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The Impact of Maternal Smoking during Pregnancy on Early Child Neurodevelopment

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Abstract

Early child neurodevelopment has major impacts on future human capital and health. However, not much is known about the impacts of prenatal risk factors on child neurodevelopment. This study evaluates the effects of maternal smoking during pregnancy on child neurodevelopment between 3 and 24 months of age and interactions with socioeconomic status (SES). Data from a unique sample of children from South America are employed. Smoking has large adverse effects on neurodevelopment, with larger effects in the low SES sample. The study results highlight the importance of early interventions beginning before and during pregnancy for enhancing child development and future human capital attainment.

Keywords

Smoking; child development; neurodevelopment; prenatal behaviors; child health; human capital

I. Introduction

Maternal smoking during pregnancy contributes to a variety of infant health problems present at birth as well as long lasting behavioral and neurodevelopmental impairments, and remains arguably one of the most important modifiable risk behaviors for child and long-

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term health and human capital (Buka, Shenassa, and Niaura 2003; Dunn et al. 1976; Fried 1989; Fried and Watkinson 1988; Key et al. 2007; Lanting 2009; Obel et al. 1998; Olds, Henderson, and Tatelbaum 1994; Richardson, Walker, and Horne 2009; Weitzman, Gortmaker, and Sobol 1992). Maternal smoking increases the risk for several adverse birth outcomes including infant death, preterm birth, low birth weight and poor intrauterine growth (Buka et al. 2003; Dunn et al. 1976; Lanting 2009; Richardson et al. 2009; Weitzman et al. 1992)[1]. Further child health implications due to smoking during pregnancy may include respiratory problems and infections (DiFranza, Aligne, and Weitzman 2004; Weitzman et al. 1992)[2].

Several studies have shown that the early physical health problems increased by smoking have adverse effects on human capital accumulation throughout life in both developed and less developed countries. For example, infants who are born at low birth weight have reduced educational achievement in the form of lower test scores, fewer school years completed, and higher rates of dropping out of school and lower economic performance in the form of lower income and living in areas with high poverty later in life (Button, Maughan, and McGuffin 2007; Case, Fertig, and Paxson 2005; Saigal and Rosenbaum 2007; Taylor et al. 2000; Victora et al. 2008).[3] Some of the pathways through which early health conditions such as low birth weight reduce human capital are through increasing risks for developmental, behavioral and chronic health problems (Button et al. 2007; Case 2010; Saigal and Rosenbaum 2007; Taylor et al. 2000; Victora et al. 2008).[4]

In addition to affecting physical health, in utero exposure to maternal smoking may have adverse effects on cognitive ability, neurological health and behavior of infants and children. Neurodevelopment encompasses several neurological and psychomotor skills including fine and gross motor, language, and social adaptation skills and may be considered an early form of not only health but also human capital as several of these earlier skills are strongly predictive of standard measures of human capital such as education and cognitive performance later in life as highlighted below. The adverse effects of prenatal smoking on child neurodevelopment may include poor language development and reduction in cognitive functioning. Key et al. (2007) find that infants exposed to maternal smoking in utero have both delayed response to sound and a lower ability to discriminate between sounds after birth, which impact later language skills (Fried 1989; Molfese 2000). Prenatal exposure to smoking may also reduce the child's motor performance, mental development (measured by the Bayley Scales of Infant Development), IQ scores, and language development through age three years (Fried 1989; Fried and Watkinson 1988; Gusella and Fried 1984; Obel et al. 1998; Richardson, Day, and Goldschmidt 1995).[5]

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[1]Maternal smoking may impair the sleep arousal processes including a decreased cortical arousal, which increases the risk for sudden infant death syndrome (Kato et al. 2003; Richardson et al. 2009). Lanting et al. (2009) reports a 7 times increased risk of preterm birth (≤ 28 gestational weeks) with prenatal smoking, and that 23.5% of infants of smoking mothers were under the 10th percentile for weight at birth, compared to 8.8 % for non-smoking mothers. Several Studies report reductions in birth weight of between 90-300 grams due to prenatal smoking (Haug 2000; Lumley 1989; Rosenzweig 1983).

[2]These include middle ear disease, upper respiratory problems and complications, decrease in pulmonary function, and tonsil/throat infection.

[3]Furthermore, performance on school tests also declines with birth weight among children of very low birth (Button et al. 2007; Case et al. 2005; Saigal and Rosenbaum 2007; Taylor et al. 2000; Victora et al. 2008).

[4]A variety of behavior and health problems have been documented in children with low birth weight (DiFranza et al. 2004; Gilman, Gardener, and Buka 2008; McCarton 1998; Stene-Larsen 2009). Low birth weight has also been found to be related to a variety of long term adverse outcomes such as lower intelligence, language, reading, quantitative skills, education, and wealth (Fried, James, and Watkinson 2001; Mortensen et al. 2005; Naeye and Peters 1984; Olds et al. 1994; Victora et al. 2008). Taylor et al (2000) found that infants born at less than 750 grams have a significantly higher risk of lower IQ than babies born at a higher birth weight.

[5]Assessment at 12 months using the Bayley Mental Development Index, 24 month assessment with Cattell Scales, 36 and 48 month evaluation with Stanford-Binet measure. Average difference between case and control IQ at 12 and 24 months was 2.59 points, and at 36 and 48 months was 4.35 points after controlling for confounding background variables.

Prenatal smoking may also increase the risks of several child behavioral problems including externalization of aggressive and hyperactive behavior, prolonged periods of verbal or physical aggression and/or socially undesirable behavior (conduct disorder) throughout childhood, and delinquency in later childhood (Faden and Graubard 2000; Herrmann, King, and Weitzman 2008; Olds et al. 1994). Several of these behavioral health problems have adverse effects on future human capital. For example, Currie et al. (2010) report lower probability of 12^{th} grade completion by age 17 years and increases in welfare use for children who had ADHD earlier in life compared to their siblings without ADHD.

There is evidence for long-lasting adverse effects of prenatal smoking on some human capital measures throughout childhood, adolescence and adulthood. Individuals who were exposed to maternal smoking in utero have lower scores on spelling, language and math assignments and tests through later childhood and teenage years (Bastra 2003) as well as deficits in auditory and visual processing (Fried 2002). Milberger et al. (1998) find that male children aged 6–17 years of women who smoked during pregnancy have significantly lower IQ scores overall compared to those who were born of non-smoking women. Case et al. (2005) report reduced employment at age 33 and 42 years among men exposed to moderate or heavy prenatal smoking. Other adverse long-term effects on human capital through increased prevalence of ADHD, externalizing behavior (Stene-Larsen 2009), criminal arrests, hospitalization for psychiatric disorders and conduct disorder (Wakschlag et al. 1997) are also found to have a dose-response relationship to maternal smoking during pregnancy (Brennan et al. 2002; Ernst, Moolchan, and Robinson 2001; Fergusson, Woodward, and Horwood 1998; Indredavik et al. 2007; Milberger 1998). It is also important to note that children of mothers who smoked during pregnancy are more likely to become smokers themselves later in life (Buka et al. 2003; Cornelius et al. 2000; Ernst et al. 2001).

In addition to the evidence linking prenatal smoking to measures of human capital at various ages either directly or indirectly through physical and behavioral health problems, a main motivation for studying child neurodevelopment as a form of early human capital is the strong evidence linking early neurodevelopmental skills to human capital attainment later in life. Suboptimal child neurodevelopment may reduce cognitive outcomes and educational achievement later in life (Capute et al. 1985; Fernald, Perfors, and Marchman 2006; Murray et al. 2007; Murray et al. 2006; Taanila et al. 2005). Murray et al. (2006) find a significant relationship between the age at which a child learns to stand without aid – an important neurodevelopmental milestone – and performance on cognitive tasks involving categorization. Murray et al. (2007) find that earlier age at walking without aid and speaking names other than those of the parents is associated with higher IQ scores during childhood (age 8 years) and better reading comprehension and verbal ability during later adulthood. Suboptimal child neurodevelopment may increase the risks of mental health and behavioral problems later in adolescence and adulthood (Fergusson 1999; Fergusson, Horwood, and Lynskey 1993; Isohanni 2001; Jones 1994; Sigurdsson 1999; van Os 1997), which is expected to have adverse effects on human capital attainment.

It is generally well accepted that prenatal factors such as maternal smoking, nutrition, and body size influence fetal adaptive responses and subsequently have significant impacts on the risk of disease throughout life (Gluckman et al. 2008). One of the mechanisms by which smoking during pregnancy is thought to affect child neurodevelopment is by restricting fetal access to oxygen-rich blood, leading to fetal neurodevelopment impairments (Ernst et al. 2001; Gennser, Marsal, and Brantmark 1975; Maritz 2008). This is thought to occur through impacting uterine blood flow and the level of carboxyhemoglobin (hemoglobin with carbon monoxide) in both the infant's and mother's blood (Morrow, Ritchie, and Bull 1988; Soothill et al. 1996).[6] In addition, toxins introduced into the mother's body via smoking readily cross the placenta during gestation and are absorbed easily by the developing fetus

(Matta et al. 2007). Some of the early detrimental smoking effects may involve changes in brain activation that affect children's ability to appropriately respond to stimuli (Bennett et al. 2009).

Given the importance of early child health in general and neurodevelopment specifically for future human capital and that neurodevelopment may be considered an early form of human capital, identifying the effects of maternal risk behaviors during pregnancy, such as smoking, on early child neurodevelopment becomes essential for identifying ways to improve not only neurodevelopment but also human capital throughout life. Therefore, studying the effects of prenatal smoking on neurodevelopment has direct implications for identifying early determinants of human capital that can be addressed by interventions very early in life, including during pregnancy. Identifying these effects may allow for developing such interventions that can have positive multiplicative lifetime effects on health and human capital. Prenatal interventions that improve early child neurodevelopment are likely to be cost-effective and result in large social returns due to the self-producing effects of child developmental skills over time and their complementarity effects with investments later in life (Cunha and Heckman 2007; Doyle et al. 2009). In other words, early child development has direct positive (self-producing) effects on development later in life and may also enhance the effects of later investments. For example, children who have acquired more skills earlier in life may benefit more from later investments compared to those who have acquired fewer skills.

The increasing knowledge and publicity of the negative smoking effects on health have resulted in reductions in maternal smoking over the past two decades, though only small reductions during certain periods (CDC 2009; Ebrahim 2000).[7] Nonetheless, the rates of smoking among women of childbearing age and prenatal smoking are still high worldwide. For example, about 12% of women reported smoking during pregnancy in 2005 in the US and about 22.4% of women of reproductive age continue to smoke (CDC 2008, 2009).[8]

This study assesses the effects of maternal smoking during pregnancy on child neurodevelopment between ages 3 to 24 months. The study evaluates the smoking effects both pooled and stratified by socioeconomic status (SES), which is a significant predictor of smoking participation and intensity. The paper contributes significantly to understanding the impacts of smoking as a major maternal risk behavior on early child neurodevelopment as a form of human capital. Previous studies of smoking effects during pregnancy on early life neurodevelopment are limited by fairly small sample sizes and descriptive statistical methods that do not account for unobserved confounders that may correlate with both smoking and child neurodevelopment. Another limitation in several studies is relying on maternal report of child developmental measures, which may be biased. Further, previous studies of prenatal smoking effects on child neurodevelopment in populations from less developed countries such as in South America are rare. Such studies are essential given the comparable, and in certain countries, higher prenatal smoking rates compared to developed countries (Bloch et al. 2008).

[6]Prenatal smoking decreases the alveolar surface used for air exchange within the lungs which decreases fetal access to oxygen. This decrease in surface area may mimic lung aging and also induce greater susceptibility to respiratory disease later in life (Collins et al; 1985; Maritz; 2008). Also, nicotine has a significant effect on placental development and can cause an increase in placental lesions, disrupt placental function, and increase the risk for placentomegaly, all of which may decrease fetal access to oxygen rich blood via the placenta (Ernst et al. 2001; Longo 1972; Naeye 1978; Sastry 1991).

[7]For example, the rate of quitting smoking among pregnant women decreased only from 26.3% to 25.2% between 1987 and 1996 in the US (Ebrahim 2000).

[8]Furthermore, quitting rates of pregnant women have been similar to those of non-pregnant women over time (Ebrahim 2000). Percentage of women who became pregnant and then quit smoking decreased at a similar rate (-1.1%) compared with the percentage of women who had no reported pregnancy and quit smoking (-1.9%) between 1987 and 1996.

We address these limitations by studying a unique and large sample of children from South America with systematic neurodevelopmental screening measurements by trained physicians for all sample children. The study estimates the smoking effects accounting for several observed relevant factors and evaluates the potential effects of maternal self-selection into smoking, based on unobserved relevant factors, on the estimated smoking effects.

II. Methods

A. Analytical Framework

The study follows the standard health production approach that has been employed in several previous seminal studies of child health production (such as Rosenzweig and Schultz, 1983; Grossman and Joyce, 1990). The model is based on a maternal utility function *U* during pregnancy that includes "anticipated" child's health/development and other utility-enhancing constructs and consumption (**Z**), which may include maternal health (*H*), smoking (*S*), and others as follows:

$$\mathrm{U}=U(D,\mathbf{Z}) \tag{1}$$

Child development (D) is produced by maternal inputs and investments (**I**) during pregnancy such as nutrition and prenatal care use and by maternal health. *D* is also impacted by smoking but also by other behavioral factors (**B**) of Z such as alcohol use, stress, exercise, and others, and by exogenous technological factors such as genetic factors (**T**). The child development production function can be specified as follows:

$$D=f(S,H,\mathbf{I},\mathbf{B},\mathbf{T}) \tag{2}$$

The mother maximizes her utility during pregnancy subject to the child development production function (2) and to the following budget constraint of income (G) being equal to expenditures on utility-enhancing consumption and inputs of child health development:

$$G=\sum_{z} Zp_z+\sum_{i} Ip_i, \tag{3}$$

where p are prices. Utility maximization allows deriving reduced-form functions for **Z**, **I** and *D* that include prices, income, "unobserved" utility-function preferences (**R**) and "unobserved" exogenous genetic endowments **T**, assumed known, at least partially, to the mother. For example, the reduced-form function for smoking is as follows:

$$S=f(p,G,\mathbf{R},\mathbf{T}). \tag{4}$$

As shown in Rosenzweig and Schultz (1983), the presence of **T** in the reduced-form function for behavioral factors such as smoking complicates the estimation of the child development function. Mothers may decide to continue or quit smoking during pregnancy in part because of their perceptions of **T** based on informal and formal risk indicators such as her and her family's history of health problems, health professionals' assessments and recommendations and other indicators that are largely unobserved. For example, mothers who perceive larger developmental risks (lower **T**) may decide to quit smoking. If so, standard estimation of input effects, even if all relevant inputs are observed, reflects the real effects in equation (2), the impacts of **T** on development and the relationships between inputs and **T** and results, therefore, in biased estimates of input effects.

Of course, it is virtually impossible to observe all relevant production inputs, which further biases the classical estimations and results in a theoretically ambiguous net bias. For example, in this study, we do not observe prenatal nutritional inputs and healthcare inputs. Maternal smoking may be correlated with unobserved inputs and risk behaviors that may impact child neurodevelopment. Specifically, the "unobserved" maternal preferences for child development and for risk taking (**R**) that impact the smoking decision may also impact other prenatal investments such as prenatal care use and nutrition and risk behaviors such as alcohol use and others, which are unobserved. This "omitted variable" bias due to unobserved preferences and inputs may result in a negative bias in smoking effects on development (i.e. overestimation of adverse smoking effects), as smoking may be positively correlated with risky behaviors that have adverse effects on development. Conversely, smoking may be negatively correlated with healthy behaviors that enhance development. However, the bias due to unobserved endowments **T** is likely to result in an opposite bias (i.e. a positive bias or underestimation of the adverse smoking effects), as women who perceive larger fetal health and developmental risks face a larger incentive to avoid smoking during pregnancy, but may be more likely to have children with neurodevelopmental problems due to these health risks. Therefore, the net bias is a function of the relative contribution of each of these self-selection biases.

B. Empirical Model and Study Measures

We employ a quasi-structural child development production function that includes development production inputs and exogenous factors that may relate to maternal preferences towards development as follows:

$$D_i=\alpha_0+\beta S_i+\mathbf{M}_i\boldsymbol{\lambda}+\delta E_i+\mathbf{H}_i\boldsymbol{\gamma}+\mathbf{C}_i\boldsymbol{\omega}+e_i. \quad (5)$$

The observed production inputs are maternal smoking during pregnancy (*S*) and maternal health status (**M**), measured by the mother having chronic physical and mental health conditions. We also include maternal socioeconomic status (*E*), defined below in detail, as it may have direct effects on development by impacting maternal self-esteem and efficiency in health/development production (Currie 2009; Grossman 1972), beyond its effects on income. However, as discussed below, we evaluate the model sensitivity to this assumption. Also included are demographic characteristics (**H**) including the child's ethnic ancestry, maternal age and marital status, and number of child's older siblings, which are assumed to impact maternal preferences for development and to modify child development production. Further, given that we employ a multiple-country sample as described below, the model includes country fixed effects (**C**) in order to account for differences in child neurodevelopment production between the sample countries. We describe below how evaluate the sensitivity of the smoking effects to the model specification.

B.1 Neurodevelopment—We measure neurodevelopment based on the child's performance on the Bayley Infant Neurodevelopmental Screener (BINS) (Aylward 1995).[9] The BINS screens children between the age of 3 and 24 months for risk of neurodevelopmental problems by evaluating cognitive processes, receptive functions, expressive functions and basic neurological functions. The BINS predicts child's development assessed using diagnostic instruments including as the McCarthy Scales of Children's Abilities and the Bayley-II very well (Aylward 1995, 2004; Aylward and Verhulst 2000). The BINS has 11–13 items based on age which are scored 1 if the child

[9]Derived from the Bayley Infant Neurodevelopment Screener. Copyright @ 2004. Harcourt Assessment Inc. Used with Permission. All rights Reserved. risk measure, is a "positive" measure of neurodevelopmental status (higher values on the neurodevelopment rate indicate better neurodevelopment).

performs the task or 0 if the child does not perform the task. The items are summed to obtain a total score, which may be classified into a three- (high, moderate, low) or two-category (high versus low) risk status for neurodevelopmental delay based on the instrument norms (Aylward 1995; Aylward and Verhulst 2000). The study physicians administered the BINS to all the study children.

This study employs two neurodevelopment measures based on the BINS score. The first measure is a binary risk status of high versus low risk for neurodevelopmental delay based on the instrument norms. The second measure is a continuous measure of the child's neurodevelopment relative to the sample average neurodevelopment. Specifically, this measure is the percentage deviation of each child's total bins score from the sample mean of the BINS score for the child's age, and is therefore referred to here as the child neurodevelopment rate. Unlike the binary risk status measure, this sample-based measure is "norm-free" as it does not utilize the BINS population norms, which are developed based on a sample from the United States. Since the study sample is from South America, we employ this "norm-free" measure in part to evaluate if the smoking effects are sensitive to employing norms from another population. The sign of the smoking effect is expected to be positive for the binary risk status measure and negative for the child neurodevelopment rate, which unlike the binary

B.2 Smoking—Smoking is measured by smoking participation during pregnancy (after pregnancy occurrence) and by the number of cigarettes smoked per day, based on maternal self-report. We do not observe maternal smoking post birth at the time of measuring child's neurodevelopment. If postnatal smoking impacts neurodevelopment, the estimated prenatal smoking effects reflect both the "prenatal smoking" effect and the "postnatal smoking" effect, as well as changes in smoking status between the two periods. However, the evidence is still unclear in terms of the importance of postnatal smoking on neurodevelopment at the ages evaluated in this study (Faden and Graubard 2000; Herrmann et al. 2008).

B.3 Socioeconomic Status—SES is measured by an index of maternal human capital and household wealth using principal component analysis (Kolenikov 2004). Maternal human capital is measured by ordinal scales for education and employment/occupational status. Household wealth is measured by asset ownership and housing quality conditions.[10] The index uses the first principal component scoring coefficients as weights for the index variables.[11] The first principal component explains about 30.5% of the variation in the asset ownership, housing quality and human capital indicators. In order to better interpret the socioeconomic status index, Table A1 in the Appendix reports the distribution of the index variables for the low and high SES groups that are identified based on having negative and positive SES index values, respectively. As expected, there are marked differences in the distribution of the index variables between the two groups with greater assets and improved household quality conditions in the high SES group. We also estimate an alternative specification of the child neurodevelopment function that includes indicators for maternal education and employment/occupational level in order to evaluate their direct effects on development, and a wealth index using PCA that includes the asset ownership and household quality conditions.

[10]The wealth characteristics include the following asset ownership and housing quality indicators: ownership of radio, TV, fridge and car; source of drinking water; type of toilet/sewage facility; type of flooring, wall, and principal roof material; the presences of a domestic worker in the home; working on family's agricultural land; and the number of household members per sleeping room. PCA is estimated using maximum likelihood with polychoric correlations between the ordinal indicators (Kolenikov 2004).

[11]In PCA, the first principal component explains the largest percent of variation in the index variables among the principal components. Table A1 in the Appendix lists the scoring coefficients (weights) of the indicators included in the SES index. The assumption made in using the PCA index is that long-term socioeconomic status explains the majority of the common variation in the used indicators (Filmer and Pritchett 2001).

Table 1 includes the distribution of the study variables.

C. Study Sample—The study sample includes 1,584 children between ages 3 and 24 months who attended 24 pediatric practices in Argentina (671 infants), Brazil (525 infants) and Chile (388 infants) for routine well-child care in 2005 and 2006. These children participated in a study of child neurodevelopment in South America, which was part of the Global Network for Women's and Children's Health Research study (Wehby et al. 2006; McCarthy 2010). Given its focus on normal development, the main study that provides the data for this paper included only children with normal birth outcomes and without major health complications such as requiring oxygen after birth, hospitalization for more than 5 days before hospital discharge after birth, or admission to the intensive neonatal care unit. Also for this purpose, the main study did not enroll children who are low birth weight (<2500 grams) and born prematurely (<37 weeks).[12] The study physicians, the majority of whom were pediatricians, were affiliated with a longstanding epidemiological research and surveillance program in South America, ECLAMC, which has been conducting infant health studies in South America for over three decades (Castilla and Orioli 2004; Wehby, Castilla, and Lopez-Camelo 2010; Wehby et al. 2009). As part of their involvement with ECLAMC, these physicians are routinely involved in infant health research studies.

The study physicians administered the BINS to evaluate neurodevelopment for all study children and obtained data on other characteristics using the same instruments and study questionnaires across all study sites. Before initiating data collection, the study investigators provided training to the study physicians in how to administer the BINS and assessed their reliability in using the instrument. The average physicians' agreement with the gold standard scores for BINS case studies during the training was 84%. The physicians also received standardized training in data collection and study procedures. The mothers were interviewed by study physicians and staff for household demographic and socioeconomic characteristics, health conditions and behaviors using the same instruments and data collection procedures across all sites.

D. Model Estimation—The child neurodevelopment production function is first estimated treating smoking as exogenous with probit regression for the binary child neurodevelopment risk status and ordinary least squares (OLS) for the child neurodevelopment rate. These models are estimated for the total sample and separately for individuals with low and high SES, given the strong SES effects on smoking in this sample. For the purposes of this estimation, low SES and high SES are assigned for negative (798 children) and positive (786 children) SES index values, respectively.

In order to evaluate the potential bias due to maternal self-selection into smoking based on unobserved factors as described above, the neurodevelopment production function is also estimated treating smoking as endogenous. For smoking participation, the sample rate of smoking during pregnancy at each of the study sites (clinics), excluding the individual's smoking status, is employed as an instrument. For each mother in the study sample, we estimate the smoking rate among the mothers of the other children recruited at the same study site (total of 24 sites), and use that as an instrument. This measure is expected to be a good proxy for the smoking rate in the community where the mother lives. Community smoking rates reflect the effects of local cigarette prices and smoking-related policies, but may also have direct effects on the mother's propensity to smoke by representing the social acceptability of smoking during pregnancy.

[12]Other complications that made the child ineligible to participate in the main study included a five-minute Apgar score of 5 or less, being twin or multiple birth, having a chronic illness that requires regular treatment for more than two weeks (excluding allergies and ear infections), documented developmental problems and delay, and receiving a major surgery.

The conditions under which the used area-level instruments provide consistent estimates of the mother's smoking effects are that the area-level smoking measures based on the other mothers' smoking status are not related to: 1- the unobserved child's own developmental endowments (**T**) that may affect the mother's smoking behaviors and 2- the mother's own preferences for risk taking, healthy behaviors, and child health (**R**). Under these conditions, the area-level instruments as constructed are not expected to affect the child's neurodevelopment other than through affecting the child's mother propensity to smoke by reflecting area differences in smoking regulations and cigarette prices/costs.

The first condition is likely to hold given that it is not expected that the behaviors of other mothers affect or are related to the child's neurodevelopmental endowments. The second condition holds if mothers do not sort themselves into areas based on either their smoking status or their smoking-related preferences for risk taking, child health, and health behaviors that are relevant for child neurodevelopment. Of course, "general" preferences for health, wellbeing and risk taking such as for area and neighborhood safety and quality certainly affect residential choice. However, it seems reasonable to assume that the mother's own smoking status and her "specific" preferences for smoking are not "major" determinants of self-selection into areas defined by the study sites. Individuals may choose their "neighborhood" based on certain physical characteristics that relate to smoking such as the concentration of bars, restaurants and nightclubs. However, the "area" measure employed in this study reflects a wider geographic area than a single residential neighborhood and each "area" likely encompasses multiple neighborhoods that differ in their physical characteristics that may relate to smoking. Therefore, while some self-sorting may occur between neighborhoods within a certain study area based on neighborhood-physical characteristics related to smoking, it is expected that such characteristics vary less between than within the area-levels at which we calculate the instruments. For example, most areas are expected to have neighborhoods with bars, restaurants and nightclubs. Of course, we cannot completely verify the assumption that the area-level instruments do not affect child neurodevelopment other than through maternal smoking behaviors due to the lack of data on neighborhood selection within the study areas and on area and neighborhood physical characteristics. However, we describe below several checks that we employ to further evaluate the instrument exogeneity.

The square of the smoking rate is also added as an instrument given the likely diminishing marginal effects of community smoking rates on individual smoking propensity. Similar instruments for smoking and other risk behaviors have been employed in other studies (Fang, Ali, and Rizzo 2009; Morris 2006). For cigarette number, we use the average number of cigarettes smoked per day at the individual's community (defined at the study site level), excluding the individual's cigarette number, as an instrument. We also include an interaction between the area cigarette number average and the individual's SES index, given that increasing SES may lessen the adverse area-level effects such as tobacco advertisements, may change sensitivity to prices and taxes, and may increase access to available resources to reduce or quit smoking.

We find these instruments to be significantly related to smoking participation and cigarette number, with F-statistics of 10 for smoking participation and 42 for cigarette number in the total sample.[13] Smaller but significant F-statistics are observed in the samples stratified by SES, which we account for by employing weak-instrument robust inference as described below. The only exception is for cigarette number in the high SES subsample, where the instruments have insignificant effects. The reason is the very limited distribution and variation of cigarette number in this subsample. Therefore, we only estimate models

[13]Instrument F-statistics are calculated accounting for the clustering of the sample across the study sites.

assuming exogenous cigarettes when using the cigarette number in this subsample. Commonly used instruments such as local cigarette prices/taxes and smoking policy measures are not available for use as instruments due to the lack of data.

When treating smoking as endogenous, the child neurodevelopment risk status function (the first binary development measure) is estimated with conditional maximum likelihood (Wooldridge 2002). The model estimates simultaneously the neurodevelopment risk function and the smoking/cigarette function, which includes the instruments and other model variables. The model is estimated by bivariate probit regression when measuring smoking by participation status, and by instrumental variables (IV) probit regression when measuring smoking by the number of cigarettes. The neurodevelopment rate function (second development measure) is estimated using two-stage least squares (2SLS) when treating smoking as endogenous. Given that the instrument F-statistics for smoking participation are less than 10 in the subsamples stratified by SES, we estimate 95% confidence bounds for the 2SLS smoking participation effects that are robust for weak instruments using the conditional Likelihood Ratio (CLR) statistic (Andrews, Moreira, and Stock 2006; Finaly and Magnusson 2009). Standard over-identification tests are employed in the IV probit and 2SLS models to evaluate if the instruments fit the over-identification restrictions.[14] Evaluating the over-identification restrictions for the bivariate probit model is less straightforward – the model may be identified without instruments. Therefore, 2SLS is used to test the over-identification restrictions in the model of child neurodevelopment risk status and smoking participation.

We estimate the variance-covariance matrices for all models with a Huber-type estimator that accounts for the clustering of the sample across the study clinics (Wooldridge 2002). We assume that the error term is correlated for children from the same area (clinic site) due to area-level "random effects" that are not related to smoking behaviors and the instruments and not due to non-random effects that vary systematically with smoking behavior. In other words, these random effects are assumed to be not correlated to maternal preferences for smoking, smoking status, and average smoking rates, and may include some unobserved area characteristics that affect child health and neurodevelopment such as transportation costs. Under this assumption, the Huber-type estimator accounting for clustering by study area is expected to provide more accurate estimates of the standard errors than those assuming classical error terms given the clustered nature of the sample and that certain covariates are measured at the area-level (Moulton 1986). Clustering the standard errors would contradict the assumptions needed for the validity of the instruments if the shared cluster-level error term is related to the mother's smoking behaviors and to the instruments (i.e. if non-random effects resulted in correlations between the error terms of individuals in the same area). However, the inference of the results as a whole is generally unaffected by clustering the standard errors, which suggests that the unobserved cluster-level effects in the error term are less relevant and overall unrelated to the instruments. We note below when differences in significance levels are observed between clustered and classical standard errors.

E. Further Instrument Checks—In addition to the standard over-identification tests described below for evaluating the excludability of instruments from the development function, we further evaluate the exogeneity of the constructed area-level instruments by assessing their relationships with the model control variables. The expectation is that the instruments should not be systematically related to the individual-level characteristics that are related to the individual-level smoking measures. Therefore, we regress both the area-

[14]In the 2SLS model, the Hansen over-identification test is used (Hayashi 2000). In the IV Probit model, Lee's over-identification test based on the Newey's two-step IV probit model is used (Baum 1999; Newey 1987).

level instruments and the individual-level smoking measures on the model control variables and compare the effects of these variables on the area- and individual-level smoking measures. Table 2 reports the effects of the individual-level characteristics on the area- and individual-level smoking measures. The area-level smoking rate is not systematically related to the individual-level characteristics as is individual-level smoking participation. Individual-level smoking participation significantly increases with mental health problems, being unmarried, and with the number of children, and decreases with socioeconomic status and maternal age. However, none of these characteristics is significantly related to the area-level smoking rate, which is only significantly and positively related to maternal chronic physical health conditions. Individual-level cigarette number decreases significantly with socioeconomic status and maternal age and increases with the number of children. However of these variables, only maternal age is significantly and negatively related to the area-level cigarette number average, which is also positively related to maternal chronic physical health conditions.

We employ additional checks for the exogeneity of the instruments by evaluating their relationships with other area-level characteristics that reflect prenatal and obstetric care availability and quality at the study communities for the same years in which the development study sample was born. We measure these characteristics from *another* sample. As mentioned above, the study physicians were affiliated with ECLAMC, which is an epidemiological research and surveillance program for birth defects that routinely obtains prenatal and birth outcome data on samples of infants born in the hospitals that are attended by the ECLAMC-affiliated physicians (Castilla and Orioli, 2004). The physicians enroll in ECLAMC all infants born with birth defects as well as a sample of unaffected infants from the same hospitals who are matched one-to-one to the affected infants by sex, hospital of birth, and birth date. The unaffected infant sample essentially represents a random sample of about 2–3% of all babies without birth defects born in the ECLAMC hospitals. ECLAMC employs systematic data collection questionnaires and procedures across all its affiliated hospitals, which allows for constructing the same area-level measures across all sites. The physicians obtain the data by interviewing the mothers before hospital discharge after delivery and by abstracting medical records. The differences in the sampling frame and inclusion criteria between the routine ECLAMC data collection and the child development study suggest that the majority of the infants in the ECLAMC sample are not enrolled in the child development sample.

We estimate the additional area-level characteristics using the prenatal data of the ECLAMC sample of infants born without birth defects in the ECLAMC-affiliated hospitals that are attended by the same study physicians who recruited the development study children at their pediatric practices, and match these to the development study sample. These characteristics include the rates of cesarean delivery, medication use and immunizations during pregnancy, and the averages of prenatal care visits and delay of prenatal care initiation. We evaluate if the area-level smoking instruments are systematically related to these area-level indicators by regressing the instruments on each of them, one at a time, controlling for the country fixed effects.

Table 3 reports the coefficients of the regressions of the area-level instruments on the other area-level characteristics. The instruments are not related to these characteristics. The only exception is that the area-level smoking rate is negatively related to the prenatal immunization rate.

III. Results

The smoking rates during pregnancy are 10.9% in the total sample and 15.4% and 6.2% in the low and high SES subsamples, respectively. Among smokers, the average number of cigarettes per day is 7.6 and 5.2 cigarettes for low and high SES, respectively. About 18.1% of the total sample children are at high risk for neurodevelopmental problems, based on the binary risk classification.

A. Child Neurodevelopment Risk Status

Table 4 reports the effects of smoking participation on the probability of being at high risk for neurodevelopmental problems as estimated from the standard and conditional maximum likelihood probit functions both for the total sample and the low and high SES subsamples.[15] When treated as exogenous, smoking has a significant adverse effect on high neurodevelopment risk in the total sample, increasing the probability of being at high neurodevelopment risk by about 0.07 points. A similar and marginally significant effect is observed for low SES. The smoking effect is slightly larger but insignificant for high SES.

When treated as endogenous, the positive smoking effect on high neurodevelopment risk increases by about 5 times for the total sample and 7 times for the low SES subsample and is significant – smoking increases the probability of being at high neurodevelopment risk by about 0.4 and 0.5 points, respectively. The exogeneity of smoking participation is rejected in the total sample (marginally significant) and the low SES subsample. The positive smoking participation effect also increases for the high SES subsample by about 3 times when treated as endogenous, but remains insignificant.

The instruments have significant effects on smoking status with an F statistic of 10.3 in the total sample and 7.3 and 6.2 in the low and high SES subsamples respectively.[16] The over-identification restrictions are not rejected in either sample (see Table 4).[17]

Table 4 also reports the effects of cigarette number on neurodevelopment risk status. When treated as exogenous, cigarettes have a marginally significant positive effect on neurodevelopment risk in the total sample and low SES subsample, increasing the probability of being at high neurodevelopment risk by about 0.006–0.007 points per cigarette. A similar but insignificant effect is observed for the high SES sample.

When treated as endogenous, the positive cigarette number effect increases by about 5 times in both the total sample and low SES subsample but becomes insignificant and the exogeneity of cigarettes is not rejected.[18] The instruments have significant effects on cigarette number in the total sample and low SES subsamples, with F-statistics of 42 and 24, respectively,[19] and the over-identification restrictions cannot be rejected. As mentioned above, the instruments have insignificant effects on cigarette number in the high SES sample, and therefore, the CML model is not estimated for this subsample.

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[15]Tables A2 through A4 in the Appendix report the full regression coefficients of the standard and conditional maximum likelihood probit models. Supplementary Table O1 online reports the equivalence of Table 4 with non-clustered error terms.

[16]The instrument F-statistics for smoking participation are larger in the model that uses non-clustered classical standard errors; the F-statistics become 15.8 in the total sample, 10.2 in the low SES sample, and 9.2 in the high SES sample.

[17]We perform another ad-hoc partial test of the instrument exogeneity by regressing the error term from the classical models for child development assuming exogenous smoking on the area-level smoking rates and average cigarettes and find that the instruments have insignificant effects on these error terms. For the high risk development function, the p values are 0.392 and 0.615 for the smoking rate and average cigarette number instruments, respectively. For the neurodevelopment rate function, the p values are 0.565 and 0.192 for the smoking rate and average cigarette number instruments, respectively.

[18]When using non-clustered standard errors, the cigarette number effects on neurodevelopment risk become statistically significant at $p<0.05$ in both samples, and the exogeneity of cigarette number is rejected at $p<0.1$ in the total sample.

[19]The F-statistics for cigarette number are lower in the model with non-clustered standard errors; the F-statistics become 32.4 in the total sample and 19.7 in the low SES sample.

B. Child Neurodevelopment Rate

Table 5 reports the OLS and 2SLS effects of smoking participation and cigarette number on the child neurodevelopment rate both pooled and stratified by SES.[20] A similar result pattern is generally observed as with the binary neurodevelopment risk measure, with larger negative smoking effects on the neurodevelopment rate in the low SES subsample compared to the high SES sample where smoking has insignificant effects.

When treated as exogenous, smoking participation decreases the child neurodevelopment rate by about 2.9 and 3.4 percentage-points in the total sample and low SES subsample, respectively. The smoking effect is smaller and insignificant in the high SES subsample. When treated as endogenous, the negative smoking effect increases in absolute value by about 10 times in both the total sample and low and high SES subsamples, but is significant only in the low SES sample,[21] decreasing the neurodevelopment rate by about 37 percentage-points. Also in this subsample, the 2SLS smoking effect is significant using the 95% weak-instrument robust confidence bounds and the exogeneity of smoking is rejected. The over-identification restrictions are not rejected for either sample (see Table 5).

When treated as exogenous, cigarettes decrease the child neurodevelopment rate by about 0.25 percentage points per cigarette in both the total sample and low SES subsample (marginally significant), and has a comparable yet insignificant effect in the high SES sample. When treated as endogenous, the negative cigarette effect increases by about 10 times in the total sample and low SES subsample and is significant, reducing the child neurodevelopment rate by about 2.5 percentage-points per cigarette. The exogeneity of the cigarette number is rejected in both of these samples. The over-identification restrictions are not rejected (see Table 5).

C. Alternative Specifications/Robustness Check

While the dataset is unique for assessing the smoking effects on neurodevelopment, it has some limitations that need to be evaluated. The study has no data on other theoretically relevant prenatal inputs and risk behaviors that may impact neurodevelopment such as alcohol use, nutrition, exercise and others. As discussed above, the employed estimation with the area-level smoking instruments will account for this problem if the area-level rates and smoking intensity are not related to the mother's own and "unobserved" relevant inputs and behaviors. While this is reasonable to assume, it is theoretically possible that the instruments may be correlated with some unobserved inputs. For instance, the instruments may be correlated with maternal alcohol use if alcohol taxes/prices vary between the study sites in the same way as cigarette taxes/prices. Further, satisfying the over-identification restrictions and the instrument checks described above does not rule out this potential bias given that these are only partial evaluations of the instrument exogeneity. Unfortunately, we have no access to data on alcohol use or prices at the community-level to account for such potential omitted variable bias, which is expected to result in overestimation of smoking adverse effects. Another complication of the model specification is that maternal health **(M)** is potentially endogenous to child development and we lack instruments to account directly for its endogeneity.

In order to evaluate the effect of omitted variable bias and endogenous maternal health on the study results, the study models are re-estimated excluding all maternal socioeconomic, demographic and health characteristics. The assumption is that these variables are correlated

[20]Tables A6 through A9 in the Appendix report the full OLS and 2SLS regression coefficients of the child neurodevelopment rate function. Supplementary Table O2 online reports the equivalence of Table 5 with non-clustered error terms.

[21]In the total sample, the smoking effect on neurodevelopment rate becomes significant when using non-clustered standard errors and the exogeneity of smoking is rejected at $p<0.05$.

with maternal preferences for health and risk taking (**R**) and consequently with unobserved risk behaviors and health inputs in the same direction as with smoking. For example, if maternal health problems are positively correlated with smoking, we assume that they would also be consistently and positively correlated with unobserved risk behaviors that are relevant to child neurodevelopment such as alcohol use, but would be negatively correlated with unobserved healthy behaviors such as nutrition – i.e., health problems would be consistently and positively correlated to preferences for risk taking and negatively correlated with preferences for health. Similarly, we assume that if socioeconomic status is negatively related to smoking, it would also be consistently and negatively related to unobserved risk behaviors but positively related to unobserved healthy behaviors, and so on. Therefore under this assumption, omitting these variables is expected to result in a positive bias in the smoking effects in the classical models ignoring the endogenous selection of smoking for the binary neurodevelopment risk status measure and a negative bias for the child neurodevelopment rate models, but not in the models that account for endogenous smoking selection using the employed instruments if the instruments are unrelated to the individual's preferences. Further, unlike the main specification, this specification assumes that socioeconomic status has no direct effects on development and evaluates the effects of including socioeconomic status in the main specification on the estimated smoking effects.

Table 6 reports the smoking participation and cigarette number effects on neurodevelopment risk status in the specification excluding maternal health, socioeconomic status, and demographic characteristics.[22] Table 7 reports these results for the child neurodevelopment rate. The results as a whole are generally similar to the main specification. As expected, the classical model estimates of smoking participation and cigarette effects assuming exogenous smoking are generally more positive for the binary neurodevelopment risk measure and more negative for the neurodevelopment rate measure. An exception is for cigarette number effects for the binary risk measure when stratified by SES, which are similar to main specification.

The endogenous smoking model estimates using the nested specification are generally comparable to the main specification. Opposite to what is expected, the smoking participation and cigarette number effects on the binary neurodevelopment risk measure in the total sample are larger in this nested specification than the main specification (by about 25%). However, in the low SES sample, the cigarette number effects on the binary risk status measure and neurodevelopment rate and the smoking participation effects on the latter are slightly lower than those in the main specification. Furthermore, the 25-percent increase in smoking effects in the total sample in the nested specification is still markedly smaller than the difference in estimates between the exogenous and endogenous smoking models. The over-identification restrictions are not rejected in the nested specification. In sum, there is no consistent evidence of a strong omitted variable bias due to positively correlated risk behaviors with smoking based on this assessment. Of course, the validity of this sensitivity analysis relies on the assumption that the variables omitted from the nested specification (maternal health, socioeconomic status and demographic characteristics) are systematically related to unobserved risk behaviors in the same direction as with smoking, which may be reasonable to assume but cannot be completely verified. Nonetheless, as a whole, these results provide some assurance that omitted risk behaviors are unlikely to have large effects on the study results.

We evaluate another specification that controls for the observed area-level characteristics related to prenatal and obstetric care in the child development function in order to assess the sensitivity of the smoking effects to their inclusion. These area-characteristics have jointly

[22]Full regression results are available from the authors upon request.

significant effects on child development but their inclusion has generally minimal effects on the smoking effects both quantitatively and qualitatively. Table A10 in the Appendix reports the effects of smoking and these area-level characteristics on child development in the specifications that include them.

Another check that we employ includes maternal education and occupation directly in the neurodevelopment function instead of as part of the socioeconomic status index. This specification also includes a wealth index based on the asset ownership and household quality conditions. Table A11 in the Appendix reports the results of this specification. Maternal education generally has insignificant effects on neurodevelopment, but the effects have the expected sign of being negative for high neurodevelopment risk and positive for the neurodevelopment rate. Having a university education has a marginally significant positive effect on neurodevelopment rate under OLS but not under 2SLS – increases neurodevelopment rate by 3.7 percentage points compared to incomplete primary schooling or lower education. Conditional on education, maternal occupation has overall insignificant effects on development except for skilled blue collar occupation, which has positive effects on development compared to an executive, professional, or owner occupation. The wealth index has insignificant effects on development. The smoking effects in this specification are generally similar both quantitatively and qualitatively to the main specification.

As mentioned before, only infants who have normal birth weights (≥2500) and gestational age (≥37 weeks) were enrolled in the main child development study that provides the data for our study. Birth weight and gestational age may be on the causal pathway between smoking and neurodevelopment (i.e. smoking can affect these birth outcomes which in turn affect neurodevelopment). In order to investigate the direct and indirect effects of smoking via birth outcomes in our sample, we estimate an alternative specification that controls for birth weight and gestational age.[23] Table A12 in the Appendix reports the effects of smoking, birth weight and gestational age in this specification. The smoking effect estimates are virtually the same when including birth weight and gestational age in the model, suggesting that the smoking effects on development in this sample are occurring through other pathways besides birth outcomes. Birth weight has significant positive effects on child neurodevelopment rate and marginally significant negative effects on high neurodevelopment risk in the exogenous smoking models but smaller and insignificant effects in the endogenous smoking models. Gestational age has insignificant effects on neurodevelopment.

IV. Discussion and Conclusions

The study finds large adverse effects of maternal smoking during pregnancy on child neurodevelopment between the ages of 3 and 24 months. Smoking effects are larger in the low SES sample, which, in part, is because of a higher smoking intensity among smokers – by more than 2 cigarettes per day – compared to the high SES sample. However, this does not explain entirely the larger adverse smoking participation effect with low SES. Further, the OLS cigarette number effects on neurodevelopment rate are slightly larger with lower SES in both the main and nested model specifications. This might be due to offsets of smoking adverse effects in the high SES sample through improved health behaviors compared to the low SES sample such as better nutrition, earlier and higher quality prenatal care use and cleaner environments. While we cannot fully evaluate such offsets due to the lack of data, differences in some of the observed inputs by SES support this argument. For

[23]Birth weight and gestational age are not confounders for smoking. They can be correlated with smoking due to unobserved inputs and endowments that are also correlated to smoking but these unobservables are the confounders for smoking and not birth weight and gestational age.

instance, the rate of maternal mental health problems (including depression) is about twice as high in the low SES subsample than in the high SES sample. This suggests higher stress rates in the low SES subsample, which may exacerbate the smoking effects.

Ignoring self-selection into smoking based on relevant unobservables may result in underestimating the adverse smoking effects on child neurodevelopment. This is consistent with most previous economic studies that evaluate smoking effects on child health and find larger adverse smoking effects on birth weight and other birth outcomes after accounting for the endogenous selection of smoking (Grossman 1972; Rosenzweig 1983; Grossman and Joyce 1990; Lien 2005). These results suggest that women who select into prenatal smoking may have certain unobserved characteristics that are positively related to child development (these are not impacted by smoking but just correlated with smoking). For example, factors such as maternal and family history of developmental and health problems may be negatively related to both maternal smoking during pregnancy and child neurodevelopment, potentially resulting in underestimation of smoking adverse effects on neurodevelopment when ignored.

The effects assuming endogenous smoking exceed those of exogenous smoking by more than 5 times and may appear to be unreasonably large. The 37 percentage-point decrease in neurodevelopment rate in the low socioeconomic status sample with smoking participation when treated as endogenous represents a change from being at average neurodevelopment rate to slightly below the 5th percentile. Slightly lower effects are observed when using the cigarette number as the smoking measure; a child exposed to the average number of cigarettes among smokers (7.6 cigarettes) in the low SES sample may experience a decrease from being at average neurodevelopment rate to slightly below the 15th percentile. While seemingly large, some clinical studies have reported large differences in child neurodevelopmental outcomes by maternal smoking during pregnancy that are generally close to the effects that we find in this study. For example, Fried and Watkinson (1988) report that 39% of the infants in their study who were exposed to high nicotine levels during pregnancy had suboptimal scores on the Bayley Mental Development Index at age 12 months, compared to 6% of the other study infants. Milberger et al. (1998) report that maternal smoking during pregnancy increased the risk of the child having ADHD by 4.4 times and reduced IQ by 5 points (about half a standard deviation). Of course, there are several constraints with comparing our study estimates directly to the literature as none of the previous studies account for the endogenous selection of smoking and several studies are based on fairly small samples and descriptive analyses. Nonetheless, some previous study results are suggestive of the large adverse prenatal smoking effects that we find in this study.

As mentioned above, the estimation bias due to unobservables may involve both favorable and adverse self-selection effects. In this study, the suggested net bias is underestimation of the smoking adverse effects on neurodevelopment in classical models. It is possible that the instruments may be accounting more for adverse self-selection and less for favorable self-selection, which may contribute to the large effects in the models assuming endogenous smoking. We employ several checks for the instrument exogeneity and find no significant systematic relationships between the instruments and several area-level characteristics that may reflect some of the unobserved behaviors that are related to favorable self-selection. Also, the smoking effects with instrumentation are virtually the same when controlling for these area-level characteristics. Furthermore, the area-level smoking instruments are overall not systematically related to observed individual-level characteristics, unlike the individual-level smoking measures. As discussed above, the consistency of the estimation with the instruments hinges on the condition that differences in area-level smoking rates (as constructed from the smoking behaviors of the other mothers in the sample) are not systematically correlated with area-level differences in unobserved relevant inputs/behaviors

for neurodevelopment that are correlated with smoking (assuming that area-differences in these other inputs/behaviors affect the mother's own choice of these inputs/behaviors). The checks described above provide some assurance and support the exogeneity of the instruments, although we are unable to completely evaluate this condition. While the magnitude of the smoking effect may be theoretically exaggerated by the instruments, it is unlikely that the suggested bias direction of underestimation in classical models is affected given the overall evidence supporting the instruments. Therefore, the classical estimates, which suggest clinically relevant smoking effects, may be thought of as lower bounds for the real smoking effects.

The study results suggest stronger self-selection into smoking based on unobservable child development endowments in the low SES subsample compared to the high SES subsample. This is consistent with an expected greater knowledge about smoking adverse effects on health with higher SES. With more knowledge, women may be less likely to choose to smoke or not based on factors such as family child health and development history since they are more aware of the harmful smoking effects regardless of family history, and are more likely to choose based on their preferences for health and risk taking. As discussed above, unobserved child development endowments are expected to result in underestimation of adverse smoking effects, while unobserved maternal preferences, which result in positive correlations between smoking and other risk unobserved behaviors such as alcohol use and poor nutrition, are expected to result in a negative omitted variable bias. The study suggests a larger net positive bias in the low SES sample.

The study results support the thesis that maternal smoking during pregnancy has adverse effects on child neurodevelopment and human capital. As discussed above, prenatal smoking may affect several physical and behavioral health conditions that have been shown to reduce human capital in the form of lower educational and cognitive achievement reduced income. Also, some studies show direct decreases in certain measures of human capital later in life with exposure to prenatal smoking. Smoking effects may extend over life through several health, development, and behavior pathways that lead to reduced human capital. Examples of these pathways include higher risks of chronic respiratory illness, poor language and cognition, lower school test scores, ADHD, criminal arrest, psychiatric hospitalization, adult health problems, and obesity (Koshy, Delpisheh, and Brabin 2010; Victora et al. 2008), all of which may adversely impact educational attainment and economic performance later in life. The specific pathway between prenatal smoking and human capital that our study supports is through reducing neurodevelopment, which may be viewed as an early form of human capital given that early neurodevelopmental skills are strongly predictive of cognitive abilities and educational outcomes later in life. Given the importance of early child neurodevelopment in influencing future human capital accumulation, designing policies and interventions to reduce maternal smoking during pregnancy will likely result in large social and economic returns throughout life.

Higher SES may compensate for early developmental deficits, which are likely to have more adverse effects on future human capital in lower SES families (Feinstein 2003). This effect, combined with the larger adverse smoking effects among low SES children, suggests that focused interventions to reduce smoking participation and intensity among low SES mothers may be needed in addition to population-level interventions such as through cigarette taxation and prohibiting smoking in public places. Such interventions may involve increasing the awareness of low SES women of the harmful effects of smoking through advertisement campaigns and enhanced pre-pregnancy and prenatal care counseling.

This study is one of the first to evaluate the prenatal smoking effects on early child neurodevelopment using a large sample and an econometric approach that evaluates the role

of unobservables in self-selection into smoking. The study provides significant insights into developing future studies in this area. Examples include studying smoking effects on neurodevelopment in other populations and evaluating the effects of other prenatal risk behaviors including alcohol use, nutrition and obesity on child neurodevelopment.

The study has limitations due to the lack of data on certain theoretically relevant inputs for child development production. We attempt to account for these limitations by employing instrumental variables for smoking. However, the instruments in some specifications including those for smoking participation when stratified by SES are considered weak. While we find that inference for the smoking effects is generally robust to employ weak-instruments, re-evaluating this question using alternative instruments is needed for evaluating the sensitivity of the results to the employed instruments. We estimate a nested specification that excludes observed inputs and compare the effects of this exclusion between models that assume exogenous smoking and the instrumental variable models, and find overall no consistent evidence of a strong omitted variable bias that is correlated with the instruments. Also, the study physicians received standard training and reliability assessment in administering the BINS. Therefore, systematic variations in neurodevelopment measurement between the study sites that may be correlated with the site-level smoking rates are unlikely. These results along with the over-identification test results provide support for the exogeneity of the instruments. However, it is still theoretically possible that the instruments are biased by being correlated with unobserved risk behaviors, which also highlight the importance of future work with other identification approaches and instruments for smoking effects.

In conclusion, we find that smoking during pregnancy may significantly reduce early child neurodevelopment. This emphasizes the importance of developing interventions to reduce prenatal smoking in order to enhance early child neurodevelopment, which represents an early form of human capital given its strong effects on cognitive and education outcomes later in life. Such interventions are expected to have positive effects on long-run human capital attainment given the importance and multiplicative effects of enhanced early neurodevelopment over life. Children in low SES households may be more adversely affected and may benefit more from focused interventions to reduce prenatal smoking. Such interventions are particularly relevant given that low SES in early life also reduces future human capital.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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APPENDIX

Table A1

Principal Component Analysis Scoring Coefficients of the Socioeconomic Status Index and Variable Distributions by Low and High SES

		% of Low SES	% of High SES
Radio			
No	−0.632185	4.89	0.13
Yes	0.016128	95.11	99.87
TV			
No	−0.755131	6.89	0.38
Yes	0.028397	93.11	99.62
Fridge			
No	−0.694741	13.91	0.00
Yes	0.052056	86.09	100.00
Car			
No	−0.233947	91.35	32.44
Yes	0.383183	8.65	67.56
Domestic Worker in the household			
No	−0.057167	99.25	81.81
Yes	0.548867	0.75	18.19
Works on own of family's agricultural land			
No	0.001094	95.74	94.78
Yes	−0.021888	4.26	5.22
Source of drinking water			
Piped drinking water in residence	0.029651	85.21	94.53
Piped drinking water outside residence	−0.209026	7.64	0.25
Bottled water	−0.248698	2.01	3.31
Connected to a river or creek	−0.274512	0.88	1.78
Inside well or spring	−0.307492	2.38	0.13
Outside well or spring	−0.377437	1.50	0.00
Other sources of drinking water	−0.466433	0.38	0.00
Type of toilet and sewage facility			
Connected to a sewer	0.144828	50.25	87.91
Connected to an open sewer	−0.19787	19.17	7.63
Latrine with connection to sewer	−0.30963	11.90	3.44
Latrine not connected to sewer	−0.388643	5.51	0.25
Pit Latrine	−0.521288	12.28	0.76
Bush, field as latrine	−0.765067	0.50	0.00
Other type of latrine	−0.880206	0.38	0.00

		% of Low SES	% of High SES
Principal type of flooring in dwelling			
Earth, sand	−0.63901	2.76	3.31
Wood, plank	−0.433934	9.15	10.69
Cement	−0.207166	44.11	51.65
Clay tile	0.04324	33.96	12.34
Polished wood or parquet	0.223571	1.63	3.56
Carpeted flooring	0.267852	0.25	18.45
Other type of flooring	0.404263	8.15	0.00
Principal wall material			
Cane, palm, trunks	−0.167255	2.76	0.13
Mud walls	−0.113471	5.01	0.89
Wood planks	−0.085943	68.92	1.15
Alvenaria (finished) walls	−0.010544	13.66	82.82
Polished wood	0.04932	9.65	4.20
Other material for walls	0.081458	0.00	10.81
Principal roofing material			
Natural material	−0.250747	0.88	0.89
Raw wood	−0.181209	2.26	5.22
Roofing tiles	−0.14499	4.01	1.27
Cement or concrete	−0.100623	18.67	9.41
Zinc materials	−0.032672	35.71	25.32
Polished wood	0.018732	12.91	11.58
Eternit, amianto roof	0.038528	2.88	5.22
Other roofing	0.103674	22.68	41.09
Number of individuals per sleeping room	−0.25028	2.99 (1.1206)	2.18 (.5876)
Maternal education			
None – illiterate	−1.101032	0.50	1.65
Primary – incomplete	−0.546629	26.82	4.58
Primary – complete	−0.27423	25.69	12.21
Secondary – incomplete	−0.093297	27.44	43.77
Secondary – complete	0.140047	17.67	16.54
University – incomplete	0.365543	1.63	21.25
University – complete	0.608683	0.25	0.00
Maternal Occupation			
Unemployed	−0.157354	80.08	47.46
Unqualified worker (blue collar)	0.122612	10.90	3.94
Qualified worker (blue collar)	0.168018	2.13	6.36
Independent worker	0.204266	2.26	6.23
Clerk (white collar)	0.30241	4.51	22.90
Boss, chief, owner	0.411081	0.13	1.27
Professional, executive	0.532899	0.00	11.83

Table A2

Standard and Bivariate Probit Regression Coefficients of the Child Development Risk[a] Function

	Probit - Total Sample	Bivariate Probit - Total Sample	Probit - Low SES	Bivariate Probit - Low SES	Probit - High SES	Bivariate Probit - High SES
Smoking during Pregnancy	0.262** (0.108)	1.174** (0.476)	0.247* (0.136)	1.527*** (0.424)	0.354 (0.216)	0.923 (1.380)
Maternal mental health problems	−0.014 (0.277)	−0.109 (0.268)	−0.038 (0.371)	−0.210 (0.403)	0.008 (0.280)	−0.017 (0.300)
Maternal chronic physical health problems	0.159(0.158)	0.128(0.155)	−0.104 (0.171)	−0.120 (0.184)	0.434* (0.231)	0.412* (0.233)
Socioeconomic status index	−0.065 (0.049)	−0.045 (0.048)	0.018 (0.084)	0.052 (0.078)	−0.080 (0.098)	−0.082 (0.097)
African ancestry	0.563*** (0.131)	0.552*** (0.142)	0.715*** (0.150)	0.687*** (0.156)	0.414** (0.197)	0.408* (0.210)
Native ancestry	0.231 (0.193)	0.242 (0.180)	0.375* (0.210)	0.391** (0.180)	0.102 (0.231)	0.099 (0.228)
Maternal age	0.102*** (0.039)	0.112*** (0.039)	0.098 (0.075)	0.101 (0.070)	0.132* (0.071)	0.137** (0.069)
Maternal age squared	−0.002*** (0.001)	−0.002*** (0.001)	−0.002 (0.001)	−0.002 (0.001)	−0.002* (0.001)	−0.002* (0.001)
Mother is single	0.199* (0.116)	0.147 (0.119)	0.200 (0.205)	0.114 (0.209)	0.197 (0.176)	0.162 (0.174)
Mother is in a stable relationship	0.184** (0.086)	0.150* (0.083)	0.178 (0.137)	0.115 (0.125)	0.165 (0.113)	0.150 (0.117)
Number of older child's siblings	0.045 (0.037)	0.021 (0.042)	0.079** (0.039)	0.041 (0.048)	−0.041 (0.060)	−0.054 (0.065)
Brazil	0.133 (0.242)	0.155 (0.233)	0.080 (0.290)	0.085 (0.246)	0.251 (0.250)	0.284 (0.249)
Chile	0.456 (0.348)	0.459 (0.328)	0.532 (0.344)	0.500* (0.297)	0.494 (0.388)	0.510 (0.387)
Constant	−2.860*** (0.617)	−3.066*** (0.624)	−2.746** (1.107)	−2.838*** (0.994)	−3.342*** (1.041)	−3.456*** (1.001)
Observations	1584	1584	798	798	786	786

Note: Standard errors are in parentheses.

*, ** *and* *** indicate p <0.1, <0.05 and <0.01, respectively.

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Table A3

Coefficients of the Smoking Participation Function of the Bivariate Probit Model of Child Neurodevelopment Risk Status[a]

	Total	Low SES	High SES
Maternal mental health problems	0.450*** (0.132)	0.449 (0.298)	0.510 (0.530)
Maternal chronic physical health problems	0.063 (0.161)	0.030 (0.231)	0.206 (0.341)
Socioeconomic status index	−0.114*** (0.041)	−0.133*** (0.047)	0.061 (0.090)
African ancestry	0.116 (0.133)	0.009 (0.121)	0.148 (0.405)
Native ancestry	−0.051 (0.109)	−0.203 (0.148)	0.178 (0.163)
maternal age	−0.090** (0.041)	−0.083 (0.060)	−0.073 (0.102)
maternal age	0.001 (0.001)	0.001 (0.001)	0.001 (0.002)
Mother is single	0.341** (0.162)	0.239 (0.209)	0.560* (0.296)
Mother is in a stable relationship	0.289*** (0.105)	0.256* (0.134)	0.308** (0.156)
Number of child's older siblings	0.138*** (0.039)	0.100* (0.057)	0.218*** (0.081)
Brazil	−0.289** (0.145)	−0.146 (0.123)	−0.824*** (0.303)
Chile	−0.142 (0.170)	−0.171 (0.173)	−0.443** (0.222)
Smoking rate	17.331*** (4.694)	16.518*** (4.656)	25.337*** (8.741)
Smoking rate squared	−57.190*** (19.669)	−52.045*** (18.485)	−97.514*** (37.713)
Constant	−0.956 (0.664)	−0.967 (0.837)	−1.473 (1.660)
Observations	1584	798	786

Note: Standard errors are in parentheses.
*, ** *and* *** indicate p <0.1, <0.05 and <0.01, respectively.

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Table A4

Standard and IV Probit Regression Coefficients of the Child Neurodevelopment Risk Status[a] Function with Cigarettes

	Probit - Total Sample	IV Probit - Total Sample	Probit - Low SES	IV Probit - Low SES	Probit - High SES
Number of cigarettes during pregnancy	0.023** (0.012)	0.121 (0.101)	0.024* (0.014)	0.119 (0.090)	0.033 (0.028)
Maternal mental health problems	−0.003 (0.281)	−0.075 (0.301)	−0.018 (0.376)	−0.083 (0.438)	0.000 (0.283)
Maternal chronic physical health problems	0.165 (0.157)	0.143 (0.148)	−0.100 (0.168)	−0.125 (0.187)	0.448* (0.232)
Socioeconomic status index	−0.065 (0.048)	−0.039 (0.062)	0.020 (0.084)	0.059 (0.097)	−0.078 (0.098)
African ancestry	0.552*** (0.131)	0.489*** (0.171)	0.706*** (0.151)	0.642*** (0.184)	0.403** (0.199)
Native ancestry	0.231 (0.193)	0.237 (0.178)	0.376* (0.210)	0.392** (0.181)	0.102 (0.228)
maternal age	0.102*** (0.039)	0.116*** (0.039)	0.100 (0.074)	0.116 (0.072)	0.129* (0.073)
maternal age squared	−0.002*** (0.001)	−0.002*** (0.001)	−0.002 (0.001)	−0.002* (0.001)	−0.002* (0.001)
Mother is single	0.210* (0.116)	0.178* (0.103)	0.208 (0.204)	0.155 (0.174)	0.208 (0.168)
Mother is in a stable relationship	0.188** (0.086)	0.153** (0.077)	0.177 (0.137)	0.116 (0.117)	0.175 (0.112)

	Probit - Total Sample	IV Probit - Total Sample	Probit - Low SES	IV Probit - Low SES	Probit - High SES
Number of child's older siblings	0.047 (0.036)	0.023 (0.049)	0.079** (0.039)	0.048 (0.060)	−0.036 (0.059)
Brazil	0.118 (0.242)	0.090 (0.235)	0.060 (0.293)	−0.011 (0.281)	0.239 (0.247)
Chile	0.457 (0.349)	0.459 (0.328)	0.536 (0.346)	0.527* (0.310)	0.497 (0.387)
Constant	−2.835*** (0.606)	−3.011*** (0.600)	−2.750** (1.084)	−2.896*** (1.008)	−3.279*** (1.059)
Observations	1584	1584	798	798	786

Note: Standard errors are in parentheses.
*, ** *and* *** indicate p <0.1, <0.05 and <0.01, respectively.

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Table A5

Coefficients of the Cigarette Number Function of the Bivariate Probit Model of Child Neurodevelopment Risk Status[a]

	Total sample	Low SES sample
Number of cigarettes during pregnancy		
Maternal mental health problems	0.820 (0.566)	0.904 (1.122)
Maternal chronic physical health problems	0.088 (0.375)	0.285 (0.721)
Socioeconomic status index	0.131 (0.089)	0.103 (0.157)
African ancestry	0.337 (0.276)	0.216 (0.314)
Native ancestry	−0.310* (0.162)	−0.572** (0.235)
maternal age	−0.120** (0.054)	−0.147* (0.076)
maternal age squared	0.002** (0.001)	0.002* (0.001)
Mother is single	0.266 (0.175)	0.354 (0.284)
Mother is in a stable relationship	0.258** (0.121)	0.412 (0.266)
Number of child's older siblings	0.218** (0.090)	0.233** (0.117)
Brazil	−0.180 (0.174)	−0.057 (0.319)
Chile	−0.115 (0.133)	−0.020 (0.182)
Area-level average cigarette number	0.516*** (0.084)	0.324* (0.174)
Area-level average cigarette number × socioeconomic status index	−0.526*** (0.163)	−0.759*** (0.281)
Constant	1.847** (0.864)	2.135** (1.082)
Observations	1584	798

Note: Standard errors are in parentheses.
*, ** *and* *** indicate p <0.1, <0.05 and <0.01, respectively.

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Table A6

Regression Coefficients of the Child Neurodevelopment Rate[a] Function with Smoking

	OLS - Total Sample	2SLS - Total Sample	OLS - Low SES	2SLS - Low SES	OLS - High SES	2SLS - high SES
Smoking during Pregnancy	−2.849** (1.359)	−29.847 (24.500)	−3.389** (1.249)	−37.270** (19.011)	−1.602 (2.280)	−11.910 (28.748)
Maternal mental health problems	−0.994 (2.109)	1.787 (3.799)	−2.020 (2.521)	2.614 (5.133)	0.455 (2.978)	0.942 (3.217)
Maternal chronic physical health problems	−1.249 (1.747)	−0.201 (1.830)	0.744 (1.963)	2.002 (2.115)	−3.077 (3.005)	−2.621 (3.237)
Socioeconomic status index	0.691 (0.454)	0.131 (0.571)	0.037 (0.896)	−0.967 (1.072)	0.939 (0.750)	0.980 (0.772)
African ancestry	−5.530*** (1.370)	−5.488*** (1.652)	−6.683*** (1.304)	−7.049*** (1.667)	−4.573* (2.227)	−4.531* (2.341)
Native ancestry	−3.230 (2.196)	−3.629* (1.886)	−5.082** (2.342)	−6.123*** (2.110)	−2.078 (2.081)	−1.995 (2.082)
Maternal age	−0.807** (0.373)	−1.257* (0.717)	−1.308** (0.603)	−1.807* (1.010)	−0.984 (0.636)	−1.130 (0.839)
Maternal age squared	0.014** (0.006)	0.019* (0.011)	0.026** (0.011)	0.032* (0.017)	0.014 (0.011)	0.015 (0.013)
Mother is single	−2.242 (1.489)	−0.548 (2.214)	−3.046 (2.312)	−0.509 (3.193)	−1.403 (1.327)	−0.789 (2.234)
Mother is in a stable relationship	−1.929* (0.958)	−0.879 (1.298)	−2.311* (1.208)	−0.651 (1.832)	−1.495 (1.394)	−1.172 (1.464)
Number of child's older siblings	−0.710 (0.446)	0.023 (0.947)	−1.137* (0.562)	−0.290 (1.107)	−0.214 (0.515)	0.094 (0.891)
Brazil	−3.648 (2.348)	−4.581** (2.303)	−3.952 (2.769)	−4.384** (2.033)	−3.879* (2.228)	−4.492 (2.905)
Chile	−4.638 (3.792)	−5.055 (3.571)	−6.248 (4.136)	−6.317* (3.631)	−4.499 (3.662)	−4.841 (3.799)
Constant	18.138*** (6.288)	27.765** (13.161)	23.744** (8.544)	34.541** (15.487)	22.105** (9.691)	25.241* (14.206)
Observations	1584	1584	798	798	786	786

Note: Standard errors are in parentheses.

*, ** *and* *** indicate p <0.1, <0.05 and <0.01, respectively.

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Table A7

First Stage Regression Coefficients for Smoking in the 2SLS Child Neurodevelopment Rate[a] Model

	Total Sample	Low SES sample	High SES sample
Maternal mental health problems	0.11*** (0.04)	0.14 (0.09)	0.05 (0.09)
Maternal chronic physical health problems	0.02 (0.03)	0.01 (0.06)	0.03 (0.05)
Socioeconomic status index	−0.02** (0.01)	−0.03** (0.01)	0.01 (0.01)
African ancestry	0.00 (0.02)	−0.01 (0.03)	0.00 (0.04)
Native ancestry	−0.01 (0.02)	−0.05 (0.03)	0.02 (0.01)
Maternal age	−0.02* (0.01)	−0.01 (0.01)	−0.01 (0.01)
Maternal age squared	0.0002 (0.0001)	0.0001 (0.0003)	0.0001 (0.0002)
Mother is single	0.06* (0.03)	0.05 (0.05)	0.07 (0.04)
Mother is in a stable relationship	0.04** (0.02)	0.05 (0.03)	0.03* (0.02)
Number of child's older siblings	0.03** (0.01)	0.03 (0.02)	0.03** (0.01)
Brazil	−0.04 (0.03)	−0.03 (0.03)	−0.06** (0.03)
Chile	−0.02 (0.03)	−0.03 (0.04)	−0.05* (0.02)
Smoking rate	1.98** (0.79)	2.75** (1.24)	2.01*** (0.65)
Smoking rate squared	−6.05* (3.38)	−8.17 (4.98)	−7.17** (2.70)
Constant	0.22 (0.14)	0.15 (0.21)	0.16 (0.20)
Observations	1584	798	786

Note: Standard errors are in parentheses.

*, ** *and* *** indicate p <0.1, <0.05 and <0.01, respectively. Standard errors are in parentheses.

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Table A8

Regression Coefficients of the Child Neurodevelopment Rate[a] Function with Cigarette Number

	OLS - Total Sample	2SLS - Total Sample	OLS - Low SES	2SLS - Low SES	OLS - High SES
Number of cigarettes during pregnancy	−0.245** (0.108)	−2.476** (1.110)	−0.258* (0.127)	−2.488** (0.975)	−0.225 (0.198)
Maternal mental health problems	−1.113 (2.117)	0.481 (2.787)	−2.309 (2.462)	−0.804 (4.357)	0.536 (2.942)
Maternal chronic physical health problems	−1.318 (1.757)	−0.936 (1.848)	0.723 (2.059)	1.636 (2.611)	−3.149 (3.013)
Socioeconomic status index	0.695 (0.451)	0.196 (0.483)	0.045 (0.887)	−0.749 (1.032)	0.944 (0.755)
African ancestry	−5.423*** (1.373)	−4.400** (1.936)	−6.575*** (1.327)	−5.957*** (1.845)	−4.498* (2.255)
Native ancestry	−3.223 (2.203)	−3.542* (2.006)	−5.068** (2.366)	−5.841*** (2.089)	−2.068 (2.078)
Maternal age	−0.802** (0.359)	−1.185*** (0.456)	−1.316** (0.582)	−1.825*** (0.691)	−0.975 (0.641)
Maternal age squared	0.014** (0.006)	0.020*** (0.007)	0.027** (0.010)	0.035*** (0.012)	0.014 (0.011)
Mother is single	−2.361 (1.518)	−1.817 (1.531)	−3.193 (2.320)	−2.272 (2.286)	−1.422 (1.320)
Mother is in a stable relationship	−1.976* (0.960)	−1.387 (1.063)	−2.351* (1.206)	−1.262 (1.325)	−1.522 (1.404)

	OLS - Total Sample	2SLS - Total Sample	OLS - Low SES	2SLS - Low SES	OLS - High SES
Number of child's older siblings	−0.732 (0.438)	−0.225 (0.607)	−1.156** (0.550)	−0.581 (0.763)	−0.221 (0.517)
Brazil	−3.509 (2.341)	−3.140 (2.121)	−3.754 (2.814)	−2.414 (2.477)	−3.855* (2.212)
Chile	−4.649 (3.811)	−5.143 (3.625)	−6.310 (4.177)	−6.903* (3.890)	−4.535 (3.663)
Constant	17.828*** (6.031)	24.249*** (7.671)	23.528*** (8.220)	30.998*** (10.182)	21.876** (9.772)
Observations	1584	1584	798	798	786

Note: Standard errors are in parentheses.
*, ** *and* *** indicate p <0.1, <0.05 and <0.01, respectively.

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Table A9

First Stage Regression Coefficients for Cigarettes in the 2SLS Child Neurodevelopment Rate[a] Model

	Total Sample	Low SES
Maternal mental health problems	0.82 (0.57)	0.90 (1.13)
Maternal chronic physical health problems	0.09 (0.38)	0.29 (0.73)
Socioeconomic status index	0.13 (0.09)	0.12 (0.15)
African ancestry	0.34 (0.28)	0.21 (0.32)
Native ancestry	−0.31* (0.16)	−0.57** (0.24)
maternal age	−0.12** (0.05)	−0.15* (0.08)
Maternal age squared	0.00** (0.00)	0.00 (0.00)
Mother is single	0.27 (0.18)	0.36 (0.28)
Mother is in a stable relationship	0.26** (0.12)	0.41 (0.27)
Number of child's older siblings	0.22** (0.09)	0.23* (0.12)
Brazil	−0.18 (0.18)	−0.05 (0.33)
Chile	−0.11 (0.13)	−0.03 (0.17)
Average number of cigarettes	0.52*** (0.08)	0.29 (0.18)
Average number of cigarettes x SES	−0.52*** (0.16)	−0.78** (0.29)
Constant	1.84** (0.87)	2.17* (1.14)
Observations	1584	798

Note: Standard errors are in parentheses.
*, ** *and* *** indicate p <0.1, <0.05 and <0.01, respectively.

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Table A10

Effects of Smoking and Area-level Prenatal and Obstetric Care Characteristics on Child Neurodevelopment in the Alternative Specifications including Area-level Characteristics

	High Neurodevelopment Risk[a]				Neurodevelopment Rate[a]			
	Probit	**Biprobit**	**Probit**	**IV Probit**	**OLS**	**2SLS**	**OLS**	**2SLS**
Smoking during Pregnancy	0.056** (0.023)	0.494*** (0.157)			−2.335** (0.992)	−20.529 (25.018)		
Number of cigarettes during pregnancy			0.005** (0.002)	0.035(0.026)			−0.208** (0.093)	−2.291** (0.911)
Cesarean delivery rate	−0.448*** (0.152)	−0.432*** (0.144)	−0.445*** (0.152)	−0.387** (0.151)	18.327*** (6.224)	15.665*** (5.828)	18.276*** (6.241)	14.341*** (5.225)
Average number of prenatal visits	−0.015 (0.013)	−0.015 (0.013)	−0.015 (0.013)	−0.012 (0.013)	0.720 (0.566)	0.597 (0.497)	0.715 (0.559)	0.499 (0.519)
Average number of weeks delayed before initiating prenatal care	−0.034*** (0.012)	−0.033*** (0.012)	−0.034*** (0.012)	−0.029** (0.012)	1.113*** (0.386)	0.914** (0.381)	1.104*** (0.375)	0.764** (0.368)
Average number of ultrasounds during pregnancy	−0.057*** (0.022)	−0.058*** (0.021)	−0.058*** (0.022)	−0.061*** (0.023)	1.203 (1.068)	0.956 (1.011)	1.240 (1.062)	1.297 (1.038)
Medication use rate during pregnancy	0.167 (0.116)	0.163 (0.118)	0.172 (0.116)	0.194* (0.116)	−7.385** (3.447)	−6.112 (4.286)	−7.616** (3.453)	−8.292*** (2.735)
Immunization rate during pregnancy	−0.041 (0.162)	−0.017 (0.162)	−0.047 (0.161)	−0.047 (0.155)	−6.297 (7.418)	−8.085 (6.389)	−6.039 (7.382)	−5.751 (6.558)
F or Chi2 statistics [df] for joint-effects of area-level characteristics	38.74*** [6]	38.49*** [6]	39.56*** [6]	33.59*** [6]	5.63*** [6, 22]	12.35* [6]	5.83*** [6, 22]	34.63*** [6]
Observations	1545	1545	1545	1545	1545	1545	1545	1545

Note: This table reports the effects of the smoking measures and area-level characteristics related to prenatal and obstetric care availability and quality. The regressions included all the other control variables in the main model but these are suppressed in this table. The sample includes 1545 observations (one site with 30 observations did not have ECLAMC data to allow estimating the area-level characteristics). The marginal/incremental effects are estimated and reported for the standard probit, biprobit and IV probit models. Standard errors are in parentheses.

*, ** *and* *** indicate p <0.1, <0.05 and <0.01, respectively.

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Table A11

Effects of Smoking, Education, Occupation and Wealth on Child Development

	High Neurodevelopment Risk[a]				Neurodevelopment Rate[a]			
	Probit	Biprobit	Probit	IV Probit	OLS	2SLS	OLS	2SLS
Smoking during Pregnancy	0.068** (0.031)	0.365* (0.208)			−2.559* (1.391)	−29.760 (24.826)		
Number of cigarettes during pregnancy			0.005* (0.003)	0.033 (0.029)			−0.211* (0.111)	−2.523** (1.102)
Completed primary school	−0.009 (0.039)	0.008 (0.044)	−0.007 (0.039)	0.027 (0.057)	1.973 (1.665)	−0.165 (3.021)	1.918 (1.643)	−0.881 (2.280)
Incomplete secondary school	−0.059 (0.038)	−0.047 (0.041)	−0.057 (0.038)	−0.031 (0.051)	3.158 (1.846)	1.476 (2.658)	3.097 (1.814)	0.696 (2.522)
Complete secondary school	−0.041 (0.039)	−0.022 (0.041)	−0.040 (0.039)	−0.007 (0.055)	2.448 (1.692)	−0.164 (3.100)	2.437 (1.686)	−0.370 (2.386)
Attended university	−0.062 (0.043)	−0.043 (0.044)	−0.061 (0.044)	−0.030 (0.052)	3.745* (1.854)	0.918 (2.867)	3.743* (1.866)	0.812 (2.089)
Unemployed	−0.033 (0.053)	−0.024 (0.055)	−0.033 (0.053)	−0.013 (0.057)	0.926 (1.500)	−0.175 (2.190)	0.886 (1.517)	−0.684 (2.070)
Unskilled blue collar worker	−0.031 (0.067)	−0.023 (0.068)	−0.033 (0.066)	−0.029 (0.067)	0.998 (3.048)	0.077 (2.979)	1.063 (3.068)	0.826 (3.069)
Skilled blue collar worker	−0.103*** (0.036)	−0.092** (0.042)	−0.103*** (0.036)	−0.086* (0.050)	5.947** (2.809)	3.002 (3.886)	5.997** (2.775)	3.512 (3.453)
Independent worker	−0.059 (0.060)	−0.051 (0.064)	−0.062 (0.059)	−0.060 (0.065)	1.720 (2.625)	0.357 (2.946)	1.818 (2.647)	1.492 (3.271)
Clerk	−0.034 (0.041)	−0.027 (0.045)	−0.034 (0.041)	−0.019 (0.047)	0.571 (1.514)	−0.490 (2.350)	0.550 (1.492)	−0.771 (1.828)
Wealth index	−0.002 (0.015)	0.001 (0.015)	−0.001 (0.014)	0.003 (0.017)	0.070 (0.522)	−0.229 (0.590)	0.066 (0.520)	−0.293 (0.526)
Observations	1584	1584	1584	1584	1584	1584	1584	1584

Note: This table reports the effects of maternal smoking, education, occupational status and wealth in the specification that replaces the socioeconomic status index with the later four characteristics. The regressions included all the other control variables in the main model but these are suppressed in this table. The marginal/incremental effects are estimated and reported for the standard probit, biprobit and IV probit models. Standard errors are in parentheses.

*, ** *and* *** indicate p <0.1, <0.05 and <0.01, respectively.

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Table A12

Effects on Child Development in the Function Including Birth Weight and Gestational Age

	High Neurodevelopment Risk				Neurodevelopment Rate			
	Probit	**Biprobit**	**Probit**	**IV Probit**	**OLS**	**2SLS**	**OLS**	**2SLS**
Smoking during Pregnancy	0.0696** (0.0311)	0.4281*** (0.1527)			−2.6150* (1.3825)	−29.6425 (24.0059)		
Number of cigarettes during pregnancy			0.0055* (0.0031)	0.0318 (0.0274)			−0.2261** (0.1092)	−2.4856** (1.0925)
Birth weight (in 100 grams)	−0.0046* (0.0026)	−0.0034 (0.0025)	−0.0047* (0.0026)	−0.0036 (0.0032)	0.2209** (0.0936)	0.0719 (0.1659)	0.2254** (0.0935)	0.1262 (0.1182)
Gestational age (in weeks)	0.0121 (0.0086)	0.0122 (0.0086)	0.0118 (0.0088)	0.0117 (0.0096)	0.2367 (0.4195)	0.1860 (0.4067)	0.2435 (0.4245)	0.2628 (0.4491)
Observations	1581	1581	1581	1581	1581	1581	1581	1581

Note: This table reports the effects of maternal smoking, birth weight, and gestational age on development in the alternative specification that includes birth weight and gestational age. The regressions included all the other control variables in themain model but these are suppressed in this table. The marginal/incremental effects are estimated and reported for the standard probit, biprobit and IV probit models. Standard errors are in parentheses.

*, ** *and* *** indicate p <0.1, <0.05 and <0.01, respectively. The specification is estimated for 1581 infants as 3 infants of the main study sample had missing gestational age data.

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Table 1

Distribution of study variables

Variable	Mean (SD)		
	Total	Low SES	High SES
Child developmental risk status (high versus low)[a]	0.181 (0.395)	0.217 (0.142)	0.145 (0.352)
Child neurodevelopment rate[a]	0.00 (14.581)	−1.596 (15.157)	1.620 (13.793)
Maternal smoking during pregnancy	0.109 (0.311)	0.154 (0.361)	0.062 (0.242)
Number of cigarettes per day during pregnancy	0. 754 (3.007)	1.175 (3.827)	0.326 (1.733)
African ancestry	0.154 (0.361)	0.211 (0.408)	0.097 (0.296)
Native ancestry	0.426 (0.495)	0.451 (0.498)	0.399 (0.490)
Birth weight (in 100 grams)	33.47 (4.26)	33.30 (4.31)	33.64 (4.21)
Gestational age (in weeks)	39.3 (1.05)	39.39 (1.04)	39.21 (1.05)
Socioeconomic status index	−0.002 (1.238)	−0.954 (0.819)	0.965 (0.741)
Completed primary school[b]	0.298 (0.458)	0.530 (0.500)	0.062 (0.242)
Incomplete secondary school[b]	0.199 (0.399)	0.274 (0.447)	0.122 (0.328)
Complete secondary school[b]	0.306 (0.461)	0.177 (0.382)	0.438 (0.496)
Attended university[b]	0.197 (0.398)	0.019 (0.136)	0.378 (0.485)
Unemployed[c]	0.639 (0.480)	0.801 (0.400)	0.475 (0.500)
Unskilled blue collar worker[c]	0.074 (0.263)	0.109 (0.312)	0.039 (0.195)
Skilled blue collar worker[c]	0.042 (0.201)	0.021 (0.144)	0.064 (0.244)
Independent worker[c]	0.042 (0.201)	0.023 (0.149)	0.062 (0.242)
Clerk[c]	0.136 (0.343)	0.045 (0.208)	0.229 (0.420)
Wealth index	0.038 (0.981)	−0.624 (0.87)	0.71 (0.524)
Maternal mental health problems	0.037 (0.188)	0.045 (0.208)	0.028 (0.165)
Maternal chronic physical health problems	0.052 (0.222)	0.050 (0.218)	0.053 (0.225)
Maternal age	27.076 (6.571)	25.197 (6.267)	28.985 (6.322)
Maternal age squared	776.287 (376.990)	674.099 (345.748)	880.036 (379.256)
Mother is single	0.169 (0.374)	0.212 (0.409)	0.125 (0.330)
Mother is in a stable relationship	0.409 (0.492)	0.509 (0.500)	0.308 (0.462)
Number of older child’s siblings	1.007 (1.368)	1.214 (1.553)	0.796 (1.111)
Area smoking rate	0.109 (0.070)	0.120 (0.072)	0.097 (0.066)
Area smoking rate squared	0.016 (0.017)	0.020 (0.019)	0.014 (0.015)
Area-level average cigarette number	0.754 (0.740)	0.875 (0.793)	0.63 (0.66)
Cesarean delivery rate	0.385 (0.153)	0.361 (0.158)	0.410 (0.143)
Average number of prenatal visits	6.997 (1.589)	6.864 (1.592)	7.129 (1.577)
Average number of weeks delayed before initiating prenatal care	13.046 (2.745)	13.364 (2.885)	12.726 (2.561)
Average number of ultrasounds during pregnancy	2.287 (1.012)	2.207 (1.057)	2.367 (0.959)
Medication use rate during pregnancy	0.715 (0.281)	0.684 (0.286)	0.747 (0.272)
Immunization rate during pregnancy	0.548 (0.294)	0.581 (0.277)	0.516 (0.308)
Brazil[d]	0.331 (0.471)	0.381 (0.486)	0.281 (0.450)

Variable	Mean (SD)		
	Total	Low SES	High SES
Chile[d]	0.245 (0.430)	0.167 (0.373)	0.321 (0.468)

Note: The table reports the means and standard deviation of the study variables.

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[b] The reference category is incomplete primary schooling or lower education.

[c] The reference category is executive, professional, or owner occupation.

[d] The reference country is Argentina.

Table 2

Coefficients of Area- and Individual-Level Smoking Measure Regressions on Control Variables

	Individual-level smoking - Probit	Area-level smoking rate – OLS	Individual-level cigarette number - OLS	Area-level average cigarette number - OLS
Maternal mental health problems	0.464*** (0.134)	−0.007 (0.014)	0.715 (0.589)	−0.098 (0.142)
Maternal chronic physical health problems	0.230 (0.161)	0.020** (0.008)	0.171 (0.375)	0.150** (0.061)
Socioeconomic status index	−0.121*** (0.040)	−0.005 (0.005)	−0.224** (0.098)	−0.024 (0.045)
African ancestry	0.091 (0.158)	0.000 (0.020)	0.458 (0.411)	−0.047 (0.338)
Native ancestry	−0.083 (0.144)	0.012 (0.022)	−0.143 (0.186)	0.112 (0.138)
Maternal age	−0.095** (0.044)	−0.003 (0.002)	−0.172*** (0.061)	−0.056** (0.027)
Maternal age squared	0.001* (0.001)	0.000 (0.000)	0.003** (0.001)	0.001** (0.000)
Mother is single	0.374** (0.170)	0.011 (0.008)	0.244 (0.184)	0.013 (0.067)
Mother is in a stable relationship	0.264** (0.112)	0.001 (0.007)	0.264 (0.154)	0.016 (0.052)
Number of child's older siblings	0.132*** (0.040)	0.000 (0.002)	0.227** (0.092)	0.012 (0.022)
Brazil	−0.275 (0.188)	−0.024 (0.034)	0.165 (0.295)	0.477 (0.409)
Chile	−0.102 (0.158)	−0.040 (0.032)	−0.222 (0.186)	−0.436** (0.182)
Constant	0.086 (0.671)	0.169*** (0.051)	2.879*** (0.954)	1.459*** (0.413)
Observations	1584	1584	1584	1584

Note: The table reports the coefficients from the regressions of the area-level instruments and the individual-level smoking measures on the individual-level characteristics included as control variables in the child development functions. The models also include country fixed effects, which are suppressed from the table. The regressions for the instruments and number of cigarettes are estimated using OLS. The regression for individual-level smoking participation is estimated using probit. Standard errors are in parentheses.

*, ** *and* *** indicate p <0.1, <0.05 and <0.01, respectively.

Table 3

Coefficients of Area-Level Instrument Regressions on Other Area-level Characteristics

Other-Area Characteristics	Smoking Rate	Average number of cigarettes
Cesarean delivery rate	−0.119 (0.097)	−0.763 (0.641)
Average number of prenatal visits	.008 (.008)	0.052 (0.110)
Average number of weeks delayed before initiating prenatal care	−0.002 (.006)	−0.041 (0.047)
Average number of ultrasounds during pregnancy	0.006 (0.014)	0.133 (0.160)
Medication use rate during pregnancy	0.034 (0.065)	−0.174 (0.474)
Immunization rate during pregnancy	−0.136* (0.065)	−0.424 (0.572)

Note: The table reports the coefficients of the regression of the area-level instruments on the other area-level characteristics, one at a time, controlling for country fixed effects (which are suppressed in the table). The regressions are estimated using OLS. Standard errors are in parentheses.

*, ** *and* *** indicate p <0.1, <0.05 and <0.01, respectively.

Table 4

Effects of Smoking Participation and Number of Cigarettes during Pregnancy on the Probability of High Neurodevelopment Risk Status[a]

Model	Total Sample	Low Socioeconomic Status	High Socioeconomics status
	Smoking participation		
Probit	0.072** (0.031)	0.075* (0.042)	0.089 (0.062)
Bivariate Probit	0.401** (0.180)	0.544*** (0.140)	0.283 (0.533)
F-statistic	10.3*** [2, 23]	7.33** [2, 22]	6.19*** [2, 23]
Over-identification Chi-square [1]	1.51	1.45	1.89
Exogeneity Chi-square [1]	3.4*	5.63**	0.16
	Cigarettes		
Probit	0.006* (0.003)	0.007* (0.004)	0.007 (0.006)
IV Probit	0.032 (0.028)	0.035 (0.029)	-
F-statistic [df]	42.1*** [2,23]	23.96*** [2, 22]	-
Over-identification Chi-square [1]	0.09	0.19	-
Exogeneity Chi-square [1]	1.04	1.24	

Note: Standard errors of effects are in parentheses.

*, ** *and* *** indicate p <0.1, <0.05 and <0.01, respectively.

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Table 5

Effects of Smoking and Number of Cigarettes during Pregnancy on the Child Neurodevelopment Rate[a]

Model	Total Sample	Low Socioeconomic Status	High Socioeconomic status
	Smoking participation		
OLS	−2.85** (1.36)	−3.39** (1.25)	−1.60 (2.28)
2SLS	−29.85 (24.50) [−88.68,24.37]	−37.27** (19.01) [−85.91, −0.57]	−11.91 (28.75) [−72.82,68.86]
F-statistic [df]	10.3*** [2, 23]	7.33** [2, 22]	6.19*** [2, 23]
Over-identification Chi-square [1]	0.99	0.04	0.19
Exogeneity F-statistic [df]	1.17 [1, 23]	3.26* [1, 22]	0.12 [1, 23]
	Cigarettes		
OLS	−0.25** (0.11)	−0.26* (0.13)	−0.22 (0.20)
2SLS	−2.48** (1.11)	−2.49** (0.97)	-
Instrument F-statistic [df]	42.1*** [2,23]	23.96*** [2, 22]	-
Over-identification Chi-square [1]	0.82	0.33	-
Exogeneity F-statistic [df]	5.62** [1, 23]	7.23** [1, 22]	-

Note: Standard errors of effects are in parentheses.

*, ** *and* *** indicate p <0.1, <0.05 and <0.01, respectively. 95% Weak-instrument robust confidence bounds for the smoking participation effects are included in brackets.

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Table 6

Effects of Smoking Participation and Number of Cigarettes during Pregnancy on the Probability of High Neurodevelopment Risk Status[a] Excluding Maternal Characteristics

Model	Total Sample	Low Socioeconomic Status	High Socioeconomics status
	Smoking participation		
Probit	0.091*** (0.030)	0.079** (0.040)	0.099 (0.063)
Bivariate Probit	0.503** (0.207)	0.546*** (0.161)	0.253 (0.635)
F-statistic	22.88*** [2, 23]	11.86*** [2, 22]	7.24*** [2, 23]
Over-identification Chi-square [1]	2.08	1.8	1.98
Exogeneity Chi-square [1]	2.73*	3.93**	0.07
	Cigarettes		
Probit	0.007** (0.003)	0.007* (0.004)	0.007 (0.006)
IV Probit	0.042* (0.022)	0.029 (0.021)	-
F-statistic [df]	48.35*** [2,23]	20.36*** [2, 22]	-
Over-identification Chi-square [1]	0.81	0.63	-
Exogeneity Chi-square [1]	4.14**	1.38	

Note: The model is a nested specification of equation (5) that excludes maternal health, socioeconomic status and demographic characteristics, and includes only smoking (or cigarette number), child's ancestry, number of older siblings, and country fixed effects. Standard errors are in parentheses.

*, ** *and* *** indicate p <0.1, <0.05 and <0.01, respectively.

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Table 7

Effects of Smoking and Number of Cigarettes during Pregnancy on the Child Neurodevelopment Rate[a] Excluding Maternal Characteristics

Model	Total Sample	Low Socioeconomic Status	High Socioeconomics status
	Smoking participation		
OLS	−3.55** (1.33)	−3.93*** (1.17)	−1.53 (2.37)
2SLS	−29.36 (21.55) [−77.04, 14.95]	−36.35* (19.38) [−80.46, 2.28]	−12.67 (28.53) [−76.71, 58.53]
F-statistic [df]	22.88*** [2, 23]	11.86*** [2, 22]	7.24*** [2, 23]
Over-identification Chi-square [1]	0.69	0.02	0.13
Exogeneity F-statistic [df]	1.47 [1, 23]	2.75 [1, 22]	0.15 [1, 23]
	Cigarettes		
OLS	−0.30*** (0.10)	−0.29** (0.12)	−0.21 (0.19)
2SLS	−2.64*** (0.94)	−2.21*** (0.75)	-
Instrument F-statistic [df]	48.35*** [2,23]	20.36*** [2, 22]	-
Over-identification Chi-square [1]	0.25	0.69	-
Exogeneity F-statistic [df]	11.85*** [1, 23]	10.19*** [1, 22]	-

Note: The model is a nested specification of equation (5) that excludes maternal health, socioeconomic status and demographic characteristics, and includes only smoking (or cigarette number), child's ancestry, number of older siblings, and country fixed effects. Standard errors are in parentheses. 95% Weak-instrument robust confidence bounds for the smoking participation effects are included in brackets.

*, ** *and* *** indicate p <0.1, <0.05 and <0.01, respectively.

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