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MATEUS FERRAZ DIAS

EFFECTS OF GLYPHOSATE ON INFANT HEALTH INDICATORS

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Dissertação apresentada à Escola de Economia de São Paulo da Fundação Getulio Vargas como requisito para obtenção do título de Mestre em Economia de Empresas

Campo de Conhecimento:
Microeconomia Aplicada – Economia da Saúde
Orientador: Prof. Dr. Rodrigo Reis Soares

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To my family.

Si cada día cae
dentro de cada noche,
hay un pozo
donde la claridad está encerrada.

Hay que sentarse a la orilla
del pozo de la sombra
pescar luz caída
con paciencia.

– Pablo Neruda, El Mar y las Campanas.

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ABSTRACT

This work estimates the impact of glyphosate on infant health indicators in Brazil, between 2000 and 2009, exploiting the adoption of genetically engineered soy in Brazil and the country's hidrographic structure (ottobasins). Our results indicate an increase in low weight birth rate and infant mortality rate, concentrated on death causes associated to glyphosate's expected effects and on children exposed to glyphosate during the first trimester of pregnancy (when the fetus is more susceptible to negative developmental effects). Hence, the results suggest that regulation regarding use of glyphosate as herbicide can be improved taking into account the nowadays neglected negative effects on human health.

Key-words: Glyphosate, genetically engineered soy, ottobasins, infant health, infant mortality.

RESUMO

Este trabalho estima o impacto do glifosato sobre indicadores de saúde infantil no Brasil, no período de 2000 a 2009, explorando a adoção da soja transgênica no Brasil e a estrutura hidrográfica do país (ottobacias). Nossos resultados indicam um aumento nas taxas de nascimentos de baixo peso e mortalidade infantil, concentradas em causas de morte associadas aos efeitos esperados do glifosato e em crianças expostas ao glifosato durante o primeiro trimestre de gravidez (período em que o feto é mais suscetível a efeitos negativos sobre seu desenvolvimento). Assim, os resultados sugerem que a regulação do glifosato como herbicida pode ser melhorada levando-se em conta os efeitos negativos sobre a saúde humana, hoje negligenciados.

Palavras-chaves: Glifosato, soja transgênica, ottobacias, saúde infantil, mortalidade infantil.

List of Figures

Figura 1 – Output per worker in soy production, from Bustos, Caprettini, and Ponticelli (2016) 44
Figura 2 – Effect timing on infant mortality rate - 90% confidence interval 44
Figura 3 – Effect timing on infant mortality rate - by causes 44
Figura 4 – Effect timing on low weight births rate - 90% confidence interval 45

List of Tables

Tabela 1 – Descriptive Statistics 32
Tabela 2 – First Stage - Main specification 33
Tabela 3 – Second Stage - Mortality Results - Main Specification 34
Tabela 4 – Second Stage - Mortality by Age Group 35
Tabela 5 – Second Stage - Other Infant Health Indicators - Main Specification 36
Tabela 6 – Second Stage - Fetal mortality and log(births) - Main Specification 37
Tabela 7 – Results by Gender - With controls - IV results 38
Tabela 8 – Mortality results by trimester - Reduced Form 39
Tabela 9 – Mortality results using population 0-1 years old 40
Tabela 10 – First Stage - Using data of position in the ottobasin 41
Tabela 11 – Second Stage - Mortality Results - Using data of position in the ottobasin . . 42
Tabela 12 – Second Stage - Other Infant Health Indicators - Using data of position in the ottobasin 43

TABLE OF CONTENTS

1 INTRODUCTION 13

2 BACKGROUND 17
2.1 Glyphosate 17
2.1.1 Genetically Engineered Soy 18
2.1.2 Glyphosate and Infant Health 20

3 DATA 22

4 EMPIRICAL STRATEGY 24

5 RESULTS 27
5.1 Main results 27
5.2 Timing of exposure 28
5.3 Robustness 29

6 CONCLUSION 31

7 TABLES 32

8 FIGURES 44

REFERENCES 46

1 Introduction

In modern agriculture, many technological advances are employed in order to increase productivity of crops. In particular, pests and weeds can destroy or compete with the crop, causing losses and, hence, diminishing productivity. This problem, present since the beginning of agriculture, was addressed by using pesticides, substances that can kill these pests or weeds. Since the first known use of a substance to that end – sulfur, used in Sumer around 2000 BC (TAYLOR; HOLLEY; KIRK, 2007) –, many other substances with similar effects have been discovered. However, pesticides can also have negative effects over environment and human health, which makes these substances subject to regulation and can ultimately lead to the prohibition of some of them – the most emblematic case is that of DDT, once a widely used insecticide which adverse environmental and human health effects were neglected, until the publication of Rachel Carson's book, Silent Spring (CARSON; DARLING; DARLING, 1962), which resulted in a public outcry against DDT and to its ban.

Nowadays, glyphosate (N-phosphonomethylglycine) is the herbicide under the spotlight. It is the most used herbicide in the world, and its use rose specially after the introduction of genetically engineered crops resistant to its action. It is currently classified as a low toxicity pesticide, with little to no effect considering exposure to environmental relevant concentrations. Recently, however, this lack of toxicity has been challenged, with studies showing that this might not be the case and glyphosate can have serious effects on human health, even at concentrations below regulatory limits (BENACHOUR et al., 2007; MESNAGE et al., 2014; MESNAGE et al., 2015).

This work provides empirical evidence of glyphosate's adverse effects on human health (specifically, on infant health), using data from Brazil at municipality level between 2000 and 2009. Unlike previous literature that studies the relationship between glyphosate and health outside a laboratory environment (SATHYANARAYANA et al., 2010; RULL; RITZ; SHAW, 2006; ARBUCKLE; LIN; MERY, 2001), this work establishes a causal relationship, by exploiting the introduction of genetically engineered soy in Brazil (which made glyphosate use in cultivation of soy rise significantly) and the country's hydrological structure. Our results show an increase in low weight births and infant mortality, with effects concentrated on causes most likely affected by glyphosate exposure and on infants exposed during the first trimester of pregnancy, when the fetus is more susceptible to adverse developmental effects by pesticides (SADLER, 2012; FRANK, 2016).

Regarding the literature on pesticides effects on health, most of the existing studies focus on small populations directly exposed to pesticides, living in agricultural communities, and/or only look at correlations, not discussing causality. Also, some works do not focus on infant health,

which can raise concerns about the results, since it would be important to have an exposure history for the population studied. Antle e Pingali (1994) use farm-level surveys and health data collected from farmers in Philippines, in rice producing areas, to investigate health effects of pesticides on farmers and the consequence it has on production, finding a negative effect of pesticides on farmer health and a positive impact of farmer health on production. The authors use a health production function, based on the environmental economics literature, to assess the health effects on production and evaluate the health effects of pesticides simply estimating a model of the health impairment variable as a function of age, nutritional status (proxied by weight/height ratio), dummies indication smoking and drinking, and number of times and types of chemicals applied. When estimating the effect of pesticides on health, the authors do not look at effects of pesticides separately; they look at the impact of herbicides and insecticides in general, only distinguishing between toxicity categories using the classification created by the World Health Organization. Antle, Cole e Crissman (1998) replicate Antle e Pingali (1994) for a potato producing region of Ecuador, also finding a negative effect of pesticides on farmer health and a positive effect of health on production.

Arbuckle, Lin e Mery (2001) use the Ontario Farm Family Health Study to analyze the relationship between pesticide exposure of farmers population in Ontario and spontaneous abortion, finding an increased risk of spontaneous abortion for populations exposed to various types of pesticides, including glyphosate. The authors exploit information they have on timing of exposition and on more specific group of parents, but they only use odds ratios, not discussing causality of the associations they find. Sathyanarayana et al. (2010) use the Agricultural Health Survey to study the relationship between maternal pesticide use and birth weight in Iowa and North Carolina. Results of the study show an association of carbaryl with birth weight, but no association between birth weight and first-trimester pesticide tasks, although, as the authors indicate, they have no data on temporal specificity of individual pesticide exposures prior to or during pregnancy. Furthermore, there is no discussion regarding causality.

Winchester, Huskins e Ying (2009) investigate whether births with conception during months when surface water has highest concentration of agrochemical have higher risk of birth defects, using United States Geological Survey's National Water Quality Assessment data and United States Centers for Disease Control and Prevention natality data sets. The authors find a significant association between season of elevated agrochemicals and birth defects in children conceived in these months but, as the authors observe, their study does not prove a causal link. Siqueira et al. (2010) study the the association between pesticide use and prematurity, low weight and congenital abnormality at birth, infant death by congenital abnormality, and fetal death in Brazil, finding a correlation between pesticide use and prematurity, low birth weight, and congenital abnormality.

The main problem with these studies is that none of them address the endogeneity issue that arises because of the possible correlation between exposure to pesticides and other variables

that also affect health. It is likely that people who expose more themselves to pesticides also engage in other risky behaviors that also affect health, like drinking, drug use, disregard for hygiene, among others. Without addressing this problem, the studies previously mentioned are most likely overestimating the effects of pesticides on health. Even in studies that try to control for some of these factors, this problem most likely still exists, since many of these behaviors are unobserved.

The only empirical study we know that has an explicit concern in identifying a causal effect of agrochemicals on health (particularly on infant health) is Frank (2016), which exploits a mortality shock to bats (a predator of some insects that attack crops) caused by a disease to draw a causal relationship between insecticides and fungicides and infant health. In some sense, our work complements Frank (2016), since we study the effects of an herbicide on infant health.

Because our work exploits exposure through contaminated water, it also contributes to the large body of literature regarding causal effects of pollution on health – and particularly on infant health. Most of this literature focus on air pollution, but there are also some works that study adverse effects of exposure to water pollution. Regarding air pollution, Currie e Neidel (2005) investigate the impact of reduction of air pollution in California in the 1990s on infant health, using weekly variation in pollution within zip codes, months, and years, finding that high levels of postnatal exposure to CO have an important effect on infant mortality. Chay e Greenstone (2003) assess the effect of a reduction in total suspended particulates on infant health using recession as an exogenous shock, finding a decline in the infant mortality rate and suggesting that fetal exposure is the main mechanism, since most of this effect is due to less deaths occurring within one month of birth. Clay, Lewis e Severnini (2016) exploit 20th century expansion of US power grid, with opening of new coal-fired electricity generation facilities, to investigate the effects of air pollution on infant health and its links with housing values and rental prices. The authors find that air pollution caused by burning coal for electricity lead to higher infant mortality rates and lower housing values and rental prices. Regarding the effect of water pollution on health, Brainerd e Menon (2014) study the effect of fertilizers in water on infant and child health using water quality data and data on child health outcomes from Demographic and Health Surveys of India, exploiting the seasons of fertilizer application on different crops (summer crops an winter crops). They find that higher concentrations of chemicals in month of conception increases mortality, specially neonatal mortality, and presence of chemical in water during the first month is associated with worse health outcomes for children. Ebenstein (2012), exploiting variation in pollution across China's river basins measured by the country's nationwide monitoring system, investigate the relationship between water quality and cancer incidence, using OLS, finding that a deterioration of water quality increases incidence of digestive cancers. The author addresses concerns regarding causality by exploiting exogenous variation in rainfall and distance from river's headwaters and estimating 2SLS models.

The main contribution to the literature of our work is to provide estimates of the causal

effect on health of the most used agrochemical in the world nowadays – something that, to the best of our knowledge, has not been made before. Our study helps to show that glyphosate can affect health negatively at environmentally relevant concentrations. Therefore, there is room to change policies regarding glyphosate use in order to increase welfare, considering these generally neglected negative health effects and the positive effect glyphosate has on agricultural productivity.

This document is organized as follows: Section 2 has a discussion about glyphosate, the introduction of genetically engineered soy in Brazil and its relationship with glyphosate use, and infant health effects of glyphosate. Section 3 describes the data and the empirical strategy is presented in Section 4. In Section 5, we report our findings, and conclude in Section 6.

2 Background

2.1 Glyphosate

Glyphosate is, nowadays, the most used herbicide in the world. Discovered as an herbicide in 1970 by Monsanto and first commercialized in 1974, under the name Roundup, it is a systemic, non-selective, foliar applied herbicide, also used as a crop desiccant – desiccation is the process of applying herbicides before harvest to speed up the maturation process. It was rapidly adopted by farmers, specially after genetically modified seeds resistant to glyphosate were introduced – notably, the glyphosate resistant soybean, also developed by Monsanto and commercialized under the name Roundup Ready soybean.

In order to understand glyphosate's action and its application process, it is helpful to understand how herbicides can be classified and, particularly, how glyphosate is classified among the existing categories. Following Vats (2015), we can classify herbicides:

1. According to translocation
    - Systemic: herbicides that are translocated in the plant through its vascular system and, hence, affect the whole plan. Systemic herbicides do not act fast, requiring days or weeks to kill weeds.
    - Non-systemic: a non-systemic herbicide affects only the portion of the plant it came in contact with, i.e., it is not translocated through the plant. Non-systemic herbicides act fast, but may require reapplications to kill regrowth or underground plant parts.
2. According to time of application
    - Preplant: herbicides applied to soil before planting. This kind of herbicide needs to get incorporated into the soil (to prevent dissipation) and it kills weeds as they grow.
    - Preemergence: herbicides applied before weeds emerge through the soil. These herbicides let weeds germinate, but kill them as they grow affecting weeds' cell division; preemergence herbicides do not affect weeds after they emerge.
    - Postemergence: herbicides used after weeds emerge through the soil surface. These herbicides are particularly susceptible to rain, since they can be washed off to the soil.
3. According to method of application
    - Soil Applied: herbicides applied directly to the soil and taken up by root or shoot of the emerging seedlings. Can be used either as preplant or preemergence.

- Foliar applied: herbicides applied to the above-ground part of the plant and absorbed by exposed tissues; hence, these herbicides are, in general, postemergence herbicides.

4. According to specificity

   - Selective: herbicides that act on specific plants without affecting others.
   - Non-selective: herbicides that act on every plant they come in contact.

Glyphosate is a systemic, postemergence, foliar applied, non-selective herbicide, i.e., it is used after emergence of weeds, absorbed by their exposed parts, and translocated through the whole plant. Also, it can affect any kind of plant, with the exception of crops genetically modified to resist glyphosate.

Regarding specifically the application in soy, according to the Roundup Ready herbicide leaflet[1], glyphosate can be applied in a single dose or sequentially, in two doses with an interval of 15-20 days between doses. The leaflet also indicates that weeds are best controlled when the herbicide is applied from 20 to 30 days after soy emergence – which, considering Brazilian characteristics, is expected to happen 7-10 days after planting, according to Mundstock e Thomas (2005). Hence, this means that glyphosate is applied from 27 to 60 days after planting. Since soy is planted between October and January in Brazil, glyphosate application season range from November to March.

Glyphosate is applied after mixed with water, by spraying it in the desired area either manually, using sprayers adequate to herbicide application, or by plane. The security interval – minimum interval between the last application and the harvest – is 56 days. There is also an indication of the ideal climatic conditions for application: no more than 28ºC, minimum relative humidity of 55% and maximum wind velocity of 10km/h (3m/s).

2.1.1 Genetically Engineered Soy

Genetically engineered soybean was developed by Monsanto and first commercialized in the US in 1996. In Brazil, the authorization to cultivate genetically engineered soybeans was given, initially, in 1998, but the Judiciary suspended it. In 2003, the government, through a Provisory Measure (*Medida Provisória*), MP 113, later transformed in law 10.688/2003, temporarily authorized commercialization of the transgenic soy production, but also established that producers should incinerate the remaining stock in order to prevent use of genetically engineered seeds in the next crop. However, through the MP 131 (later, law 10.184/2003), the government authorized the producers who still had genetically engineered seeds from the previous season to cultivate them and renewed the authorization to commercialize the product of transgenic soybeans through the MP 223 (transformed in law 11.092/2005). Finally, in 2005, the New Bio-Safety Law (law 11.105/2005) authorized permanently production and commercialization

[1] Available at http://www.monsanto.com/global/br/produtos/documents/roundup-ready-bula.pdf

of genetically engineered soy. The genetically engineered soy use spread fast and, according to USDA (2016), the adoption rate of these seeds in Brazil are at 93%.

The use of genetically engineered soybean is advantageous to farmers since it is resistant to glyphosate-based herbicides (of which the main commercial formulation is Monsanto's Roundup). This facilitates the control of weeds, since producers can use the herbicide even after emergence without harming the crop, and allows farmers to use more productive techniques, like no-tillage planting techniques [2]. In contrast, with traditional seeds, the soil needs to be prepared before planting (tillage) and use of glyphosate-based herbicides after planting and emergence is bound to harm the crop, since this kind of herbicide is non-selective. Hence, one of the consequences is that glyphosate use is expected to rise significantly with adoption of genetically engineered seeds. Indeed, according to the Brazilian Institute of Geography and Statistics (IBGE, 2004; IBGE, 2012), glyphosate use, in terms of percentage of total weight of active ingredients used in herbicides, rose from 48.38% in 2001, when it was used to kill weeds in non cultivated areas, orchards, reforestation, and in cultivated areas before emergence of the culture, to 71.1% in 2009.

An important question about the adoption of genetically engineered soy is about the adoption of the technology by farmers. Two points are of importance in this matter. First, since at least 2001, there are reports of transgenic soy seeds being smuggled from Argentina (USDA, 2001). Second, the Provisory Measures in 2003 and 2004 may also have induced the farmers to adopt the new technology before the New Bio-Safety Law in 2005. Regarding the smuggling, since genetically engineered soy induces a technical change that is labor saving, as argue Bustos, Caprettini e Ponticelli (2016), we can expect an increase in productivity (in terms of output per worker); the same authors show that output per worker in soy is crescent since the 1990's, but there is a sharp increase in mid 2000's (Figure 1), which indicates that a substantial adoption of genetically engineered soy only occurred with the laws regarding the issue, and not with the smuggling in early 2000's. About the second point, the measures adopted by the government, specially in 2003, resulted from a pressure to solve (at least temporarily) the situation of producers mainly from Rio Grande do Sul, where most of the smugglers were located (because of the proximity to Argentina). In 2004, although the commercialization of genetically engineered seeds wasn't definitely authorized yet, there was expectation of another governmental permission to cultivate genetically engineered soy, as Roessing e Lazzarotto (2005) point out. So, it is reasonable to define 2004 as the year of adoption of genetically engineered soy in Brazil for practical purposes.

[2] Tillage is a technique used in agriculture in order to preparate the soil before planting. It consists in mechanical agitation of various types and is used to aerate the soil, loosen the top layer of the soil and mix organic matter and nutrients evenly. However, it also has some important downsides, as it makes the soil lose nutrients and its ability to store water, reduces organic matter, dries the soil before seeding and induces erosion.

2.1.2 Glyphosate and Infant Health

Manufacturers always marketed glyphosate-based herbicides as low toxicity pesticides but, as time passed, claims of adverse health and environmental effects gained attention and many studies tried to assess the hazards that glyphosate-based herbicides can pose. Although there is not a consensus regarding the effects yet (specially the health effects), there is a body of compelling evidence that demonstrates pathways through which glyphosate can act on human body and affect human health. Some works, in particular, show mechanisms of action that are of importance to infant health.

According to Cox (1998), people can be exposed to glyphosate through direct contact in the workplace, through drift[3], by eating contaminated food, by coming in contact with contaminated soil, and by contact with contaminated water (by drinking or bathing). Regarding contamination of water, glyphosate has been found in surface and ground water (BORTLESON; DAVIS, 1997; FRANK et al., 1990; EDWARDS; JR.; KRAMER, 1980; RASHIN; GRABER, 1993; SMITH; MARTIN; CROIX, 1996) and its persistence in water can go up to 60 days (GOLDSBOROUGH; BECK, 1989; GOLDSBOROUGH; BROWN, 1993).

An infant, in particular, can be exposed to glyphosate *in utero*, through contamination of the mother. Regarding the effects on infants *in utero*, Richard et al. (2005) and Benachour et al. (2007) demonstrate that glyphosate (and, in particular, Monsanto's commercial formulation, Roundup) has a toxic effect on human placental cells. Benachour et al. (2007) investigate the effects of glyphosate on human embryonic and placental cells and how these effects are amplified with dose and time, strongly suggesting that exposure to glyphosate may affect fetal development. Also, Benachour e Séralini (2009) show that, even in low concentrations, glyphosate-based herbicides can induce apoptosis and necrosis (thus, have toxic effects) in human embryonic, umbilical, and placental cells. Another possibility is that the infant is exposed directly to glyphosate – and this can happen even *in utero*, since glyphosate can cross the placenta, as Poulsen et al. (2009) show. This can affect the balance of estrogen through its endocrine disruptor activity, affecting the development of testicular cells and testosterone production Richard et al. (2005); Clair et al. (2012); Haverfield et al. (2011)).

Given all this information, we can define how we expect that infants should be affected by glyphosate. Since it damages the placenta,which is responsible for fetus' nutrition and oxygenation (and, hence, for fetus' proper development), we expect glyphosate to increase the proportion of low weight births, preterm births (since placental insufficiency can lead to preterm birth), and births with APGAR score lower than normal. Ultimately, these problems can cause the infant to die, which would be classified by Brazilian Ministry of Health as a fetal death (if death happens before birth) or a death caused by a perinatal period affection (if death occurs after birth) – so, glyphosate is likely to increase fetal deaths and deaths by perinatal affections. Also, since

[3] Exposure through drift is the exposure caused by off-target movement after the application of the pesticide.

glyphosate can also affect the testis, we can expect an increase in deaths caused by geniturinary system diseases (although this effect is expected to be significantly lower, since it affects the testis and, thus, concerns male infants only). The negative developmental effects can also cause malformations, ultimtely leading to infant death, so we also expect an increase in deaths caused by malformations. These effects are likely to be stronger when the fetus is more susceptible to negative developmental effects, what happens early in the pregnancy, during the first trimester (SADLER, 2012; FRANK, 2016); hence, we expect to find stronger effects when looking to those exposed to glyphosate during the first trimester of pregnancy. Also, as Frank (2016) points out, some recent work report sex-selective effects of pesticides (RAUH et al., 2012; LASSITER et al., 2008; HAVILAND; BUTZ; PORTER, 2010) and, although there is no evidence of such effects specifically for glyphosate, sex-selective effects remain a possibility.

3 Data

The main sources of data are the Municipal Agricultural Production dataset, from the Brazilian Institute of Geography and Statistics (IBGE), the mortality and birth database from the Brazilian Ministry of Health and data from the Vegetal Defense Industries Union (SINDIVEG in portuguese). Also, we use data from the FAO Global Agro-Ecologial Zones database, and from the National Waters Agency (ANA in portuguese). All data span the period from 2000 to 2009.

The Municipal Agricultural Production is a annual survey conducted by IBGE which collects information on crops areas, production, average revenue and production value for diverse temporary and permanent crops at municipality level for the whole country. The information is collected by an IBGE's agent in each municipality and, in general, the information is a result of the agent's contacts with producers and agricultural sector technicians, and of her own knowledge about the municipality's agricultural activity. For our purposes, data from soy planted area at municipality level was used. We also used IBGE's estimations of municipalities' GDP and population.

All the data regarding infant mortality and births by municipality is from the Brazilian Ministry of Health, through its system of information (DATASUS). We also obtain from the Ministry of Health data regarding number of hospital beds per municipality, presence of hospitals in each municipality, immunization coverage, and information about municipalities with teams of a major program of basic attention called Family Health Program (*Programa Saúde da Familia*).

We also use hydrological data from the National Waters Agency. The agency provides georreferenced data about the drainage basins of water courses in Brazil, coded using the method developed by Otto Pfafstetter – and, hence, these drainage basins are called ottobasins. A drainage basin of a water course is the area of land (topographically defined) where all precipitation flows to this water course. It includes all the surface water from snowmelt, rain runoff, and the tributaries of the water course, as well as the groundwater. Drainage basins (in our case, ottobasins) are separated by boundaries called drainage divides; precipitation on different sides of a drainage divide will flow into different drainage basins. ANA provides data at different levels of detail, starting from level 1 ottobasins – which are drainage basins at continental level – and with the next levels being subdivisions of these basins. Since levels 1 and 2 ottobasins are excessively large (with some ottobasins covering entire states) and level 4 ottobasins are too small, with an excessive number of municipalities crossing ottobasins and even containing entire ottobasins, we work in our main specifications with ottobasins detailed at level 3.

Ottobasins at this level are 345 in number and have, on average, 19.57 municipalities in each (entirely or partially) and an area of $39532.3km^2$. The median ottobasin has 4 municipalities in it and an area of $9165km^2$. Since the coding is consistent over levels and it provides information

about areas downstream and upstream the main water courses, we also use in some robustness exercises level 4 ottobasins (which are subdivisions of level 3 ottobasins) to identify upstream and downstream areas in each level 3 ottobasin.

From SINDIVEG we obtained data regarding consumption of herbicides. Since data at municipality level is not available, we use data of herbicides consumption by State, in terms of weight of active ingredient consumption, and data on herbicide consumption in soy for the country to construct a variable of herbicide for each municipality. To construct the variable, we take the soy planted area in the municipality, divide by the total soy planted area in the State, multiply by the ratio of herbicides used in the State, and multiply by the use of herbicides in soy. Hence, we assume that use of herbicides in soy is, across municipalities in the same State, proportional to the soy planted area, and that the ratio of herbicides used in any give State and the ratio of herbicides used in soy in the same State are equal. In other words, we are calculating h_{it} according to the following equation:

$$h_{it} = \frac{soyarea_{it}}{soyareastate_{it}} * \frac{herbstate_{it}}{herbbrazil_t} * herbsoybrazil_t \tag{3.1}$$

Here, $soyarea_{it}$ is the soy planted area in municipality i in year t, $soyareastate_{it}$ is the soy planted area in the State of municipality i in year t, $herbstate_{it}$ is the quantity (in tons of active ingredient) of herbicides used in the State of municipality i in year t, $herbbrazil_t$ is the quantity (in tons of active ingredient) of herbicides used in Brazil in year t, and $herbsoybrazil_t$ is the quantity (in tons of active ingredient) of herbicides used in soy in Brazil in year t.

Finally, we use data of potential soy yields from FAO-GAEZ database to construct our instrument. Descriptive statistics (including constructed variables, which construction will be described in the next section) are reported in table 1.

4 Empirical Strategy

We want to estimate the causal effect of herbicides on infant health indicators, exploiting the rise in use of herbicides in soy that occurred in Brazil between 2000 and 2009 as a result of adoption of genetically engineered soybean in the country. Since genetically engineered soy is resistant to a particular active ingredient, glyphosate, the effect we want to estimate should be closely related to the effect of glyphosate on infant health.

A naive strategy to estimate the effect we want would be simply to regress infant health outcomes on a measure of herbicides and a set of controls at municipality level[1]. However, it is likely that the quantity of herbicides used in a municipality is related to unobserved variables that also affect infant health indicators (like rainfall, temperature, agricultural production, and GDP). More specifically, we deal with two sources of endogeneity. First, considering that the rise in herbicide use stem from the adoption of genetically engineered soybean and the consequent rise in glyphosate use, it is likely that the adoption of genetically engineered soybean is related to some characteristics of the municipality that can also be related to infant health indicators, like geographic characteristics or entrepreneurship characteristics. Second, the increased productivity of genetically engineered soybean can generate effects that also affect infant health (e.g., through higher incomes or through a change in the share of rural population).

To deal with the first endogeneity source, we use as instrument the potential yields from FAO-GAEZ database, also used by Bustos, Caprettini e Ponticelli (2016). These potential yields are calculated using a model that accounts for soil and weather characteristics and predicts the maximum attainable yields for soy in a given area. The database also reports these potential yields under different technologies: yields under low technology are those obtained using traditional seeds, no use of chemicals and without mechanization, whereas yields under high technology are those obtained using improved seeds, fertilizers and herbicides, and mechanization. Therefore, areas with greater differences between low and high potentials should have more incentive to switch from traditional soy to genetically engineered soy and, consequently, use more herbicides (glyphosate-based herbicides, in particular) after adoption of genetically engineered soy. Thus, since we consider the adoption to happen in 2004, potential of each area is equal to low potential until 2003 and equal to high potential from 2004 onwards.

To deal with the second source of endogeneity, we use the hydrological structure to construct a variable of exposure to herbicides (per unit of area) for each municipality. The main idea behind this variable is that use of herbicides in a given municipality affects not only that municipality, but also others through contamination of bodies of water. Therefore, use of

[1] Since borders of municipalities can change over time, we use the concept of Minimum Comparable Areas (in portuguese, *Áreas Mínimas Comparáveis – AMCs*) developed by IBGE, to be able to compare municipalities over time. We also use the update made by Bustos, Caprettini e Ponticelli (2016) of the AMCs up to 2010.

herbicides in one municipality will affect other municipalities in the same ottobasin, since these municipalities share the same water resources. It is important to notice that we assume that, conditional on our control variables (income per capita, number of hospital beds, existence of hospitals, immunization coverage, and existence of Family Allowance and Family Health programs), the expansion in soy production in any given municipality does not affect other municipalities through channels other than the contamination of bodies of water.

We define the exposition to herbicides in soy of a given municipality as the sum of the estimated use of herbicides in soy of all municipalities of the ottobasin except the given municipality divided by the total area of the ottobasin. If one municipality is in more than one ottobasin, its contribution to each ottobasin is multiplied by the proportion of its area in each ottobasin; in a similar way, if one municipality is in more than one ottobasin, the contribution of each ottobasin to the exposition of the municipality is weighted by the proportion of the municipality area in each ottobasin.

Since we want to instrument the constructed exposure variable, we have to construct our instrument in a similar fashion. To do this, we assign to each municipality the weighted average of the other municipalities' potentials, with each municipality area in the ottobasin as weight. If a municipality is in more than one ottobasin, we take as instrument the average weighted by the municipality area in each ottobasin.

Formally, combining the two strategies – use of exposition to herbicides and the instrument –, we have the following estimating equations

First stage:

$$herb_{it} = \tilde{\alpha} + \tilde{\gamma} instrument_{it} + \tilde{\beta} X_{it} + \tilde{\delta}_i + \tilde{\pi_{st}} + \epsilon_{it} \tag{4.1}$$

Second stage:

$$health_{it} = \alpha + \gamma \hat{herb}_{it} + \beta X_{it} + \delta_i + \pi_{st} + \varepsilon_{it} \tag{4.2}$$

where $health_{it}$ is an infant health indicator for municipality i in year t, $herb_{it}$ is the exposure to herbicides variable (in tons of active ingredient per km^2) for municipality i in year t, $instrument_{it}$ is the instrument for municipality i in year t, X_{it} are controls, $\tilde{\delta}_i$ and δ_i are municipality fixed effects and we also control for a State-year interaction, $\tilde{\pi_{st}}, \pi_{st}$, since some policies are designed and/or implemented at the State level. Our controls are: log of municipality's GDP per capita, since income can affect infant health; log of hospital beds per capita in municipality, a dummy for hospital presence, and immunization coverage, variables that reflect the municipality's health infrastructure and, hence, related to infant health; and dummies for existence of Family Health Program and Family Allowance Program, federal programs with positive effects on health.

Finally, we weight our estimations by mean births in the period for each municipality.

Also, because of the way our exposure to herbicides variable is constructed, this variable should be correlated between municipalities in the same ottobasin – for example, if two municipalities, A and B, are in an ottobasin with ten other municipalities, the exposure variable for both municipalities will consider the sum of the estimated herbicide use of eleven municipalities: ten common municipalities and only one different (A will consider use in B and B will consider use in A); hence, because of the ten common municipalities, the exposure to herbicides variable of A and B will be correlated. Because of this, we cluster standard errors at the ottobasin level; if a municipality is in more than one ottobasin, we assign to it the ottobasin where most of its area is located in (since, by construction, this is the ottobasin that will contribute more to the variable for the municipality).

5 Results

5.1 Main results

In table 3, we report the results for our main specification, with and without controls, including OLS and reduced form results, for infant mortality. First stages for IV regressions are reported in table 2, with Kleinbergen-Paap rk Wald F statistic reported. We find a significant positive effect of herbicides on infant mortality rate for our main specification, with and without controls. Mean variation of the exposure variable from 2000 to 2009 is approximately 0.013 tons/km^2, which, using our main specification with controls, would result in a rise of approximately 1.55 infants deaths per 1000 births. Taking only a group of causes of infant mortality that we expect to be affected by glyphosate (perinatal period affections, genitourinary tract diseases, and malformations, in terms of chapters of the International Disease Code), we find a significant impact on our main specification with controls, but not without controls[1]. Also, the point estimate is much higher than the point estimate for all the other causes and close to the point estimate for full infant mortality rate, which indicates that the effect we find on infant mortality is concentrated on expected causes. Reduced form coefficients follow the same pattern, but with point estimates for affected causes significant in both cases. IV and reduced form estimates are very different from OLS estimates, even qualitatively, which indicates that, indeed, there is an important bias stemming from endogeneity of genetically engineered soy adoption.

In table 4, we report results for Infant Mortality Rate by age groups: 0-6 days old, 7-27 days old, and 28-364 days old (only the second stage is reported, since the first stage is the same as in table 1). IV and reduced form results indicate that most of the infant mortality effect is due to the effect on infants between 0-6 days old. This is expected, since glyphosate affects infants *in utero* and infants between 0 and 6 days old are most likely to die from factors that affect them during gestational period (since period of exposition to other factors are extremely reduced). There is also a statistically significant effect on infants with age between 7 and 27 days old, albeit much smaller than the effect on infants with age between 0 and 6 days old. We do not find any effect on infants with 28 or more days old, when death is most likely to be caused by factors to which infants are exposed after birth.

Regarding results for other indicators of infant health, reported in table 5, we find positive and significant results, both with and without controls, for Low Weight Birth Rate (births with less than 2500g per 1000 births), with reduced form results following the exact same pattern. Using again the mean variation of the exposure variable from 2000 to 2009, approximately 0.013 tons/km^2, we estimate that there was a rise of approximately 2.13 low weight births per 1000 births. For Preterm Birth Rate (births with less than 37 gestational weeks per 1000 births) and

[1] This lack of significance in this case can be due to imprecision on estimating the coefficient.

Low APGAR Scores Birth Rates (here, less than 6) for APGAR scores at 1 minute and at 5 minutes after birth, all point estimates are positive, which also points in the direction of worse infant health conditions (as in the case of Low Weight Birth Rate), but none of these results are significant, either in reduced form or in IV, with or without controls. In table 6, we report results for other indicators: fetal mortality rate (fetal deaths per 1000 births plus fetal deaths), log of fetal deaths and log of births. IV and reduced form estimates, although positive, are not significant, with or without controls.

We report IV results with controls for male and female infants separately in table 7, for Infant Mortality Rate (for full rate and breaking in affected and other causes), Low Weight Birth Rate, Preterm Birth Rate, and Low APGAR Scores Rates. We do this since some recent studies indicate that pesticides can have a sex-selective effect, as Frank (2016) points out, but we find very similar point estimates for both groups and results very similar to our previous results [2]. Since these sex-selective effects are not reported in literature for glyphosate specifically, this could be an indication that exposure to glyphosate do not have sex-selective effects like other kinds of pesticides, but this issue certainly requires further investigation in medical literature. We also report IV results for the ratio of female/male births, which is not significant.

5.2 Timing of exposure

In table 8, we assess, through reduced form estimates, the effect of exposure to herbicides during pregnancy on infant mortality rate, estimating the month of conception from data on year and month of birth, considering 9 months of pregnancy, and using information about the period of herbicide use in soy, from November to March. We calculate the infant mortality rate for each month-year (by month-year of birth; in other words, for each month-year, we are calculating the IMR for infants born in that month-year) and, for each trimester of exposure, regress it on potentials interacted with dummies of exposure in the trimester; in other words, considering exposure in trimester T, our independent variable is

$$\widetilde{instrument}_{imy} * 1\{\text{exposed in trimester T}\} \tag{5.1}$$

where the subscripts i, m, y indicate, respectively, municipality, month, and year, and $\widetilde{instrument}_{imy}$ is the same instrument as before, but adjusted considering exposition in trimester T. For instance, if we consider the first trimester of pregnancy, since the shift from low potential to high potential happens in 2004, an infant born in January 2004 will face the low potential, since the first trimester of pregnancy is entirely in 2003, whereas an infant born in July 2004 will have one month of the first trimester of pregnancy in 2004 and, hence, face the high potential.

Our estimates for the first trimester of pregnancy, when the fetus is more susceptible to negative developmental effects caused by pesticides (SADLER, 2012; FRANK, 2016), are

[2] Some estimates are significant for one group, but not for the other. Since the point estimates are similar, it is likely that this is due to a lack of precision, not that the effects are different between groups.

the highest and consistently significant. Moreover, all the estimates for the first trimester of pregnancy are similar, which gives us more confidence on this result. The positive and significant results we found for 1st trimester before conception and for 1st trimester of life also make sense. In the first case, there is a possibility that a residual remains on mother and affects the embryo – the lower coefficient than that of first trimester exposure supports this idea and, also, other works (like Arbuckle, Lin e Mery (2001)) look to windows of exposure right before conception. Another possibility is that we find an effect before the conception due to measurement error, since we estimate the month of conception considering that the length of all pregnancies is 9 months. In the second case, since infants are more fragile in the first trimester of life than in subsequent trimesters, and since, when they are born, children may be exposed to glyphosate not only through their mother (via breastfeeding), but also through contaminated water, it is not necessarily unexpected to have a significant positive effect for exposure during the first trimester of life.

5.3 Robustness

In table 9, results for Infant Mortality Rate using population 0-1 years old are reported, since it has less variability than births and, hence, the estimates may gain precision [3]. As before, we report results for our main specification without controls and with controls. Qualitatively, the infant mortality rate results are identical to the former ones, but the estimates are lower. Using the mean variation of the herbicide exposure variable between 2000 and 2009, 0.013 tons/km^2, the estimate for infant mortality rate with controls yield a rise of 1.03 more infant deaths per 1000 individuals with 0-1 years old – which still seems quantitatively high. Results for ICD-10 chapters more likely affected by glyphosate and other chapters are also qualitatively similar to the main results, but the IV estimation without controls is more precise for the affected chapters, becoming significant.

Since level 4 ottobasins are subdivisions of level 3 ottobasins and with their codes we can identify, inside each level 3 ottobasin, which level 4 ottobasins are upstream and which are downstream, we can use them to assess the relative position of each municipality in each level 3 ottobasin. We do this in tables 10, 11, and 12, modifying our variable of estimated exposure to herbicides to include, for each municipality, only the contribution of the municipalities in the same level 3 ottobasin upstream. Our instrument is also adjusted to correspond to the same areas. The idea is that use of herbicides in one municipality will affect only other municipalities in the same ottobasin downstream. As before, we report results without controls and with controls. Results for Infant Mortality Rate, reported in table 11, are similar to our previous results, with point estimates close to the previous Infant Mortality Rate point estimates. As in our main specification, reduced form and IV results for affected causes are positive, significant, and point estimates are similar to IMR point estimates, with estimates for other causes being statistically

[3] More specifically, we take the mortality rates as infant deaths per 1000 individuals with 0-1 years old.

insignificant and estimates close to 0. Regarding the other indicators (Low Weight Birth Rate, Preterm Birth Rate, and Low APGAR Scores Rates), reported in table 12, we do not find any significant effect – even for Low Weight Birth Rate, the one we have found a positive significant effect before.

We also analyze the timing of the effects in the following fashion. For each year t, starting from 2001, we regress the difference of the indicator between t and 2000 on our instrument, assuming that the timing of adoption of genetically engineered soy is in year t, and on dummies for State. We do this for the results we find significant in our main specification, Infant Mortality Rate – using full Infant Mortality Rate and breaking in rates for affected causes and other causes – and Low Weight Birth Rate. Figure 2 shows that, for Infant Mortality Rate, the effect seems to appear in 2004. Moreover, if we observe our two groups of mortality causes, affected and other causes, although we do not find significant effects, the pattern suggests what we expected: before 2004, the estimated coefficients are close to 0 and seem to follow parallel paths and, in 2004, the coefficient for affected causes rises, whereas coefficient for other causes stays close to the previous values (Figure 3). Low Weight Birth Rate coefficients follow a similar pattern than Infant Mortality Rate coefficient, but with a delay, as can be seen from Figure 4: it starts to rise in 2005.

6 Conclusion

In this work, we assess the effect of herbicides (and particularly of glyphosate) on infant health in Brazil, between 2000 and 2009, exploiting the introduction of genetically engineered soybean in the country and the consequent rise in glyphosate use. Since we believe that endogeneity is an issue in the analysis, we deal with it by using the country's hydrological structure and also an instrument based on potential soy yields obtained under high and low technologies, calculated by FAO-GAEZ. In our results, we find a positive impact of our variable of exposure to herbicides on infant mortality – particularly on causes of death that can be linked to glyphosate via recent medical and biochemical literature regarding effects of glyphosate on human cells – and on the proportion of low weight births (births with less than 2500g). Our main specification indicates that, on average, from 2000 to 2009, the rise in herbicide use resulted in additional 1.55 infant deaths per 1000 births and 2.13 low weight births per 1000 births in Brazil. Although quantitatively our results can be unreasonably high (particularly in the case of Infant Mortality Rate), the consistency of qualitative results under different specifications gives us confidence that there is a causal and negative effect of glyphosate on infant health.

Recently, there has been a reexamination of claims that glyphosate is a safe pesticide, with little to no effect on human health, by scientists, specially by biochemists, using controlled laboratory experiments. Our work increments this literature providing evidence that glyphosate can affect human health in a real setting. Since these effects are generally neglected by current regulation of glyphosate use, this can have important policy implications, providing subsidy to new regulatory marks for glyphosate-based herbicides that take into account the effects of glyphosate on human health, even in environmentally relevant concentrations.

As more detailed data of pesticide use become available from Brazilian Institute of the Environment and Renewable Natural Resources (IBAMA), it will be possible to investigate further the issue, mitigating the error we have on our measure of herbicide use. Also, further research can assess health impact of pesticides using data on watercourses instead of drainage basins. Another direction of further research is to exploit introduction of other genetically engineered seeds using similar strategies.

7 Tables

Tabela 1 – Descriptive Statistics

Variable	Mean	SD	Min	Max	N
Births	707.3	3685	2	203922	42580
Infant Mortality Rate	18.51	15.73	0	1000	42580
Infant Mortality Rate - Affected Causes	12.71	11.97	0	666.7	42580
Infant Mortality Rate - Other Causes	5.807	8.791	0	333.3	42580
Low Weight Births Rate (< 2500g)	73.46	30.32	0	454.5	42580
Preterm Births Rate (< 36 weeks)	60.78	48.84	0	844.3	42580
Hospital Beds (annual mean)	108.3	634.8	0	28563	42580
Hospital Dummy	0.765	0.424	0	1	42580
Family Health Program Dummy	0.842	0.364	0	1	42580
Family Allowance Program Dummy	0.600	0.490	0	1	42580
Vaccination Coverage	0.7863	0.1168	0.1531	6.374	42580
Population	42432.7	223493.1	789	11039573	42580
Population 0-1 years old	1544	7246	18	370864	42580
GDP (R$ 1000,00)	494128.9	4983790	2464.9	389284929.3	42580
Herbicide Exposition (tons/km^2)	0.0132	0.0214	0	0.117	42580
Δ Herbicide Exposition 2000-2009	0.0128	0.0202	$-3.95*10^{-6}$	0.0862	4258
Low Potential	0.303	0.0989	0	0.551	4258
High Potential	2.130	0.636	0	3.464	4258
Δ Potential in Ottobasin	1.827	0.594	0	3.048	4258
Number of AMCs in Ottobasin	19.57	44.00	1	403	3450

Tabela 2 – First Stage - Main specification

	Herbicides Ottobasin	Herbicides Ottobasin
Instrument	0.00714***	0.00716***
	(0.00171)	(0.00170)
F-statistic	17.39	17.67
AMC FE	Yes	Yes
Controls	No	Yes
State-Year FE	Yes	Yes
Observations	42580	42580
Clusters	184	184

Controls are GDP per capita, existence of hospitals, hospital beds per capita, existence of Family Health Program, existence of Family Allowance program and vaccination coverage. Observations weighted by average number of births or average population 0-1 years old in the AMC between 2000 and 2009. Standard errors clustered by ottobasin. Since one AMC can be in more than one ottobasin, to each AMC is assigned the ottobasin in which the most part of its area is located in. Kleibergen-Paap rk Wald F statistic reported.
*** $p<0.01$, ** $p<0.05$, * $p<0.1$

Tabela 3 – Second Stage - Mortality Results - Main Specification

	OLS			Reduced Form			IV		
	IMR	IMR Affected	IMR Others	IMR	IMR Affected	IMR Others	IMR	IMR Affected	IMR Others
A. No Controls									
Herbicides Ottobasin (Tons AI/km^2)	−2.811	−0.396	−2.415	0.885**	0.834*	0.0517	123.9**	116.7	7.241
	(16.87)	(9.229)	(10.53)	(0.359)	(0.447)	(0.227)	(63.31)	(74.04)	(31.37)
Observations	42580								
Clusters	184								
B. With Controls									
Herbicides Ottobasin (Tons AI/km^2)	−1.654	1.536	−3.190	0.886**	0.802*	0.0535	119.6**	112.1*	7.479
	(17.62)	(9.307)	(10.77)	(0.341)	(0.411)	(0.218)	(59.25)	(67.71)	(30.11)
Observations	42580								
Clusters	184								
AMC FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
State-Year FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Controls are GDP per capita, existence of hospitals, hospital beds per capita, existence of Family Health Program, existence of Family Allowance program and vaccination coverage. Observations weighted by average number of births in the AMC between 2000 and 2009. Standard errors clustered by ottobasin. Since one AMC can be in more than one ottobasin, to each AMC is assigned the ottobasin in which the most part of its area is located in.
*** p<0.01, ** p<0.05, * p<0.1

Tabela 4 – Second Stage - Mortality by Age Group

	OLS			Reduced Form			IV		
	IMR 0-6 days	IMR 7-27 days	IMR 28-364 days	IMR 0-6 days	IMR 7-27 days	IMR 28-364 days	IMR 0-6 days	IMR 7-27 days	IMR 28-364 days
A. No Controls									
Herbicides Ottobasin (Ton IA/km^2)	−5.297	5.174**	−3.162	0.667**	0.146*	0.0573	93.39*	20.45*	8.025
	(8.131)	(2.505)	(10.43)	(0.320)	(0.0811)	(0.152)	(55.38)	(12.05)	(21.00)
Observations	42580								
Clusters	184								
B. With Controls									
Herbicides Ottobasin (Ton IA/km^2)	−4.278	5.390**	−3.216	0.644**	0.143*	0.0546	89.94*	19.94*	7.635
	(8.104)	(2.584)	(10.70)	(0.297)	(0.0815)	(0.152)	(51.18)	(11.95)	(20.95)
Observations	42580								
Clusters	184								
AMC FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
State-Year FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Controls are GDP per capita, existence of hospitals, hospital beds per capita, existence of Family Health Program, existence of Family Allowance program and vaccination coverage. Observations weighted by average number of births in the AMC between 2000 and 2009. Standard errors clustered by ottobasin. Since one AMC can be in more than one ottobasin, to each AMC is assigned the ottobasin in which the most part of its area is located in.
*** p<0.01, ** p<0.05, * p<0.1

Tabela 5 – Second Stage - Other Infant Health Indicators - Main Specification

	OLS				Reduced Form				IV			
	Low Weight	Preterm	Apgar 1min <6	Apgar 5min <6	Low Weight	Preterm	Apgar 1min <6	Apgar 5min <6	Low Weight	Preterm	Apgar 1min <6	Apgar 5min <6
A. No Controls												
Herbicides Ottobasin (Tons AI/km^2)	44.41	135.1**	−13.22	−10.80	1.200**	1.220	1.146	2.431	167.9**	170.8	160.4	340.2
	(32.55)	(56.85)	(45.18)	(22.94)	(0.530)	(1.940)	(2.082)	(2.105)	(76.41)	(257.9)	(289.7)	(303.1)
Observations	42580											
Clusters	184											
B. With Controls												
Herbicides Ottobasin (Tons AI/km^2)	45.69	128.7**	−11.96	−13.81	1.172**	1.383	1.159	2.466	163.7**	193.2	161.9	344.6
	(32.53)	(56.22)	(46.34)	(22.48)	(0.531)	(1.824)	(2.045)	(2.069)	(74.90)	(241.6)	(284.5)	(299.0)
Observations	42580											
Clusters	184											
AMC FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
State-Year FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Controls are GDP per capita, existence of hospitals, hospital beds per capita, existence of Family Health Program, existence of Family Allowance program and vaccination coverage. Observations weighted by average number of births in the AMC between 2000 and 2009. Standard errors clustered by ottobasin. Since one AMC can be in more than one ottobasin, to each AMC is assigned the ottobasin in which the most part of its area is located in.
*** p<0.01, ** p<0.05, * p<0.1

Tabela 6 – Second Stage - Fetal mortality and log(births) - Main Specification

	OLS			Reduced Form			IV		
	FMR	log(fetal deaths)	log(births)	FMR	log(fetal deaths)	log(births)	FMR	log(fetal deaths)	log(births)
A. No Controls									
Herbicides Ottobasin (Tons AI/km^2)	−21.58**	−1.685**	−0.161	0.428	0.0509	0.0154	60.00	7.894	2.157
	(8.580)	(0.816)	(0.463)	(0.429)	(0.0468)	(0.00990)	(65.29)	(8.006)	(1.601)
Observations	42580								
Clusters	184								
B. With Controls									
Herbicides Ottobasin (Tons AI/km^2)	−20.06**	−1.596**	−0.181	0.408	0.0489	0.0157	57.13	7.584	2.192
	(8.141)	(0.803)	(0.442)	(0.402)	(0.0435)	(0.00993)	(60.74)	(7.426)	(1.602)
Observations	42580								
Clusters	184								
AMC FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
State-Year FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Controls are GDP per capita, existence of hospitals, hospital beds per capita, existence of Family Health Program, existence of Family Allowance program and vaccination coverage. Observations weighted by average number of births in the AMC between 2000 and 2009 or, for fetal mortality, average number of births plus fetal deaths. Standard errors clustered by ottobasin. Since one AMC can be in more than one ottobasin, to each AMC is assigned the ottobasin in which the most part of its area is located in.
*** p<0.01, ** p<0.05, * p<0.1

Tabela 7 – Results by Gender - With controls - IV results

	Herbicides Ottobasin	IMR	IMR Affected	IMR Others	Low Weight	Preterm	Apgar 1min < 6	Apgar 5min < 6	Ratio female/male
A. Male									
First Stage									
Instrument	0.00716***								
	(0.00170)								
F stat	17.66								
Second Stage									
Herbicides		114.8*	101.5	13.30	187.3**	181.7	177.6	363.5	−0.255
		(60.77)	(67.29)	(33.47)	(74.34)	(224.3)	(284.3)	(297.8)	(0.210)
Observations	42580								
Clusters	184								
B. Female									
First Stage									
Instrument	0.00716***								
	(0.00170)								
F stat	17.66								
Second Stage									
Herbicides		109.7*	109.9*	−0.165	145.5	227.2	141.7	321.6	
		(57.34)	(65.09)	(29.87)	(101.6)	(267.5)	(287.8)	(300.2)	
Observations	42580								
Clusters	184								
AMC FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
State-Year FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Controls	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Controls are GDP per capita, existence of hospitals, hospital beds per capita, existence of Family Health Program, existence of Family Allowance program and vaccination coverage. Observations weighted by average number of births in the AMC between 2000 and 2009. Standard errors clustered by ottobasin. Since one AMC can be in more than one ottobasin, to each AMC is assigned the ottobasin in which the most part of its area is located in. Kleibergen-Paap rk Wald F statistic reported.
*** p<0.01, ** p<0.05, * p<0.1

Tabela 8 – Mortality results by trimester - Reduced Form

	IMR	IMR	IMR	IMR	IMR	IMR	IMR	IMR	IMR	IMR	IMR	IMR	IMR	IMR
2nd trimester before conception	−0.147													0.00157
	(0.158)													(0.150)
1st trimester before conception		0.0233												0.197*
		(0.140)												(0.109)
1st trimester of pregnancy			0.403*										0.584*	0.498*
			(0.223)										(0.327)	(0.288)
2nd trimester of pregnancy				0.135									0.0969	0.161
				(0.159)									(0.147)	(0.157)
3rd trimester of pregnancy					−0.185								−0.0598	0.0139
					(0.172)								(0.223)	(0.208)
1st trimester of life						−0.0751							0.242	0.412**
						(0.165)							(0.151)	(0.181)
2nd trimester of life							−0.0114						−0.369	−0.265
							(0.159)						(0.404)	(0.304)
3rd trimester of life								0.274					0.235*	0.0999
								(0.194)					(0.126)	(0.136)
4th trimester of life									−0.270					−0.306
									(0.170)					(0.284)
5th trimester of life										−0.270				−0.332*
										(0.211)				(0.181)
6th trimester of life											−0.100			−0.286
											(0.206)			(0.257)
7th trimester of life												0.375		0.292
												(0.265)		(0.224)
AMC FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
State-Month FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
State-Year FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Observations	504746													
Clusters	184													

Observations weighted by average number of births in the AMC between 2000 and 2009. Standard errors clustered by ottobasin.
Since one AMC can be in more than one ottobasin, to each AMC is assigned the ottobasin in which the most part of its area is located in.

Tabela 9 – Mortality results using population 0-1 years old

	OLS			Reduced Form			IV		
	IMR	IMR Affected	IMR Others	IMR	IMR Affected	IMR Others	IMR	IMR Affected	IMR Others
A. No Controls									
Herbicides Ottobasin (Tons AI/km^2)	0.309	0.874	−0.565	0.590***	0.487**	0.103	82.98**	68.48*	14.49
	(9.507)	(5.304)	(5.315)	(0.209)	(0.242)	(0.105)	(39.26)	(41.19)	(14.49)
Observations	42580								
Clusters	184								
B. With Controls									
Herbicides Ottobasin (Tons AI/km^2)	0.810	1.615	−0.805	0.569***	0.466**	0.103	79.81**	65.41*	14.40
	(9.626)	(5.301)	(5.341)	(0.195)	(0.220)	(0.104)	(36.24)	(37.38)	(14.66)
Observations	42580								
Clusters	184								
AMC FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
State-Year FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Controls are GDP per capita, existence of hospitals, hospital beds per capita, existence of Family Health Program, existence of Family Allowance program and vaccination coverage. Observations weighted by average number of individuals with 0-1 years old in the AMC between 2000 and 2009. Standard errors clustered by ottobasin. Since one AMC can be in more than one ottobasin, to each AMC is assigned the ottobasin in which the most part of its area is located in.
*** p<0.01, ** p<0.05, * p<0.1

Tabela 10 – First Stage - Using data of position in the ottobasin

	Herbicides Ottobasin	Herbicides Ottobasin
Instrument	0.00482***	0.00486***
	(0.00134)	(0.00134)
F-statistic	12.99	13.20
AMC FE	Yes	Yes
Controls	No	Yes
State-Year FE	Yes	Yes
Observations	42580	42580
Clusters	184	184

Controls are GDP per capita, existence of hospitals, hospital beds per capita, existence of Family Health Program, existence of Family Allowance program and vaccination coverage. Observations weighted by average number of births in the AMC between 2000 and 2009. Standard errors clustered by ottobasin.
Since one AMC can be in more than one ottobasin, to each AMC is assigned the ottobasin in which the most part of its area is located in. Kleibergen-Paap rk Wald F statistic reported.
*** p<0.01, ** p<0.05, * p<0.1

Tabela 11 – Second Stage - Mortality Results - Using data of position in the ottobasin

	OLS			Reduced Form			IV		
	IMR	IMR Affected	IMR Others	IMR	IMR Affected	IMR Others	IMR	IMR Affected	IMR Others
A. No Controls									
Herbicides Ottobasin (Tons AI/km^2)	10.76	5.492	5.272	0.530***	0.543**	−0.0129	110.0**	112.7*	−2.678
	(12.47)	(8.649)	(7.440)	(0.171)	(0.262)	(0.139)	(45.80)	(64.29)	(28.86)
Observations	42580								
Clusters	184								
B. With Controls									
Herbicides Ottobasin (Tons AI/km^2)	11.29	6.515	4.772	0.488***	0.508**	−0.0197	100.4**	104.5*	−4.053
	(12.79)	(8.594)	(7.666)	(0.165)	(0.237)	(0.129)	(41.47)	(57.01)	(26.67)
Observations	42580								
Clusters	184								
AMC FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
State-Year FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Controls are GDP per capita, existence of hospitals, hospital beds per capita, existence of Family Health Program, existence of Family Allowance program and vaccination coverage. Observations weighted by average number of births in the AMC between 2000 and 2009. Standard errors clustered by ottobasin. Since one AMC can be in more than one ottobasin, to each AMC is assigned the ottobasin in which the most part of its area is located in.
*** p<0.01, ** p<0.05, * p<0.1

Tabela 12 – Second Stage - Other Infant Health Indicators - Using data of position in the ottobasin

	OLS				Reduced Form				IV			
	Low Weight	Preterm	Apgar 1min <6	Apgar 5min <6	Low Weight	Preterm	Apgar 1min <6	Apgar 5min <6	Low Weight	Preterm	Apgar 1min <6	Apgar 5min <6
A. No Controls												
Herbicides Ottobasin (Tons AI/km^2)	44.30	126.7***	−76.49	−17.00	0.260	1.019	−0.585	0.116	53.95	211.4	−121.4	24.09
	(30.58)	(41.99)	(57.29)	(24.64)	(0.457)	(1.353)	(1.044)	(0.680)	(89.72)	(256.5)	(212.8)	(139.7)
Observations	42580											
Clusters	184											
B. With Controls												
Herbicides Ottobasin (Tons AI/km^2)	45.03	122.4***	−75.71	−18.41	0.250	1.116	−0.495	0.167	51.47	229.7	−101.9	34.31
	(30.38)	(41.72)	(58.02)	(24.64)	(0.457)	(1.284)	(1.032)	(0.643)	(86.04)	(239.0)	(208.3)	(131.0)
Observations	42580											
Clusters	184											
AMC FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
State-Year FE	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

Controls are GDP per capita, existence of hospitals, hospital beds per capita, existence of Family Health Program, existence of Family Allowance program and vaccination coverage. Observations weighted by average number of births in the AMC between 2000 and 2009. Standard errors clustered by ottobasin. Since one AMC can be in more than one ottobasin, to each AMC is assigned the ottobasin in which the most part of its area is located in.
*** p<0.01, ** p<0.05, * p<0.1

8 Figures

Figura 1 – Output per worker in soy production, from Bustos, Caprettini, and Ponticelli (2016)

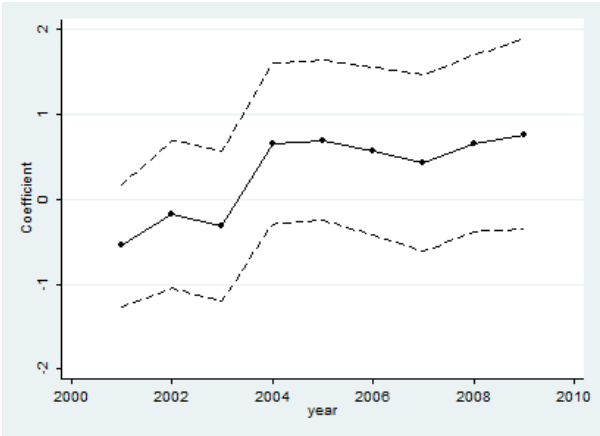

Figura 2 – Effect timing on infant mortality rate - 90% confidence interval

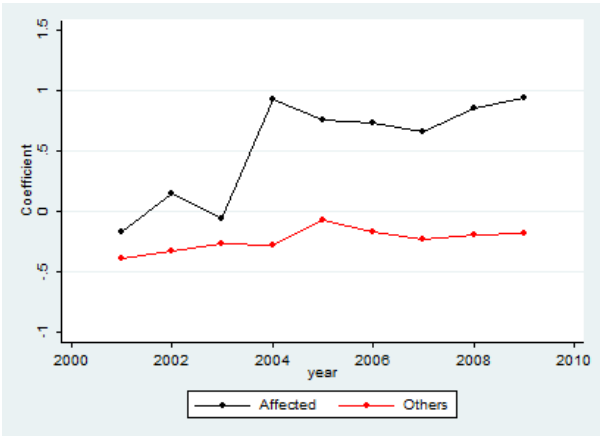

Figura 3 – Effect timing on infant mortality rate - by causes

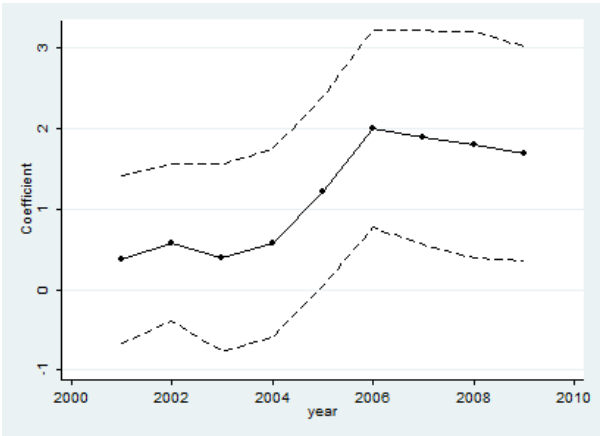

Figura 4 – Effect timing on low weight births rate - 90% confidence interval

References

ANTLE, J. M.; COLE, D. C.; CRISSMAN, C. C. Further evidence on pesticides, productivity and farmer health: Potato production in Ecuador. *Agricultural Economics*, v. 18, n. 2, p. 199–207, 1998.

ANTLE, J. M.; PINGALI, P. L. Pesticides, productivity, and farmer health: A Philippine case study. *Am. J. Agric. Econ.*, v. 76, n. 3, p. 418–430, 1994.

ARBUCKLE, T. E.; LIN, Z.; MERY, L. S. An Exploratory Analysis of the Effect of Pesticide Exposure on the Risk of Spontaneous Abortion in an Ontario Farm Population. *Environmental Health Perspectives*, v. 109, n. 8, p. 851–857, 2001.

BENACHOUR, N. et al. Time- and Dose-Dependent Effects of Roundup on Human Embryonic and Placental Cells. *Arch. Environ. Contam. Toxicol.*, v. 53, p. 126–133, 2007.

BENACHOUR, N.; SéRALINI, G. E. Glyphosate formulations induce apoptosis and necrosis in human umbilical, embryonic, and placental cells. *Chem. Res. Toxicol.*, v. 22, n. 1, p. 97–105, 2009.

BORTLESON, G. C.; DAVIS, D. A. *Pesticides in selected small streams in the Puget Sound Basin, 1987-1995*. [S.l.], 1997.

BRAINERD, E.; MENON, N. Seasonal effects of water quality: The hidden costs of the Green Revolution to infant and child health in India. *Journal of Development Economics*, v. 107, p. 49–64, 2014.

BUSTOS, P.; CAPRETTINI, B.; PONTICELLI, J. Agricultural Productivity and Structural Transformation: Evidence from Brazil. *American Economic Review*, v. 106, n. 6, p. 1320–1365, 2016.

CARSON, R.; DARLING, L.; DARLING, L. *Silent Springer*. [S.l.]: Boston : Houghton Mifflin ; Cambridge, Mass. : Riverside Press, 1962.

CHAY, K. Y.; GREENSTONE, M. The Impact of Air Pollution on Infant Mortality: Evidence from Geographic Variation in Pollution Shocks Induced by a Recession. *The Quarterly Journal of Economics*, v. 118, n. 3, p. 1121–1167, 2003.

CLAIR Émilie et al. A glyphosate-based herbicide induces necrosis and apoptosis in mature rat testicular cells in vitro, and testosterone decrease at lower levels. *Toxicology in Vitro*, v. 26, n. 2, p. 269–279, 2012.

CLAY, K.; LEWIS, J.; SEVERNINI, E. Canary In A Coal Mine: Infant Mortality, Property Values, And Tradeoffs Associated With Mid-20th Century Air Pollution. NBER Working Paper 22155. Available at: <http://www.nber.org/papers/w22155.pdf>. 2016.

COX, C. Glyphosate (Roundup). *J. Pest. Reform*, v. 18, p. 3–17, 1998.

CURRIE, J.; NEIDEL, M. Air Pollution and Infant Health: What Can We Learn from California's Recent Experience? *The Quarterly Journal of Economics*, v. 120, n. 3, p. 1003–1030, 2005.

EBENSTEIN, A. The Consequences of Industrialization: Evidence from Water Pollution and Digestive Cancers in China. *The Review of Economics and Statistics*, v. 94, n. 1, p. 186–201, 2012.

EDWARDS, W. M.; JR., G. B. T.; KRAMER, R. M. A Watershed Study of Glyphosate Transport in Runoff. *Journal of Environmental Quality*, v. 9, n. 4, p. 661–665, 1980.

FRANK, E. The Effects of Bat Population Losses on Infant Mortality through Pesticide Use in the U.S. Working Paper. Available at: $cdep.sipa.columbia.edu/sites/default/files/cdep/Frank_JMP.pdf$. 2016.

FRANK, R. et al. Contamination of rural ponds with pesticide, 1971-85, Ontario, Canada. *Bull. Environ. Contam. Toxicol*, v. 44, n. 3, p. 401–409, 1990.

GOLDSBOROUGH, L. G.; BECK, A. E. Rapid dissipation of glyphosate in small forest ponds. *Archives of Environmental Contamination and Toxicology*, v. 18, n. 4, p. 537–544, 1989.

GOLDSBOROUGH, L. G.; BROWN, D. J. Dissipation of glyphosate and aminomethylphosphonic acid in water and sediments of boreal forest ponds. *Environmental Toxicology and Chemistry*, v. 12, p. 1139–1147, 1993.

HAVERFIELD, J. T. et al. Teasing out the role of aromatase in the healthy and diseased testis. *Spermatogenesis*, v. 1, n. 3, p. 240–249, 2011.

HAVILAND, J. A.; BUTZ, D. E.; PORTER, W. P. Long-term sex selective hormonal and behavior alterations in mice exposed to low doses of chlorpyrifos in utero. *Reproductive Toxicology*, v. 29, n. 1, p. 74–79, 2010.

IBGE. *Indicadores de Desenvolvimento Sustentável*. 2004.

IBGE. *Indicadores de Desenvolvimento Sustentável*. 2012.

LASSITER, T. L. et al. Exposure of neonatal rats to parathion elicits sex-selective reprogramming of metabolism and alters the response to a high-fat diet in adulthood. *Environmental Health Perspectives*, v. 116, n. 11, p. 1456–1462, 2008.

MESNAGE, R. et al. Major Pesticides Are More Toxic to Human Cells Than Their Declared Active Principles. *BioMed Research International*, v. 2014, 2014.

MESNAGE, R. et al. Potential toxic effects of glyphosate and its commercial formulations below regulatory limits. *Food and Chemical Toxicology*, v. 84, p. 133–153, 2015.

MUNDSTOCK, C. M.; THOMAS, A. L. *Soja: fatores que afetam o crescimento e o rendimento de grãos*. [S.l.]: Porto Alegre: Departamento de Plantas de Lavoura - UFRGS: Evengraf, 2005.

POULSEN, M. S. et al. Modeling placental transport: correlation of in vitro BeWo cell permeability and ex vivo human placental perfusion. *Toxicology in Vitro*, v. 23, n. 7, p. 1380–1386, 2009.

RASHIN, E.; GRABER, C. *Effectiveness of best management practices for aerial application of forest pesticides*. [S.l.], 1993.

RAUH, V. A. et al. Brain anomalies in children exposed prenatally to a common organophosphate pesticide. *PNAS*, v. 109, n. 20, p. 7871–7876, 2012.

RICHARD, S. et al. Differential Effects of Glyphosate and Roundup on Human Placental Cells and Aromatase. *Environmental Health Perspectives*, v. 113, n. 6, p. 716–720, 2005.

ROESSING, A. C.; LAZZAROTTO, J. J. Soja transgênica no brasil: situação atual e perspectivas para os próximos anos. In: *53º Congresso Brasileiro de Economia e Sociologia Rural*. [S.l.: s.n.], 2005.

RULL, R. P.; RITZ, B.; SHAW, G. M. Neural Tube Defects and Maternal Residential Proximity to Agricultural Pesticide Applications. *American Journal of Epidemiology*, v. 163, n. 8, p. 743–753, 2006.

SADLER, T. W. *Langman's Medical Embryology*. 12. ed. [S.l.]: Philadelphia : Wolters Kluwer Health/Lippincott Williams and Wilkins, 2012.

SATHYANARAYANA, S. et al. Maternal Pesticide Use and Birth Weight in the Agricultural Health Study. *Journal of Agromedicine*, v. 15, n. 2, p. 127–136, 2010.

SIQUEIRA, M. T. de et al. Correlation Between Pesticide Use in Agriculture and Adverse Birth Outcomes in Brazil: An Ecological Study. *Bull Environ Contam Toxicol*, v. 84, p. 647–651, 2010.

SMITH, N. J.; MARTIN, R. C.; CROIX, R. S. Neural Tube Defects and Maternal Residential Proximity to Agricultural Pesticide Applications. *Bull Environ Contam Toxicol.*, v. 57, n. 5, p. 759–765, 1996.

TAYLOR, E. L.; HOLLEY, A. G.; KIRK, M. *Pesticide Development: A Brief Look at the History*. 2007. Southern Regional Extension Forestry. Publication ID: SREF-FM-010. Available at http://www.sref.info/resources/publications/pesticide-development—a-brief-look-at-the-history.

USDA. *National Agricultural Statistics Service*. 2001.

USDA. *National Agricultural Statistics Service*. 2016.

VATS, S. Herbicides: history, classification and genetic manipulation of plants for herbicide resistance. In: LICHTFOUSE, E. (Ed.). *Sustainable Agriculture Reviews*. [S.l.]: Springer, 2015. v. 15, p. 153–192.

WINCHESTER, P. D.; HUSKINS, J.; YING, J. Agrichemicals in surface water and birth defects in the United States. *Acta Paediatrica*, v. 98, n. 4, p. 664–669, 2009.