HEALTH ECONOMICS
Health Econ. **23**: 69–92 (2014)
Published online 22 January 2013 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/hec.2901

FETAL HEALTH SHOCKS AND EARLY INEQUALITIES IN HEALTH CAPITAL ACCUMULATION†

GEORGE L. WEHBY[a,*], KWAME A. NYARKO[a] and JORGE S. LOPEZ-CAMELO[b]

[a]*Department of Health Management and Policy, University of Iowa, Iowa City, IA, USA*
[b]*Centro de Educación Médica e Investigaciones Clínicas (CEMIC), Buenos Aires, Argentina*

ABSTRACT

Several studies report socioeconomic inequalities in child health and consequences of early disease. However, not much is known about inequalities in health capital accumulation in the womb in response to fetal health shocks, which is essential for finding the earliest sensitive periods for interventions to reduce inequalities. We identify inequalities in birth weight accumulation as a result of fetal health shocks from the occurrence of one of the most common birth defects, oral clefts, within the first 9 weeks of pregnancy, using quantile regression and two datasets from South America and the USA. Infants born at lower birth weight quantiles are significantly more adversely affected by the health shock compared with those born at higher birth weight quantiles, with overall comparable results between the South American and US samples. These results suggest that fetal health shocks increase child health disparities by widening the spread of the birth weight distribution and that health inequalities begin in the womb, requiring interventions before pregnancy. Copyright © 2013 John Wiley & Sons, Ltd.

Received 25 October 2011; Revised 16 November 2012; Accepted 5 December 2012

KEY WORDS: child health; inequalities; disparities; quantile regression; health production; pregnancy

1. INTRODUCTION

Health inequalities are common and occur early in life. For example, several socioeconomic, racial, and geographic disparities are reported in the prevalence of early adverse infant health outcomes such as low birth weight or infant mortality worldwide (Thompson *et al*., 2005; Matijasevich *et al*., 2008; Currie, 2009; Heron *et al*., 2010). More importantly, inequalities may result from *differential responses* to disease occurrence or health shocks due to differences in economic, social, environmental, or biological factors that not only affect the risk of exposure to or severity of disease and shocks but also modify their health consequences. Identifying these differential responses to health shocks is essential for identifying approaches to reduce health inequalities. Many diseases occur in a 'random' fashion and involve very complex etiologies including genetic factors that until now cannot be modified through preventive interventions. For these reasons, public policy interventions may be limited in being able to prevent several diseases and more suited to influence factors that may reduce the negative consequences of these diseases such as by improving population health care and socioeconomic conditions. Such interventions may serve as a secondary prevention that reduces the adverse effects of disease on individual well-being and human capital and may be more effective in improving health outcomes until cost-effective primary prevention approaches are available for complex diseases.

*Correspondence to: Department of Health Management and Policy, College of Public Health, University of Iowa, 105 River Street, N248 CPHB, Iowa City, IA 52242, USA.
E-mail: george-wehby@uiowa.edu
†This article was published online on January 22, 2013. Errors were subsequently identified. This notice is included in the online and print versions to indicate that both have been corrected May 30, 2013.

Several studies report compensatory effects from socioeconomic endowments that lessen disease consequences. However, most previous studies evaluate inequalities in responses to diseases and health shocks that occur after birth, and little is known about the extent to which inequalities develop in response to health shocks during pregnancy. In this study, we assess inequalities in fetal health accumulation, in the form of birth weight, after health shocks in the form of oral clefts, which are one of the most common birth defects occurring within the first 9 weeks of pregnancy. Using multiple datasets including a unique dataset with detailed measures of oral cleft types and quantile regression to evaluate differences in fetal responses to the shocks, we find that these shocks reduce early health capital significantly more for infants at low birth quantiles who may generally be thought of as having lower health endowments than for infants at high birth weight quantiles who are much less affected by these shocks. The results indicate significant inequalities in fetal responses to early health shocks.

2. BACKGROUND

Some studies have reported that improved socioeconomic backgrounds lessen the adverse consequences of health shocks during childhood. For example, Feinstein (2003) found that children with delayed development in poor families are more adversely affected in terms of their educational attainment during adulthood compared with those in richer families. Currie and Lin (2007) found that poor children are significantly more likely to have activity limitations as a result of chronic conditions such as asthma and mental health conditions compared with wealthier children with these conditions. Currie (2009) highlighted that inequalities between poor and nonpoor children in activity limitations as a result of chronic conditions exceed inequalities in the prevalence of these conditions. Such compensatory effects of higher socioeconomic status are likely due to enhanced parental investments in child health and healthcare treatments that may reduce the burden of disease.

Although informative, the majority of previous studies evaluate inequalities in health responses to diseases and health shocks that occur after birth. Not much is known about the extent to which inequalities develop in response to health shocks during pregnancy. Such inequalities may have long-lasting and multiplicative effects on health inequalities throughout life. Therefore, evaluating inequalities in health capital formation during pregnancy is important to identify the earliest sensitive period when such disparities develop to devise early and cost-effective interventions that can reduce health gaps. A few studies motivated by the fetal origin hypothesis evaluate differences in the effects of health shocks during pregnancy on subsequent health capital accumulation by socioeconomic indicators.[1] However, these studies evaluate collective shocks, which unlike individual shocks may be inaccurately measured at the individual level.

We examine inequalities in responses to health shocks in the womb. Specifically, we investigate how the effects of fetal health shocks, in the form of craniofacial birth defects that occur by the ninth week of pregnancy, on early health capital accumulation, in the form of birth weight, vary across the entire birth weight distribution. We employ oral clefts as the measure of fetal health shocks for several reasons. As birth defects, oral clefts represent a marker of abnormal fetal development. Furthermore, oral clefts are highly genetic in etiology, with genetic heritability estimated to be around 70–90% (Christensen and Fogh-Andersen, 1993; Christensen, 1999; Schliekelman and Slatkin, 2002). The high genetic heritability suggests that much of the variation in oral cleft risks may be considered exogenous. Furthermore, oral clefts occur very early in pregnancy—between 6 and 9 weeks of pregnancy (Sperber, 2002). This supports the exogeneity of oral clefts as shocks as they are unlikely to be affected by prenatal care use and other healthcare interventions during pregnancy. We do not aim at estimating the causal effects of oral clefts on fetal growth but rather use them as an indicator of a developmental shock and assess differential responses to these shocks. Therefore, it is

[1]For example, Lindeboom *et al*. (2010) found that individuals born in a lower social status (based on father's occupation) who were exposed to the Dutch potato famine in 1884–1887 had larger reductions in survival during adulthood compared with individuals from higher social class born during the same period.

DOI: 10.1002/hec

not critical for our purposes whether oral clefts are exogenous or not. However, the fact that they largely occur because of exogenous factors strengthens the interpretation of the effects.

Oral clefts and fetal growth may share some underlying genetic and environmental/behavioral etiology, which supports their use as a marker of a shock to fetal development. Some of the genes that may be involved in oral cleft risks may also affect fetal growth and consequently birth weight.[2] Furthermore, a few behavioral factors including smoking, multivitamin/folic acid use, and excessive alcohol consumption have been suggested to play a role in oral clefts (Wyszynski *et al*., 2003; Wehby and Murray, 2010; Wehby *et al*., 2011). These behaviors have also been associated in the same direction with fetal growth and/or birth weight as with oral clefts (Scholl *et al*., 1997; Lien and Evans, 2005; Okah *et al*., 2005; Wehby *et al*., 2009a, 2011).[3] Also, there is some evidence that lower socioeconomic status increases the risks of oral clefts (Clark *et al*., 2003; Durning *et al*., 2007) and that lower socioeconomic status has well-documented negative effects on birth weight (Currie, 2009).

Another motivation for studying oral clefts as health shocks is that they are commonly considered one of the most prevalent birth defects worldwide. More than 7000 infants were born annually with oral clefts in the USA between 2004 and 2006 (Parker *et al*., 2010). Furthermore, oral clefts are easily diagnosed and have varying severity levels that can be easily measured and evaluated as indicators of different intensities of health shocks. In sum, the etiological, epidemiological, and clinical characteristics of oral clefts provide several advantages for studying them as fetal health shocks compared with other common birth defects, which may be harder to diagnose, are highly heterogeneous, and have an etiology that may not well overlap with that of fetal growth and birth weight. An additional significance of studying oral clefts is that they have a significant burden on early and long-term individual health, quality of life, psychosocial status, and human capital and increase mortality risks (Kapp-Simon, 1986; Kapp-Simon *et al*., 1992; Thomas *et al*., 1997; Nackashi *et al*., 2002; Forrester and Merz, 2003; Christensen *et al*., 2004; Wehby *et al*., 2006; Wehby and Cassell, 2010; Wehby *et al*, 2012a).

Several clinical and epidemiological studies using descriptive designs have reported negative associations between oral clefts and birth outcomes including birth weight and/or gestational age (Menegotto and Salzano, 1991; Becker *et al*., 1998; Wyszynski and Wu, 2002; Wyszynski *et al*., 2003; Forrester and Merz, 2004).[4] This epidemiological research literature supports the premise of using oral clefts as markers of health shocks for fetal growth and birth weight. However, none of these studies assessed the inequalities in the effects of oral clefts on fetal health capital accumulation. We are aware of no other study that undertakes our approach to identify inequalities in fetal health capital accumulation after health shocks. Therefore, our study makes a novel contribution to the literature on inequalities in responses to very early health shocks.

Several genetic, biologic, socioeconomic, and environmental factors or endowments may modify fetal responses to health shocks during pregnancy. Parsing these factors out and defining a single comprehensive measure of endowment are challenging because of the limited knowledge to date of the specific relevant factors and how to identify and measure them. Therefore, we do not evaluate inequalities resulting from differences in specific measurable endowments. Instead, we employ quantile regression to evaluate the inequality in effects of oral clefts between various quantiles of the birth weight distribution. By evaluating changes in the spread of the birth weight distribution, quantile regression provides information about whether these fetal shocks widen

[2]Fetal growth and birth weight are thought to have a genetic heritability of 34–37% (Clausson *et al*., 2000). Fibroblast growth factor genes and transforming growth factor genes, which have been implicated in certain forms of oral clefts occurring either alone or with other malformations (Dixon *et al*., 2011), may be related to other fetal growth aspects (Forbes and Westwood, 2010). Of course, most of the genetic etiologies of oral clefts and fetal growth are yet to be identified. However, there is theoretical support for some common genetic risk factors.

[3]Furthermore, genetic variants have been found to modify the effects of some of these behaviors on both oral clefts and fetal growth/birth weight. For example, variants in *GSTT1* and other genes of the detoxification pathway have been reported to modify the effects of maternal smoking on oral clefts (Shi *et al*., 2008). Similarly, there is evidence that the effects of maternal smoking on birth weight and preterm birth are modified by fetal (*GSTT1* and *HLA-DQ*) and maternal (*GSTT1*) genes (Nukui *et al*., 2004; Taylor *et al*., 2006).

[4]For example, using data from Sweden on infants with oral clefts compared with the entire birth population, Becker *et al*. (1998) found that infants born with isolated clefts of both the lip and the palate (without other defects) had two times higher risk of low birth weight. Similarly, using US natality data, Wyszynski and Wu (2002) reported a 1.6–1.7 times increased risk of low birth weight among children with isolated oral clefts compared with unaffected infants.

DOI: 10.1002/hec

(or shrink) inequalities in birth weight. Also, the unobservable factors that determine the child's quantile ranking on the birth weight distribution (conditional on the observable characteristics) may be thought of as representing unmeasured fetal health endowments as less (better) endowed infants are expected to rank on the lower (higher) quantiles of birth weight. Therefore, quantile regression serves as a useful tool to assess the heterogeneity in fetal responses to the health shocks.

3. ANALYTICAL APPROACH

We study inequalities in early health accumulation in the form of birth weight production in response to fetal health shocks. We use birth weight as an early measure of health capital because it is very well reflective of fetal growth and health accumulation, is an important measure of early health that is related to neonatal hospitalization and infant mortality, and is strongly predictive of future health and human capital accumulation. Several studies find that low birth weight is adversely associated with subsequent child development and adult health and human capital outcomes (Frankel *et al*., 1996; Anderson and Doyle, 2003; Gluckman *et al*., 2008; Victora *et al*., 2008; Currie, 2009). Our study follows standard infant health production models that have been commonly employed in previous studies (Rosenzweig and Schultz, 1983; Wehby *et al*., 2009b) but adds the fetal health shock that has direct effects on infant health.

We employ quantile regression to identify how the effects of fetal health shocks vary at different locations of the birth weight distribution. The infant health production function can be considered within the quantile regression framework as

$$H = Q(\mathbf{X}, S, U), \tag{1}$$

where H is the birth weight, $\mathbf{X}$ are the observed relevant inputs and risk factors, S is the fetal health shock, and Q is the quantile function of H. U is uniformly distributed between 0 and 1 and represents the infant's ranking on the net level of unobserved factors that determine how each infant ranks on the distribution of H, conditional on $\mathbf{X}$ and S (Chernozhukov and Hansen, 2005). In other words, U results in different ranks on H for infants with the same values of $\mathbf{X}$ and S. Substituting the quantile order q of H for U, where q is between 0 and 1, we find that Q($\mathbf{X}$, S, q) is the conditional qth quantile of H.

Quantile regression is useful for identifying inequalities in fetal responses to health shocks. The model allows for evaluating how the spread of the birth weight distribution is changing with these shocks. The spread of the distribution is one measure of inequality. The spread would widen if the shock reduces birth weight more at lower than at higher quantiles, indicating an increase in inequality. In contrast, the spread would shrink if the shock reduces birth weight more at higher than at lower quantiles, indicating a decrease in inequality. Another advantage of quantile regression is that the effects of S (and $\mathbf{X}$) on Q can be interpreted as holding U constant at the quantile order q. By estimating the effect of S on Q at a certain q, the model evaluates an effect of the fetal health shock that essentially applies to infants, with U resulting in their ranking at that q. U may be generally thought of here as representing the net level of 'unobserved' fetal health endowments (genetic/biologic, socioeconomic, and environmental) that are relevant for H.[5] By varying q, the model can evaluate the heterogeneity in responses to S because it traces the effects of S on H by q as follows:

$$\mathrm{H} = Q\left(\alpha_{0q} + \mathbf{X}\boldsymbol{\lambda}_q + \beta_q S\right) \tag{2}$$

[5]See other quantile regression applications for related interpretations (Chernozhukov and Hansen, 2004; Wehby *et al*., 2009b; Wehby and Courtemanche, 2012).

DOI: 10.1002/hec

Quantile regression is *not* estimated by stratifying the sample by the quantiles of H and regressing H on the model variables in stratified samples (such as by using ordinary least squares, OLS). At each q, quantile regression is estimated *using the whole sample* by minimizing the sum of weighted absolute deviations of H from the predicted value as follows (Koenker and Bassett, 1978; Koenker and Hallock, 2001):

$$\min\left[q\sum_{H_i\geq Q_i}^{n}|H_i-Q_i|+(1-q)\sum_{H_i<Q_i}^{n}|H_i-Q_i|\right] \tag{3}$$

We estimate the quantile regression for q from 0.05 to 0.95 in increments of 0.05. The variance–covariance matrices are estimated by bootstrap with 500 replications. We test for the differences in the effects of the health shocks on H by q using Wald tests (Hao, 2007). For comparison purposes, we also estimate the infant health production function using OLS to obtain the effects of the health shocks at the mean of H. We employ a Huber-type estimator for the OLS variance–covariance matrix that accounts for the nonindependence of observations from the same area, which is defined later (Moulton, 1986; Wooldridge, 2002).

As mentioned earlier, our goal is not to estimate the 'causal effects' of oral clefts *per se* on birth weight but rather to evaluate the heterogeneity in their effects as a marker of fetal health shocks across the birth weight distribution. In other words, we employ oral clefts as an indicator of a strong health shock to fetal health that can result from either genetic, behavioral, or socioeconomic effects that are also relevant for birth weight. Therefore, a general evaluation of our question may be achieved by simply regressing birth weight quantiles on the oral cleft indicator alone. However, we are able to further evaluate the 'source' of the shock and whether it is generated mainly by 'genetic' or 'behavioral' effects that are common to oral clefts and birth weight. As indicated earlier, even though oral clefts have a very high genetic etiology, they may also be affected by behavioral and socioeconomic factors.

We first estimate a specification that excludes individual-level characteristics in $\mathbf{X}$ and only includes area and year fixed effects described in the following in addition to S. Next, we estimate a specification that additionally controls for several theoretically relevant individual-level characteristics including maternal health, behavioral, demographic, and socioeconomic factors. By comparing the effects of S between these two specifications, we are able to evaluate the extent to which S represents genetic versus nongenetic effects on birth weight.

4. DATA AND EMPIRICAL MODEL

4.1. Datasets

We employ two data sources and analyze them separately for this study. The goal is to evaluate the stability and generalizability of the results across different samples and settings. The first is a unique data source from the Latin American Collaborative Study of Congenital Anomalies (ECLAMC). Since 1967, ECLAMC has been established as a research program for epidemiological investigations and surveillance of congenital anomalies in several South American countries (Castilla and Orioli, 2004). ECLAMC is built on a model of voluntary participation of several hospitals and physicians (who are mostly pediatricians) in its surveillance activities. The physicians receive standard training from ECLAMC to monitor the incidence of congenital anomalies in all the births in their hospitals and to systematically obtain—using standardized infant identification and data collection methods across all physicians and hospitals including infant examination, maternal interviews, and hospital record abstraction—detailed information

DOI: 10.1002/hec

on the birth defects, infant health, and prenatal risk factors (such as maternal health and fertility history). The physicians examine the infants and conduct the interviews with the mothers before the infant is discharged from the hospital after birth. The same data are obtained on all infants born with congenital anomalies in the ECLAMC-affiliated hospitals. The physicians routinely transmit collected data to the ECLAMC headquarters for data cleaning and storage. The physicians attend annual meetings of ECLAMC at which refresher training is provided.

In addition to the infants with congenital anomalies, the physicians identify infants who are born in the same hospitals without congenital anomalies and who are matched one to one to the affected infants by sex and date of birth. The majority of eligible infants who are identified participate in the program (more than 95%).[6] The physicians obtain the same information on infants without congenital malformations using the same data collection procedures as for affected infants. The sample of unaffected infants can be thought of as essentially representing a 2–3% random sample of all infants without congenital anomalies in the ECLAMC-affiliated hospitals. ECLAMC data have been successfully employed in several previous studies of infant health production in South America (Lopez Camelo *et al*., 2006; Wehby *et al*., 2009a, 2010, 2012b).

The study sample that we employ from ECLAMC includes infants with oral clefts and infants without congenital anomalies who were born in ECLAMC-affiliated hospitals between 1970[7] and 2007 in eight South American countries[8] and enrolled in the ECLAMC program. The total sample includes 2665 infants with isolated oral clefts (i.e., clefts without other congenital malformations), 1417 infants with nonisolated oral clefts (i.e., clefts with other congenital malformations), and 40,528 infants without congenital anomalies. We include all nonmalformed infants who were recruited into ECLAMC and born in the same month as the infants with oral clefts.

The ECLAMC sample offers several advantages over other potential data sources for this study such as other birth defect registry data. The sample is larger than most samples from other birth defect registry programs and is unique in being identified by physicians who receive the same training in the study procedures and who systematically and prospectively obtain all the study data by examining infants, interviewing mothers, and abstracting hospital records. To our knowledge, many registry programs in other settings rely solely on record abstraction, which can result in missed cases or birth defect misclassifications. Because of the physical examination of children, the dataset includes detailed measures of birth defect types, allowing for measuring birth defect severity and studying the effects of different severity levels. Another advantage of the ECLAMC sample is that it covers several communities that are diverse in their geographic location, socioeconomic conditions, and demographic characteristics. Specifically, the sample that we employ includes infants born in 144 hospitals, 91 cities, and 57 provinces/states in eight countries. As described later, the sample involves significant variation in infant and maternal health and in demographic and socioeconomic characteristics. We cannot directly evaluate the sample representativeness of the entire birth populations in these countries because of the lack of population-level data on comparable measures. However, the sample diversity significantly enhances its representativeness and generalizability of results. Further, ECLAMC does not impose inclusion or exclusion criteria on hospital participation, which further enhances representativeness.

The second data source that we employ for this study is the US natality live birth data for 2004. The dataset includes birth certificate information on virtually all (>99%) births in the USA (Natality User Guide, 2006) and is publicly available through the National Center of Health Statistics at the Centers for Disease Control. Standard reporting and data collection methods have been developed for the states. The natality datasets include, for each birth, data on birth outcomes such as birth weight, maternal health,

[6]Participation in ECLAMC, personal communication with Eduardo E. Castilla, ECLAMC Coordinator, on December 4, 2009.
[7]ECLAMC started in 1967, but several relevant inputs and demographic characteristics were added in 1970. Further, the sample was markedly smaller in the first 3 years.
[8]These include Argentina, Bolivia, Brazil, Chile, Colombia, Ecuador, Uruguay, and Venezuela.

DOI: 10.1002/hec

and prenatal behaviors and risk factors (prenatal care, smoking, alcohol, weight gain, health complications during pregnancy, and live birth order); demographic and socioeconomic characteristics (marital status, age, race, and education); and presence of selected congenital malformations, including oral clefts. We choose 2004 instead of more recent years as it includes state of birth, which we control for in our models.

The natality dataset provides a much larger sample of unaffected births but is limited to birth certificate data and does not provide the same accuracy of birth defect classification as the ECLAMC data. There are concerns that congenital malformations (especially less visible ones) may be underreported in birth certificates. However, this has minimal implications, if anything, for our study because we are interested in evaluating the effects of oral cleft occurrence as a health shock measure and not in estimating the prevalence of oral clefts. Given that we draw a random sample of 'unaffected' infants from the natality dataset as the reference group, any 'measurement error' of unaffected status is likely to have minimal effects because of the relatively low oral cleft incidence in the population. The natality sample that we study includes 1751 infants with isolated oral clefts, 436 infants with oral clefts with other birth defects, and 306,618 infants without birth defects. The unaffected group is based on a 10% random sample of all infants without any birth defect in the natality dataset, which provided an unbiased estimate of the birth weight mean of the entire population of unaffected infants. The 'unaffected' sample may include 307 undiagnosed oral cleft cases, assuming an average incidence of one case of oral clefts per 1000 births (Mossey *et al*., 2009). We expect this to result in underestimation of the health shock effect, which still allows for using the estimated effects as the lower bounds of the real effects.

4.2. Health shock measures

As mentioned earlier, we measure fetal health shocks by whether the infant has an oral cleft, which occurs by the ninth week of pregnancy. In the ECLAMC dataset, oral cleft status was recorded by the affiliated pediatricians through examination of the infant before discharge from the hospital after birth. Oral clefts are commonly defined as those that occur alone without other birth defects (isolated forms) or with other birth defects (nonisolated forms). The three types of typical oral clefts include cleft lip alone, cleft lip with palate, and cleft palate alone. Isolated forms are the majority of cases, including about 70% of cases with cleft lip with or without cleft palate and about 50% of cases with cleft palate alone (Jones, 1988; Marazita, 2002). Isolated clefts have significantly less severe adverse effects on individual health than nonisolated cases. Unlike the ECLAMC sample, the 2004 natality dataset does not include specific measures for the type of oral clefts but combines the three types together. However, the data allow for measuring isolated and nonisolated status on the basis of the presence of other birth defects.

We separately evaluate the effects of isolated and nonisolated oral clefts as fetal health shocks given their different severity levels in both the ECLAMC and natality datasets. Additionally, in the ECLAMC dataset, we measure the shocks within the isolated and nonisolated groups by the three cleft types of cleft lip alone, cleft lip with palate, and cleft palate alone as they vary in severity and effects on infant health.

4.3. Empirical model

Our basic empirical model is defined as

$$H_i = \alpha_0 + \sum_{s=1}^{S} \alpha_s SHOCK_{si} + \sum_{a=1}^{A} \alpha_a AREA_{ai} + \sum_{y=1}^{Y} \alpha_y YEAR_{yi} + u_i, \tag{4}$$

where, for infant i, H is the birth weight and *SHOCK* is the oral cleft status as described earlier. *AREA* includes country fixed effects when using ECLAMC data and state fixed effects when using natality data. *YEAR* includes year of birth fixed effects when using ECLAMC data.

DOI: 10.1002/hec

Next, we estimate an expanded model that includes observable inputs and risk factors to evaluate the different sources of the shock,

$$H_i = \alpha_0 + \sum_{s=1}^{S} \alpha'_s SHOCK_{si} + \sum_{m=1}^{M} \alpha_m MATERNAL_{mi} + \sum_{f=1}^{F} \alpha_f FAMILY_{fi} + \sum_{d=1}^{D} \alpha_d INFANT\_DEMOGRAPHICS_{di} + \sum_{a=1}^{A} \alpha'_a AREA_{ai} + \sum_{y=1}^{Y} \alpha'_y YEAR_{yi} + v_i, \quad (5)$$

where differences in coefficients from the previous model are indicated by ($'$). The specification of the added vectors on the right-hand side varies slightly between the ECLAMC and US natality data because of differences in data measures. *MATERNAL* includes several maternal health, behavioral, demographic, and socioeconomic indicators such as fertility history indicators, age, prenatal behaviors, and schooling.[9] *FAMILY* is only measured for the ECLAMC dataset and includes father's employment/occupational level and family history of oral clefts. *INFANT_DEMOGRAPHICS* includes the infant's sex and race/ethnicity.[10] As mentioned earlier, we estimate all models separately for isolated and nonisolated clefts.

Tables I and II report all the model variables and their distributions for the ECLAMC and natality samples, respectively.

5. RESULTS

5.1. Health shock effects—basic specification

We first report how the effects of health shocks on birth weight accumulation vary between different quantiles of the birth weight distribution as estimated from the quantile regression of Equation (4), which excludes observable inputs and risk factors and only adjusts for area and year (for ECLAMC) fixed effects. For the ECLAMC sample, Table III reports these effects for birth weight quantiles 0.1, 0.25, 0.5, 0.75, and 0.9, and Figures 1 and 2 show these effects for quantiles 0.05 through 0.95 in 0.05 increments. Table IV and Figure 3 show these results for the US natality data.

The results are overall comparable between the two data samples. The health shocks have significant negative effects on birth weight that are significantly larger (in absolute value) for infants born at lower birth weight quantiles. Therefore, the spread of the birth weight distribution widens with these shocks, indicating an increase in inequality. Furthermore, because infants ranking at lower birth weight are generally expected to have lower health endowments, the results suggest that these health shocks have larger effects for less-endowed infants. This particular interpretation of the quantile effects requires a rank similarity assumption, in that the unobserved endowments thought to determine the ranking of the child on the birth weight distribution do not systematically vary between infants exposed to the shocks and those not exposed to the shocks. In other words, there are no disproportionate shock effects that

[9]For the ECLAMC analysis, *MATERNAL* includes indicators for acute and chronic health conditions during pregnancy, number of previous live births and miscarriages/still births, maternal age, receiving vaccinations, taking medications and folic acid during pregnancy, and schooling level. For the natality analysis, *MATERNAL* includes indicators for acute and chronic health conditions during pregnancy, number of previous live births and still births, maternal age, smoking during pregnancy, and schooling level.

[10]These are based on maternal report in ECLAMC. The infant may have multiple ancestries reported, which are represented by separate indicators.

DOI: 10.1002/hec

Table I. Variable description for Latin American Collaborative Study of Congenital Anomalies data

	Percent/mean (SD)			
Variable	Total sample	Isolated cases ($N = 2665$)	Nonisolated cases ($N = 1417$)	Nonaffected ($N = 40{,}528$)
Any oral cleft	9.100	—	—	—
Cleft lip only[a]	1.800	25.600	9.000	—
Cleft palate only[a]	2.400	16.000	44.900	—
Cleft lip and palate[a]	5.000	58.400	46.100	—
Infant characteristics				
Birth weight between 500 and 6000 g only	3177.510 (589.790)	3094.240 (650.890)	2518.630 (867.860)	3206.840 (558.380)
Gestational age from 19.5 to 46.5 weeks	39.040 (2.779)	38.950 (3.063)	37.390 (4.042)	39.110 (2.704)
Female infant[a]	46.400	42.700	49.500	46.500
African ancestry[a]	17.200	10.900	15.300	17.400
Native ancestry[a]	81.400	83.100	81.100	80.600
European Latin ancestry[a]	43.200	43.300	44.700	43.100
European non-Latin ancestry[a]	7.400	7.800	8.200	7.700
Other ancestry[a]	2.400	2.400	3.200	2.400
Cleft relative[a]	2.200	16.600	8.700	1.000
Maternal characteristics				
Acute illnesses[a]	27.400	33.900	37.200	27.400
Chronic illnesses[a]	10.300	12.700	15.600	10.300
Conception difficulty[a]	6.900	7.700	8.800	6.900
Number of live births the mother has had	1.577 (1.884)	1.915 (2.139)	1.877 (2.137)	1.545 (1.853)
Number of spontaneous and stillbirths	0.211 (0.590)	0.264 (0.668)	0.325 (0.756)	0.201 (0.572)
Vaccine taken during the first trimester[a]	7.500	7.200	8.300	7.500
Medication taken during the first trimester[a]	27.600	33.000	37.300	27.000
Folic acid taken during the first trimester[a]	2.600	2.400	3.200	2.500
Maternal age, 13 to 49 years	25.452 (6.463)	26.067 (6.617)	27.051 (7.219)	25.343 (6.428)
Maternal age squared	689.570 (355.230)	723.270 (369.070)	783.860 (414.620)	683.590 (352.130)
Primary school complete[a,b]	24.600	26.000	25.900	24.500
Secondary school incomplete[a,b]	0.250	0.235	0.215	0.250
Secondary school complete[a,b]	17.400	15.000	18.1	17.5
University incomplete[a,b]	3.300	3.900	3.900	3.200
University complete[a,b]	2.700	3.600	3.400	2.600
Father's employment/occupational status				
Blue collar workers[a,c]	18.500	16.900	18.900	18.600
White collar workers[a,c]	24.900	24.500	22.600	24.700
Independent workers[a,c]	9.100	10.300	10.700	9.100
Executive workers[a,c]	8.100	8.200	7.500	8.000
Country indicators				
Bolivia[a,d]	3.400	8.000	3.900	3.000
Brazil[a,d]	23.700	15.700	23.200	25.200
Chile[a,d]	21.200	16.400	17.500	20.700
Colombia[a,d]	1.400	2.300	2.300	1.200
Ecuador[a,d]	6.000	6.700	4.900	5.700
Uruguay[a,d]	2.100	2.800	2.300	1.900
Venezuela[a,d]	14.700	11.900	10.200	14.300

Standard deviations (SD) of study variables are in parentheses. Year indicators are omitted for brevity.
[a]A binary 0/1 indicator is used.
[b]The reference for maternal education is no schooling and incomplete primary education.
[c]The reference for father's employment or occupation status is unemployed.
[d]The reference country is Argentina.

DOI: 10.1002/hec

Table II. Variable description for US natality data

Variable	Percent/mean (SD)			
	Total sample	Isolated cases ($N = 1751$)	Nonisolated cases ($N = 436$)	Nonaffected ($N = 306{,}618$)
Any oral cleft[a]	0.60	—	—	—
Infant characteristics				
Birth weight between 500 and 6000 g only	3255.27 (619.55)	3196.20 (621.78)	2682.87 (831.31)	3255.61 (619.52)
Gestational age from 19.5 to 46.5 weeks	38.50 (2.60)	38.51 (2.61)	37.18 (3.52)	38.51 (3.52)
Female infant[a]	47.92	42.55	51.61	47.96
Maternal characteristics				
Acute illnesses[a]	7.27	9.25	15.14	7.26
Chronic illnesses[a]	9.74	11.94	11.47	9.72
Number of live births the mother has had	1.05 (1.22)	1.10 (1.20)	1.21 (1.38)	1.05 (1.22)
Number of spontaneous stillbirths	0.38 (0.83)	0.42 (0.88)	0.46 (0.97)	0.38 (0.82)
Maternal age, 13 to 49 years	27.34 (6.17)	26.79 (6.01)	27.85 (6.50)	27.35 (6.17)
Maternal age squared	785.64 (348.95)	753.63 (337.10)	817.56 (376.79)	785.83 (349.00)
High school[a,b]	30.25	35.12	30.96	30.23
University incomplete[a,b]	21.45	20.56	22.25	21.45
University complete[a,b]	27.32	21.36	23.62	27.35
Maternal race White[a,c]	77.67	85.44	84.63	77.62
Maternal race Black[a,c]	16.32	7.71	9.63	16.37
Smoked during pregnancy (yes)[a]	10.36	17.13	14.45	10.33

Standard deviations (SD) of study variables are in parentheses. State indicators are omitted for brevity.
[a]A binary 0/1 indicator is used.
[b]The reference for maternal education is less than a high school graduate.
[c]The reference for maternal race is other race.

systematically modify the rankings of the well-endowed infants relative to the less-endowed ones.[11] This assumption does not affect the interpretation that the shocks increase the spread of the birth weight distribution. As expected, more severe shocks (nonisolated clefts and more severe cleft types) have larger adverse effects on birth weight. However, more importantly, the decrease in the adverse shock effects on birth weight with the increase in quantile order is monotonous for more severe shocks (nonisolated clefts) but generally flattens out quickly especially in the ECLAMC sample beyond fairly low quantile ranks for less severe shocks (isolated clefts).[12] In other words, the effects of severe shocks decrease at a fairly constant rate with moving to higher birth weight quantiles, whereas the effects of less severe shocks overall decrease at an increasing rate (which again is more prominent in the ECLAMC sample). This suggests that an

[11]This may be considered a strong assumption in our case because some of the unobserved endowments (such as genetic or environmental factors) that determine the birth weight ranking may also relate to the risk of having an oral cleft. The extent to which this assumption holds depends on the importance of these particular endowments (related to both oral clefts and birth weight ranking) relative to other unobserved endowments that determine birth weight ranking but are not related to oral clefts. As we show later, controlling for several observable socioeconomic and maternal health factors does not change the observed pattern of heterogeneous shock effects across the quantiles. If these controls proxy for a large extent of the variation in these endowments (that vary between infants with and without oral clefts *and* relate to their birth weight ranking), then this may reduce the risk of seriously violating this assumption. However, it is possible that some of these endowments are not accounted for by the controls. Therefore, the interpretation of heterogeneous effects by unobservable endowments should be considered within this qualification.

[12]In most cases, the effect decreases (in absolute value) with an increase in the quantile order, but in a few cases, especially with isolated clefts in the natality sample, the effect increases. There is no prior expectation that the effects should always decrease monotonously across adjacent quantiles. The underlying unobserved heterogeneity may influence the effects of isolated clefts in different ways at different quantiles compared with the effects of nonisolated clefts, resulting in different patterns of effects.

DOI: 10.1002/hec

Table III. Fetal health shock effects on birth weight using Latin American Collaborative Study of Congenital Anomalies data—basic specification

	Quantile					
Model	0.1	0.25	0.5	0.75	0.9	Ordinary least squares
Isolated clefts[a] ($N=43{,}193$)	−280.0*** (30.8)	−130.0*** (20.2)	−70.0*** (15.2)	−48.0*** (14.7)	−45.0** (20.1)	−110.0*** (13.0)
Isolated cleft types ($N=43{,}193$)						
Cleft lip only[b]	−190.0*** (53.1)	−68.0** (30.1)	−30.0 (27.4)	−35.0 (29.5)	−5.0 (32.9)	−65.7*** (11.0)
Cleft palate only[b]	−190.0** (79.9)	−90.0** (35.8)	8.0 (34.1)	10.0 (32.3)	−45.0 (38.1)	−46.9* (24.0)
Cleft lip with palate[a]	−330.0*** (39.1)	−182.0*** (22.7)	−100.0*** (16.8)	−60.0*** (15.5)	−65.0*** (25.8)	−147.0*** (21.2)
Nonisolated clefts[a] ($N=41{,}945$)	−1326.0*** (49.9)	−1020.0*** (30.7)	−610.0*** (36.6)	−400.0*** (19.6)	−265.0*** (28.4)	−693.6*** (43.0)
Nonisolated cleft types ($N=41{,}945$)						
Cleft lip only[a]	−1412.5*** (136.3)	−1130.0*** (148.6)	−550.0*** (116.9)	−260.0*** (77.6)	−220.0* (126.9)	−657.8*** (72.9)
Cleft palate only[a]	−1132.5*** (72.1)	−920.0*** (60.8)	−530.0*** (35.8)	−350.0*** (28.6)	−220.0*** (30.9)	−599.5*** (73.9)
Cleft lip with palate [a]	−1397.5*** (53.7)	−1086.0*** (51.4)	−770.0*** (54.5)	−450.0*** (34.7)	−380.0*** (49.7)	−792.3*** (38.4)

The table reports the health shock effects on birth weight quantiles and mean from the basic specification in Equation (4). Standard errors are in parentheses.
[a]The coefficients are significantly different between the five quantiles at $p < 0.0001$.
[b]The coefficients are significantly different between the five quantiles at $p < 0.05$.
*$p < 0.1$; **$p < 0.05$; ***$p < 0.01$.

DOI: 10.1002/hec

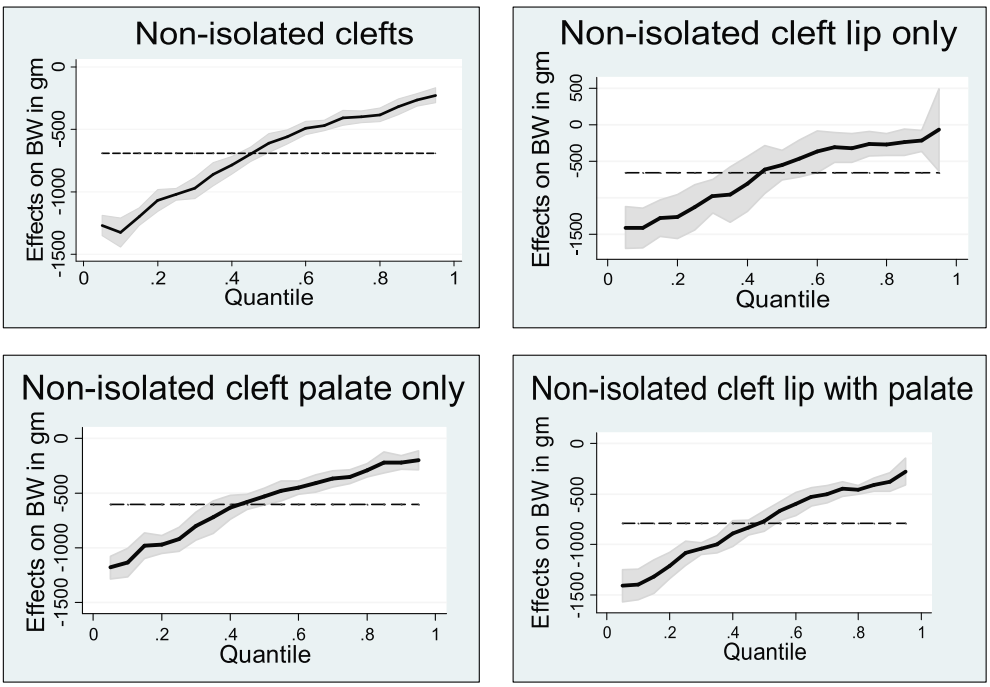

Figure 1. Effects of nonisolated oral clefts on birth weight (BW) quantiles and mean using the Latin American Collaborative Study of Congenital Anomalies data—basic specification. The figure reports the effects of nonisolated oral clefts (both overall and by type) on birth weight quantiles (solid line) and mean (dashed line). The effects are estimated from the basic specification that only controls for country and year of birth fixed effects (Equation (4)). The 95% CIs for the quantile effects estimated using 500 bootstrap applications are in the shaded area

increase in the quantile rank (which may be generally thought of as an increase in endowment) has close to constant marginal returns with severe shocks but diminishing marginal returns with less severe shocks.

In the ECLAMC sample, the severe shocks (nonisolated clefts) decrease birth weight by 1326 g at the 0.1 quantile and by 265 g at the 0.9 quantile. Within these, the most severe type (cleft lip with palate) generally has larger effects than the less severe types (except in a few cases at low quantiles when compared with cleft lip alone) and reduces birth weight by 1398 g at the 0.1 quantile and 380 g at the 0.9 quantiles. In contrast, isolated clefts, which represent the less severe shocks, decrease birth weight by 280 g at the 0.1 quantile and by 45 g at the 0.9 quantile. Within the isolated clefts, the more severe type (cleft lip with palate) has overall larger effects than less severe types and reduces birth weight by 330 g at the 0.1 quantile and by 65 g at the 0.9 quantile. Clearly, the shock effects for the 'average child' (at the median or at the mean) mask the heterogeneity in the effects at other locations of the birth weight distribution. The more severe (nonisolated cleft) and less severe (isolated cleft) shocks decrease birth weight by 610 and 70 g, respectively, at the 0.5 quantile, which are very different from the effects at the low or high quantiles. The differences in the health shock effects between the five quantiles reported in Table III are statistically significant.

Slightly lower effects are observed in the natality dataset, but the trend is remarkably similar to that in the ECLAMC dataset, especially for the severe shocks. The severe shocks (nonisolated clefts) reduce birth weight by 987 g at the 0.1 quantile and by 255 g at the 0.9 quantile. At the 0.5 quantile, severe shocks reduce birth weight by 567 g. Similarly, the less severe shocks reduce birth weight by 109 g at the 0.1 quantile, by 57 g at the 0.9 quantile, and by 85 g at the 0.5 quantile. The severe health shock effects (nonisolated) are significantly different between the five quantiles reported in Table IV, but the less severe shock effects are not statistically different.

DOI: 10.1002/hec

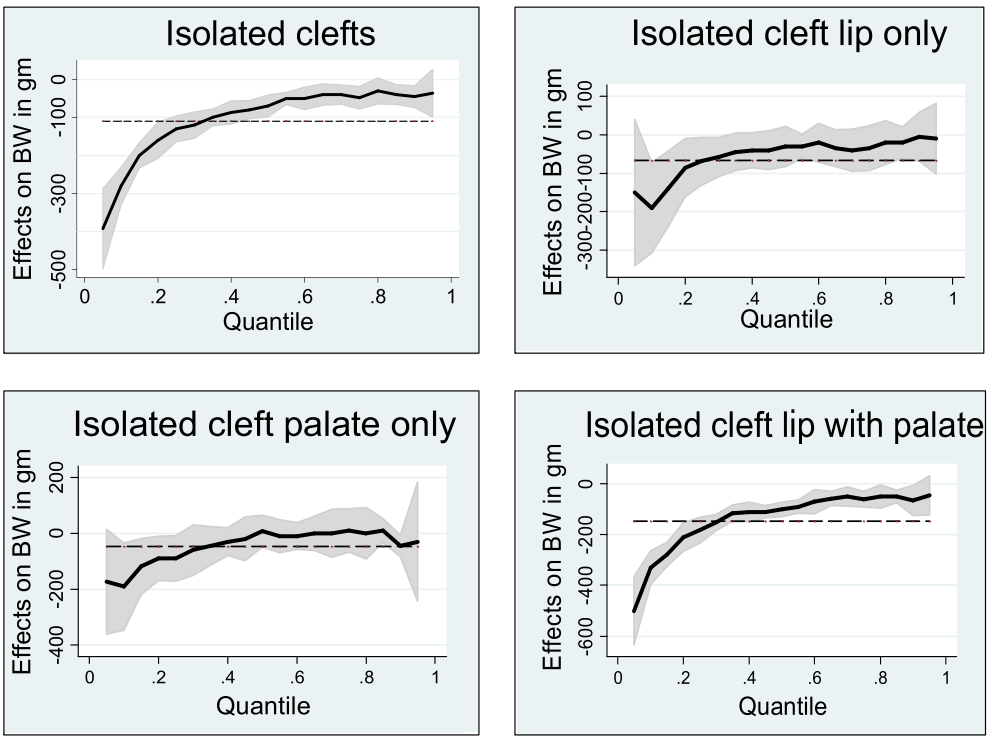

Figure 2. Effects of isolated oral clefts on birth weight (BW) quantiles and mean using the Latin American Collaborative Study of Congenital Anomalies data—basic specification. The figure reports the effects of isolated oral clefts (both overall and by type) on birth weight quantiles (solid line) and mean (dashed line). The effects are estimated from the basic specification that only controls for country and year of birth fixed effects (Equation (4)). The 95% CIs for the quantile effects estimated using 500 bootstrap applications are in the shaded area

5.2. Health shock effects—expanded specification

Tables V and VI report the health shock effects on the selected five birth weight quantiles and the mean in the expanded specification (Equation (5)), which includes observable risk factors and inputs for the ECLAMC and natality samples, respectively.[13] Figures 4 and 5 show the effects of nonisolated and isolated clefts, respectively, for quantiles 0.05 through 0.95 in the ECLAMC sample. Figure 6 shows these effects for the natality sample.

The health shock effects are generally insensitive to controlling for the observed maternal health, demographic, behavioral, and socioeconomic characteristics. The same pattern of differences in shock effects across the birth weight quantiles is virtually observed in both the ECLAMC and natality datasets. Some effects slightly increase after controlling for these factors, whereas others slightly decrease. Differences in the effects of isolated clefts between the five quantiles become significant in the natality dataset.[14] As a whole, these results support the hypothesis that genetic effects common to both oral clefts and birth weight are likely to be the main source of the shock.

[13]Detailed regression results for these covariates are available in the Appendix.

[14]Overall, there are no consistent differences in the magnitude and pattern of changes in shock effects from the basic (Table IV) to the expanded (Table VI) specification between isolated and nonisolated clefts. The differences are likely driven by differences in how the cleft group indicators (isolated versus nonisolated) are correlated with some of the control variables with significant effects on birth weight. For example, isolated cleft status is positively correlated with smoking status and chronic illnesses (in a regression of isolated status on all control variables), but these variables are not significantly correlated with nonisolated oral cleft status.

DOI: 10.1002/hec

Table IV. Fetal health shock effects on birth weight using natality data—basic specification

Model	Quantile					Ordinary least squares
	0.1	0.25	0.5	0.75	0.9	
Isolated clefts ($N = 308,369$)	−109.0***	−98.0***	−85.0***	−53.0***	−57.0**	−62.1***
	(35.2)	(21.5)	(18.9)	(15.1)	(19.6)	(16.8)
Nonisolated clefts[a]	−987.0***	−782.0***	−567.0***	−397.0***	−255.0***	−574.1***
($N = 307,054$)	(67.7)	(61.7)	(35.5)	(61.7)	(51.7)	(31.9)

The table reports the health shock effects on birth weight quantiles and mean from the basic specification in Equation (4). Standard errors are in parentheses.
[a]The coefficients are significantly different between the five quantiles at $p < 0.0001$.
**$p < 0.05$; ***$p < 0.01$.

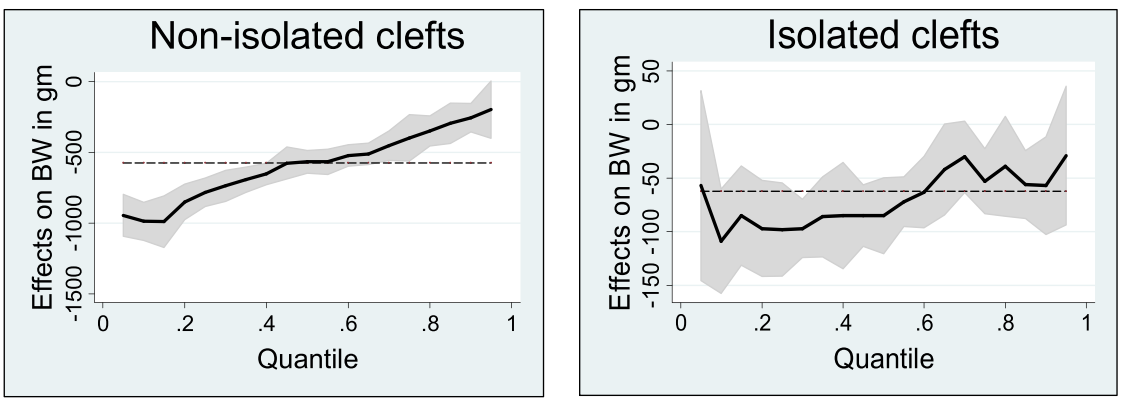

Figure 3. Effects of oral clefts on birth weight (BW) quantiles and mean using the natality data—basic specification. The figure reports the effects of nonisolated and isolated oral clefts on birth weight quantiles (solid line) and mean (dashed line). The effects are estimated from the basic specification that only controls for state fixed effects (Equation (4)). The 95% CIs for the quantile effects estimated using 500 bootstrap applications are in the shaded area

Several of the included risk factors and inputs have the expected effects on birth weight.[15] In the ECLAMC and natality datasets, birth weight increases with maternal age (at a decreasing rate), number of previous live births (with larger increases at higher quantiles), and maternal education. In contrast, birth weight generally decreases with maternal illnesses and number of miscarriages and stillbirths, with larger reductions at lower birth weight quantiles. Also, female infants have lower birth weight (particularly at higher quantiles). In the ECLAMC sample, a history of difficulty in conceiving and intake of folic acid supplements in the first trimester are negatively associated with birth weight at low quantiles (especially in the model with isolated clefts), whereas father's employment is positively associated with birth weight. Also, children of Native and African ancestries have lower birth weight (especially at lower quantiles). In the natality sample, infants of Black mothers have lower birth weight, whereas infants of White mothers have higher birth weight than infants of non-White, non-Black mothers. Finally, maternal smoking is associated with a decrease in birth weight. The overall similarity in these results between the two datasets provides further validity for the comparable patterns of the shock effects.

[15]See detailed results in the Appendix.

DOI: 10.1002/hec

Table V. Fetal health shock effects on birth weight using Latin American Collaborative Study of Congenital Anomalies data—expanded specification

Model	Quantile					Ordinary least squares
	0.1	0.25	0.5	0.75	0.9	
Isolated clefts[a] ($N = 43{,}193$)	−277.8***	−137.1***	−85.6***	−53.1***	−36.6*	−117.8***
	(28.5)	(18.9)	(15.2)	(13.0)	(19.9)	(14.4)
Isolated cleft types ($N = 43{,}193$)						
Cleft lip only[b,c]	−174.8***	−83.3**	−58.4**	−41.6*	−8.33	−75.3***
	(49.0)	(34.9)	(26.5)	(24.6)	(31.3)	(8.2)
Cleft palate only[d]	−206.6** (81.2)	−84.6**	−21.9	7.0	8.7	−40.0
		(34.8)	(32.6)	(36.0)	(42.7)	(22.2)
Cleft lip with palate[a]	−327.5***	−190.7***	−130.4***	−77.1***	−75.3***	−159.1***
	(42.3)	(23.8)	(18.9)	(17.2)	(24.3)	(22.5)
Nonisolated clefts[a]	−1290.6***	−1017.3***	−604.1***	−409.2***	−253.0***	−693.1***
($N = 41{,}945$)	(54.9)	(30.0)	(32.5)	(25.3)	(36.3)	(42.9)
Nonisolated cleft types ($N = 41{,}945$)						
Cleft lip only[a]	−1307.0***	−1188.0***	−563.0***	−254.4***	−126.4	−658.9***
	(185.0)	(128.0)	(133.3)	(88.2)	(133.1)	(73.7)
Cleft palate only[a]	−1104.1***	−892.9***	−494.7***	−345.4***	−218.3***	−594.9***
	(81.5)	(63.2)	(36.7)	(34.6)	(39.2)	(76.0)
Cleft lip with palate[a]	−1363.3***	−1103.0***	−779.2***	−508.7***	−406.8***	−797.1***
	(68.8)	(51.4)	(52.2)	(37.0)	(69.3)	(36.1)

The table reports the health shock effects on birth weight quantiles and mean from the expanded specification in Equation (5). Standard errors are in parentheses.
*$p < 0.1$; **$p < 0.05$; ***$p < 0.01$.
[a]The coefficients are significantly different between the five quantiles at $p < 0.0001$.
[b]The coefficients are significantly different between the five quantiles at $p < 0.1$.
[c]The coefficients are significantly different between the 0.1 and 0.9 quantiles at $p < 0.01$ (only evaluated when the coefficients are not significantly different between the five quantiles at $p < 0.05$).
[d]The coefficients are significantly different between the 0.1 and 0.9 quantiles at $p < 0.05$ (only evaluated when the coefficients are not significantly different between the five quantiles at $p < 0.05$).

Table VI. Fetal health shock effects on birth weight using natality data—expanded specification

Model	Quantile					Ordinary least squares
	0.1	0.25	0.5	0.75	0.9	
Isolated clefts[a] ($N = 308{,}369$)	−87.3** (40.8)	−114.6*** (18.4)	−67.3*** (14.5)	−48.6*** (16.9)	−35.5* (19.8)	−61.0*** (15.1)
Nonisolated clefts[b] ($N = 307{,}054$)	−932.9*** (86.9)	−769.7*** (50.5)	−578.8*** (36.2)	−377.1*** (44.1)	−212.1*** (50.8)	−550.0*** (28.9)

The table reports the health shock effects on birth weight quantiles and mean from the expanded specification in equation (5). Standard errors are in parentheses.
[a]The coefficients were significantly different between the five quantiles at $p < 0.01$.
[b]The coefficients were significantly different between the five quantiles at $p < 0.0001$.
*$p < 0.1$; **$p < 0.05$; ***$p < 0.01$.

6. CONCLUSIONS

We find that fetal health shocks increase inequalities in health capital accumulation by more adversely affecting infants at lower birth weight quantiles and widening the spread of the birth weight distribution. Specifically, severe health shocks reduce birth weight at low quantiles by up to five times more than at high quantiles. This

DOI: 10.1002/hec

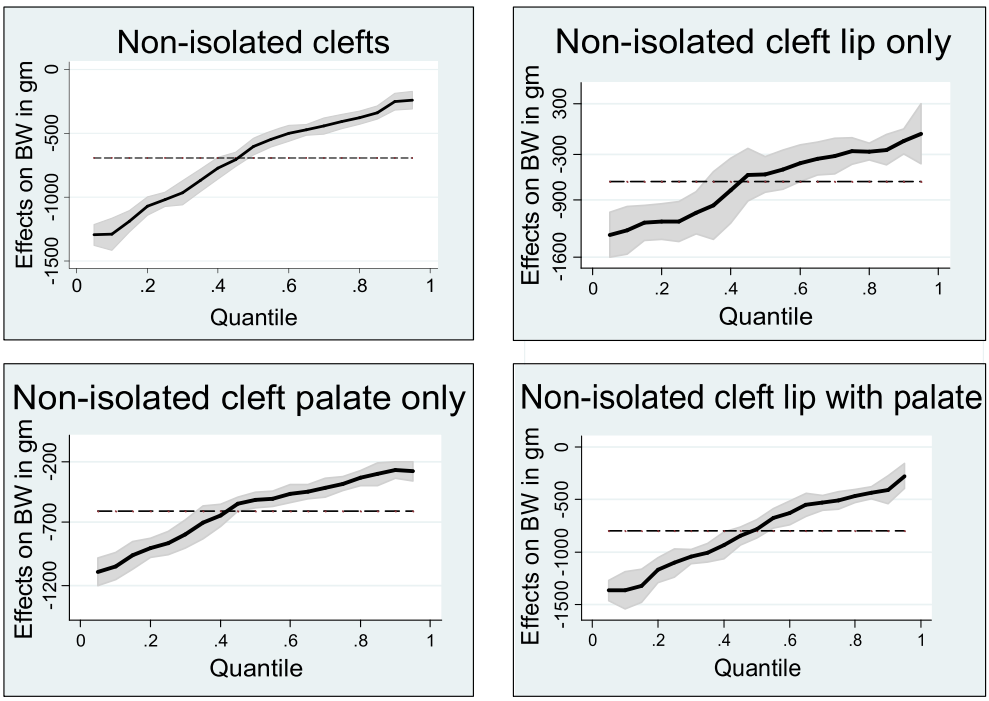

Figure 4. Effects of nonisolated oral clefts on birth weight quantiles and mean using the Latin American Collaborative Study of Congenital Anomalies data—expanded specification. The figure reports the effects of nonisolated oral clefts (both overall and by type) on birth weight quantiles (solid line) and mean (dashed line). The effects are estimated from the expanded model that includes all control variables (Equation (5)). The 95% CIs for the quantile effects estimated using 500 bootstrap applications are in the shaded area.

is also observed for less severe shocks, with birth weight decreasing by about six and two times more at low than at high quantiles in South America and the USA, respectively. Although we cannot evaluate the long-term effects of these inequalities, the large gaps in birth weight loss due to these shocks between infants at low versus high quantiles and the wide literature on the importance of birth weight as a predictor of future health and human capital suggest that these disparities may translate into large differences in these outcomes later in life. These results strongly indicate that inequalities in response to health shocks begin before birth and that policies aiming at improving child health and human development and reducing disparities in these outcomes should consider interventions that can reduce these inequalities during pregnancy, which is a highly sensitive period for health disparities.

Interestingly, the results are replicated across two samples from developed and less-developed countries. Although the absolute effects of the fetal health shocks are lower in the USA than in South America, the inequalities as a result of severe shocks are generally comparable between the two samples. This suggests that economic growth may proportionally reduce the adverse effects of severe fetal health shocks across the entire birth weight distribution but may not substantially affect the disparity in responses to these shocks between infants at different birth weight quantile ranks. However, economic growth appears to reduce the effects of less severe shocks much more for infants at low birth weight quantiles. For example, the effect of isolated clefts at the 0.1 quantile is about three times larger (in absolute value) in the South American sample than in the US sample, but the effect is comparable between the two samples at the median and higher quantiles. The comparable results between two unrelated samples from developed and less-developed countries suggest no sample selection bias in this study. However, replicating the study in other samples may be important for evaluating the generalizability of the results across different population characteristics.

DOI: 10.1002/hec

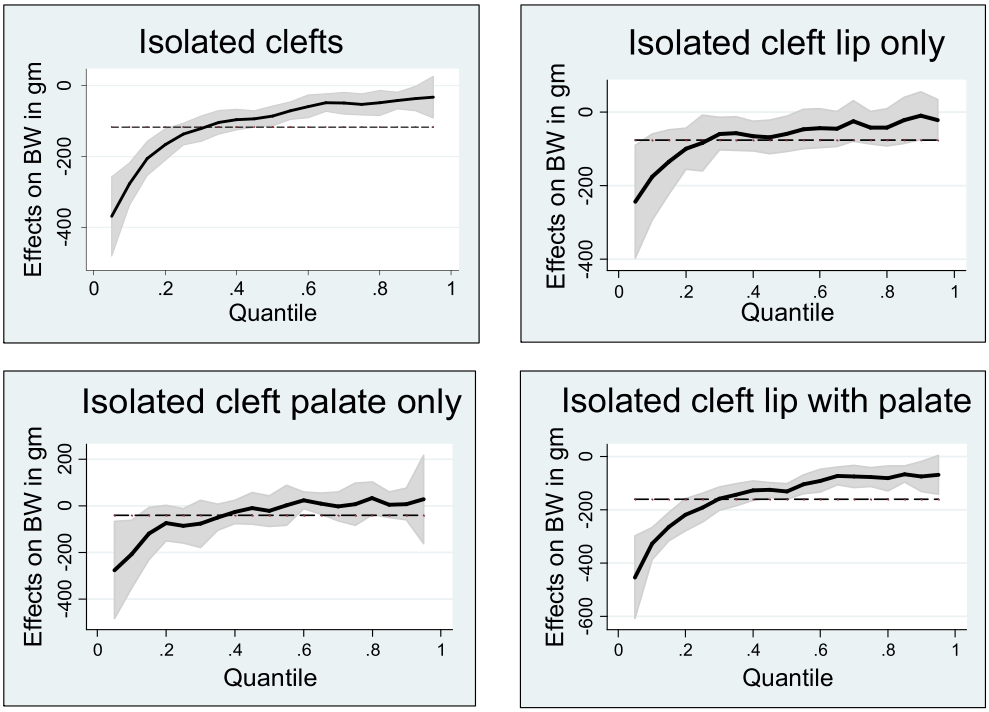

Figure 5. Effects of isolated oral clefts on birth weight quantiles and mean using the Latin American Collaborative Study of Congenital Anomalies data—expanded specification. The figure reports the effects of isolated oral clefts (both overall and by type) on birth weight quantiles (solid line) and mean (dashed line). The effects are estimated from the model that includes all control variables (Equation (5)). The 95% CIs for the quantile effects estimated using 500 bootstrap applications are in the shaded area.

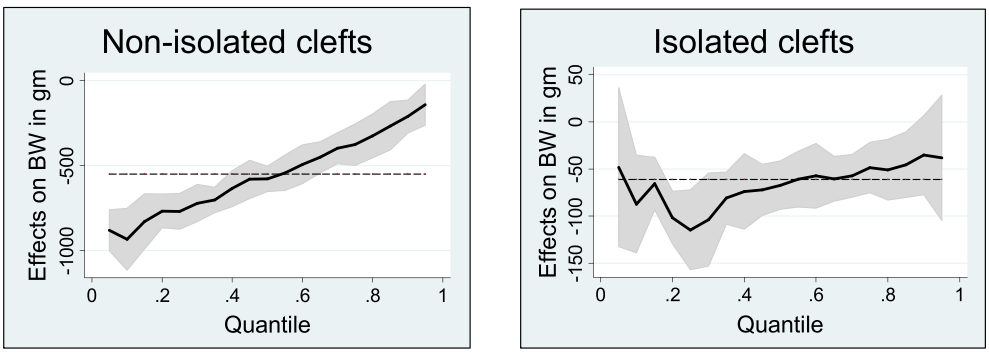

Figure 6. Effects of oral clefts on birth weight quantiles and mean using the natality data—expanded specification. The figure reports the effects of nonisolated and isolated oral clefts on birth weight quantiles (solid line) and mean (dashed line). The effects are estimated from the model that includes all control variables (Equation (5)). The 95% CIs for the quantile effects estimated using 500 bootstrap applications are in the shaded area.

The unobservable heterogeneity resulting in different birth weight rankings for infants of similar observable characteristics may be thought of as reflecting differences in unobservable fetal health endowments, which may include a wide range of genetic/biologic, socioeconomic, and environmental factors. Because infants ranking at lower birth weight quantiles may have fewer of these endowments on average, the findings suggest that health shocks result in larger health losses for less-endowed than better-endowed infants. Previous research has suggested that less-endowed infants at lower birth weight quantiles benefit more from prenatal care than

DOI: 10.1002/hec

better-endowed ones (Wehby *et al*., 2009a, 2009b). Together, these results suggest that less-endowed infants at lower birth weight quantiles are more sensitive to either gaining from healthcare interventions or losing from health shocks. We cannot directly identify in our analysis the specific fetal health endowments that may play a role in these inequalities and how they differ across the birth weight distribution. However, most of these seem unrelated to the typically observable and studied inputs such as maternal health, education, employment, and fertility history. These results highlight a complex underlying structure of causes for inequalities in early health accumulation and the need to expand the traditional health production framework in future research to be able to measure and study additional less-evaluated inputs and endowments such as psychosocial and genetic factors, besides the typically evaluated socioeconomic endowments, and to understand their role in the observed inequalities.

The 'shock' effects of oral clefts on birth weight appear to be mainly due to common genetic etiologic factors between these two conditions and to a lesser extent due to socioeconomic and behavioral factors. This is supported by observing virtually similar effects of oral clefts in the two specifications that alternatively exclude and include several socioeconomic, demographic, and behavioral factors. Of course, it is still possible that some unobserved behavioral factors such as alcohol use, maternal nutrition and body weight, and others that are relevant to both oral clefts and birth weight may be contributing to these shocks. Nonetheless, it is unlikely that the large effects of oral clefts on birth weight can be explained by differences in such behaviors between mothers of children with and without oral clefts as this would suggest very large behavioral effects on birth weight as well as large differences in these behaviors between these two maternal groups, which are not supported in the literature. As mentioned previously, oral clefts have a high genetic hereditability that further supports the role of genetic factors in these shocks. However, the main implications of the study are not dependent on the specific pathway of how oral clefts are associated with birth weight reduction as we use oral clefts as a marker of a health shock to normal fetal development.

APPENDIX A

Table A1. Detailed results for the birth weight regression specification with the less severe shocks in the Latin American Collaborative Study of Congenital Anomalies dataset

Model	Quantile					Ordinary least squares
	0.1	0.25	0.5	0.75	0.9	
Isolated clefts	−277.8*** (28.5)	−137.1*** (18.9)	−85.6*** (15.2)	−53.1*** (13.0)	−36.6* (19.9)	−117.8*** (11.5)
Maternal age, 13 to 49 years	54.5*** (7.0)	45.1*** (4.2)	34.0*** (4.0)	38.9*** (3.8)	41.2*** (5.0)	40.9*** (3.1)
Maternal age squared	−1.0*** (0.1)	−0.8*** (0.1)	−0.5*** (0.1)	−0.6*** (0.1)	−0.6*** (0.1)	−0.7*** (0.1)
Female infant	−77.7*** (10.7)	−97.1*** (6.7)	−105.9*** (6.0)	−126.3*** (6.1)	−140.1*** (8.2)	−110.1*** (5.3)
Acute illnesses	−100.7*** (14.2)	−45.2*** (8.8)	−18.8** (7.6)	−15.7** (7.6)	0.3 (9.7)	−39.6*** (6.6)
Chronic illnesses	−90.7*** (20.7)	−54.2*** (13.5)	−51.6*** (11.4)	−29.6** (11.5)	1.0 (17.9)	−52.9*** (9.1)
Number of live births the mother has had	11.9*** (4.1)	10.1*** (2.5)	16.0*** (2.0)	20.5*** (2.4)	22.0*** (3.1)	16.3*** (1.9)
Conception difficulty	−53.7** (22.6)	−29.0** (14.2)	−1.8 (12.4)	−0.8 (12.1)	−13.4 (15.1)	−11.9 (10.7)
Number of spontaneous stillbirths	−59.9*** (15.8)	−16.4*** (6.0)	−5.6 (5.1)	8.0 (6.6)	9.2 (7.4)	−16.5*** (4.7)

(*Continues*)

DOI: 10.1002/hec

Table A1. Continued

Model	Quantile					Ordinary least squares
	0.1	0.25	0.5	0.75	0.9	
Vaccine taken during the first trimester	26.4 (24.4)	3.8 (15.0)	8.1 (13.9)	7.3 (13.2)	13.3 (16.1)	17.4 (11.0)
Medication taken during the first trimester	16.8 (14.0)	5.5 (8.4)	3.9 (6.8)	6.3 (7.8)	3.6 (11.0)	3.5 (6.6)
Folic acid taken during the first trimester	−75.5** (33.8)	−38.4* (21.0)	−13.1 (24.3)	−21.0 (24.7)	−4.8 (33.8)	−28.3 (17.8)
Primary school complete	10.9 (15.6)	10.1 (9.7)	15.7* (9.0)	1.0 (9.1)	19.4 (12.1)	11.6 (7.7)
Secondary school incomplete	15.8 (15.5)	21.4** (9.6)	23.9*** (8.9)	−2.7 (10.0)	5.7 (12.4)	12.6 (8.0)
Secondary school complete	60.2*** (18.1)	38.6*** (12.3)	52.2*** (10.1)	17.8* (10.6)	15.0 (13.9)	39.9*** (9.2)
University incomplete	60.1* (35.6)	12.7 (19.1)	30.2 (18.7)	−27.9 (17.8)	−21.7 (23.7)	4.0 (16.4)
University complete	144.4*** (42.6)	66.3*** (19.5)	44.9** (18.3)	−15.5 (21.5)	−29.3 (31.4)	28.5 (18.5)
Cleft relative	51.2 (37.5)	49.7* (30.0)	19.4 (23.0)	26.3 (20.7)	−43.4 (30.5)	11.7 (19.7)
European Latin ancestry	−33.6** (13.2)	−14.8* (7.6)	0.1 (6.8)	12.6* (7.4)	13.4 (9.0)	−4.7 (6.0)
European non-Latin ancestry	0.9 (25.2)	19.5 (14.2)	30.2** (13.1)	15.4 (11.2)	13.3 (18.1)	23.8** (10.7)
Native ancestry	−52.8*** (19.3)	−42.1*** (11.5)	−24.0** (9.3)	−14.3 (9.4)	−8.6 (14.1)	−24.7*** (8.7)
African ancestry	−63.8*** (20.4)	−34.3*** (12.9)	−20.0** (10.0)	−26.5** (10.5)	−9.9 (15.4)	−27.6*** (9.0)
Other ancestry	−0.6 (35.5)	−29.9 (22.5)	−42.6** (21.7)	−29.1 (18.8)	−50.8** (25.2)	−26.5 (17.7)
Independent workers	67.9*** (21.0)	33.0*** (11.3)	22.0* (12.1)	6.8 (10.5)	−13.0 (15.4)	25.7** (10.1)
Blue collar workers	52.3*** (16.5)	21.2** (9.8)	19.7** (8.6)	25.0*** (8.9)	6.9 (11.4)	21.8*** (7.7)
White collar workers	43.6*** (15.3)	32.4*** (9.1)	24.1*** (7.8)	22.9** (9.2)	1.5 (11.6)	24.5*** (7.4)
Executive workers	39.1* (22.3)	34.3** (14.7)	30.6** (12.5)	40.0*** (13.8)	22.6 (16.7)	33.3*** (11.5)

$N = 43{,}193$. The table reports the regression coefficients from Equation (5) with standard errors in parentheses. Country and year fixed effects and the intercept are omitted for brevity.
**$p < 0.05$; *$p < 0.1$; ***$p < 0.01$.

Table A2. Detailed results for the birth weight regression specification with the severe shocks in the Latin American Collaborative Study of Congenital Anomalies dataset

Model	Quantile					Ordinary least squares effect
	0.1	0.25	0.5	0.75	0.9	
Nonisolated clefts	−1290.6*** (54.9)	−1017.3*** (30.0)	−604.1*** (32.5)	−409.2*** (25.3)	−253.0*** (36.3)	−693.1*** (15.3)
Maternal age, 13 to 49 years	51.9*** (7.2)	46.2*** (4.5)	36.1*** (4.1)	40.7*** (4.0)	43.4*** (5.0)	42.5*** (3.2)
Maternal age squared	−0.9*** (0.1)	−0.8*** (0.1)	−0.6*** (0.1)	−0.6*** (0.1)	−0.6*** (0.1)	−0.7*** (0.1)
Female infant	−76.1*** (11.2)	−94.0*** (6.3)	−103.8*** (6.1)	−125.5*** (6.2)	−133.6*** (8.3)	−107.2*** (5.5)
Acute illnesses	−92.5*** (15.4)	−45.3*** (8.8)	−16.2*** (7.8)	−15.4*** (8.5)	0.6 (10.6)	−37.5*** (6.8)
Chronic illnesses	−82.9*** (21.5)	−49.7*** (13.4)	−48.6*** (10.5)	−30.7*** (11.8)	−8.6 (16.2)	−50.5*** (9.3)
Number of live births the mother has had	14.5*** (4.2)	10.4*** (2.5)	17.0*** (2.2)	20.9*** (2.4)	22.7*** (3.2)	17.5*** (1.9)
Conception difficulty	−42.5* (21.9)	−25.3* (14.7)	−3.7 (12.7)	−1.3 (13.0)	−10.5 (15.9)	−9.6 (11.0)
Number of spontaneous stillbirths	−59.7*** (15.2)	−16.7** (6.5)	−7.3 (5.3)	6.8 (6.9)	10.0 (7.7)	−18.8*** (4.8)

(*Continues*)

DOI: 10.1002/hec

Table A2. Continued

Model	Quantile					Ordinary least squares effect
	0.1	0.25	0.5	0.75	0.9	
Vaccine taken during the first trimester	18.6 (25.5)	14.4 (14.6)	18.0 (13.7)	14.9 (14.3)	13.2 (17.4)	24.2** (11.3)
Medication taken during the first trimester	7.4 (15.3)	6.6 (9.2)	3.5 (7.3)	4.7 (7.5)	2.8 (10.7)	1.1 (6.8)
Folic acid taken during the first trimester	−50.4 (34.6)	−35.5* (21.5)	−17.4 (24.2)	−16.2 (24.2)	−6.3 (34.0)	−21.0 (18.2)
Primary school complete	13.3 (15.3)	11.4 (9.5)	15.3* (8.5)	−0.3 (8.9)	14.2 (12.2)	9.4 (8.0)
Secondary school incomplete	17.4 (15.0)	18.9* (9.8)	20.0** (8.7)	−3.7 (9.6)	3.3 (12.6)	8.9 (8.2)
Secondary school complete	61.1*** (18.1)	35.4*** (12.3)	51.3*** (10.6)	17.2 (11.1)	15.0 (14.0)	37.6*** (9.5)
University incomplete	70.7** (34.6)	25.1 (20.8)	27.3 (18.3)	−22.8 (17.6)	−20.8 (25.2)	11.5 (16.9)
University complete	111.0** (49.4)	51.7** (22.6)	36.8* (20.6)	−15.9 (22.6)	−35.7 (28.6)	8.6 (19.1)
Cleft relative	47.6 (42.8)	72.4** (32.3)	38.3 (26.1)	48.6* (24.9)	−21.9 (49.6)	60.0** (24.2)
European Latin ancestry	−35.2** (14.6)	−12.6* (7.6)	3.0 (6.8)	11.4 (7.1)	7.7 (8.6)	−2.1 (6.1)
European non-Latin ancestry	−6.6 (25.0)	25.1* (14.8)	26.3* (13.7)	18.1 (12.0)	9.3 (17.8)	24.4** (11.0)
Native ancestry	−54.8*** (19.2)	−39.0*** (11.9)	−27.4*** (10.0)	−15.5 (10.0)	−14.5 (13.6)	−27.4*** (8.9)
African ancestry	−64.6*** (20.3)	−35.1*** (12.3)	−23.6** (10.0)	−26.1*** (10.0)	−13.9 (15.4)	−30.9*** (9.2)
Other ancestry	8.6 (35.4)	−26.7 (22.5)	−35.3 (22.6)	−21.9 (19.6)	−55.2** (25.4)	−20.9 (18.2)
Independent workers	55.8** (23.1)	27.3** (12.0)	26.3** (12.4)	6.0 (11.3)	−9.0 (14.7)	22.9** (10.4)
Blue collar workers	42.7** (17.4)	20.4** (10.1)	20.4** (9.0)	22.8** (8.8)	2.0 (11.9)	21.3*** (7.9)
White collar workers	39.6** (16.1)	31.6*** (9.4)	24.3*** (8.0)	20.5** (8.8)	−2.3 (12.1)	23.5*** (7.6)
Executive workers	28.6 (23.2)	32.7** (14.9)	29.0** (13.2)	39.4*** (14.0)	15.9 (17.4)	32.1*** (11.8)

$N = 41{,}945$. The table reports the regression coefficients from Equation (5) with standard errors in parentheses. Country and year fixed effects and the intercept are omitted for brevity.
*$p < 0.1$; **$p < 0.05$; ***$p < 0.01$.

Table A3. Detailed results for the birth weight regression specification with the less severe shocks in the natality dataset

Model	Quantile					Ordinary least squares
	0.1	0.25	0.5	0.75	0.9	
Isolated clefts	−87.31*** (40.82)	−114.56*** (18.36)	−67.26*** (14.53)	−48.56*** (16.87)	−35.46* (19.82)	−61.01*** (14.40)
Maternal age, 13 to 49 years	61.65*** (3.243)	38.26*** (2.16)	28.95*** (1.49)	29.50*** (1.65)	30.23*** (2.09)	37.40*** (1.49)
Maternal age squared	−1.14*** (0.06)	−0.67*** (0.04)	−0.47*** (0.03)	−0.45*** (0.03)	−0.44*** (0.04)	−0.64*** (0.03)
Female infant	−56.50*** (4.36)	−97.30*** (2.59)	−118.48*** (2.14)	−130.99*** (2.29)	−141.60*** (2.99)	−107.88*** (2.16)
Acute illnesses	−674.29*** (14.51)	−404.95*** (8.91)	−230.02*** (5.29)	−146.52*** (5.70)	−89.81*** (6.47)	−291.38*** (4.19)
Chronic illnesses	−96.49*** (9.85)	−31.30*** (5.03)	−1.77 (3.62)	25.32*** (4.24)	47.22*** (5.20)	−8.17** (3.69)

(*Continues*)

DOI: 10.1002/hec

Table A3. Continued

Model	Quantile					Ordinary least squares
	0.1	0.25	0.5	0.75	0.9	
Number of live births the mother has had	9.36*** (2.21)	14.10*** (1.32)	17.68*** (1.13)	18.13*** (1.22)	19.96*** (1.62)	18.02*** (1.03)
Number of spontaneous stillbirths	−35.91*** (3.71)	−17.38*** (1.98)	−10.17*** (1.44)	−4.93*** (1.69)	−3.41* (2.07)	−16.20*** (1.35)
High school	13.15* (6.72)	19.52*** (3.83)	23.25*** (3.21)	19.78*** (3.65)	18.95*** (4.80)	18.00*** (3.20)
University incomplete	40.79*** (8.21)	46.95*** (4.49)	50.02*** (3.62)	41.55*** (4.12)	39.63*** (5.50)	43.66*** (3.65)
University complete	59.80*** (8.66)	73.08*** (4.68)	72.98*** (3.71)	51.30*** (4.36)	39.84*** (5.62)	59.12*** (3.90)
Maternal race White	92.33*** (9.93)	124.03*** (5.95)	131.86*** (4.95)	122.6*** (5.43)	127.54*** (8.14)	118.49*** (4.79)
Maternal race Black	−167.86*** (12.43)	−80.94*** (6.95)	−49.35*** (5.55)	−55.62*** (6.24)	−43.43*** (9.23)	−86.47*** (5.48)
Smoked during pregnancy (yes)	−232.37*** (8.42)	−211.80*** (4.84)	−193.46*** (3.68)	−189.23*** (4.18)	−179.01*** (5.48)	−200.15*** (3.70)

$N = 308{,}369$. The table reports the regression coefficients from Equation (5) with standard errors in parentheses. State fixed effects and the intercept are omitted for brevity.
*$p < 0.1$; **$p < 0.05$; ***$p < 0.01$.

Table A4. Detailed results for the birth weight regression specification with the severe shocks in the natality dataset

Model	Quantile					Ordinary least squares effect
	0.1	0.25	0.5	0.75	0.9	
Nonisolated clefts	−932.86*** (86.94)	−769.70*** (50.45)	−578.76*** (36.20)	−377.14*** (44.12)	−212.09*** (50.76)	−549.99*** (28.79)
Maternal age, 13 to 49 years	61.87*** (3.55)	38.71*** (2.07)	29.10*** (1.38)	29.74*** (1.43)	30.30*** (2.11)	37.68*** (1.50)
Maternal age squared	−1.14*** (0.06)	−0.68*** (0.04)	−0.48*** (0.02)	−0.46*** (0.02)	−0.45*** (0.04)	−0.64*** (0.03)
Female infant	−55.77*** (4.63)	−97.38*** (2.58)	−118.45*** (2.20)	−131.10*** (2.45)	−141.99*** (3.07)	−107.87*** (2.17)
Acute illnesses	−673.61*** (13.56)	−406.11*** (8.39)	−230.25*** (5.45)	−147.50*** (5.53)	−90.58*** (6.37)	−292.02*** (4.20)
Chronic illnesses	−95.62*** (10.05)	−30.90*** (4.99)	−1.84 (3.79)	25.04*** (4.11)	47.04*** (5.63)	−8.24** (3.70)
Number of live births the mother has had	9.03*** (2.22)	14.06*** (1.28)	17.54*** (1.04)	18.25*** (1.18)	20.28*** (1.68)	18.00*** (1.03)
Number of spontaneous stillbirths	−36.47*** (3.56)	−17.92*** (2.04)	−10.32*** (1.52)	−4.96*** (1.62)	−3.36 (2.12)	−16.38*** (1.36)
High school	12.59** (6.33)	19.54*** (3.51)	23.26*** (2.91)	19.63*** (3.53)	19.03*** (4.71)	17.89*** (3.21)
University incomplete	40.34*** (7.95)	47.00*** (4.29)	49.69*** (3.46)	41.03*** (4.10)	39.66*** (5.35)	43.19*** (3.66)
University complete	57.95*** (8.63)	73.00*** (4.50)	72.59*** (3.67)	50.87*** (4.32)	40.13*** (5.59)	58.69*** (3.91)

(*Continues*)

DOI: 10.1002/hec

Table A4. Continued

Model	Quantile					Ordinary least squares effect
	0.1	0.25	0.5	0.75	0.9	
Maternal race White	92.03*** (9.64)	124.43*** (5.24)	132.39*** (4.82)	123.10*** (5.45)	127.74*** (8.02)	118.95*** (4.81)
Maternal race Black	−167.58*** (12.22)	−80.20*** (6.36)	−48.65*** (5.33)	−54.80*** (6.35)	−43.12*** (8.68)	−85.82*** (5.50)
Smoked during pregnancy (yes)	−232.94*** (8.69)	−212.45*** (5.06)	−193.08*** (3.88)	−189.46*** (4.09)	−178.98*** (5.46)	−200.09*** (3.71)

$N = 307{,}054$. The table reports the regression coefficients from Equation (5) with standard errors in parentheses. State fixed effects and the intercept are omitted for brevity.
*$p < 0.1$; **$p < 0.05$; ***$p < 0.01$.

ACKNOWLEDGEMENTS

This work was supported by grant 1R03 DE018394 from the National Institutes of Health (NIH), National Institute of Dental and Craniofacial Research (NIDCR) [Correction made here after initial online publication.].

REFERENCES

Anderson P, Doyle LW. 2003. Neurobehavioral outcomes of school-age children born extremely low birth weight or very preterm in the 1990s. *JAMA: The Journal of the American Medical Association* **289**(24): 3264–3272.
Becker M, Svensson H, Kallen B. 1998. Birth weight, body length, and cranial circumference in newborns with cleft lip or palate. *The Cleft Palate–Craniofacial Journal* **35**(3): 255–261.
Castilla EE, Orioli IM. 2004. ECLAMC: the Latin-American collaborative study of congenital malformations. *Community Genetics* **7**(2–3): 76–94.
Chernozhukov V, Hansen C. 2004. The effects of 401(k) participation on the wealth distribution: an instrumental quantile regression analysis. *The Review of Economics and Statistics* **86**(3): 735–751.
Chernozhukov V, Hansen C. 2005. An IV model of quantile treatment effects. *Econometrica* **73**(1): 245–261.
Christensen K. 1999. The 20th century Danish facial cleft population—epidemiological and genetic–epidemiological studies. *The Cleft Palate–Craniofacial Journal* **36**(2): 96–104.
Christensen K, Fogh-Andersen P. 1993. Cleft lip (+/− cleft palate) in Danish twins, 1970–1990. *American Journal of Medical Genetics* **47**(6): 910–916.
Christensen K, Juel K, Herskind AM, Murray JC. 2004. Long term follow up study of survival associated with cleft lip and palate at birth. *British Medical Journal* **328**(7453): 1405.
Clark JD, Mossey PA, Sharp L, Little J. 2003. Socioeconomic status and orofacial clefts in Scotland, 1989 to 1998. *The Cleft Palate–Craniofacial Journal* **40**(5): 481–485.
Clausson B, Lichtenstein P, Cnattingius S. 2000. Genetic influence on birthweight and gestational length determined by studies in offspring of twins. *BJOG: An International Journal of Obstetrics and Gynaecology* **107**(3): 375–381.
Currie J. 2009. Healthy, wealthy, and wise: socioeconomic status, poor health in childhood, and human capital development. *Journal of Economic Literature* **47**(1): 87–122.
Currie J, Lin W. 2007. Chipping away at health: more on the relationship between income and child health. *Health Affairs (Millwood)* **26**(2): 331–344.
Dixon MJ, Marazita ML, Beaty TH, Murray JC. 2011. Cleft lip and palate: understanding genetic and environmental influences. *Nature Reviews Genetics* **12**(3): 167–178.
Durning P, Chestnutt IG, Morgan MZ, Lester NJ. 2007. The relationship between orofacial clefts and material deprivation in Wales. *The Cleft Palate–Craniofacial Journal* **44**(2): 5.
Feinstein L. 2003. Inequality in the early cognitive development of British children in the 1970 cohort. *Economica* **70**(277): 73–97.
Forbes K, Westwood M. 2010. Maternal growth factor regulation of human placental development and fetal growth. *Journal of Endocrinology* **207**(1): 1–16.

DOI: 10.1002/hec

Forrester MB, Merz RD. 2003. First-year mortality rates for selected birth defects, Hawaii, 1986–1999. *American Journal of Medical Genetics. Part A* **119A**(3): 311–318.
Forrester MB, Merz RD. 2004. Descriptive epidemiology of oral clefts in a multiethnic population, Hawaii, 1986–2000. *The Cleft Palate–Craniofacial Journal* **41**(6): 622–628.
Frankel S, Elwood P, Sweetnam P, Yarnell J, Smith GD. 1996. Birthweight, body-mass index in middle age, and incident coronary heart disease. *Lancet* **348**(9040): 1478–1480.
Gluckman PD, Hanson MA, Cooper C, Thornburg KL. 2008. Effect of in utero and early-life conditions on adult health and disease. *The New England Journal of Medicine* **359**(1): 61–73.
Hao L, *Naiman D*. 2007. Quantile Regression. Sage Publications: Thousand Oaks, CA.
Heron M, Sutton PD, Xu J, Ventura SJ, Strobino DM, Guyer B. 2010. Annual summary of vital statistics: 2007. *Pediatrics* **125**(1): 4–15.
Jones MC. 1988. Etiology of facial clefts: prospective evaluation of 428 patients. *The Cleft Palate Journal* **25**(1): 16–20.
Kapp-Simon K. 1986. Self-concept of primary-school-age children with cleft lip, cleft palate, or both. *The Cleft Palate Journal* **23**(1): 24–27.
Kapp-Simon KA, Simon DJ, Kristovich S. 1992. Self-perception, social skills, adjustment, and inhibition in young adolescents with craniofacial anomalies. *The Cleft Palate–Craniofacial Journal* **29**(4): 352–356.
Koenker R, Bassett G Jr. 1978. Regression quantiles. *Econometrica* **46**(1): 33–50.
Koenker R, Hallock KF. 2001. Quantile regression. *Journal of Economic Perspectives* **15**(4): 143–156.
Lien DS, Evans WN. 2005. Estimating the impact of large cigarette tax hikes. *Journal of Human Resources* **40**(2): 373–392.
Lopez Camelo JS, Campana H, Santos R, Poletta FA. 2006. Effect of the interaction between high altitude and socioeconomic factors on birth weight in a large sample from South America. *American Journal of Physical Anthropology* **129**(2): 305–310.
Marazita M. 2002. *Segregation Analysis*. Oxford University Press: New York, NY.
Matijasevich A, Victora CG, Barros AJ, Santos IS, Marco PL, Albernaz EP, Barros FC. 2008. Widening ethnic disparities in infant mortality in Southern Brazil: comparison of 3 birth cohorts. *American Journal of Public Health* **98**(4): 692–668.
Menegotto BG, Salzano FM. 1991. Epidemiology of oral clefts in a large South American sample. *The Cleft Palate–Craniofacial Journal* **28**(4): 373–376; discussion 76–77.
Mossey PA, Little J, Munger RG, Dixon MJ, Shaw WC. 2009. Cleft lip and palate. *Lancet* **374**(9703): 1773–1785.
Moulton BR. 1986. Random group effects and the precision of regression estimates. *Journal of Econometrics* **32**(3): 385–397.
Nackashi J, Dedlow R, Dixon-Wood V. 2002. In *Cleft Lip and Palate: From Origin to Treatment*, Wyszynski DF (ed.), Health care for children with cleft lip and palate: comprehensive services and infant feeding. Oxford University Press: New York, NY, 303–318.
Nukui T, Day RD, Sims CS, Ness RB, Romkes M. 2004. Maternal/newborn GSTT1 null genotype contributes to risk of preterm, low birthweight infants. *Pharmacogenetics* **14**(9): 569–576.
Okah FA, Cai J, Hoff GL. 2005. Term-gestation low birth weight and health-compromising behaviors during pregnancy. *Obstetrics and Gynecology* **105**(3): 543–550.
Parker SE, Mai CT, Canfield MA, Rickard R, Wang Y, Meyer RE, Anderson P, Mason CA, Collins JS, Kirby RS, Correa A. 2010. Updated national birth prevalence estimates for selected birth defects in the United States, 2004–2006. *Birth Defects Research. Part A, Clinical and Molecular Teratology* **88**(12): 1008–1016.
Rosenzweig MR, Schultz TP. 1983. Estimating a household production function: heterogeneity, the demand for health inputs, and their effects on birth weight. *Journal of Political Economy* **91**(5): 723–746.
Schliekelman P, Slatkin M. 2002. Multiplex relative risk and estimation of the number of loci underlying an inherited disease. *American Journal of Human Genetics* **71**(6): 1369–1385.
Scholl TO, Hediger ML, Bendich A, Schall JI, Smith WK, Krueger PM. 1997. Use of multivitamin/mineral prenatal supplements: influence on the outcome of pregnancy. *American Journal of Epidemiology* **146**(2): 134–141.
Shi M, Wehby GL, Murray JC. 2008. Review on genetic variants and maternal smoking in the etiology of oral clefts and other birth defects. *Birth Defects Research. Part C, Embryo Today* **84**(1): 16–29.
Sperber G. 2002. In *Cleft Lip and Palate: From Origin to Treatment*, Wyszynski D (ed.), Formation of the primary palate. Oxford University Press: New York, NY; 5–13.
Taylor GM, Alexander FE, D'Souza SW. 2006. Interactions between fetal HLA-DQ alleles and maternal smoking influence birthweight. *Paediatric and Perinatal Epidemiology* **20**(5): 438–448.
Thomas PT, Turner SR, Rumsey N, Dowell T, Sandy JR. 1997. Satisfaction with facial appearance among subjects affected by a cleft. *The Cleft Palate–Craniofacial Journal* **34**(3): 226–231.
Thompson LA, Goodman DC, Chang CH, Stukel TA. 2005. Regional variation in rates of low birth weight. *Pediatrics* **116**(5): 1114–1121.
Victora CG, Adair L, Fall C, Hallal PC, Martorell R, Richter L, Sachdev HS. 2008. Maternal and child undernutrition: consequences for adult health and human capital. *Lancet* **371**(9609): 340–357.

DOI: 10.1002/hec

Wehby GL, Cassell CH. 2010. The impact of orofacial clefts on quality of life and healthcare use and costs. *Oral Diseases* **16**(1): 3–10.
Wehby GL, Courtemanche CJ. 2012. The heterogeneity of the cigarette price effect on body mass index. *Journal of Health Economics* **31**(5):719–729.
Wehby GL, Jugessur A, Moreno LM, Murray JC, Wilcox A, Lie RT. 2011. Genes as instruments for studying risk behavior effects: An application to maternal smoking and oraofacial clefts. *Health Services and Outcomes Research Methodology* **11**: 54–78.
Wehby GL, Murray JC. 2010. Folic acid and orofacial clefts: a review of the evidence. *Oral Diseases* **16**(1): 11–19.
Wehby GL, Ohsfeldt RL, Murray JC. 2006. Health professionals' assessment of health-related quality of life values for oral clefting by age using a visual analogue scale method. *The Cleft Palate–Craniofacial Journal* **43**(4): 383–391.
Wehby GL, Murray JC, Castilla EE, Lopez-Camelo JS, Ohsfeldt RL. 2009a. Prenatal care effectiveness and utilization in Brazil. *Health Policy and Planning* **24**(3): 175–188.
Wehby GL, Murray JC, Castilla EE, Lopez-Camelo JS, Ohsfeldt RL. 2009b. Quantile effects of prenatal care utilization on birth weight in Argentina. *Health Economics* **18**(11): 1307–1321.
Wehby GL, Castilla EE, Lopez-Camelo J. 2010. The impact of altitude on infant health in South America. *Economics and Human Biology* **8**(2): 197–211.
Wehby GL, Fletcher J, Lehrer S, Moreno Uribe L, Murray J, Wilcox A, Lie R. 2011. A genetic instrumental variables analysis of the effects of maternal smoking during pregnancy on birth weight. *Biodemography and Social Biology* **57**(1): 29.
Wehby GL, Pedersen D, Murray J, Christensen K. 2012a. The effects of oral clefts on hospital use throughout the lifespan. *BMC Health Services Research*.
Wehby GL, Lopez-Camelo J, Castilla E. 2012b. Hospital volume and mortality of very low-birthweight infants in South America. *Health Services Research* **47**(4): 1502–1521.
Wooldridge JM. 2002. *Econometric Analysis of Cross Section and Panel Data*. MIT Press: Cambridge.
Wyszynski DF, Wu T. 2002. Prenatal and perinatal factors associated with isolated oral clefting. *The Cleft Palate–Craniofacial Journal* **39**(3): 370–375.
Wyszynski DF, Sarkozi A, Vargha P, Czeizel AE. 2003. Birth weight and gestational age of newborns with cleft lip with or without cleft palate and with isolated cleft palate. *Journal of Clinical Pediatric Dentistry* **27**(2): 185–190.

DOI: 10.1002/hec