

II. 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 online Appendix D.

A. *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, 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 percent 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.

B. *Infant Mortality Data*

The second dataset comes from vital statistics death records from the Brazilian Mortality Information System (Sistema de Informações sobre Mortalidade, in Portuguese) (HSMG 2022c). This dataset contains information on all natural and nonnatural 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.

C. *Hospitalization Data*

The third dataset comprises hospitalization records from the Hospital Information System (Sistema de Informações Hospitalares, 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]

D. *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, and rash; 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 percent) of pregnancies with a positive dengue diagnosis, meaning that 2,282 dengue infections occur in our

[3] In 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.

[4] Compared 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 successfully just over 30 percent 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.

Table 1—Descriptive Statistics

	All mothers		Maternal FE	
	Mean	SD	Mean	SD
Birth outcomes				
Birth weight	3,160.583	511.191	3,174.865	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
First minute APGAR	8.414	1.219	8.448	1.184
Fifth minute APGAR	9.380	0.825	9.381	0.821
Newborn characteristics				
Female	0.488	0.500	0.482	0.500
Pregnancy and delivery characteristics				
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
Mothers characteristics				
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	1,578,599		281,497	

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 online Appendix B, we provide detailed information on the temporal and spatial distribution of the dengue incidence over the period of interest.

[5] To 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 $((\div 9 \times 0.00097 = 0.0087))$.

[6] This 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 percent) and second pregnancies (48 percent); the same is not true for exposure during the 2016 wave, which largely affects second and later births, with only 2 percent first births being exposed, contributing to the higher dengue incidence for higher birth order pregnancies.

E. *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-Range Weather Forecasts 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.

F. *Sample Restrictions*

We restrict the sample to singleton births (97.60 percent) of mothers between the ages of 13 and 50 at the time of delivery (99.97 percent) and drop cases where there is information missing regarding the identity of the mother (0.1 percent 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 2015–2016. 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]

[7] The 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 percent for 2015–2017).

III. 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 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:

$$y_{itm} = \beta_0 + \beta_1 dengue_{itm} + \gamma_t + \theta_m + \mathbf{X}_i'\tau + \mu_{itm}, \tag{1}$$

where 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, and θ_m is a maternal fixed effect, while the vector $\mathbf{X}_i$ 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 the mother, alleviating concerns regarding the nonrandom detection of infections or the nonrandom 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 effects[9] 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.

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

[9] Bairros 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.

IV. Results

A. *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 percent and 5 percent, 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 2.5 kg. We find that dengue infections during pregnancy increase the chance for low BW by 1.1 percent, compared to the mean prevalence of 7 percent: a 15 percent 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., children with a BW below 2 kg and 1.5 kg, 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 percent, a 67 percent increase compared to the baseline and by 0.4 percent for extremely low BW, a 133 percent increase given a baseline rate of 0.3 percent, with both coefficients being significant at the 5 percent 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

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

Table 2—Effect of Dengue on Birth Outcomes

	BW		*Low BW*		*Very low BW*		*Extremely low BW*	
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Panel A. Birth weight (BW)								
Dengue	−31.328	−27.480	0.013	0.011	0.006	0.006	0.004	0.004
(*pregnancy*)	(11.416)	(11.306)	(0.007)	(0.007)	(0.003)	(0.003)	(0.002)	(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
	Gestatation (days)		*Gestation* (< 259 days)		*Gestation* (< 224 days)		*Gestation* (< 196 days)	
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Panel B. Gestational length								
Dengue	−0.500	−0.474	0.005	0.005	0.011	0.010	0.002	0.002
(*pregnancy*)	(0.407)	(0.401)	(0.008)	(0.008)	(0.004)	(0.004)	(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

Notes: 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), and 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. Robust standard errors are clustered at the mother level in parentheses.

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

[11] In online 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.

Table 3—Effect of Dengue on Birth Outcomes by Trimester

	BW		*Low BW*		*Very low BW*		*Extremely low BW*	
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Dengue	−24.116	−18.880	0.020	0.017	0.007	0.006	0.004	0.004
(*First trimester*)	(19.605)	(19.368)	(0.012)	(0.012)	(0.005)	(0.005)	(0.003)	(0.003)
Dengue	−20.978	−13.202	−0.005	−0.008	0.008	0.007	0.007	0.006
(*Second trimester*)	(20.148)	(19.870)	(0.012)	(0.012)	(0.005)	(0.005)	(0.003)	(0.003)
Dengue	−50.811	−52.846	0.025	0.027	0.003	0.003	0.002	0.002
(*Third trimester*)	(19.315)	(19.265)	(0.011)	(0.011)	(0.005)	(0.005)	(0.004)	(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

Notes: 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. 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). Robust standard errors are clustered at the mother level in parentheses.

to either intrauterine growth retardation and/or reduced gestational length and the effects documented for late pregnancy point to a mechanism of of maternal dengue through growth retardation (Almond et al. 2005; Kramer 1987; and Foureaux 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 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 setof 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

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

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

Table 4—Effect of Dengue on Birth Outcomes—Sensitivity Analysis

	(1)	(2)	(3)	(4)	(5)	(6)	(7)
BW							
Dengue	−8.657	−27.480	−30.186	−33.981	−26.548	−27.666	−50.063
(*pregnancy*)	(11.003)	(11.306)	(15.001)	(16.687)	(12.569)	(12.438)	(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
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Low BW							
Dengue	0.002	0.011	0.013	0.014	0.011	0.011	0.021
(*pregnancy*)	(0.006)	(0.007)	(0.009)	(0.010)	(0.007)	(0.008)	(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
	(1)	(2)	(3)	(4)	(5)	(6)	(7)
Very low BW							
Dengue	0.003	0.006	0.007	0.008	0.005	0.006	0.009
(*pregnancy*)	(0.002)	(0.003)	(0.004)	(0.005)	(0.003)	(0.003)	(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
Extremely low BW							
Dengue	0.003	0.004	0.005	0.005	0.004	0.004	0.007
(*pregnancy*)	(0.002)	(0.002)	(0.003)	(0.003)	(0.003)	(0.003)	(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

Notes: 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. 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.

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 percent, and a small increase

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

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 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 percent level. We document a 28 percent increase in low BW compared to the baseline. Effects for very and

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

extremely low BW are also accentuated, with an increase by 100 percent and 175 percent compared to the mean, respectively.

We probe the robustness and sensitiveness of the results further in online 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.

B. *Additional Results*

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 percent 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 (less than 37 weeks) of about 0.5 percent, but the coefficient is not significant. In contrast, we find a positive and strong effect of maternal dengue on very short gestation of 1 percentage point, a 77 percent 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, 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 percent increase compared to the baseline). We do not find an effect on the sex ratio at birth, indicating

[16] Estimating the effect on gestation separately by trimester in online 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 percent compared to the baseline.

Table 5—Effect of Dengue on Additional Outcomes

	Emergency C-section	*APGAR* (First minute)	*APGAR* (Fifth minute)	*Prenatal visits*	*Female*
	(1)	(2)	(3)	(4)	(5)
Panel A. Additional outcomes					
Dengue	0.008	−0.019	−0.015	0.209	0.016
(*pregnancy*)	(0.009)	(0.036)	(0.023)	(0.063)	(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

	Mortality (1 week)	*Mortality* (4 weeks)	*Mortality* (22 weeks)	*Mortality* (1 year)
	(1)	(2)	(3)	(4)
Panel B. Mortality				
Dengue	0.003	0.002	0.002	0.001
(*pregnancy*)	(0.002)	(0.002)	(0.003)	(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

Notes: 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). Robust standard errors are clustered at the mother level in parentheses.

that maternal dengue infections in utero unlikely lead to an increase in (selective) survival in utero.[17]

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

[17] The 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.

[18] More 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 percent, compared to a mean of 0.8 percent 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.

child mortality. This is confirmed estimating the effect separately by trimester in online Appendix A, with none of the trimester coefficients being significant.

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 percent, significant at the 5 percent level, a 27 percent 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 percent, compared to the 26 percent 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 the International Statistical Classification of Diseases and Related Health Problems (ICD-10) 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 percent 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

Table 6—Effect of Dengue on Hospitalization

	Hospitalization				*Intensive care unit*			
	Total	First year	Second year	Third year	Total	Neonatal	First year	Second year
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Panel A								
Dengue	0.032	0.025	0.016	0.001	0.005	0.007	0.004	0.001
(*pregnancy*)	(0.013)	(0.012)	(0.006)	(0.004)	(0.006)	(0.006)	(0.006)	(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

	Length of stay				*Cost*			
	Total	First year	Second year	Third year	Total	First year	Second year	Third year
	(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
Panel B								
Dengue	0.414	0.234	0.157	0.024	0.366	0.283	0.172	0.011
(*pregnancy*)	(0.316)	(0.276)	(0.112)	(0.019)	(0.150)	(0.142)	(0.070)	(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

Notes: The analysis includes mothers over the period between 2011 and 2017. Hospitalization outcomes are dummies indicating whether the infant was hospitalized in the respective time period, where "Total" refers to the first three years of life. Length of stay is the number of days in hospital. Intensive care unit outcomes 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). Robust standard errors are clustered at the mother level in parentheses.

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 percent 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 percent 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 percent and 45 percent 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$3,327.95[19] as expected with very substantial variability (SD: 9759.79).[20] We find a positive and significant effect on log cost of 0.366 over the three-year period, a 44 percent 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 percent and 19 percent. 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; 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.

V. 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 of in 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 percent 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.

[19] Based on the average 2014 R$-US$ exchange rate US$136 and US$1,418.70, respectively.
[20] The mean is skewed heavily, indicated by a median of R$606.43 and the top 1 percentile of R$54.82.

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 (Wylie et al. 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.

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