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Brazil's Missing Infants: Zika Risk Changes Reproductive Behavior

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Abstract

Zika virus epidemics have potential large-scale population effects. Controlled studies of mice and nonhuman primates indicate that Zika affects fecundity, raising concerns about miscarriage in human populations. In regions of Brazil, Zika risk peaked months before residents learned about the epidemic and its relation to congenital anomalies. This spatiotemporal variation supports analysis of both biological effects of Zika infection on fertility and the effects of learning about Zika risk on reproductive behavior. Causal inference techniques used with vital statistics indicate that the epidemic caused reductions in birth cohort size of approximately one-quarter 18 months after Zika infection risk peaked but 10 months after public health messages advocated childbearing delay. The evidence is consistent with small but not statistically detectable biological reductions in fecundity, as well as large strategic changes in reproductive behavior to temporally align childbearing with reduced risk to infant health. The behavioral effects are larger for more-educated and older women, which may reflect facilitated access to information and to family planning services within high-risk, mosquito-infested urban locations as well as perceptions about the opportunity costs of risks to pregnancy and infant survival.

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Data Availability All data sets used in the article are public and can be retrieved from the sources listed. STATA-SE programs utilized on compiling analysis samples can be obtained from the corresponding author.

Ethics and Consent All analyses presented in the article are based on secondary public-use de-identified data. No informed consent forms were utilized.

Conflict of Interest The authors declare that they have no conflict of interest.

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Keywords

Zika; Fecundity; Fertility; Avoidance; Tempo effects

Introduction

The Zika virus epidemic has spread rapidly across the Americas, with recent emergence in South Asia, raising a number of concerns about its impacts on population welfare. Such impacts include threats to infant health as well as to male and female reproductive health and viability. In this study, we use multiple data sources from Brazil to show the effects of the epidemic on population fertility. We employ a study design developed for causal inference that highlights both the epidemic's biological and behavioral effects while considering contemporaneous political and economic upheaval in Brazil. The design allows us to expand on the observation that fertility rates have fallen in affected nations. The research produces three important results: (1) the fecundity effects documented in controlled animal studies have not manifested as large drops in births in human populations; (2) there is evidence of a remarkable and relatively immediate behavioral response to information about the epidemic; and (3) the behavioral response differs across education and age groups, corresponding to significant changes not only in the size but also in the composition of birth cohorts.

Demographic responses to new health risks provide a window into a central component of fertility: whether and when people adjust reproductive behavior to time births with favorable environmental conditions. Most models of fertility suggest behavioral links between reproduction and contextual conditions, such as epidemiologic threats, agricultural yield, and macroeconomic change. In these models, fertility preferences and behaviors vary across the life course and may respond to shifting circumstances, including costs of investing in children, desirability of being pregnant, and changes in expectations about the future (Becker and Lewis 1973; Hayford 2009; Hotz et al. 1997; Johnson-Hanks et al. 2011; Jones et al. 2015; Kim and Prskawetz 2010; Preston 1978; Schultz 1997). Some of these changes manifest in increases or decreases in the total number of children born (*quantum* effects), but they may also manifest in temporal shifting of births (*tempo* effects), such that births are timed to occur when parents are better positioned to bear and raise a child (Jones 2014; Schultz 2001).

Empirically, fertility has been observed to decline during periods of hardship, such as conflict, disease exposure, and economic decline (Agadjanian and Prata 2002; Lindstrom and Berhanu 1999; Sobotka et al. 2011; Terceira et al. 2003), but to increase following the eradication of some forms of disease, such as malaria (Lucas 2013). Nevertheless, interpreting the alignment of demographic rates and contextual health threats as evidence of strategic change in reproductive behavior is difficult (Alam and Portner 2018; Barreca et al. 2018; Kim and Prskawetz 2010; National Research Council 2004). In many cases, factors that increase the costs and/or risks of childbearing also affect other proximate determinants of fertility. Disaster, conflict, or epidemic may result in family separation and an accompanying reduction in coital frequency. Health threats may also reduce biological fecundity (e.g., Barreca et al. 2018; Terceira et al. 2003); changes in exposure to nutrition,

infection, and multiple forms of physiological stress have effects on organ systems centrally involved in establishing a pregnancy and carrying it to term (Arck et al. 2008; Larsen et al. 2013). In addition to these alternative explanations, the standard threats to interpretation in observational research are also relevant. Other coterminous phenomena that exacerbate disease risk, such as political or economic instability, may simultaneously shape fertility through biological and behavioral pathways.

The recent observation of fertility reductions in populations affected by Zika are similarly difficult to interpret (Castro et al. 2018; Coelho et al. 2015). Zika may have both biological and behavioral effects, and the biological effects are potentially serious. Most evidence on these effects comes from the study of animals. For example, Zika significantly reduces male fecundity in mice: infection damages testes and renders one-third of infected male mice infertile (Govero et al. 2016; de La Vega et al. 2019). Among nonhuman primates, Zika infection increases miscarriage risk three- to sevenfold (Dudley et al. 2018). In humans, Zika infection is associated with a 10- to 20-fold increase in stillbirth risk (Hoen et al. 2018; Walker et al. 2019). Because human population infection rates appear to have been high in Brazil—exceeding 50% in high-risk areas—scholars have questioned whether Zika contributes to population-level reductions in fecundity, raising concerns about the global implications of the epidemic (Coelho et al. 2015; Esposito et al. 2017; Gonc et al. 2018).

At the same time, fertility effects via changes in reproductive behavior are plausible (Marteleteo et al. 2020). The health risks associated with Zika were elevated in public consciousness through widespread media depictions of infants with microcephaly. These were accompanied by unequivocal public health recommendations to delay fertility. Qualitative evidence from northeastern Brazil describes women with clear knowledge of Zika's health risks (Borges et al. 2018) and for some, a desire to delay childbearing (Marteleteo et al. 2017).

It is also, of course, possible that population fertility declines could be entirely unrelated to Zika risk. Since 2014, Brazil has faced significant political and economic unrest, including the impeachment of the nation's president and a reversal of the nation's previously strong gross domestic product (GDP) growth. As we demonstrate, fertility in Brazil has closely followed economic conditions for many years. Accounting for these coterminous effects is necessary to ascribe population-level fertility change to any factor related to the epidemic.

To distinguish these interpretations, we leverage the spatiotemporal spread of Zika in Brazil. We pay particular attention to the period when residents in Northeast Brazil were at risk of infection but had not yet learned about Zika. We compare the plausibly biological effects with the changes in fertility observed after information about Zika was widely distributed. We use two complementary quasi-experimental design approaches to rule out competing explanations for behavioral change.

We draw on multiple data sources, including complete natality files from the Brazilian Birth Registry, data on the geospatial penetration of the primary mosquito vector (*Aedes aegypti*) for Zika spread, data from hospital and health post accounting records that document regional counts in procedure codes (*Sistema Unico de Saude*; read more about this in the

upcoming Data section), census population data, information on labor markets and inflation, and United Nations (UN) data on regional socioeconomic development.

By unpacking Brazilian demographic change accompanying the Zika epidemic, our analysis sheds light on a central aspect of fertility: whether, when, and which people time the birth of their offspring to align with reduced risks to maternal and infant health. Behavioral timing effects are widely theorized but not well documented empirically. The results also demonstrate evidence of public response to explicit antinatalist policy recommendations from the federal administration. This particular case is all the more striking because realized fertility reductions occurred in a region of Brazil where the majority of births are unintended and abortion is illegal and difficult to access safely. Before turning to the study design, we describe the Brazilian context and the spread of Zika risk in more detail.

Zika Virus Epidemic in Brazil

The Onset of a Public Health Emergency

Although Zika was identified in 1947, the virus received little global attention until outbreaks in humans occurred in Micronesia (2007) and French Polynesia (2013) (see McNeil 2016; World Health Organization 2016). It was not until April 2015, when the Brazilian Ministry of Health identified a Zika outbreak in the northeastern region of the country and notified the World Health Organization, that the virus gained global notoriety.¹ Over the following year, the outbreak intensified and spread, reaching into the southern United States and more than 40 countries and territories in the Americas.

The arrival of Zika in northeastern Brazil made its clinical detection difficult to distinguish from the more common Dengue and Chikungunya fevers, which have seasonally afflicted urban populations across Brazil for more than two decades. Up to four-fifths of Zika-infected adults are asymptomatic (Duffy et al. 2009), and to date, there is no indication that Zika affects prime-age adult mortality. The epidemic raised concerns after evidence suggested that Zika increases the risk of severe neurological congenital disorders among infants and the risk of Guillain-Barré Syndrome among adults (Epelboin et al. 2017; Mlakar et al. 2016; Molnar and Kennedy 2016; Oliveira et al. 2017). By late October 2015, Brazilian health authorities were informed of an unusual increase in cases of microcephaly among newborns within the same region. Because cranial growth accompanies brain increase, microcephaly indicates serious risk of developmental delay, including problems with speech, standing, walking, and multiple intellectual disabilities.

On November 17, 2015, the detection of Zika virus in amniotic fluid samples triggered the declaration of a national medical emergency. The Ministry of Health encouraged pregnant women to take preventive action against disease-spreading mosquitos, and women in family planning were advised to consult with doctors about risks to their fetuses. Cases of congenital complications started being tracked and reported weekly; Zika suspected and confirmed cases were tracked as well.

¹Reports of a new disease appeared as early as the third trimester of 2014. Laboratory tests later confirmed cases in Pernambuco in December 2014; and in Maranhao, Rio Grande do Norte, and Bahia, in February and March 2015.

As the epidemic evolved, government agencies across the Americas, including the Centers for Disease Control and Prevention (CDC) in the United States, advised pregnant women to avoid mosquito-infested areas. Soon after the declaration of medical emergency, officials in the Brazilian Ministry of Health took the unprecedented step of advising women to consider delaying fertility indefinitely (Castro 2016; McNeil 2016).² At the time, the increase in positive cases and their graphic display in pictures was reported regularly by the media (Ophir and Jamieson 2018; Ribeiro et al. 2018). We reproduce the timeline of these events overlaid with the dramatic increase in the incidence of microcephaly across the country in panel a of Fig. 1. The number of microcephaly cases recorded per live birth in December 2015 is approximately 28 times larger than the norm since 2005.

Not all geographic regions in Brazil are equally suited to support sustained autochthonous transmission of the Zika virus. *Aedes* mosquitoes, which transmit the virus from person to person, reproduce in warm humid regions with high levels of rainfall. Scholars have constructed geospatial Zika suitability indices based on detailed climate, topographic, and land use data (e.g., Messina et al. 2016) alongside information about population density and mobility to model the spread of the disease (Zhang et al. 2017). This type of modeling is preferred to the use of Zika diagnosis counts to understand the spatiotemporal distribution of infection risk because diagnosis counts are widely understood to underestimate risk. Diagnosis counts also skew the picture of the geographic/socioeconomic distribution of risk; undercounts are likely worse in lower-income relative to higher-income communities. This type of modeling, alongside information about microcephaly incidence, quickly elevated the microregion of Recife and other urban centers in the state of Pernambuco and across the Northeast as the main areas of Zika risk in 2015 and early 2016.³ Indeed, as depicted in panel b of Fig. 1, a higher incidence microcephaly can be observed in these locations. This figure contrasts the location-specific average microcephaly rates in Recife and in other microregions in Pernambuco (17 microregions), across the Northeast (113 microregions), and elsewhere (281 microregions).⁴

Fertility Impacts of a Public Health Emergency

The Zika epidemic emerged in a period of ongoing fertility decline in Brazil. The nation's total fertility rate (TFR) fell from 6 births per woman in 1960 to 2.1 by 2005 and 1.8 by 2014. Contraceptive use increased, although with considerable variation across the country. Data from the most recent Demographic and Health Survey (2006) indicated that 55% of pregnancies were unintended.

Whether a contextual change like the Zika epidemic affects fertility behavior depends in large part on (1) how its risks are perceived by the population and (2) the resources available for adjusting behavior (Akwawara et al. 2003; Yeatman 2009). To date, research on the effects of disease risk on fertility has largely focused on disease eradication. Many of these studies relied on a framework in which parents adjust fertility behavior to expectations about

²Zika was then added to the list of microcephaly-correlated factors, such as severe malnutrition, substance abuse, infections with rubella or toxoplasmosis, and some conditions that interrupt blood supply to the fetus.

³See the Pan American Health Organization website (https://www.paho.org/hq/index.php?option=com_topics&view=rdmore&cid=8095&item=zika-virus-infection&type=statistics&lang=en).

⁴See the online appendix, Figs. A1 and A2, for a map of the Northeast region and of its microregional subdivisions.

child survival and the needed investments to raise children (Boucekkine et al. 2009; Preston 1978). For example, Bleakley and Lange (2009) studied the eradication of hookworm in the American South and observed associated decreases in fertility. They argued that because hookworm had minimal effects on adult health, fertility reductions resulted from an increase in the returns to investments made in children (triggered by quality-quantity substitution).⁵ Ager et al. (2018) observed reductions in the number of children ever born in Sweden following smallpox vaccination and attributed them to reductions in child mortality. McCord et al. (2017) similarly found positive effects of child mortality from malaria on population fertility. Lucas (2013), by contrast, observed an increase in fertility after malaria eradication in Sri Lanka, a change largely attributed to increases in pregnancy survival versus effects on fertility behavior specifically.

The primary example of a *new* epidemic threat in this literature is HIV/AIDS. However, a distinguishing aspect of the HIV epidemic is its effects on adult mortality. Several studies have suggested that some families seek to initiate births earlier, in part because of concern about future risk of HIV infection and associated lifespan uncertainty (see Hayford et al. 2012; Nattabi et al. 2009; Trinitapoli and Yeatman 2011; Yeatman 2009). Other studies similarly identified population-level fertility increases associated with HIV risk (Chin and Wilson 2018), although the general conclusions about population-level associations in this research appear sensitive to identification (Kalemli-Ozcan 2012).

A general insight from the disease risk literature is that fertility effects depend on risk perception. For example, perceptions of risk are amplified by experiences within individuals' social networks and their local communities; spatial clustering of disease risk may have an outsized effect on behavior. Institutions with political authority may exert stronger effects on risk perception. Too, perceptions may respond asymmetrically to increases and decreases in true health risk; risk increase may more acutely observed than risk reduction (Kohler et al. 2007; Montgomery 2000). As a result, information media—both formal reporting and social media—likely impact the construction of risk perception.⁶

Each of these factors appears relevant to population perception of risk in the case of the Zika epidemic. In Brazil, information about Zika has been distributed through official government bulletins, professional journalism, and social media. During February 2016, more than 200,000 members of the armed forces went door to door in a targeted attempt to distribute information and disrupt mosquito breeding grounds (Jacobs 2016). Although that action was warranted for vector control, the presence of the armed forces may have been more effective in raising concerns regarding the prevalence of mosquito vectors than in assuring population confidence that the epidemics could be controlled. Such interactions from the formal authority of military and public health institutions provided relatively transparent information about area-level Zika risk. By contrast, variation in individual-level risk may have been more difficult for residents to assess. The risk of infant congenital anomaly,

⁵Aaronson et al. (2014), used similar reasoning and argued that these “cheaper-quality” substitution effects operate among those who already have children, whereas fertility is stimulated among the childless.

⁶Social media are an increasingly important conduit for health risk information (Fung et al. 2014; Panagiotopoulos et al. 2016). Media representations often inflate infectious illness threats relative to their contribution to population morbidity and mortality (Frost et al. 1997; McComas 2006).

conditional on infection, was not known at the time and is still estimated with considerable uncertainty. Risk estimates range from 0.03% to 17% (Honein and Jamieson 2019; Jaenisch et al. 2017; Mulkey et al. 2019; Rice et al. 2018). Cases of microcephaly occurred at a lower rate among higher-resourced families in the population (see Fig. A3 in the online appendix), but given the rarity of microcephaly, this may have reflected differential access to pregnancy termination. It is not clear that high-resourced women perceived lower Zika infection risk.

For women and couples in Brazil, integrating this new threat into fertility plans may have been challenging (Martelete et al. 2017; Simmons and Rigby 2016). Several of the regions more suitable for Zika transmission are also the least-resourced parts of the country. Delaying fertility indefinitely may not be an option for women and families, especially where access to contraception is incomplete and childbearing is a central feature of family life. Moreover, several of Zika virus' hypothesized effects cannot be discerned via ultrasound until the second trimester (Oliveira Melo et al. 2016), which may limit the ability to legally interrupt pregnancies or to do it without elevated risks to maternal health.

The capacity to react to these risks almost certainly varies across the population. Although contraceptive access in Brazil is widespread and quite high by global standards (Ponce de Leon et al. 2019), it varies significantly by region. In 2012, contraceptive use among women aged 15–49 was close to 75% in the wealthier southern states but only 30% in Pernambuco in the Northeast (Minowa et al. 2015). Abortion is illegal, and the access to safe clandestine alternatives varies by socioeconomic conditions (Dias et al. 2015), which are heterogeneous even within well-defined urban microregions like those examined in this study. Well-resourced areas in the Southeast (and households within any locality) are more connected to up-to-date information about the epidemic and have higher density of social media networks, even though risk of local infection may be lower among them.

Ultimately, a differential temporal change in behaviors depends on the salience of both the risk perceptions of individuals *and* the ability to react to those.

In Brazil, a monthly count of live births indicates a decrease of up to 15% in the months following the outbreak compared with the months preceding it (Castro et al. 2018), raising significant media attention. In the present study, we seek evidence that these declines represent a causal impact of the epidemic. We then build on other research examining the population-level fertility effects of disease by accounting for evidence of behavioral responses to the disaster and, as others have emphasized, the concerning effects of the epidemic over human fecundity (Coelho et al. 2015).

Indeed, the biological effects of Zika infection on population fertility could have been sizable. Although infection risk in the population is difficult to discern, most studies have suggested that it was much higher than indicated by reported cases. Epidemiologic studies of microcephaly risk assumed population infection rates ranging from 10% to 80% (Cauchemez et al. 2016; Johansson et al. 2016) based on evidence from Micronesia and French Polynesia that population infection rates exceeded 50% by the fourth and seventh months, respectively, of those outbreaks (Keegan et al. 2017). In northeastern Brazil, serum studies identified Zika antibodies in nearly two-thirds of new mothers recruited to be

controls in case-control studies in late 2015 and early 2016 (Araujo et al. 2016; Netto et al. 2017).

What does this mean for expected changes in birth cohort size? The Zika virus has been associated with pregnancy loss at multiple points in gestation, although the magnitude of increase in miscarriage risk is still not well understood.⁷ Multiple case studies have documented spontaneous pregnancy terminations between 7 and 10 weeks' gestation associated with Zika virus replication in amniotic stem cells (Gonç et al. 2018; Van der Eijk et al. 2016). There is also evidence of late-gestation termination; estimates of stillbirth risk associated with maternal Zika infection in the first trimester are estimated to be between 1% and 2%—10–20 times the rate in noninfected populations (Hoen et al. 2018; Walker et al. 2019). Animal models suggest multiple biological mechanisms responsible for termination, including vertical transmission and subsequent fetal infection and immunological responses that operate even in the absence of fetal infection (Dudley et al. 2019).

Estimates of complete Zika-associated miscarriage risk are harder to generate because of the difficulty of measuring early pregnancy in humans. Spontaneous abortion is clustered in the first weeks of pregnancy before pregnancies are recorded in registries or electronic health records (Wilcox 2010). An estimated 12% of human clinical pregnancies (those that reach 7–9 weeks' gestation) terminate, whereas an even larger fraction (potentially one-third) of pregnancies of 4–5 weeks' gestation terminate (Larsen et al. 2013; Wang et al. 2003).

Data from nonhuman primates indicate miscarriage rates that are three to seven times as high in Zika-infected versus noninfected mothers (Dudley et al. 2018; Walker et al. 2019). If the effect detected in nonhuman primates were applicable only to human *clinical* pregnancies, a tripling of miscarriage risk among 10% of the population by March 2015 would reduce birth cohort sizes by more than 2.5% six to nine months later. If infection rates reached 50% by March 2015, the reduction in cohort size from increased pregnancy loss and stillbirth could exceed 13.5%. If this effect were applicable to *pre-clinical* pregnancies, the associated birth cohort reductions would be even larger. The associated birth cohort reduction could also be larger if Zika infection reduces male fertility in humans, as it appears to do in mice (Govero et al. 2016; Walker et al. 2019).

A primary issue in identifying the effect of Zika exposure over fertility in Brazil is the potential effect of contemporaneous economic and political instability. In 2014, the Brazilian economy initiated a downward spiral, becoming the worst recession since 1981. Between 2014 and 2016, the GDP for the country fell 7.2%. From the first contraction in 2014, the expectation of economic agents already appeared to reflect the turbulent conditions that would follow.⁸ Figure 2 overlays the trends for year-to-year changes in 12-month birth cohorts with the year-to-year changes in consumer prices and unemployment rates. Any study of Zika effects over population change must be attentive to the potential impacts of broader macroeconomic conditions (and expectations) over fertility decisions.⁹

⁷In a recent review in the *Annual Review of Virology*, Dudley et al. (2018) argued that macaque studies could provide an important source of information on Zika-associated fetal death given how difficult it has been to study in humans.

⁸See <http://g1.globo.com/economia/noticia/2014/12/o-que-esperar-da-economia-em-2015.html> and <http://g1.globo.com/economia/noticia/2015/12/o-que-esperar-para-economia-em-2016.html>.

Political instability also affected the country during this period. Between December 2015 and April 2016, President Dilma Rousseff was under a Congress-led investigation that led to impeachment halfway through her second term in office. Her vice president and successor, with little popular and political support, faced challenges to govern. The combination of economic and political crises may have contributed to an overall belief that health shocks like Zika could not be combated by a failing public sector apparatus, increasing the perception of risk during the epidemic.

For all these reasons, methods that generate expected period changes in fertility in the absence of Zika exposure need to resemble as closely as possible a case-control exercise. Castro et al. (2018), for example, employed auto-regressive integrated moving average (ARIMA) time series forecasting methods to generate expected fertility rates in Brazil based on past trends. This is a useful strategy to demonstrate temporal deviation from the past but does not provide leverage to interpret trends if other factors that affect fertility are changing concomitantly with the exposure of interest. To advance our understanding, we must attend to the macroeconomic and political turbulence of the time. We delineate inference strategies that leverage spatiotemporal variations in order to quantify changes in fertility and a potential behavioral explanation for the observed decline: health-risk avoidance on the part of some would-be parents.

Data and Methods

Data¹⁰

To investigate fertility patterns in the wake of the Zika epidemics, we use information on all births in Brazil between January 2011 and December 2017 from the Brazilian Birth Registry. The registry has high coverage rates, exceeding 98% as early as the mid-2000s (Mello-Jorge et al. 2007). These records include information on mothers' age and educational attainment, municipality of maternal residence, and municipality of delivery. Records include birth outcomes, including the diagnosis of any congenital anomaly, coded per the World Health Organization's International Classification of Diseases (ICD-10). These vital records are public and posted on the Ministry of Health web portal.¹¹ As of this writing, records do not exist beyond December 2017.¹² The registry includes microdata on every live birth across 5,570 municipalities, the smallest administrative unit in Brazil.

We aggregate this information to generate monthly birth counts by microregion (*Região Geográfica Imediata*). Microregions are defined as areas containing common employment and goods markets; they also provide catchment areas for health and education services. We use the boundaries published by the Brazilian Statistical Institute (*Instituto Brasileiro de*

⁹A large literature spanning the social sciences suggests that fertility co-moves with the economic business cycles, with improvements in the latter generating increased fertility (see Adsera 2004, 2011), for example. A recent contribution by Buckles et al. (2018) has even uncovered evidence that fertility decisions are a leading economic indicator, with conceptions moving in anticipation of bad and good future economic tides.

¹⁰Because we employ numerous data sets, to help readers, we include in Table A1 (online appendix) a list of all information and the respective sources.

¹¹See *Sistema de Informacao de Nascidos Vivos* (SINASC-DATASUS) for live births; see *Sistema de Informacao de Mortalidade* (SIM-DATASUS) for a registry of fetal deaths (<http://www2.datasus.gov.br/DATASUS/index.php?area=0901&item=1>).

¹²We last updated our analysis files with data uploaded on May 23, 2019, by Brazilian authorities.

Geografia e Estatística (IBGE)) in 2017. The birth registry data contain information for all 510 microregions (see map in Fig. A1 in the online appendix). To ensure that the monthly estimates are not driven by noise from sparsely populated regions, we restrict the working sample by trimming the most rural areas: microregions that between 2011 and 2013 had at least one month with live-birth counts in the bottom 10% of the microregion-month live births counts' distribution. The resulting sample includes 412 unique microregions, representing 96.3% of all births for residents in the Brazilian territory during that period.

We use several data sources to characterize socioeconomic and demographic variation across the regions. We measure variation in poverty and economic development with the UN Human Development Index (HDI), constructed for each municipality in 2010. To do so, we aggregate the municipal HDI data to the microregion level using 2010 population counts as weights. We also draw on three subcomponents of the HDI index that classify regional variation in income, health, and educational attainment, respectively.¹³ We compute urbanization rates, population size, and population age composition using microdata from IBGE's 2010 census. To describe the evolution of macroeconomic conditions in the country, we employ information regarding labor markets and inflation—IPEADATA—from the *Instituto de Pesquisas em Economia Aplicada* (IPEA).¹⁴

Because this study is centered on a health emergency associated with a mosquito-transmitted disease, we retrieve reports published by the Ministry of Health's *Secretaria de Vigilância em Saúde* on the Larval Index Rapid Assessment for *Aedes aegypti* (*Levantamento de Índice Rápido do Aedes aegypti* (LIRAA)). The index is constructed from a survey of localities in which researchers search for mosquito eggs in standing water through door-to-door visits, which are followed by larval lab tests. The results are used to construct an index indicating the percentage of households visited with positive tests for *Aedes* mosquitos (*Índice de Infestação Predial*, hereafter referred to as the LIRAA index). This index is reported widely in Brazil. Locations with more than 3.9% of their households testing positive are considered high-risk and are publicly red-flagged. We use a dichotomous variable to measure microregions with red-flagged communities. The public communication of these findings is central to combating mosquito-borne diseases by incentivizing the population to take action by eliminating standing water within their households and guiding local authorities in organizing the spraying of streets with insecticide.

In supporting analysis, we also use data on hospitalizations and health post visits for institutions (public and private) that are affiliated service providers for the *Sistema Único de Saúde* (Unified Health System, or SUS). The SUS system provides routine medical services for approximately three-fourths of the population in Brazil, with the rest occurring in private clinics unaffiliated with SUS.¹⁵ To reimburse providers, SUS requires the maintenance and transmission of records on all activities, including date of visits, procedures, diagnoses, length of inpatient stays, and basic demographics on patients.¹⁶ Because this is an accounting mechanism, there is a clear financial interest for their accuracy. The municipality

¹³Retrieved from <https://www.br.undp.org/>.

¹⁴See <http://www.ipeadata.gov.br/Default.aspx>.

¹⁵Despite the high coverage, we expect more-educated, high-income, and privately insured individuals to be underrepresented within the SUS's hospitalization records.

of service provision as well as patient municipality of residence are recorded and reported in public databases with a two-month delay, undergoing recurrent updating during a 12- to 18-month moving window.¹⁷ Procedures are recorded using Ministry of Health codebooks, and diagnoses are reported following ICD-10 classification.¹⁸

Methods

The nature and timing of the Zika virus epidemic in Brazil provides unusual leverage to distinguish behavioral fertility responses. In some locations, infection risk peaked before most Brazilians knew what Zika disease was or its potential impact on infant and maternal health. If population fertility were to fall because of reductions in the probability of conception, we would expect missing births to be detectable in these data roughly 8–10 months after the outbreak peak, corresponding to the gestation period of most successful pregnancies. If spontaneous pregnancy loss contributed to fertility decline, missing pregnancies may be detectable earlier, 6–8 months after the outbreak peak. By contrast, fertility decline resulting from behavioral attempts to delay fertility and avoid pregnancies (including elective termination) would be expected at a later time, at least 6–10 months after the announcement of the epidemic and the peak in microcephaly cases.

On top of these temporal patterns, we also expect the spatial distribution of suspected Zika cases to influence fertility patterns. Biological effects should be clustered in regions where infection risk was highest. Behavioral changes should cluster in locations where the epidemic was perceived to pose the greatest threat—regions where microcephaly cases were more numerous and where insecticide campaigns and information distribution were more intense.

To identify effects on fertility, we use two complementary strategies. Both methods generate expected period changes in fertility in the absence of Zika exposure, resembling as closely as possible a case-control exercise using observational data. The first focuses on effects detectable in the metropolitan region of Recife in northeastern Brazil. Recife was unambiguously the epicenter of the Zika-related microcephaly epidemic (Fig. 1). In Recife, infection risk peaked in March 2015 (Zhang et al. 2017), months before residents knew about Zika or learned about its risks. To isolate the epidemic effects in Recife, we employ a conceptual extension of standard comparative case-control designs known as the *synthetic control* method (Abadie et al. 2010, 2015; Arkhangelsky et al. 2019; Doudchenko and Imbens 2016). This approach selects comparison series for Recife by combining information from other microregions that the analyst selects as potential donors. The method is data-driven and weights a combination of the comparison regions to find a best-fitting synthetic control during the period *prior* to the event of interest. This procedure allows us to investigate a single geographic unit (Recife), which would not be possible with a standard differences-in-differences strategy that we employ.¹⁹

¹⁶Collected under the *Sistema de Informacoes Hospitalares* (SIH-DATASUS), and the *Sistema de Informacoes Ambulatoriais* (SIA-DATASUS). Data can be found online at <http://www2.datasus.gov.br/DATASUS/index.php?area=0901&item=1>.

¹⁷See <http://www2.datasus.gov.br/DATASUS/>.

¹⁸This includes codes for vaginal and C-section deliveries (O80–O82) and deliveries with complications (O60–O69).

¹⁹In practice, there is only one treated unit, which does not provide cross-sectional variation needed for parameter identification. This method heavily relies on longer time series variation, which we accommodate by including data from as early as 2011.

When extending the analysis beyond Recife to other affected microregions in the Northeast region of Brazil, we complement the analysis with a more traditional difference-in-difference approach. In this design, we compare the fertility trajectories in exposed regions with the trajectories that we would expect had fertility in exposed regions followed the path observed in unexposed regions. We consider that both the spread of the disease and its salience to the population were functions of mosquito infestation because of evidence that infestation was highly correlated with microcephaly rates and drove targeted public health measures. We use the mosquito surveillance indices published in January–February 2015 and October–November 2015 to characterize microregions where we expect larger and earlier incidence of Zika infections and, consequently, any behavioral response to it.

Synthetic Control—Recife, the capital city of Pernambuco, Brazil experienced the earliest clustering of Zika risk and received the largest share of media attention to microcephaly cases when the outbreak was recognized and announced. To use the synthetic control method, we construct time series of monthly crude birth rates (CBR) for Recife and all potential comparison microregions. Monthly CBR are computed by dividing counts of live births by total population (in thousands) reported in the 2010 census.²⁰ In the synthetic control design, the analysts select a set of potential controls based on observed characteristics. Time series from these controls are used to predict the time series of interest (here, the CBR) in the exposed region during a period prior to exposure. Cases with low prediction error during the prediction period are weighted to create a combined synthetic control series. The vector of weights is generated by minimization of overall mean squared prediction error (Abadie et al. 2010, 2015; Doudchenko and Imbens 2016).²¹

We use potential comparison regions that (1) were exposed to Zika later than Recife and with a much lower infection rate and (2) may be similar to Recife on major characteristics that influence fertility. For this reason, we select heavily urbanized microregions located outside the Northeast region of Brazil.²² These decisions produce 187 microregions in the pool of possible controls. We then use several attributes for the matching process, in addition to the CBR time series. These include (1) the municipal-level human development index, income subindex; (2) Human Development Index, health subindex; (3) Human Development Index, education subindex; (4) the 2010 share of population in urban sectors; (5) the 2010 population share of women in seven distinct birth cohorts; (6) the 2010 share of births to women aged 35+, 30–34, 25–29, and younger than 24; (7) the 2010 share of births with very low birth weight (<1,500 grams), with low birth weight (<2,500 grams), or deemed premature; (8) the 2010 share of births to women with at least a high school education, with primary but incomplete high school education, or with less than elementary education; (9) the 2010 share of births by race and gender; (10) the 2010 share of babies born in private health units; (11) the 2010 rate of incidence for microcephaly and other congenital anomalies; (12) the 2010 share of population in urban sectors; and (13) the 2010 local Gini

²⁰We use CBR values versus TFR and explicitly adjust for variation in the population age composition.

²¹There is some discretion on the implementation of the method, including which attributes to use in the prediction and which period to use in order to fit the time series of interest. We make our choices clear in this section and examine robustness of findings with respect to those choices when discussing results.

²²We use as a cutoff for urbanization rates, measured from the 2010 census data, the rate for the least urbanized of the state capitals: approximately 77%.

coefficient for income distribution. In Table 1, we present the descriptive statistics on these dimensions for Recife (column 1) as well as for the chosen pool of microregions used to construct the synthetic contrast (column 2).

We fit the data during the period between March 2011 and March 2014, which is one year prior to the peak of Zika infections in the northeastern portion of the country. We select this window so that the calibration of the model occurs during a period that precedes the spread of the disease and related information. In Table A2 (online appendix), we report the list of locations and respective weights that form the synthetic control series. Descriptive statistics are presented in Table 1 (column 3). We visually depict the fit of the synthetic prediction in panel a of Fig. A4 (online appendix) by plotting three CBR series (in log scale): for Recife, for the average non-Northeast urban microregion, and for the “synthetic-Recife” constructed using the method. The simple average of the comparison microregions consistently underestimates the CBR level for Recife and displays month-to-month movement at odds with Recife, including during the pre-event period. By contrast, the series for synthetic Recife is constructed to produce the best match of levels and seasonal variation in the period prior to March 2014. The weights used to match during the pre-March 2014 period are applied to the data following March 2014 to provide a plausible counterfactual for the time trend in fertility in places with low to no Zika risk in 2015 to 2017.

With the synthetic control in hand, we contrast births observed in Recife relative to the synthetic control between April 2014 and December 2017. We then implement a series of placebo tests (Abadie et al. 2015), substituting the donor municipalities for Recife, one at a time, to calculate the same quantities used in the main exercise issuing matched synthetic counterfactuals. These provide an empirical distribution of the effect estimates that we would generate if exposure were randomly assigned to microregions in the working sample. We then compute exact p values by using the distribution of estimated effects normalized by the square root of the mean prediction error. Conceptually, the placebo tests consider whether conclusions from the synthetic control tests are specific to Recife, or whether we would arrive at the same outcome by studying fertility in, for example, Belo Horizonte, a region known to have limited Zika exposure.

Difference-in-Differences—The difference-in-differences extends the analysis to a broader contrast between regions with different levels of exposure to the epidemic between January 2013 and December 2017. We use a regression model that tests for the differential evolution of birth cohorts month by month during and after the onset of the Zika epidemics. We first compare microregions within Pernambuco (including Recife) with others from across the country. We then expand the regions of interest to all microregions in northeastern Brazil. Although very similar in principle to the analysis using synthetic control methods, this regression framework allows us to fully explore cross-sectional heterogeneity of impacts both within and across locations, enriching the ability to discuss the demographic and policy implications of our main findings.

The parsimonious difference-in-differences specification is

$$\ln(births)_{rt} = \gamma_r + \delta_t + \theta_{rm} + \sum_{t=t_0}^T \alpha_t \times treated_r + \sum_{t=t_0}^T \beta'_t \mathbf{X}_r \times \varepsilon_{rt}, \quad (1)$$

where (log) births in microregion r in year-month t are explained by location fixed effects (γ_r), time effects (δ_t), 11 monthly microregion-specific seasonality indicators (θ_{rm}), an interaction between a group indicator for the collection of microregions being scrutinized ($treated_r$), and time effects covering the onset and aftermath of the epidemics (January 2015 onward). The parameter estimated for this interaction (α_t) reflects the realization of a month-by-month difference-in-differences estimator (measured as the percentage change in birth cohorts due to the log transformation of the dependent variable). In an effort to reduce concerns regarding the comparability between exposed and comparison locations, we also include interactions between time effects between January 2015 and December 2017 with a microregion's economic characteristics ($\mathbf{X}_r$), such as development level, inequality, and urbanization (all measured in 2010) as well as a red-flag indicator for microregions with large infestation according to the LIRAA index (measured in January–February and October–November 2015).²³ The differential impacts of the treatment over time measured in the month-by-month parameter carry significant noise (multiple parameters are estimated). In our discussion of results, we also present results based on rolling-trimester averaged effects, reporting on $\tilde{\alpha}_t = (\alpha_t + \alpha_{t-1} + \alpha_{t-2}) / 3$ and its precision.

Table 2 presents descriptive statistics for different groups of microregions analyzed in these specifications. Pernambuco is clearly an outlier in terms of microcephaly incidence (after June 2014) and high levels of mosquito infestation. The picture is less clear but still troublesome for the whole Northeast region.

We reestimate Eq. (1) to predict variation in subgroups of the birth cohorts within locations. These include groups defined by maternal age at birth and educational attainment. Attention to this variation helps shed light on distinguishing impacts in the form of *quantum* or *tempo* effects, particularly if responses are observed among women closer to ending the most fecund portion of their life cycle. Socioeconomic differences, on the other hand, can be informative of the mechanisms behind fertility fluctuations, in particular because poorer families are more likely exposed to disease (and therefore its biological effects) but have less access to quality family planning services (and, therefore, less room for behavioral change). It is also possible that more-educated mothers have higher opportunity costs to raise a child with neurological disabilities. Because changes to fertility shift the composition of birth cohorts, these also shed light on the longer-run impacts of a short-run health shock on population patterns.

In a final piece of the analysis, we study heterogeneity across locations within the Northeast by including one additional interaction to the term measuring epidemic impact. We highlight the role of the mosquito infestation red-flagging as an important element in the salience of the message regarding disease risk. Although the disease environment is obviously connected to the presence of the mosquito (conditional on the circulation of the virus),

²³We match the municipality-level reports to the microregions in our data by taking the maximum value of the index across municipalities within a given microregion. The latter is red-flagged if at least one of the municipalities within it is red-flagged.

information regarding higher concentration of *Aedes* larvae may have magnified the impact of the call to reassess fertility plans.

Results

Fertility Change in Recife, Brazil

We begin by examining results of the synthetic control analysis focused on fertility in the center of the epidemic: Recife, Brazil. Here we concentrate attention on the section of results starting in January 2015 reproduced in panel a of Fig. 3.²⁴ Infection risk in Recife is believed to have peaked in March 2015. If infection induced miscarriage among ongoing pregnancies, we would expect to see fertility rates fall between April and December 2015, depending on when in pregnancy excess miscarriage risk is highest. We see evidence of decline in birth rates relative to expected values in December 2015, but it does not extend to the month before and after, and is not statistically distinguishable from zero. The estimation indicates a sizable and significant reduction in birth rates in Recife from September 2016 (15.3%) to February 2017 (12.1%), indicating that reductions in fertility were sustained for approximately one-half year, corresponding with pregnancy cohorts that would have been initiated one to five months after the public health emergency was announced. The reduction peaks in November 2016. At that point, the birth cohorts were 19.8% smaller than predicted in the absence of the epidemic.

We conducted several robustness checks. We reestimated the synthetic control including northeastern microregions outside Pernambuco. This increased the pool of donor microregions for comparison to 201 locations. We also tested alternative cutoff dates that expand the time during which the synthetic control is fit to March 2015 and November 2015 (vs. March 2014). The latter is particularly different in its matching principle because it matches Recife with a synthetic location inclusive of any potential early biological impact of Zika over fertility. We report the results in the online appendix; Table A4 shows estimates, and Table A5 shows the composition of the synthetic control under the three alternatives. Results confirm October to December 2016 as the months during which gaps between observed birth rates and counterfactual levels are concentrated. Some of the effects are attenuated, suggesting that fertility variations beyond Recife and across the Northeast region are pertinent.

Fertility Change in Northeastern Brazil

To capture effects beyond Recife, we turn to the difference-in-differences estimates describing Pernambuco state and other locations across the northeastern region of Brazil as *treated* (exposed) microregions. We display the results in the form of month-to-month differential birth cohort sizes changes (in a log scale) between locations more and less exposed to Zika, as approximated by the infestation risk of the primary mosquito vector and cases of reported microcephaly. We report estimates from 10 months before the public health emergency announcement to 25 months afterward.

²⁴Effect estimates are presented for the entire period of study in panel b of Fig. A4 and in Table A3 of the online appendix.

The estimates indicate a small reduction in the birth rate in the immediate aftermath of the announcement, although most prominently 9 to 17 months after it, but that contraction has not entirely disappeared by the end of 2017. Estimates describing the 18 microregions within Pernambuco are presented in panel b of Fig. 3 as well as numerically in Table A6 (online appendix). These patterns are observed even after the interaction of additional controls for location characteristics interacted with time effects are included (Table A6, column 2).²⁵ The findings indicate that birth cohort sizes within Pernambuco were 25.8% smaller than in microregions outside the Northeast in October 2016 and that most of the cohorts born 9–25 months after the public health emergency declaration are smaller in the former. These patterns can be more clearly seen once we estimate smoothed versions of the impacts by examining trimester-long moving averages of the effects in panel a of Fig. 4. In general, the difference-in-difference analysis of the full Northeast region aligns with the synthetic control analysis of Recife. Both indicate (1) at most, small fertility reductions during the window when biological effects should appear and (2) evidence that larger fertility declines clustered in the 10–15 months following the declaration of a national emergency.

To extend the analysis of impact to more recent data, we also estimate the effects of the epidemics using only data on deliveries computed by the public reimbursement system (SUS)—a potential resource for the scientific and policy communities because the SUS data allow observation of births closer to real time. Results presented in panel b of Fig. 4 suggest that shrunken birth cohorts will continue to be seen well into the first half of 2018. The smaller point estimates in the peak of behavioral changes also indicate that the response to the epidemics may have been heterogeneous within the population.

The use of difference-in-differences analysis allows us to detect evidence of a differential behavioral response *within* the Pernambuco population. We reestimate Eq. (1) for population subgroups: first by maternal education (less than primary vs. primary school or more). The results in trimester-long moving averages are presented in Fig. 5 (monthly estimates provided in Table A7 of the online appendix). We find reductions for both more- and less-educated women, but the effects are substantively larger for women with more schooling. Birth cohorts to educated women are 25% smaller than expected 8–11 months after the public health emergency, but they are 15% smaller among less-educated women, for example. The difference between these two effects is significant (at 10% significance level) and approximately 10 percentage points for about eight months (panel c, Fig. 5). The advantaged women/couples also seem to have responded earlier than their less-resourced counterparts, with significant reductions in births nine months after national alerts about the Zika-microcephaly link. In later months, cohorts remained smaller as in the overall results, but significant differences between these two groups cease to exist. Incidentally, this heterogeneity suggests that estimations of the effect of the epidemics using only data on deliveries computed by the public reimbursement system (SUS) will lead to

²⁵They are also robust to the analysis, which includes recorded miscarriages to the counts of births (online appendix, Table A6, columns 3 and 4), suggesting that fetal mortality accounted for in official records cannot explain variation in fertility we observe, particularly for the 2016 effects.

underestimation, particularly during the period when the more educated (and those more likely to use the private health system) are most responsive.

Turning to maternal age, we find clear evidence that the fertility response is smaller for women under 25 years of age, relative to older mothers, including those aged 35 or older. These results are shown in Fig. 6 (numeric estimates shown in the online appendix, Table A8). The effects are much larger among older women. The effects are also more enduring for the oldest women (aged 35+); we see more than 15% reductions in birth cohort size relative to the expected value extend to November–December 2017, 24 months after the public health emergency was declared. Because this oldest group was approaching ages of rapid declines in fecundity, the evidence suggests that Zika-related fertility delays may result in smaller completed fertility for a subset of the population.²⁶ This can also be seen in estimates by cohorts of women. Results shown in Fig. A6 in the online appendix indicate that women born between 1976 and 1980 have had fewer births in Pernambuco than in other microregions outside the Northeast from the ninth month after the public health emergency. For younger cohorts, we still see sharp initial reductions, but differences with respect to other microregions are no longer significant toward the end of 2017.

These differences in effects across groups can also be illustrated by a change in the composition of birth cohorts with respect to parental characteristics. We examine changes in average composition of birth cohorts using the same difference-in-differences specifications used earlier. Figure A7 (online appendix) summarizes the findings, presenting evidence of significant reductions (at the 10% level) in maternal age and education in the same months in which we observe an overall reduction in birth cohort size. We conclude that both size and compositional changes in birth cohorts are observed as a result of behavioral changes triggered by the Zika epidemic in Pernambuco.

In a final piece of the analysis, we ask whether evidence of fertility changes extend into locations in the Northeast beyond the state of Pernambuco. We find quite clearly that birth cohort sizes are much smaller than for this larger group of microregions (Fig. A8 and Table A9, online appendix). Moreover, when we examine heterogeneity across the region, mosquito infestation plays an important role in the observed fluctuations in birth cohort sizes. Locations where Zika transmitting mosquitos were more prevalent, and where that information was made public by the red-flagging mechanism employed by the Brazilian Ministry of Health, have a stronger reduction in birth rates than elsewhere across the Northeast (Fig. 7). We see little evidence of difference between panels a and b of Fig. 7 during the months when birth cohort size would have been a function of the biological effects of infection alone. Instead, the evidence in Fig. 7 suggests that behavioral changes were linked to the information regarding place-specific exposure to the new disease.

Before turning to a discussion of our results, we provide a numeric summary of the findings across all indicators by dividing the period studied into three distinct blocks of time: (1) February 2015 to October 2015, which captures the peak of Zika infections and solely

²⁶This reasoning is consistent with our finding that higher-parity births are also less frequent in Pernambuco as a result of the epidemics. See Fig. A5 in the online appendix.

biological impacts of the epidemics; (2) November 2015 to July 2016, when biological and behavioral responses likely coexist; and (3) the period after July 2016, when we expect the behavioral responses to the health crisis announcement to fully materialize. Each row of Table 3 summarizes information presenting the average of the previously shown month-specific estimates divided into these three longer periods. The estimates in Table 3 conform to the patterns we present throughout this section. The more coarse temporal aggregation masks some of the detectable timing differences *across* groups; nevertheless, we still observe meaningfully sized differences in fertility by age, education, and regional differences in public alerts of mosquito infestation.

Discussion

Most theoretical models of human fertility predict the adjustment of reproductive behavior in response to changing circumstances (Hotz et al. 1997; Johnson-Hanks et al. 2011; Trinitapoli and Yeatman 2018). Decades of demographic research have documented examples of changes in fertility rates in the wake of major events, including macroeconomic change, violence and conflict, environmental change, mortality shocks, and shifts in the disease landscape (Agadjanian and Prata 2002; Barreca et al. 2018; Bleakley and Lange 2009; Heuveline and Poch 2007; Lindstrom and Berhanu 1999; McCord et al. 2017). In a few cases, evidence on accompanying changes to stated fertility intentions (e.g., Agadjanian and Prata 2002) suggests that some people may try to adjust fertility timing to align births with more favorable circumstances. In this study, we examine fertility change alongside the emergence of the Zika virus, which posed a new, serious pregnancy health risk in the Americas. Although concerns have been raised about the potential biological effects of the epidemic, we find minimal evidence that the epidemic significantly reduced the size of Brazilian birth cohorts via infection-induced reductions in fecundity. Instead, we find evidence consistent with behavioral adjustments to delay fertility. Several characteristics of the epidemic support identification of these behavioral timing effects in contrast to other competing explanations that often accompany large-scale threats to population health.

By studying fertility effects in regions of Brazil where infection risk peaked before residents learned about it, we are able to distinguish biological and behavioral effects of disease spread. Case studies in humans and experimental studies in animals suggest that Zika infection increases the risk of pregnancy loss and stillbirth (Hoen et al. 2018; Walker et al. 2018); biomedical research now indicates multiple pathways through which pregnancy termination can result from maternal infection (Dudley et al. 2019). At the population level, however, the fecundity effects in humans do not appear to be large enough to account for the majority of observed declines in Brazilian birth cohorts, even with rates of population infection that appear to have exceeded 50% in high risk areas (Araujo et al. 2016; Netto et al. 2017). We see no evidence of declines in live births 7–8 months after the peak infection period; the declines 9–10 months after the peak infection period did not exceed 6% to 7%. We conclude that these fecundity effects may well exist, but they are unlikely to be as devastating in human populations as in animal populations.

Instead, we find strong evidence of a behavioral response to *learning* about the disease. Attributable fertility declines are clustered 10–15 months after the national emergency was

declared. The effects are concentrated in time and appear to be large; in the fourth quarter of 2016, birth cohorts were 25% smaller than expected in the absence of the epidemic. This effect is larger than effects resulting from other macro-level events that change risks to pregnancy or the costs of childbearing. For example, worsened economic conditions during the 2008 recession reduced U.S. fertility by about 10% (Schneider 2017). In terms of health risks specifically, hookworm eradication was associated with a 12.5% reduction in fertility over 10 years in the early twentieth century (Bleakley and Lange 2009). Other forms of epidemic threat provide a less clear comparison because of accompanying child and adult mortality (e.g., HIV, malaria, and smallpox).

We arrive at these conclusions by comparing the temporal patterns in fertility rates in the most directly affected regions (Recife as well as other microregions in Northeast Brazil) against comparison regions that were affected later and to a lesser degree. For the approaches used here—difference-in-differences and synthetic control analysis—spillover effects of Zika exposure into comparison communities will bias estimates toward 0. During the period before information about Zika was widespread, we have no reason to believe that spillover was an issue; models of the disease spread indicate that it was limited to Northeast Brazil in 2015 (e.g., Zhang et al. 2017). In the later periods, 2016 and 2017, the epidemic reached into other parts of Brazil. Risk and depictions of risk (reported *Aedes* mosquito infestation and reports on microcephaly) were still much higher in the Northeast. Nevertheless, it is possible that persons in southern Brazil, for example, also made fertility timing adjustments, given the scale of media communication about the epidemic. If this were the case, the reductions of fertility attributable to learning about Zika may be even larger.

Pregnant women or couples intending to have children may have moved away from cities in the Northeast after learning about risks to infant health. Short-term migration would be a more drastic example of the kind of mosquito-avoidance behaviors that have already been reported among women with higher socioeconomic status (SES) in Recife (Marteletto et al. 2017). Because selective migration would complicate interpretation of our results, we use data on maternal place of residence in the analysis instead of place of delivery; therefore, our estimates include short-term migrants as among the affected population. If departures are more permanent and include changes in residence, we might expect to see evidence of fertility reductions earlier in 2016, potentially as early as January or February 2016, as pregnant women exited Recife and other affected regions of Pernambuco and northeastern Brazil. At that time, no information about trimester-specific risk was included in public health campaigns, and women in the third trimester of pregnancy were also considered at risk. We do not see evidence of larger declines in births until late in 2016, long after migration would have started to be an option. When we investigate changes in birth cohorts based on birth location instead of location of maternal residence, we see equivalent effects for the later portion of 2016 (columns 5 and 6 of Table 2). The effects in 2017 seem to be larger using this accounting of births than maternal residence, suggesting that some level of exodus from these regions happened among those with fertility plans. These differences, though, are not large enough to explain the majority of the effect estimates here. In the online appendix (Table A10), we also present auxiliary exercises using data from (1) school matriculation of 7-year-olds and (2) electoral records to provide additional evidence on the

robustness of our results to migration. Neither data source indicates flows away from the areas that were most heavily affected by Zika.

Three key limitations must be considered in any discussion of the findings of this study. First, as with most population-level work, we are unable to directly measure spontaneous pregnancy loss. Unintended pregnancy terminations are clustered in the first few weeks of gestation and are largely unmeasured (e.g., Wilcox 2010). Here, we must rely on inference derived from spatiotemporal change in live birth counts. The nature of the Zika spread gives us some purchase on these effects. We also use data on recorded miscarriages; to be documented, these are miscarriages that occur later in gestation. We find that these counts are too small to explain the fertility effects here (see Table A5, online appendix, columns 3 and 4). The second and third limitations involve the inability to distinguish changes to *desired* fertility and to predict the implications for quantum changes to family size in Brazil. We discuss each in turn.

Specifically, we find evidence of fertility timing effects among both more-resourced and less-resourced populations. The findings are substantively larger among older, better-educated women, who are more likely to use private health care. That fertility avoidance happened among less-resourced women is striking given evidence that unintended pregnancy in Pernambuco is high, contraception is somewhat harder to access for low-income women (Marteletto et al. 2017), and safe abortion is very difficult to access for low-income women (Dias et al. 2015). Bahamondes and colleagues (2017a, b) used data from pharmaceutical companies and found no evidence of increases in hormonal and long-acting contraceptive sales in Brazil between 2014 and 2016. Of course, the national contraceptive supply data used in these studies may mask place-specific changes in use. In addition, women may have avoided childbearing through other means, including barrier methods (e.g., condoms), abstinence, and delayed partnering. In qualitative work, Marteletto and colleagues (2017) found that lower-SES women in Recife had less access to desired contraception relative to higher-SES women, but lower-SES women attempted to increase contraceptive protection after learning about Zika risk. More generally, the findings here lend further support to demographic research documenting evidence of fertility adjustment outside hormonal contraceptive methods (e.g., Goodkind 1993).²⁷

The behavioral explanation driving the *differences* between better- and less-educated women is harder to pin down. It is possible that wealthier families perceived lower risk because they were better able to achieve mosquito avoidance (Marteletto et al. 2017), or they noticed that microcephaly cases disproportionately occurred to less-resourced women (Fig. A3, online appendix). However, if this is the case, the fertility differences by education may be *smaller* here than would be observed in an epidemic that was perceived to equally affect families across social class. In learning about microcephaly risk, more-resourced women may have

²⁷Our full investigation of additional health records reveals interesting patterns of increase (although not statistically significantly different from 0) in use of intrauterine device and diaphragm insertion in health posts. We also see a significant reduction in abortion-related procedures (curettage), which we interpret as representing reductions in conception rates among portions of the population that were more prone to interrupting pregnancies. Finally, we see no change in counts of tubal ligation and vasectomies. See Table A11 in the online appendix for summary of these findings. See also Lautharte and Rasul (2020) for an interesting and complementary analysis.

had more tools to avoid childbearing (e.g., access to safe abortion). Alternatively or additionally, more-educated women may have had a stronger desire to avoid childbearing. Distinguishing between these explanations is difficult, and it is possible that both were in play. Although wealthier families could more easily absorb the financial aspects of caring for a child with disability, the opportunity costs of navigating pregnancy and infant health risks more generally may have differentially increased desire to avoid risk. Ongoing qualitative research in the region (see Marteleto and colleagues 2017) may be able to better capture differential effects on *desired* fertility specifically.

Scholars have highlighted Zika as a human rights issue for low-income women in high-risk areas (Rasanathan et al. 2017; Ribeiro et al. 2016). The important insights from these scholars underscore a more general observation about demographic behavior and population welfare. Temporal adjustment in fertility may have distinct implications for population inequality. Indeed, we find evidence that the differences in fertility avoidance between less-educated and better-educated women was sufficient to shift the composition of birth cohorts in the later months of 2016 and beginning of 2017. Families who are least able to shift pregnancy timing are often those who must manage the heightened pregnancy risks with the fewest resources. Although the net impact of temporal fertility adjustment on population welfare may be to improve the *average* birth conditions of the next generation, temporal adjustment will also exacerbate inequality by increasing the association between birth conditions and parental resources.²⁸

In 2017 and early 2018, fertility rates in exposed regions almost returned to pre-epidemic levels, although not above them, indicating no evidence that fertility declines in 2016 and the beginning of 2017 were subsequently recovered or offset by the end of the period that we observe here. When we disaggregate fertility across age groups, we observe that declines are larger for older women. These delays may translate into forgone fertility as women approach the end of their reproductive ages. Indeed, when we plot cohort-specific fertility, we observe no evidence of offsetting fertility among women of any cohort, including those who are aged 37–41 by the end of 2017. Because the epidemic effects were clustered in a period of a few months, it would be possible for these to be offset still. In the coming years, studying completed fertility among older cohorts of women will help to clarify the longer-run effects of Zika on population change in Brazil.

Of course, period fertility changes have implications beyond their potential effects on completed family size (Ní Bhrolcháin 2011). In Northeast Brazil, and particularly in the hardest-hit regions, children born in 2016 will move through school and enter the labor market in a smaller cohort. Children in cohorts preceding the epidemic will experience sibling spacing that is, on average, lengthened. Fertility timing may even intersect with labor market attachment, particularly among young women. In general, the impact of state-sanctioned directives for fertility delay in the wake of an epidemic may well extend beyond the most mechanical aspects of population renewal. How these changes shaped life in Brazil remains to be learned.

²⁸For an interesting empirical exercise on long-term effects of aggregate fertility changes, see Pop-Eleches (2006).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1.

Reported microcephaly cases per 10,000 live births, Brazil aggregate rates for 2006–2017 (panel a), and monthly rates by microregion for 2014–2017 (panel b). For the spatial distribution of these microregions, see Figs. A1 and A2 in the online appendix. See the definition of microregions in the Data section of the text. *Source:* SINASC-DATASUS.

Fig. 2.

Country-level year-to-year change in 12-month birth cohorts, consumer price index, and unemployment rate (in percentage points). *Sources:* SINASC-DATASUS and IPEADATA.

Fig. 3. Monthly crude live births rate (births per 1,000 inhabitants in 2010): Recife versus synthetic Recife, ln scale (panel a); and monthly difference-in-differences, live birth cohorts, Pernambuco versus non-Northeast microregions, ln scale (panel b). In panel a, differences in gray are produced from 187 placebo estimations. Dashed lines represent the top and bottom 10% of the placebo-generated differences. In panel b, reported 95% confidence intervals are based on standard errors clustered at the microregion level. The regression controls for time interactions with the local Human Development Index (HDI); urbanization rate; income inequality (Gini; mosquito infestation; and fixed effects for microregion-specific seasonality, year-month, and microregion.

Fig. 4.

Trimester moving-average difference-in-differences, live birth cohorts, Pernambuco versus non-Northeast microregions, ln scale (panel a); and deliveries in public health system, Pernambuco versus non-Northeast microregions, ln scale (panel b). Reported 95% confidence intervals are based on standard errors clustered at the microregion level. The regression controls for time interactions with local Human Development Index (HDI); urbanization rate; income inequality (Gini); mosquito infestation; and fixed effects for microregion-specific seasonality, year-month, and microregion.

Fig. 5. Difference in differences, live birth cohorts, Pernambuco versus non-Northeast microregions, by maternal level of education: completed primary or more (panel a), incomplete primary or less (panel b), and triple-differences more- versus less-educated (panel c). See the notes for Fig. 4 (panels a and b). For panel c, we depict 90% confidence intervals.

Fig. 6. Difference-in-differences, live birth cohorts, Pernambuco versus non-Northeast microregions, by maternal age group: under 25 (panel a), 25–29 (panel b), 30–34 (panel c), and 35+ (panel d). See the notes for Fig. 4.

Fig. 7. Difference-in-differences, live birth cohorts, northeast versus non-Northeast microregions, by type LIRAa index red flag: high mosquito infestation (panel a), low/unknown mosquito infestation (panel b), and difference between the two (panel c). See the notes for Fig. 4.

Table 1

Descriptive statistics for covariates in synthetic control analysis

	Recife (1)	Microregions Outside Northeast (2)	Synthetic Recife (3)
Socioeconomic Indicators			
Human Development Index (HDI)	0.730	0.739 (0.0021)	0.730
HDI, income	0.720	0.732 (0.0024)	0.731
HDI, health	0.820	0.842 (0.0012)	0.839
HDI, education	0.661	0.656 (0.0033)	0.637
Gini coefficient	0.608	0.507 (0.0029)	0.512
Share population in urban areas	0.969	0.879 (0.0043)	0.863
Demographic Composition			
Population share of females born in 1971–1975	0.043	0.037 (0.0002)	0.037
Population share of females born in 1976–1980	0.046	0.041 (0.0002)	0.041
Population share of females born in 1981–1985	0.048	0.043 (0.0003)	0.044
Population share of females born in 1986–1990	0.046	0.043 (0.0003)	0.045
Population share of females born in 1991–1995	0.042	0.043 (0.0003)	0.045
Population share of females born in 1996–2000	0.041	0.042 (0.0003)	0.044
Population share of females born after 2000	0.071	0.069 (0.0007)	0.073
Sociodemographic Indicators for Births			
Share of births to mothers aged 35+	0.096	0.105 (0.0017)	0.092
Share of births to mothers aged 30–34	0.176	0.181 (0.0018)	0.169
Share of births to mothers aged 25–29	0.256	0.258 (0.0011)	0.255
Share of births to mothers aged 24	0.472	0.456 (0.0038)	0.485
Average maternal age	25.558	25.828 (0.0578)	25.394
Share of births who are boys	0.512	0.512 (0.0007)	0.509
Share of births who are black or brown	0.724	0.295 (0.0182)	0.423
Share of births who are white	0.275	0.670 (0.0199)	0.548
Share of births to mothers with high school education or more	0.180	0.196 (0.0036)	0.162
Share of births to mothers with 8–11 years of education	0.499	0.500 (0.0054)	0.512
Share of births to mothers with 4–7 years of education	0.267	0.247 (0.0041)	0.246
Share of births to mothers with 3 years of education	0.048	0.044 (0.0017)	0.052
Share of births to mothers with unknown education level	0.005	0.013 (0.0015)	0.029
Share of births in private health units	0.618	0.771 (0.0172)	0.709
Birth Outcomes			
Microcephaly cases per 10,000	0.560	0.580 (0.1000)	0.320
Congenital anomaly cases per 10,000	93.930	73.620 (2.0400)	68.300
Share of births before term	0.076	0.075 (0.0012)	0.067
Share with very low birth weight	0.015	0.013 (0.0002)	0.011
Share with low birth weight	0.088	0.089 (0.0008)	0.080
Microregions	1	187	1

Notes: Means are reported. Standard errors, shown in parentheses, are computed using the jackknife method for the sample of microregions outside the Northeast (NE). All indicators reflect measures for year 2010.

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Table 2

Descriptive statistics for difference-in-differences analysis

	Pernambuco (PE) State (1)	Northeast Region (including PE) (2)	Non-Northeast (3)	Pernambuco vs. Non- Northeast (4)	Northeast vs. Non- Northeast (5)
Composition					
Number of microregions	18	131	281	299	412
Average number of municipalities within a microregion	10.28 (1.364)	12.43 (0.615)	11.58 (0.408)	−1.31 (1.424)	0.84 (0.739)
Disease Environment					
Average peak monthly microcephaly rate (before June 2014)	28.50 (4.132)	20.41 (1.865)	22.89 (1.545)	5.61 (4.412)	−2.48 (2.422)
Average peak monthly microcephaly rate (after June 2014)	218.356 (23.689)	116.283 (7.497)	39.642 (2.518)	178.715 (23.823)	76.641 (7.908)
Share of microregions with high LIRAA	1.00 —	0.71 (0.040)	0.64 (0.029)	0.36 (0.029)	0.07 (0.049)
Development Stage, Economic Conditions					
Average Human Development Index (HDI)	0.62 (0.009)	0.61 (0.004)	0.71 (0.003)	−0.09 (0.010)	−0.10 (0.005)
Average HDI, income	0.60 (0.010)	0.59 (0.004)	0.70 (0.004)	−0.11 (0.010)	−0.12 (0.005)
Average HDI, health	0.77 (0.005)	0.76 (0.002)	0.83 (0.002)	−0.06 (0.005)	−0.07 (0.002)
Average HDI, education	0.52 (0.012)	0.52 (0.005)	0.62 (0.005)	−0.10 (0.013)	−0.10 (0.007)
Average Gini	0.54 (0.009)	0.55 (0.003)	0.52 (0.003)	0.02 (0.009)	0.03 (0.004)
Average urbanization rate	0.68 (0.030)	0.63 (0.011)	0.80 (0.008)	−0.12 (0.031)	−0.17 (0.014)
Demographic Composition					
Average age of mother	24.76 (0.129)	24.54 (0.071)	25.47 (0.065)	−0.71 (0.144)	−0.93 (0.097)
Average share of mothers with high school or more	0.12 (0.006)	0.11 (0.004)	0.18 (0.004)	−0.06 (0.007)	−0.07 (0.005)
Average share of mothers 8 to 11 years of schooling	0.37 (0.014)	0.37 (0.006)	0.47 (0.005)	−0.10 (0.015)	−0.09 (0.008)

Notes: Standard errors, shown in parentheses, are based on the jackknife method. Microcephaly rates are per 10,000 births. All indicators (except disease environment) were measured in 2010.

Table 3

Summary results for difference-in-differences analysis

	February 2015 to October 2015 (1)	November 2015 to July 2016 (2)	August 2016 and Later (3)
A. Aggregates			
Live births	0.002 (0.019)	−0.018 (0.019)	−0.108 (0.020)
Deliveries SUS system	0.014 (0.030)	−0.018 (0.032)	−0.093 (0.031)
B. Subgroups			
More-educated mothers	0.002 (0.022)	−0.033 (0.022)	−0.140 (0.024)
Less-educated mothers	0.014 (0.029)	−0.007 (0.031)	−0.083 (0.035)
Mothers aged 24	−0.012 (0.021)	−0.015 (0.018)	−0.086 (0.020)
Mothers aged 25–29	0.030 (0.025)	−0.034 (0.031)	−0.128 (0.023)
Mothers aged 30–34	0.004 (0.027)	−0.025 (0.027)	−0.136 (0.027)
Mothers aged 35+	−0.023 (0.019)	−0.031 (0.037)	−0.204 (0.033)
First births	0.007 (0.021)	−0.002 (0.025)	−0.067 (0.025)
Second births	−0.012 (0.025)	−0.028 (0.027)	−0.130 (0.025)
Third or higher-order births	0.018 (0.028)	−0.012 (0.033)	−0.136 (0.039)
C. Microregional Differences by Mosquito Infestation Within Northeast (NE)			
Live births, Northeast all	0.011 (0.006)	0.009 (0.007)	−0.030 (0.008)
Live births, mosquito-infested NE	0.005 (0.012)	0.001 (0.013)	−0.056 (0.013)
Live births, non-mosquito-infested NE	0.013 (0.007)	0.011 (0.008)	−0.023 (0.009)

Notes: Standard errors, shown in parentheses, are clustered at the microregion level. All outcomes are measured in ln scale. For Deliveries SUS system, the final period in column (3) includes first six months of 2018. Regression controls are post-January 15 time-effect interactions with local human development index (HDI), urbanization rate, income inequality (Gini), and mosquito infestation. All models include fixed effects for microregion-specific seasonality, year-month, and microregion.