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The association between maternal smoking during pregnancy and performance on Criterion-Referenced Competency Tests (CRCT) among 1st Grade students in Georgia

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ABSTRACT

The association between maternal smoking during pregnancy and performance on Criterion-Referenced Competency Tests (CRCT) among 1st Grade students in Georgia

By Jia Feng

Background: Smoking during pregnancy has been reported to be associated with poorer cognitive function test scores. The objective of this study is to assess whether maternal smoking during pregnancy is associated with poorer performance on Criterion-Referenced Competency Tests (CRCT) among 1st Grade students in Georgia.

Methods: This study is a retrospective cohort study, in which electronic birth certificates of children born to Georgia resident mothers from 1998 to 2003 were deterministically linked with individual CRCT educational records taken from 2004 to 2010, for students of Grade 1 in Georgia. Maternal smoking during pregnancy, the exposure variable, was recorded on birth certificates. Binary fail/pass levels for CRCT Reading, Reading, English/Language Arts (ELA) and Mathematics tests were defined using standardized scaled scores. The pass/fail levels were the dependent variables in logistic and log-binomial models, with adjustment for maternal age at the time of birth; alcohol consumption during pregnancy; marital status; maternal education; prenatal care status; delivery funded by Medicaid or not; whether having prior adverse birth outcomes; child's sex; race/ethnicity; whether being preterm birth; low birth weight; small for gestational age; and parity status.

Results: In models adjusted for maternal and child characteristics, maternal smoking during pregnancy compared to non-smoking was associated with an increased risk of poor school performance. The risk ratios were 1.17 (1.13-1.21) for Reading test, 1.13 (1.10-1.16) for ELA test and 1.14 (1.10-1.17) for Mathematics test. These risk ratios remained statistically significant when we further adjusted for smoking-related adverse birth outcomes, including preterm birth, low birth weight and small for gestational age. Our results also indicated that for any CRCT test, there was a dose-response relationship between maternal smoking during pregnancy and the risk of poor offspring school performance (p-value < 0.001).

Conclusion: These results suggested that maternal smoking during pregnancy may have long-term effects on offspring school performance. Although the association may not be causal, it emphasizes the early preventive efforts health education and public health campaigns about the harmful effects of cigarette smoking by pregnant women.

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INTRODUCTION

The detrimental effects of cigarette smoking such as, respiratory diseases, lung cancers and cardiovascular diseases have been well-established. In recent decades, the overall cigarette smoking prevalence among young women of reproductive age has decreased significantly in the United States. According to the reports of the Pregnancy Risk Assessment Monitoring System (PRAMS), prevalence of smoking during pregnancy significantly declined from 15.2% to 13.8% during 2000 to 2005, on the basis of aggregated data. However, it is still reported that the prevalence of smoking during pregnancy ranged from 5.2% in New York City to 35.7% in West Virginia on the basis of site-specific data from 26 sites in 2005(1). Maternal smoking during pregnancy is of great public health concern, since it exposes the fetus to a large amount of detrimental chemicals found in cigarette smoke. Maternal smoking during pregnancy is one of the most important preventable risk factors for adverse maternal and pregnancy outcomes.

Many studies have shown that maternal smoking is associated with various adverse birth outcomes, including elevated risks of low birth weight (LBW), small for gestational age (SGA), and preterm birth (PTB) (2-8). In addition to birth outcomes, many investigators have also suggested that maternal smoking during pregnancy may have adverse effects on long-term offspring cognitive development, both structurally and functionally. The underlying biological mechanisms for how maternal smoking during pregnancy could affect offspring cognitive development are not yet well understood. Many studies on laboratory animals and on humans have shown that nicotine, a main component of cigarette smoke, is associated with reduced uterine blood flow, chronically increased resistances in the uterine, and umbilical and fetal middle cerebral arteries, and may result in hypoxia and malnutrition status of the fetus in uterine (9-11). Nicotine also has neuroteratogenic effects, by interacting with neurotransmitter systems and affecting the developing nervous system (12).

Many studies have been conducted to examine the relationship between maternal smoking during pregnancy and offspring cognitive development across a broad range of domains and at different ages. However, there are inconsistent results in this research area, because it is particularly difficult to control for various confounders. It has been reported that prenatal exposure to cigarette smoke is associated with a decrease in Motor Scale scores, and a decline in verbal comprehension at 13 months (13); lower scores on the General Cognitive Index at 3 years old (14); lower average Stanford-Binet scores at 3 and 4 years old (15); lower cognitive and receptive language scores, namely McCarthy Scales, Peabody Vocabulary Test, at 60 and 72 months (16); worse performance on arithmetic and spelling tasks among children aged 5.5 to 11 years (17); lower Full Scale IQ scores among a group of boys aged 6 to 17 years (18); deficits in verbal learning, design memory, problem solving and response on a test of eye-hand coordination among 10-year-old children (19); and lower global intelligence scores at 9 to 12 years old (20).

However, not all studies found inverse associations between maternal smoking and cognitive development in offspring. Some studies found that the association between maternal smoking during pregnancy and offspring cognitive development was eliminated or attenuated after controlling for maternal IQ and education, or not found at all when comparing between sibling pairs, suggesting that these associations may be due to familial and/or environmental confounding (21-25).

Also, due to the influence of uncontrolled confounders and the collinearity of pre- and postnatal maternal smoking, few studies can distinguish the effects of in utero exposure to maternal smoking from the effects of the child's postnatal exposure to second-hand tobacco smoke (26). A few studies have found that even after controlling for the effects of maternal smoking during pregnancy, poorer academic performance was associated with postnatal tobacco exposure (22, 27), suggesting that exposure to environmental tobacco smoke during childhood may be more hazardous to neurodevelopment than prenatal exposure. However, the authors could

not rule out the possibility that the observed association could be due to unmeasured confounders, or potential misclassification.

It remains unclear whether the association between maternal smoking during pregnancy and offspring cognitive development is causal or spurious, and to what extent the effects of maternal smoking are attributable to later poor academic performance in offspring. To add more evidence to this research area, in our current study, we assessed the association between maternal smoking during pregnancy and offspring cognitive development, as measured by academic performance using Criterion-Referenced Competency Tests (CRCT) scores among 1st Grade students in Georgia, adjusting for a wide range of important confounders, such as birth outcomes, and maternal and child characteristics.

To some extent, the maternal and child characteristics act as proxies for some important familial and environmental factors that may affect offspring cognitive development. Thus, by adjusting for maternal and child characteristics, we tried to control for these important familial and environmental factors. Birth outcomes could lie in the causal pathway between maternal smoking during pregnancy and offspring cognitive development (Figure 1). Thus, in our two-stage analyses, by only adjusting for maternal and child characteristics, we first assessed an overall effect of maternal smoking during pregnancy on long-term offspring development. Secondly, by adjusting for both maternal and child characteristics, and the birth outcomes, we assessed the direct effect of maternal smoking during pregnancy not via intrauterine growth retardation.

LITERATURE REVIEW

Maternal Smoking during Pregnancy

Maternal smoking is one of the most important preventable risk factors for many adverse maternal and fetal outcomes.

During recent decades, in the U.S, the overall cigarette smoking prevalence among women of reproductive age decreased substantially. The prevalence of cigarettes smoking was 38% for women aged 18 to 24 years, and 44% for women aged 25 to 44 years, in 1965. The corresponding figures decreased to 25% and 23% in 2000, respectively (28). In the past decade, smoking rates among women of reproductive age appears to have leveled off (29). Information on smoking prevalence during pregnancy is usually based on data from the U.S. Standard Certificate of Live Birth or self-reported information from questionnaires or interviews. Birth certificate data indicate that smoking prevalence among pregnant women decreased from about 20% in 1989 to only 12% in 2000 (28). The overall decline in smoking prevalence during pregnancy is largely due to the decrease of smoking initiation rates among women of reproductive age rather than an elevated rate of smoking cessation during pregnancy. Data collected between 1987 to 1996 from the Behavioral Risk Factor Surveillance System survey (BRFSS) indicate that among women aged 18 to 44 years from 33 states, the smoking initiation rates decreased significantly from 44.1% in 1987 to 38.2% in 1996 (30). During the same 10-year period, the prevalence of current smoking also decreased significantly from 16.3% to 11.8% for pregnant women. However, the percentage of women quitting smoking during pregnancy only decreased from 26.3% to 25.2% during that 10-year period (30).

Prevalence of maternal smoking during pregnancy differs by many factors, such as age, race, education and socioeconomic status (SES). Birth certificate data from 1990 to 2002 indicate that for every year from 1996 to 2001, mothers aged 15 to 19 years had the highest percentage of

smoking during pregnancy than any other age group (31). In 2002, the percentage of women smoking during pregnancy was 16.7% both for women aged 15 to 19 years and 20 to 24 years, and with 18.2%, the highest percentage observed, for women aged 18 to 19 years (32). In 2005, the percentage of women smoking during pregnancy was 16.6% for mothers aged 15 to 19 years, 18.6% for mothers aged 20 to 24 years, 11.5% for mothers aged 25 to 29 years and 7.1% for mothers aged 30 to 39 years (33).

Prevalence of maternal smoking during pregnancy differs across different race/ethnicity groups. In 1967, 40% of White pregnant women and 33% of Black pregnant women smoked, whereas in 1980, the corresponding numbers decreased to 25% and 23%, respectively (34). It is also reported that from 1987 to 1996, White mothers smoked more than non-White mothers, with 11.9% for Whites versus 8.5% for non-Whites in 1996 only (30). In 2000, Native Americans and Alaskan natives had the highest prevalence of maternal smoking during pregnancy (20%); for other race/ethnicity groups, 16% of non-Hispanic Whites, 9% of non-Hispanic Blacks, and 4% of Hispanics smoked during pregnancy (31). PRAMS data indicate that, in 2005, Alaska Natives still had the highest prevalence of smoking during pregnancy (36.3%), and 20.6% of American Indians, 14.0% of Hispanic women, 5.4% of Asian/Pacific Islanders smoked during pregnancy. Prevalence of maternal smoking during pregnancy among non-Hispanic Whites and non-Hispanic Blacks in 2005 were 18.5% and 10.1%, respectively (1).

Maternal education levels have been reported to be associated with maternal smoking status during pregnancy. In 2000, 2% of college-educated women self-reported smoking during pregnancy compared to 25% for women who did not complete college (35). In 2005, only 1.8% of women who completed college reported smoking during pregnancy compared to 20.2% of women with less than a high school education (33). SES status of mothers is another factor that affects maternal smoking during pregnancy. PRAMS data of 2005 show that women having 12 years of education or less, having an annual income of less than \$15,000, and being enrolled in

Medicaid were more likely to smoke during pregnancy (1). A systematic review of 9 cohorts indicate that lower education and SES were risk factors for smoking during pregnancy (36). It is also reported that smoking prevalence during pregnancy is associated with insurance coverage and delivery payor. Using Washington State 'First Steps Program' database, the investigators found that the age-adjusted maternal smoking prevalence was 44.4% for the Medicaid-funded mothers compared to 16.3% for those not Medicaid-funded; further stratified by marital status, among married mothers, smoking prevalence was 2.6 times higher in whites, 1.4 times higher in blacks, and 1.8 times higher in American Indians, when comparing mothers Medicaid-funded to those not (37). Other factors, such as, maternal marital status, whether having an unplanned pregnancy, smoking status of the partner, nicotine addiction status, age at smoking initiation, and parity are also reported to be associated with likelihood of smoking during pregnancy (1, 36, 38, 39).

Maternal smoking during pregnancy is of great public health concerns, because there are numerous detrimental chemicals in cigarette smoke, including nicotine, carbon monoxide (CO), tar, benzene and heavy metals, lead and cadmium. Many studies have focused on nicotine, because it has known addictive properties and neurotoxicity (40). To validate the accuracy of self-reported smoking status during pregnancy from birth certificate data or interviews, more objective measures of cigarette smoke exposure, such as serum cotinine concentration, the main metabolite of nicotine, were used in many studies. The accuracy of self-reported smoking status varies across different study populations. One cross-sectional study, measuring cotinine concentrations in stored blood samples in Scotland reported that self-reported smoking status during pregnancy underestimated true smoking status by 25% from serum cotinine measurement (41). One study testing serum cotinine concentrations of residual sera from early and late antenatal blood samples to assess the reliability of self-reported smoking status during pregnancy from a postal questionnaire, or obstetric booking notes, found that nearly a quarter of smoking

pregnant women did not report smoking during pregnancy and of those who did report smoking, the amount was often under reported (42). One cohort study of pregnant women who registered in the Collaborative Perinatal Project (1959-1966) reported that among their study subjects 94.9% of non-smokers and 87.0% of smokers reported their status accurately (43). Overall, due to the negative attitudes toward smoking during pregnancy, the self-reported information of smoking status during pregnancy is generally underestimated.

In Georgia, there is the same issue of underestimates of maternal smoking status during pregnancy from birth certificate data. Data from PRAMS, which is a self-administered, mailed, and confidential survey, show that, in Georgia, 10.5% of pregnant women smoked during pregnancy against 7.5% reported from birth certificate data in 2004; the corresponding figures in 2005 were 10.3% for PRAMS data and 6.5% for birth certificate data, respectively (1). PRAMS data identified more women smoking during pregnancy than birth certificate data, which suggested that women might be more comfortable to report smoking habit during pregnancy through a confidential and anonymous survey than to their healthcare providers (26). PRAMS data also show that about 46.1% in 2004 and 46.3% in 2005 pregnant women quit smoking during pregnancy in Georgia.

Offspring Cognitive Development

Because maternal smoking during pregnancy exposes the fetus to a large amount of detrimental chemicals in cigarette smoke as mentioned before, maternal smoking during pregnancy might affect birth outcomes and later cognitive development both structurally and functionally. The mechanisms for how maternal smoking during pregnancy could affect offspring cognitive development are not yet well understood. Several mechanisms are proposed to explain the short-term biological influences on birth outcomes and long-term consequences on offspring cognitive development, of maternal smoking during pregnancy.

Nicotine has received much attention and been studied in laboratory animals focusing on its neurotoxicity on the offspring. In humans, because of high lipid solubility, once absorbed, nicotine and its main metabolite, cotinine, rapidly cross the placental tissue into the fetal bloodstream; in fact, the fetal nicotine concentration is generally 15% above the levels of smoking mother (44). Maternal smoking during pregnancy was found to be associated with reduced uterine blood flow, chronically increased resistances in the uterine, umbilical and fetal middle cerebral arteries, and it is hypothesized that these biological changes both in mothers and fetus might cause a deprived nutrient and oxygen status of fetus and then result in hypoxia and malnutrition (9-11). These might cause intrauterine growth retardation and then impaired cognitive development. Studies in laboratory animals have also indicated that nicotine has neuroteratogenic effects during development, by affecting the developing nervous system (12), and that cholinergic neurotransmitter system was persistently hypoactive through adolescence and adult life of prenatal nicotine exposed rats (45). It is proposed that in humans, maternal smoking during pregnancy might also affect the long-term cognitive development via influence on the neurotransmitter systems. Once into the fetal bloodstream, nicotine interacts with nicotinic acetylcholine receptors (nAChRs), which are present very early in the human fetal brains and

involved in releasing of other neurotransmitters, suggesting important effects of prenatal cigarette smoke exposure on fetal brain development (46). Prenatal exposure to cigarette smoke was found to be associated with changes in cholinergic neurotransmitter system, which depresses amino acid transport through placenta (29, 47).

Many studies have examined the association between maternal smoking during pregnancy and alterations within specific regions of the brain, which might cause later cognitive development problems. Measured by magnetic resonance images, some cerebral cortices, including orbitofrontal, middle frontal, and parahippocampal parts, were thinner in prenatally exposed adolescents compared to those unexposed, which provides some biological evidence of the impacts of maternal smoking during pregnancy on long-term cognitive development (48).

Maternal smoking during pregnancy has been found to be associated with various adverse pregnancy outcomes, particularly in the area of fetal growth restriction indicated by subsequent low birth weight, smaller head circumference, and small for gestational age (SGA). These adverse birth outcomes might then have long-term impacts on offspring cognitive outcomes. In 1957, Simpson first reported that maternal smoking during pregnancy was associated with lower birth weight comparing mothers who smoked 10 cigarettes or more/day to non-smokers (49). The association between maternal smoking during pregnancy and the risk of LBW and SGA are consistent in the literature, and a dose-response relationship was also reported in several studies (2-8). It is also reported that smoking cessation during pregnancy can improve fetal growth. In one population-based longitudinal study of mothers and their first and second infants, among mothers who smoked during the first pregnancy but quit during the second pregnancy, the second birth weight was the same as among women who never smoked (50). This suggested the desired benefits of quitting smoking during pregnancy. Studies also found that maternal smoking during pregnancy was negatively associated with head circumference, a standard measurement reflecting total brain volume (51, 52), even when adjusting for growth retardation and gestational age.

These investigators suggested that decreased growth of infants' heads due to exposure to cigarette smoking in utero might be associated with impaired brain development and later impaired cognitive and intellectual development. It is reported that, among VLBW children, subnormal head circumference was associated with adverse cognitive functions independent of other risk factors(53). Among SGA children, head growth compromise beginning in utero has been found to impair the acquisition of some cognitive and academic abilities and postnatal head growth might improve these outcomes, but might not completely eliminate the impairments (54).

Besides birth outcomes, many studies have been conducted to directly assess the association between maternal smoking during pregnancy and offspring cognitive development across a broad range of domains and at different ages. However, there are inconsistent results about the association between maternal smoking during pregnancy and offspring cognitive development, because it is particularly difficult to control for various confounders in research of this area.

Many studies found negative relationship between maternal smoking during pregnancy and offspring intellectual and cognitive abilities.

Prenatal exposure to nicotine was found to be associated with a decrease in Motor Scale scores, and a decline in verbal comprehension and fine motor skills among offspring at 13 months, after adjusting for various confounders (13). Measured by the McCarthy Scales of Children's Abilities and the Minnesota Child Development Inventory, 3-year-old children born to women who consistently smoked during pregnancy had significant lower scores on the General Cognitive Index of the McCarthy and on each of the three subscales, compared to those whose mothers quit smoking during pregnancy (14). In one prospective cohort study of 400 families in which the mothers registered before the 30th week of pregnancy and had no previous live births, children at 3 and 4 years old, whose mothers smoked 10 or more cigarettes/day during pregnancy compared to those of non-smokers, had average Stanford-Binet Scores 4.35 points lower after controlling

for social class, maternal IQ and education, and quartiles of care-giving (15). Among children at 60 and 72 months, a negative dose-response association was observed between prenatal cigarette exposure and lower cognitive and receptive language scores, namely McCarthy Scales and Peabody Vocabulary Test (16). The prospective Dutch birth cohort study of 1186 children aged 5.5 to 11 years showed that after adjustment for socio-economic status and pre- and perinatal complications, children exposed to cigarette smoke prenatally performed worse on arithmetic and spelling tasks (17). Among a group of boys aged 6 to 17 years, maternal smoking during pregnancy was found to be significantly associated with lower Full Scale IQ scores comparing children whose mothers smoked during pregnancy to those whose mothers did not (18). One prospective cohort study, conducted from the fourth prenatal month until 10-year visit, found that after controlling for other prenatal substance use, current tobacco, other substance use, as well as multiple socio-demographic characteristics, maternal smoking during pregnancy was a significant predictor of deficits in verbal learning, design memory, problem solving and responding on a test of eye-hand coordination among 10-year-old children (19). Among 131 children aged 9 to 12 years in an ongoing longitudinal study in Canada, a dose-response relationship of maternal smoking during pregnancy on lower global intelligence scores with the verbal subtests of the WISC were detected (20).

However, not all studies found inverse association between maternal smoking and cognitive development in offspring. Results of some studies suggested that the association between maternal smoking and offspring cognitive development might be spurious, and these associations might be due to genetic and/or environmental confounding.

In the US National Longitudinal Survey of Youth 1979, 5578 offspring were analyzed. Children born to mothers who smoked one or more packs of cigarettes/day during pregnancy had a lower IQ score, Peabody Individual Achievement Test total, compared to children born to nonsmoking mothers. However, controlling for maternal IQ and education markedly attenuated

the observed association (21). In one prospective cohort study among 2,124 children aged 5 years, instead of demonstrating a consistent dose-response relation between maternal smoking during pregnancy, measured by serum cotinine concentrations, and cognitive performance in offspring, the authors found that, in fact, the children exposed to cigarette smoke prenatally had somewhat higher but not significant scores on the Peabody Picture Vocabulary Test and the Raven Colored Progressive Matrices Test, compared to children of non-smokers (22). Children born in 1983 to 1985 from inner-city and suburban communities in southeast Michigan, USA were analyzed in one cohort study; adjustment for maternal cognitive ability measured by IQ and education eliminated the association between maternal smoking during pregnancy and children's IQ, assessed at ages 6, 11, and 17, using Wechsler intelligence tests (23). Similar results were found in another cohort study. In a birth cohort of New Zealand children aged 8 to 12 years, no relationship between smoking during pregnancy and subsequent child cognitive development can be detected after controlling for SES and features of the home environment (24). In a population-based Swedish cohort study on 205,777 singleton males born between 1983 and 1988, the researchers found a significant association between maternal smoking during pregnancy and poor intellectual performance of male offspring born to smoking mothers compared to non-smokers. Their further analyses, stratified by order of birth, showed that the increased risks of poor intellectual performance were found for both sons if the mother smoked in the first pregnancy, but not found if the mother only smoked in the second pregnancy. They also found no association when comparing between sibling pairs and concluded that the association between maternal smoking during pregnancy and offspring intellectual performance might be completely confounded by familial (genetic and early environmental) factors (25).

Also, due to the influence of uncontrolled confounders and the collinearity of pre- and postnatal maternal smoking, few studies can distinguish the effects of in utero exposure to maternal smoking from the effects of the child's postnatal exposure to second-hand tobacco

smoke (26). A few studies found that even after controlling for the effects of maternal smoking during pregnancy, poorer academic performance was associated with postnatal tobacco exposure (22, 27), suggesting that exposure to environmental tobacco smoke during childhood may be more hazardous to neurodevelopment than prenatal exposure; however, the authors could not rule out that the observed association might be due to unmeasured confounders or potential misclassification.

Criterion-Referenced Competency Tests (CRCT) Scores

Studies have used different measures of offspring cognitive development. Although school performance is influenced by many factors, such as students' motivation, and ability to concentrate, school performance is generally closely associated with intelligence. Thus, in this study, we use scores from one set of standardized tests, Criterion-Referenced Competency Tests, as the indicators of offspring academic performance, one aspect of cognitive development.

The CRCT was implemented in spring 2000 in Georgia and is administered to all public school students from Grade 1 to 8. It is designed to measure how well students acquire, learn, and accomplish the knowledge, concepts and skills set forth in the Georgia Performance Standards (GPS). Required by Georgia law, students from Grade 1 to 8 take the Reading, English/Language Arts (ELA), and Mathematics CRCT each spring; two additional domains of the Science and Social Studies are administered to students from Grade 3 to 8. These tests are designed to assess student academic achievement, individual strengths and weaknesses related to the instruction of GPS, as well as the quality of education in the state. Only the knowledge, concepts, and skills outlined in the GPS are assessed on the CRCT. (55)

For Grade 1 students in Georgia, the domains tested for Reading are vocabulary and comprehension (56); for English/Language Arts are grammar/phonological awareness/phonics, sentence construction, and research (57); for Mathematics are number and operations, measurement, geometry and data analysis and probability (58).

In this study, the content areas of interests are Reading, English/Language Arts, and Mathematics CRCT.

METHODS

Specific Aim

To assess the association between maternal smoking during pregnancy and CRCT scores among 1st Grade students in Georgia, controlling for other covariates.

Hypotheses

H₀: there are no effects of maternal smoking during pregnancy on CRCT scores among 1st Grade students in Georgia, controlling for other covariates.

H_A: there are (adverse) effects of maternal smoking during pregnancy on CRCT scores among 1st Grade students in Georgia, controlling for other covariates.

Study Design

For this retrospective cohort study the exposure status, maternal smoking during pregnancy, was obtained from electronic birth certificates. The original birth cohort is followed forward in time by linking birth records to statewide individual-level educational records, using a unique identifier created by the Office of Health Indicators for Planning (OHIP) of the Georgia Department of Public Health. The outcomes, the CRCT test results in first grade, were abstracted from individual-level educational records.

Georgia Birth-Education dataset and Sample

In order to create the Georgia Birth-Education dataset, electronic birth certificate data of children born to Georgia-resident mothers from 1998 to 2003 were linked with CRCT educational data taken from 2004 to 2010, for students of Grade 1. Birth records were deterministically linked to student CRCT data using a unique ID variable constructed from portions of the child's first and last name, date of birth and sex. For this dataset, study subjects were restricted to those having matching student information, birth weights recorded between 400g to 5,000g, gestational ages between 20 to 43 weeks and without recorded congenital anomalies and chromosomal defects.

For the current study, because twin, triplet or more births might be associated with a disadvantageous fetal environment, subjects were restricted to singleton births by excluding non-singleton births. Also, very few students were born in 2003 or took CRCT tests in 2004, analysis datasets were further restricted to children born from 1998 to 2002, taking their CRCT tests between 2005 and 2009.

Measures

Maternal Smoking during Pregnancy

The birth certificate data had information on mothers' responses to question about maternal smoking during pregnancy (yes/no) and the average number of cigarettes smoked per day during pregnancy. The binary cigarettes smoking yes/no variable was used in the majority of the analyses. Also, in order to assess a potential dose-response relationship of maternal smoking during pregnancy with different academic performance outcomes, using the cigs/day variable, we categorized maternal smoking during pregnancy into four categories: non-smokers (0 cigarettes

per day), moderate smokers (1-9 cigarettes per day), heavy smokers (10-19 cigarettes per day) and very heavy smokers (20 or more cigarettes per day).

Child Academic Performance

The primary aim of this study is to assess whether prenatal exposure to cigarette smoke impairs child cognitive development. We used CRCT scores as our measures of child academic performance, one aspect of offspring cognitive development.

The Georgia Department of Education uses standardized scaled scores on the CRCT dichotomized into pass vs. fail to indicate students demonstrating the minimum expected competency in each domain for Reading, ELA and Mathematics. In general students must pass the CRCT in order to be promoted to the next grade.

Covariates

A wide range of potential covariates, including various maternal and child characteristics, which can be abstracted from birth certificate data or student CRCT data, were considered in the analyses of this study.

Covariates from birth certificates:

Maternal age at the time of birth was considered both as continuous variable and categorical variable of eight age groups, 11-14, 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, and 45-53;

Mother's alcohol consumption during pregnancy, any vs. none, defined from the yes/no question reported by mothers on birth certificates; also as continuous variable, defined from the average drinks consumed per week;

Mother's marital status at the time of birth, married vs. unmarried;

Mother's education at the time of birth, categorical variable, defined as having education of Less than 12 Grades, High School, Some College, and College Completed;

Prenatal care, any vs. none;

Delivery payor, Medicaid-funded vs. not Medicaid-funded;

Whether or not having prior adverse birth outcomes, defined as whether or not the mother had a previous delivery characterized by preterm birth, small for gestational age or low birth weight, yes vs. no;

Child's sex, male vs. female;

The year of birth, ranging from 1998 to 2003;

Parity/live birth order, defined as first, 2-3, and 4+.

Covariates for student CRCT educational records:

Child's race/ethnicity, categorical variable, defined as non-Hispanic White, non-Hispanic Black, Hispanic, and Other;

The school year CRCT tests taken, ranging from 2004 to 2009.

Derived covariate:

Child's age at the time of taking CRCT tests, defined as the year of taking CRCT test minus the year of birth.

Indicators for birth outcomes from birth certificates:

In order to assess whether maternal smoking during pregnancy affects cognitive development directly via influence on neurotransmitter systems or indirectly via intrauterine growth retardation, birth outcomes were included into analyses as covariates. Birth outcome variable included birth weight, gestational age, and computed variables, such as, preterm birth, low birth weight, and small for gestational age.

Birth weight, the weight of a baby at its birth, was measured in grams; birth weight was used as continuous variable. Dichotomous variable was created to indicate low birth weight (< 2500 g) and normal birth weight (≥ 2500 g).

Gestational age, the age of an embryo or fetus (or newborn infant), ideally measured from conception but practically from the first day of last menstrual period, was coded in weeks, as continuous variable. Gestational age was further dichotomized into preterm births (< 37 weeks) and not preterm births (≥ 37 weeks).

SGA, an indicator for whether a baby is smaller in size than normal for the baby's gestational age, was defined as a birth weight below the 10th percentile for the gestational age, using multiple reference percentiles for birth weight at each gestational age from 1999 and 2000 US nationwide Natality data (59).

Analyses

All analyses were performed using SAS 9.3 (Cary, NC). Missing and implausible values were checked for each variable of interests.

Initial data analyses included descriptive analyses of outcome variables (pass/fail on Reading, ELA, and Mathematics tests), exposure variable (maternal smoking status during pregnancy), as well as other covariates.

Univariate and bivariate analyses were performed to assess the association between maternal smoking during pregnancy and other covariates, and the association between Reading, ELA, and Mathematics CRCT scores and other covariates, respectively. Unadjusted estimated odds ratios (OR), risk ratios (RR) and 95% confidence intervals (CI) were calculated and comparisons were performed using t-tests for continuous variables and Chi-square tests for categorical variables.

Multivariable analyses were performed in two stages. Considering the facts that the OR's were non-collapsible across different levels of covariates and that the prevalence of failing on CRCT tests was not rare, both logistic and log-binomial regression models were fitted using similar model building strategies for Reading, ELA, and Mathematics, respectively.

In the first stage, to assess an overall effect of maternal smoking during pregnancy on offspring school performance, only variables of maternal and child characteristics were adjusted in the regression models. In the second stage, all the birth outcomes, including variables indicating preterm birth, small for gestational age, and low birth weight, and maternal and child characteristics were adjusted in the regression models to assess whether or not maternal smoking affects long-term offspring cognitive development indicated by school performance, mediated by adverse birth outcomes.

Collinearity diagnostics among proposed variables were assessed using a priori cutoff of 30 for the Condition Indices and 0.5 for the variance decomposition proportions (VDP), Collinearity problems were determined if at least two variables (except intercept) were related a high CI and high VDP's. Only one collinearity problem involving main exposure, child's age, and their interaction term, was detected. The collinearity problem was solved by removing the interaction term of the exposure with child's age from the model.

After solving the collinearity problem, statistical significance of the interaction terms of the main exposure variable with each other covariate was assessed using likelihood ratio tests for Proc logistic and Score tests for Proc genmod, using a backward elimination strategy. Given the large sample size and number of tests, significance of interaction terms were only reported for p-values smaller than 0.001 for all CRCT tests. Confounding was then assessed by 10% changes or more of the estimated OR/ RR for maternal smoking during pregnancy on CRCT test results.

Missing Data

The sample sizes for the analyses of different outcomes varied because of different patterns of missing values for Reading, ELA, and Mathematics CRCT scores, respectively.

For most of the covariates of the Georgia linked Birth-Education dataset, the percentages of missing values were less than 1%. The variables with more than 1% of missing data were maternal education (N = 5,061, 1.5%), and prenatal care (N = 11,428, 3.5%). Dummy variables were created for missing data of these variables with more than 1% of missing values. Logistic and log-binomial models with and without dummy variables were fitted to assess whether missing data affect the estimated effect of maternal smoking during pregnancy on the risk of failing on CRCT tests.

Human Subjects Review

The data used for this study was de-identified data from an IRB approved project. The parent project was approved by the IRB (IRB00044043, Emory University) (APPENDIX A).

RESULTS

Sample Characteristics

This study investigated the association between maternal smoking during pregnancy and offspring school performance, CRCT scores among 1st Grade students in Georgia, using the Georgia linked Birth-Education dataset. There were 783,730 live born infants to Georgia residents during 1998-2003 of whom 340,553 were successfully linked to 1st grade CRCT test results. For this study, subjects were further restricted to singleton births by excluding non-singleton births (n = 8,844). The majority of the students took their CRCT tests between 2005 and 2009. A few students, who took CRCT tests in 2004 (n = 27), were excluded from analyses. Also, a few children were born in 2003, the analysis dataset was further restricted to children born from 1998 to 2002, by excluding those born in 2003 (n = 26). The final study population for analyses comprises 331,656 1st grade students born from singleton pregnancies to Georgia residents from 1998 to 2002.

Maternal smoking status during pregnancy—indicated by the yes/no question the mothers reported on birth certificates—were not available for 1,704 (0.5%) linked records (Table 1). In the analysis dataset (n = 331,656), about 9.2% of the mothers reported smoking during pregnancy.

Among those having information on maternal smoking status during pregnancy, the percentage failing the Reading, ELA, or Math test were 9.6%, 16.3% and 12.7% respectively (Table 1). More than half (55.5%) of the pregnant women were in the age range of 20-29. A few mothers reported alcohol consumption during pregnancy (0.6%). Approximate 61.8% of women were married and most (60.4%) of the pregnant women had a high school education or less. Of those having information on prenatal care, only a few women (0.6%) reported having no prenatal

care. Nearly half (47.3%) of the deliveries were funded by Medicaid. Only 0.6% reported having previous adverse birth outcomes. About 49.4% of the students were female and 49.5% were Whites. The percentages of preterm birth, low birth weight, and small for gestational age were 10.2%, 6.6%, and 11.4%, respectively. About 41.1% of the students were the first birth of their mothers.

The mothers' mean age was 26.08 ± 6.06 years, and the average last grade mother completed was 12.51 ± 2.66 grades. For those who drank alcohol during pregnancy, the average number of alcoholic drinks per week was very small (0.013 ± 0.295). The average number of prenatal care visits received by mothers was 12.04 ± 4.08 . The average fathers' age was 29.28 ± 6.72 years. The mean birth weight of the baby was 3307 ± 557 grams and the mean gestational age was 38.72 ± 2.08 weeks.

Table 1 also presents the numbers and percentages of different covariate categories by maternal smoking status (smoking vs. not smoking) during pregnancy. The outcomes, demographic characteristics of mothers and students in exposed and unexposed groups were not comparable among almost all covariates except for child's gender.

The percentages of students failing on any of the Reading, ELA or Math test were higher for those exposed to maternal smoking during pregnancy compared to those not exposed (also see Figure 2). For instance, for reading test results, 11.7% of students exposed to maternal smoking during pregnancy failed in this test compared to 9.3% of students not exposed.

There were higher percentages of women aged 15-24 years among smokers. Percentage of alcohol consumption during pregnancy was higher among smokers than non-smokers (2.9% vs. 0.4%). Higher percentage (62.9%) of non-smokers was married compared to 50.4% of the smokers. Among smokers, only 2.7% of them had completed college education, compared to 21.2% of non-smokers. Higher percentage of non-smokers received any prenatal care than that of

smokers (99.4% vs. 98.9%). Also, women smoking during pregnancy had higher percentage (69.4%) of Medicaid-funded delivery compared to 45.1% of those not smoking during pregnancy.

Among the students, the gender distribution of the offspring was comparable, comparing those born to smokers to those born to non-smokers. Among students born to mothers who smoked during pregnancy, 75.2% were Whites compared to 46.9% of those born to non-smokers. There were more preterm births (12.3%) among students prenatally exposed to maternal smoking compared to 10.0% of those not exposed. The risk of low birth weight and small for gestational age were both higher among students prenatally exposed to maternal smoking compared to those prenatally not exposed. About 32.9% of students born to smokers were the first pregnancy of their mothers compared to 41.9% of students born to non-smokers.

Table 2a-2c presents the numbers and percentages of different covariate categories by students fail/pass status on CRCT Reading, ELA, and Math tests, respectively. In these analyses, different records were excluded due to different missing values for different CRCT tests. 329,625 out of 329,952 (99.9%) records were analyzed for Reading test scores, with 327 records of missing values excluded. 329,593 out of 329,952 (99.9%) records were analyzed for English/Language Arts, with 359 records of missing values excluded. 329,569 out of 329,952 (99.9%) records were analyzed for Mathematics, with 383 records of missing values excluded.

For each CRCT test, failing students were more likely to have mothers who smoked during pregnancy and younger mothers at the time of delivery. The habits of maternal alcohol consumption during pregnancy seemed comparable among students who failed or passed these tests. Students born to married mothers, mothers having some college or above education, having prenatal care, delivery not funded by Medicaid and not having previous adverse birth outcomes tended to have favorable results on any of the CRCT test. Female, first-born, White students who

were not born preterm, low birth weight, small for gestational age were more likely to have passing results on CRCT tests.

Among students with favorable results on CRCT tests, the maternal age at delivery and the highest grade the mother completed were higher; however, the average numbers of cigarettes per day and alcohol drinks per week were lower. They also tended to have more prenatal care, and the students tended to have higher birth weight and gestational age. The fathers' ages were also higher among students with favorable results on CRCT tests.

Crude Analyses

The Association between Maternal Smoking during Pregnancy and Covariates

Table 3 presents the crude relationship between maternal smoking during pregnancy and other risk factors. The unadjusted OR and 95%CI indicated that maternal smoking status during pregnancy was significantly associated with other covariates at all levels, except for 45-53 age group and with child's sex. Mothers having younger age at delivery, consuming alcohol during pregnancy, being unmarried, having lower education, having no prenatal care, delivery funded by Medicaid, having previous adverse birth outcomes, being White, giving births for preterm, low birth weight, or small for gestational age babies, and having previous pregnancies were more likely to be smokers during pregnancy.

The Association between Study Outcomes and Covariates

Table 4a-4c presents the crude associations between the main exposure, other covariates and risks of failing on CRCT Reading, ELA, and Math tests, respectively. For each CRCT test, except for the covariates of maternal alcohol consumption during pregnancy and whether having

previous adverse birth outcomes, risks of poor school performance indicated by failing on CRCT tests were significantly associated with the exposure and each of the other covariates at all levels. Generally speaking, for any CRCT test, maternal characteristic, such as maternal smoking during pregnancy, low maternal age at delivery, being unmarried, low maternal education, having no prenatal care, delivery funded by Medicaid, and having previous adverse birth outcomes were significantly associated with increased risks of offspring failing on CRCT tests. In terms of children's characteristics, being male, Black, Hispanic or in other race/ethnic group compared to White, being preterm birth, having low birth weight, small for gestational age and not being the first birth were also significantly associated with increased risks of failing on CRCT tests.

Regression Analyses

Different logistic and log-binomial regression models were fitted using model building strategies for Reading, ELA, and Mathematics, respectively.

From crude analyses, we found no association between maternal alcohol consumption during pregnancy, as well as whether having previous adverse birth outcomes and any CRCT test result (Table 2a-2d), indicating that these two factors might not be potential confounders. However, they were still included in initial regression models for conservative reasons. Child's gender was adjusted for the similar reason.

In the first stage, in order to assess an overall effect of maternal smoking during pregnancy on offspring school performance, maternal and child characteristics were controlled in regression models. The interaction terms of the main exposure variable with each covariate, except for child's age, which was deleted from the full model due to collinearity problem, was assessed using likelihood ratio tests for Proc logistic or Score tests for Proc genmod. For each CRCT test,

statistical interaction only between maternal smoking during pregnancy and child's race was observed on the multiplicative scale (p -value < 0.001 for interaction term in each model), and odds/risk ratios of failing on CRCT tests were significantly different in different strata of child's race (Table 5a-c). The effects of maternal smoking during pregnancy were more profound among Whites and other race/ethnicity group. The ORs/RRs of poor school performance were statistically significant smaller than one among Hispanic students.

However, the additive interactions between maternal smoking during pregnancy and child's race were not pronounced on an additive scale for race/ethnicity groups, of Black vs. White and Other vs. White, but significant for the group of Hispanic vs. White (Table 6a-c). For example, for CRCT Reading test, the relative excess risk due to interaction (RERI) was -0.065 (95%CI: $-0.276, 0.174$) for Black vs. White; -0.653 (95%CI: $-0.955, -0.291$) for Hispanic vs. White and -0.109 (95%CI: $-0.254, 0.042$) for Other vs. White, respectively.

Thus, in the following analyses, we also present results excluding the interaction between maternal smoking during pregnancy and child's race. For any other interaction, statistical significance was only detected in a subset of CRCT tests (data not shown) and not considered to be evidence of meaningful effect measure modification. None of them was included in further analyses.

Without the interaction term between maternal smoking during pregnancy and child's race in the models, Table 7a-c present the results of gold standard models, which control for all covariates of maternal and child characteristics before assessing confounding. Students born to smoking mothers had a 15% to 19% increase in odds, and 13% to 17% increase in risk of poor school performance compared to students born to non-smoking mothers.

After assessing confounding, the most parsimonious models were the ones only controlled for maternal education, delivery payor and child's race; the ORs/RRs were within 10% change of the corresponding ORs/RRs of gold standard models (Table 8a-c).

In the second stage, all the birth outcomes, including variables indicating preterm birth, small for gestational age, and low birth weight, and maternal and child characteristics were adjusted in regression models to assess whether or not maternal smoking affects long-term offspring cognitive development indicated by school performance, via adverse birth outcomes. Our results indicated that further controlling for birth outcomes (Table 9a-c), the adjusted ORs/RRs slightly decreased, but were still statistically significant, with only a 11% to 15% increase in odds, and 10% to 14% increase in risk of poor school performance compared to students born to non-smoking mothers.

Dose-Response Analyses of Maternal Smoking during Pregnancy on CRCT Test

Results

Table 10 presents the numbers and percentages of different covariate categories by ordinal maternal smoking status during pregnancy. For each CRCT test, the percentage of failing on CRCT test was higher in any maternal smoking categories compared to those of nonsmoking mothers. The crude analyses indicated that the percentages of failing on CRCT tests did not increase consistently as the numbers of cigarettes mothers smoked increased for each test. Others covariates, except for child's sex, were not comparable among different maternal smoking categories.

Table 11a-c present the results of dose-response analyses. Our results indicated that for any CRCT test, there was a dose-response relationship between maternal smoking during pregnancy

and the risk of poor offspring school performance, controlling for maternal and child characteristics. For example, for CRCT Reading test, as the numbers of cigarettes mothers smoked increased from '1-9 cigs/day' (moderate smokers), to '10-19 cigs/day' (heavy smokers), to ' ≥ 20 cigs/day' (very heavy smokers), the adjusted estimated risk ratios of offspring failing on the CRCT Reading test increased from 1.09 to 1.17 to 1.32, compared to those born to non-smokers. The dose-dependent increases in risk were consistent across different CRCT test. Similar dose-response relationship was detected for odds ratios for each CRCT test. The p-values for test of trend were less than 0.001 for both logistic and log-binomial models fitted.

DISCUSSION

Findings

Direct vs. Indirect Effects of Maternal Smoking during Pregnancy on Offspring School Performance

This study identified associations between maternal smoking during pregnancy and poor school performance on CRCT tests of Reading, English/Language Arts and Mathematics among 1st Grade students in Georgia. The associations between maternal smoking during pregnancy and offspring school performance were of modest magnitude.

Maternal smoking during pregnancy may have direct effects (through effects on the developing brain or on the neurotransmitter systems), or indirect effects (via the consequences of pregnancy complications or adverse birth outcomes) on offspring cognitive development. Previous studies found strong relationships between lower cognitive scores and adverse birth outcomes, such as low birth weight and small gestational age at birth, and no significant differences in results obtained from different countries (59). We proposed that adverse birth outcomes could lie in the causal pathway between maternal smoking during pregnancy and offspring poor school performance. If this is the true situation, after controlling for birth outcomes, as well as other covariates, we would expect to observe that the association between maternal smoking during pregnancy and poor school performance would be largely attenuated or diminished. Otherwise, we would expect to observe that the association between maternal smoking during pregnancy and offspring school performance would not be much affected.

In our first stage of analyses, we controlled only maternal and child characteristics in the regression models in order to assess an overall effect of maternal smoking during pregnancy on offspring school performance. We found that the odds of failing on CRCT tests for students born

to smoking mothers was about 1.15 to 1.19 times the corresponding odds for students born to nonsmoking mothers and the risks of poor school performance for children prenatally exposed to tobacco smoke was about 1.13 to 1.17 times the corresponding risks for children prenatally not exposed (Table 7a-c). In our second stage analyses, in addition to controlling for maternal and child's characteristics, we included indicators for low birth weight, preterm birth and small for gestational age as covariates in the regression models. We found that although further adjustment for birth outcomes slightly reduced the association between maternal smoking during pregnancy and poor school performance), with only a 11% to 15% increase in odds, and 10% to 14% increase in risk of poor school performance compared to students born to non-smoking mothers, the odds/risk ratios of failing on CRCT tests remained statistically significant (p -values < 0.001 (Table 9a-c). These results suggested that the association between maternal smoking during pregnancy and offspring cognitive development was largely through the direct effects, with a small proportion mediated by adverse birth outcomes. More appropriate interpretations would be a mixture of direct and indirect effects of maternal smoking during pregnancy on offspring school performance, which may indicate complex underlying mechanisms.

Interaction with Child's Race

We found statistically significant interaction between maternal smoking during pregnancy and child's race on a multiplicative scale (Table 5a-c). The effects of maternal smoking during pregnancy were protective among Hispanic students, which was not in line with common sense of the hazards of maternal smoking during pregnancy.

Interactions on an additive scale, which is arguably a more plausible scale for considering true effect modification as compared to statistical interaction(60), were also considered in our analyses. We found that the additive interactions between maternal smoking during pregnancy

and child's race were not pronounced on an additive scale for race/ethnicity groups, of Black vs. White and Other vs. White, but significant for the group of Hispanic vs. White (Table 6a-c). Thus, we included results both including and excluding the interaction term of the main exposure with child's race on the multiplicative scale; and found that excluding such interaction term from the regression models, did not affect our conclusions of the negative association between maternal smoking during pregnancy and offspring school performance.

This raised our concern about the relative sparse data in Hispanic race/ethnicity category compared to other race/ethnicity groups. There might be potential selection bias in Hispanic race/ethnicity group due to mismatching of birth certificates with individual education records. In order to get Georgia Birth-Education dataset, a unique ID variable was constructed from portions of the child's first and last name, date of birth and sex; however, Hispanic surnames may not be identically captured on educational data, which may lead to a larger proportion of mismatching in Hispanic groups as compared to other groups. We also did not know whether there was differential mismatching by maternal smoking status during pregnancy among Hispanic students. Further studies among Hispanic students are of great importance to validate our study results.

Dose-Response of Maternal Smoking during Pregnancy on Offspring School Performance

Our dose-response analyses revealed a significant dose-response relationship between maternal smoking during pregnancy and the risk of poor school performance on CRCT tests, controlling for maternal and child characteristics. According to the results in Table 11a-c, as the numbers of cigarettes mothers smoked increased from '1-9 cigs/day' (moderate smokers), to '≥ 20 cigs/day' (very heavy smokers), the adjusted estimated risk ratios of offspring failing on the CRCT tests also increased. Although, the results for the '≥ 20 cigs/day' category was based on a relatively small subsample (n=6,437), students born to mothers smoked '≥ 20 cigs/day' during

pregnancy, had the most serious consequences for offspring school performance, highest increase in risk of failing on CRCT tests. Such dose-response relationships were consistent across different CRCT tests. The p-values for test of trend were less than 0.001 for both logistic and log-binomial models fitted.

The exposure variable, cigarettes smoked per day, used in the dose-response analyses was likely to be less accurate compared to the binary maternal smoking question (yes vs. no), because more missing values were detected for the quantity question. Although results were subject to potential misclassification of the exposure variable, such dose-dependent relationship provided compelling evidence of the negative relationship between maternal smoking during pregnancy and offspring school performance; since confounding by other familial or environmental factors would not adequately explain such a dose-response relationship.

Strengths and Weaknesses

The strengths of this study are its sample size and its population-based retrospective cohort design. The sample size of this study ($n = 329,952$ for analysis dataset) is very large, which gives more statistical power to detect small differences in the outcomes. Because this study has a population-based retrospective cohort design, it is less likely to have differential risks for the loss of follow-up based on students failing/passing status on CRCT tests. Students in our sample were born to mothers from various ages, education categories, and marital status, which makes our sample more representative of the general population of 1st Grade students in Georgia.

The greatest concern about this study relate to the accuracy of information on maternal smoking status during pregnancy and other covariates collected on the birth certificates. Due to stigma associated with smoking during pregnancy, it is very likely that the women underreported their smoking status during pregnancy. Since the information on maternal smoking during pregnancy was collected prior to the results of offspring school performance, it is very likely that the underreporting of maternal smoking status during pregnancy is non-differential based on fail/pass status of the CRCT tests, which would result in a bias towards the null. Thus, if non-differential misclassification of maternal smoking during pregnancy occurred in this study, the observed strength of the effect of maternal smoking during pregnancy on offspring school performance is likely to be an underestimate of the true association.

Another weakness of measurement of maternal smoking during pregnancy is that there are inconsistencies between different classifications of exposure measures (self-report binary smoking status vs. average cigarettes smoked per day). Considering that some pregnant women may only answer the binary question and omit the quantity question and that more missing values were detected for the quantity question, we used the binary question as our exposure variable in most of our analyses, except for the dose-response analyses.

We also had no information on exactly when during pregnancy the mothers smoked cigarettes and the pattern of smoking during pregnancy. Studies of other outcomes (61) have indicated that the effects of maternal smoking during pregnancy might be trimester-specific. Thus, without such information we are not able to determine at which point during pregnancy the effects of maternal smoking were most profound.

Another limitation of this study was the absence of information on postnatal exposure of offspring to passive smoking. Previous studies indicated that postnatal tobacco smoke exposure may have independent effects on children's school performance, after controlling for the effects of maternal smoking during pregnancy (22, 27). We had no information on maternal and paternal smoking behaviors in early childhood. Thus, the observed association between maternal smoking during pregnancy and offspring school performance might be confounded by postnatal tobacco smoke exposure.

Mothers who smoked during pregnancy may be different from non-smokers in a variety of other ways. Maternal smoking during pregnancy may be associated with a less advantageous socioeconomic status and home environment. In our study, we tried to control for a collection of familial and environmental factors that could be associated with both maternal smoking during pregnancy and offspring school performance, by adjusting for marital status; maternal education; prenatal care status; delivery funded by Medicaid or not; child's race/ethnicity; and parity status. However, residual confounding due to unmeasured factors, such as parents' employment status, occupation, income, and household crowding, could affect the observed association.

A well-designed prospective study is needed. This would offer many advantages, including using direct biochemical measurements to verify the self-report information on smoking; determining the extent and timing of smoking during pregnancy; and more accurate evaluation of the covariates.

Conclusion

In sum, although we cannot draw a causal conclusion about the relationship between maternal smoking during pregnancy and offspring cognitive development, offspring school performance is influenced by many genetic and environmental factors, and prenatal exposure to tobacco smoke is one of these important factors. The results of our study provide additional evidence of the harmful effects of cigarette smoking, especially by pregnant women. This supports the early prevention efforts of health education and public health campaigns about the harmful effects of cigarette smoking to deter pregnant women from smoking.

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TABLES

Table 1 Characteristics of Georgia, singleton, 1st Grade students by maternal smoking status based on the linked Birth-Education Data

Variables	Total ^A (n= 331,656)		Missing smoking status (n= 1,704 0.5%)		Having smoking status (n= 329,952 99.5%)		Smoking during pregnancy (n= 30,365 9.2%)		Not smoking during pregnancy (n= 299,587 90.3%)		p- value *
	No.	%	No.	%	No.	%	No.	%	No.	%	
Outcomes											
Reading											
Fail	31,649	9.6	150	8.8	31,499	9.6	3,549	11.7	27,950	9.3	<.001
Pass	299,678	90.4	1,552	91.2	298,126	90.4	26,790	88.3	271,336	90.7	
Missing	329		2		327		26		301		
English/Language Arts											
Fail	53,932	16.3	264	15.6	53,668	16.3	6,080	20.0	47,588	15.9	<.001
Pass	277,359	83.7	1,434	84.5	275,925	83.7	24,254	80.0	251,671	84.1	
Missing	365		6		359		31		328		
Math											
Fail	42,156	12.7	211	12.4	41,945	12.7	4,478	14.8	37,467	12.5	<.001
Pass	289,112	87.3	1,488	87.6	287,624	87.3	25,848	85.2	261,776	87.5	
Missing	388		5		383		39		344		
Maternal											
Maternal age, 5 years group											
11-14	1,178	0.4	7	0.4	1,171	0.4	37	0.1	1,134	0.4	<.001
15-19	49,137	14.8	230	13.5	48,907	14.8	5,596	18.4	43,311	14.5	
20-24	95,454	28.8	439	25.8	95,015	28.8	10,685	35.2	84,330	28.2	
25-29	88,459	26.7	481	28.2	87,978	26.7	6,994	23.0	80,984	27.0	
30-34	63,900	19.3	336	19.7	63,564	19.3	4,146	13.7	59,418	19.8	

Variables	Total ^A (n= 331,656)		Missing smoking status (n= 1,704 0.5%)		Having smoking status (n= 329,952 99.5%)		Smoking during pregnancy (n= 30,365 9.2%)		Not smoking during pregnancy (n= 299,587 90.3%)		p- value *
	No.	%	No.	%	No.	%	No.	%	No.	%	
35-39	28,464	8.6	185	10.9	28,279	8.6	2,412	7.9	25,867	8.6	
40-44	4,896	1.5	25	1.5	4,871	1.5	482	1.6	4,389	1.5	
45-53	168	0.1	1	0.1	167	0.1	13	0.0	154	0.1	
Maternal alcohol consumption during pregnancy											
Yes	1,979	0.6	4	9.5	1,975	0.6	893	2.9	1,082	0.4	<.001
No	327,946	99.4	38	90.5	327,908	99.4	29,432	97.1	298,476	99.6	
Missing	1,731		1,662		69		40		29		
Mother's marital status											
Married	205,042	61.8	1,200	71.1	203,842	61.8	15,297	50.4	188,545	62.9	<.001
Unmarried	126,596	38.2	489	29.0	126,107	38.2	15,067	49.6	111,040	37.1	
Unknown	18		15		3		1		2		
Maternal education											
Less than 12 Grades	83,465	25.6	333	21.7	83,132	25.6	13,779	45.8	69,353	23.5	<.001
High School	113,652	34.8	543	35.3	113,109	34.8	11,471	38.1	101,638	34.5	
Some College	65,825	20.2	312	20.3	65,513	20.2	4,027	13.4	61,486	20.9	
College Completed	63,653	19.5	350	22.8	63,303	19.5	823	2.7	62,480	21.2	
Missing	5,061		166		4,895		265		4,630		
Prenatal care											
Yes	318,197	99.4	1,305	98.6	316,892	99.4	28,901	98.9	287,991	99.4	<.001
No	2,031	0.6	19	1.4	2,012	0.6	326	1.1	1,686	0.6	
Unknown	11,428		380		11,048		1,138		9,910		

Variables	Total ^A (n= 331,656)		Missing smoking status (n= 1,704 0.5%)		Having smoking status (n= 329,952 99.5%)		Smoking during pregnancy (n= 30,365 9.2%)		Not smoking during pregnancy (n= 299,587 90.3%)		p- value *
	No.	%	No.	%	No.	%	No.	%	No.	%	
Delivery payor											
Medicaid	156,157	47.3	594	34.9	155,563	47.3	20,955	69.4	134,608	45.1	<.001
Not Medicaid	174,159	52.7	1,109	65.1	173,050	52.7	9,253	30.6	163,797	54.9	
Missing	1,340		1		1,339		157		1,182		
Whether have prior adverse birth outcomes											
Yes	1,978	0.6	4	0.2	1,974	0.6	289	1.0	1,685	0.6	<.001
No	329,678	99.4	1,700	99.8	327,978	99.4	30,076	99.1	297,902	99.4	
Children											
Child's sex											
Female	163,775	49.4	814	47.8	162,961	49.4	14,928	49.2	148,033	49.4	0.406
Male	167,881	50.6	890	52.2	166,991	50.6	15,437	50.8	151,554	50.6	
Child's race/ethnicity											
White	164,155	49.5	981	57.6	163,174	49.5	22,828	75.2	140,346	46.9	<.001
Black	116,508	35.1	457	26.8	116,051	35.2	5,405	17.8	110,646	36.9	
Hispanic	34,047	10.3	190	11.2	33,857	10.3	694	2.3	33,163	11.1	
Other	16,946	5.1	76	4.5	16,870	5.1	1,438	4.7	15,432	5.2	
Preterm birth											
Yes	33,792	10.2	213	12.5	33,579	10.2	3,733	12.3	29,846	10.0	<.001
No	297,864	89.8	1,491	87.5	296,373	89.8	26,632	87.7	269,741	90.0	
Low birth weight											
Yes	21,855	6.6	150	8.8	21,705	6.6	3,127	10.3	18,578	6.2	<.001
No	309,801	93.4	1,554	91.2	308,247	93.4	27,238	89.7	281,009	93.8	

Variables	Total ^A (n= 331,656)		Missing smoking status (n= 1,704 0.5%)		Having smoking status (n= 329,952 99.5%)		Smoking during pregnancy (n= 30,365 9.2%)		Not smoking during pregnancy (n= 299,587 90.3%)		p- value *
	No.	%	No.	%	No.	%	No.	%	No.	%	
Small for gestational age											
Yes	37,878	11.4	218	12.8	37,660	11.4	5,546	18.3	32,114	10.7	<.001
No	293,778	88.6	1,486	87.2	292,292	88.6	24,819	81.7	267,473	89.3	
Live birth order											
1st	135,750	41.1	845	49.6	134,905	41.1	9,942	32.9	124,963	41.9	<.001
2-3	165,473	50.1	742	43.6	164,731	50.1	16,268	53.9	148,463	49.8	
4+	29,088	8.8	116	6.8	28,972	8.8	3,997	13.2	24,975	8.4	
Missing	1,345		1		1,344		158		1,186		
(Continuous Variables ^B)	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	p
Maternal											
Maternal age, years	26.08	6.06	26.66	6.17	26.08	6.06	25.13	6.05	26.18	6.05	<.001
Last degree mother completed	12.51	2.66	12.75	2.65	12.51	2.66	11.30	1.83	12.63	2.70	<.001
Mother's # of alcohol drinks/week	0.013	0.296	0.279	1.141	0.013	0.295	0.075	0.806	0.006	0.174	<.001
# of prenatal care visit	12.04	4.08	11.68	4.01	12.04	4.08	11.25	4.06	12.12	4.07	<.001
Father's age, years	29.28	6.72	29.83	6.69	29.28	6.72	28.53	7.18	29.34	6.67	<.001
Children											
Infant's birth weight, in grams	3307	557	3278	603	3307	557	3151	548	3323	555	<.001
Gestational age, in weeks	38.72	2.09	38.62	2.36	38.72	2.08	38.61	2.21	38.73	2.07	<.001

^A A total of 331,656 1st Grade students born between the 1998 to 2002 in Georgia were included into this analysis.

^B Descriptive statistics were calculated for continuous variables, excluding missing values.

* p-values were calculated among students with maternal smoking status during pregnancy, using χ^2 tests or t-tests.

Table 2a Characteristics of Georgia, singleton, 1st Grade students by CRCT Reading test Pass/Fail status based on the linked Birth-Education Data^A

Variables	Reading ^B						p-value *
	Eligible (n= 329,625)		Fail (n= 31,499)		Pass (n= 298,126)		
	No.	%	No.	%	No.	%	
Maternal							
Maternal smoking during pregnancy							
Yes	30,339	9.2	3,549	11.3	26,790	9.0	<.001
No	299,286	90.8	27,950	88.7	271,336	91.0	
Maternal age, 5 years group							
11-14	1,169	0.4	213	0.7	956	0.3	<.001
15-19	48,836	14.8	6,706	21.3	42,130	14.1	
20-24	94,908	28.8	11,276	35.8	83,632	28.1	
25-29	87,895	26.7	7,248	23.0	80,647	27.1	
30-34	63,522	19.3	3,890	12.4	59,632	20.0	
35-39	28,262	8.6	1,780	5.7	26,482	8.9	
40-44	4,866	1.5	367	1.2	4,499	1.5	
45-53	167	0.1	19	0.1	148	0.1	
Maternal alcohol consumption during pregnancy							
Yes	1,974	0.6	184	0.6	1,790	0.6	0.723
No	327,582	99.4	31,306	99.4	296,276	99.4	
Missing	69		9		60		
Mother's marital status							
Married	203,676	61.8	13,483	42.8	190,193	63.8	<.001
Unmarried	125,946	38.2	18,016	57.2	107,930	36.2	
Unknown	3		0		3		
Maternal education							
Less than 12 Grades	82,975	25.6	13,782	44.8	69,193	23.5	<.001
High School	113,015	34.8	11,723	38.1	101,292	34.5	

Variables	Reading ^B						p-value *
	Eligible (n= 329,625)		Fail (n= 31,499)		Pass (n= 298,126)		
	No.	%	No.	%	No.	%	
Some College	65,477	20.2	3,889	12.6	61,588	21.0	
College Completed	63,276	19.5	1,362	4.4	61,914	21.1	
Missing	4,882		743		4,139		
Prenatal care							
Yes	316,581	99.4	29,802	98.9	286,779	99.4	<.001
No	2,008	0.6	347	1.2	1,661	0.6	
Unknown	11,036		1,350		9,686		
Delivery payor							
Medicaid	155,362	47.3	20,882	66.5	134,480	45.3	<.001
Not Medicaid	172,924	52.7	10,521	33.5	162,403	54.7	
Missing	1,339		96		1,243		
Whether have prior adverse birth outcomes							
Yes	1,971	0.6	183	0.6	1,788	0.6	0.681
No	327,654	99.4	31,316	99.4	296,338	99.4	
Children							
Child's sex							
Female	162,830	49.4	11,594	36.8	151,236	50.7	<.001
Male	166,795	50.6	19,905	63.2	146,890	49.3	
Child's race/ethnicity							
White	163,091	49.5	8,980	28.5	154,111	51.7	<.001
Black	115,940	35.2	15,988	50.8	99,952	33.5	
Hispanic	33,745	10.2	5,434	17.3	28,311	9.5	
Other	16,849	5.1	1,097	3.5	15,752	5.3	
Preterm birth							
Yes	33,550	10.2	4,101	13.0	29,449	9.9	<.001
No	296,075	89.8	27,398	87.0	268,677	90.1	

Variables	Reading ^B						p-value *
	Eligible (n= 329,625)		Fail (n= 31,499)		Pass (n= 298,126)		
	No.	%	No.	%	No.	%	
Low birth weight							
Yes	21,678	6.6	3,188	10.1	18,490	6.2	<.001
No	307,947	93.4	28,311	89.9	279,636	93.8	
Small for gestational age							
Yes	37,620	11.4	5,238	16.6	32,383	10.9	<.001
No	292,005	88.6	26,261	83.4	265,744	89.1	
Live birth order							
1st	134,758	41.1	11,497	36.6	123,261	41.5	<.001
2-3	164,588	50.1	15,498	49.4	149,090	50.2	
4+	28,935	8.8	4,408	14.0	24,527	8.3	
Missing	1,344		96		1,248		
(Continuous Variables^C)	Mean	SD	Mean	SD	Mean	SD	p-value *
Maternal							
Maternal age, years	26.08	6.06	24.34	5.84	26.27	6.05	<.001
Last grade mother completed	12.51	2.66	11.09	2.52	12.66	2.62	<.001
Mother's # of cigs smoked/day	0.958	3.700	1.183	4.181	0.934	3.645	<.001
Mother's # of alcohol drinks/week	0.013	0.296	0.016	0.385	0.012	0.284	0.068
# of prenatal care visit	12.04	4.08	11.30	4.37	12.12	4.04	<.001
Father's age, years	29.28	6.72	27.83	6.77	29.41	6.70	<.001
Children							
Infant's birth weight, in grams	3,307	557	3,191	609	3,320	549	<.001
Gestational age, in weeks	38.72	2.08	38.50	2.47	38.74	2.04	<.001

^A 1,704 records were excluded due to missing values of maternal smoking status during pregnancy; a total of 329,952 left

^B 327 records were further excluded from 329,952 for missing values of Reading test.

^C Descriptive statistics were calculated for continuous variables, excluding missing values.

* p-values were calculated among students passing/failing CRCT Reading test, using χ^2 tests or t-tests.

Table 2b Characteristics of Georgia, singleton, 1st Grade students by CRCT ELA test Pass/Fail status based on the linked Birth-Education Data ^A

Variables	English Language Arts (ELA) ^B						p-value *
	Eligible (n= 329,593)		Fail (n= 53,668)		Pass (n= 275,925)		
	No.	%	No.	%	No.	%	
Maternal							
Maternal smoking during pregnancy							
Yes	30,334	9.2	6,080	11.3	24,254	8.8	<.001
No	299,259	90.8	47,588	88.7	251,671	91.2	
Maternal age, 5 years group							
11-14	1,169	0.4	328	0.6	841	0.3	<.001
15-19	48,826	14.8	11,263	21.0	37,563	13.6	
20-24	94,903	28.8	18,989	35.4	75,914	27.5	
25-29	87,887	26.7	12,531	23.4	75,356	27.3	
30-34	63,523	19.3	6,854	12.8	56,669	20.5	
35-39	28,253	8.6	3,083	5.7	25,170	9.1	
40-44	4,865	1.5	592	1.1	4,273	1.6	
45-53	167	0.1	28	0.1	139	0.1	
Maternal alcohol consumption during pregnancy							
Yes	1,974	0.6	311	0.6	1,663	0.6	0.523
No	327,550	99.4	53,347	99.4	274,203	99.4	
Missing	69		10		59		
Mother's marital status							
Married	203,661	61.8	24,234	45.2	179,427	65.0	<.001
Unmarried	125,929	38.2	29,434	54.8	96,495	35.0	
Unknown	3		0		3		
Maternal education							
Less than 12 Grades	82,968	25.6	22,635	43.1	60,333	22.2	<.001
High School	113,009	34.8	20,040	38.2	92,969	34.2	

Variables	English Language Arts (ELA) ^B						p-value *
	Eligible (n= 329,593)		Fail (n= 53,668)		Pass (n= 275,925)		
	No.	%	No.	%	No.	%	
Some College	65,470	20.2	7,088	13.5	58,382	21.5	
College Completed	63,262	19.5	2,706	5.2	60,556	22.2	
Missing	4,884		1,199		3,685		
Prenatal care							
Yes	316,549	99.4	50,961	98.9	265,588	99.5	<.001
No	2,009	0.6	582	1.1	1,427	0.5	
Unknown	11,035		2,125		8,910		
Delivery payor							
Medicaid	155,352	47.3	34,746	64.9	120,606	43.9	<.001
Not Medicaid	172,903	52.7	18,764	35.1	154,139	56.1	
Missing	1,338		158		1,180		
Whether have prior adverse birth outcomes							
Yes	1,972	0.6	317	0.6	1,655	0.6	0.802
No *	327,621	99.4	53,351	99.4	274,270	99.4	
Children							
Child's sex							
Female	162,802	49.4	20,627	38.4	142,175	51.5	<.001
Male	166,791	50.6	33,041	61.6	133,750	48.5	
Child's race/ethnicity							
White	163,073	49.5	17,359	32.4	145,714	52.8	<.001
Black	115,925	35.2	25,344	47.2	90,581	32.8	
Hispanic	33,745	10.2	9,015	16.8	24,730	9.0	
Other	16,850	5.1	1,950	3.6	14,900	5.4	
Preterm birth							
Yes	33,551	10.2	6,800	12.7	26,751	9.7	<.001
No	296,042	89.8	46,868	87.3	249,174	90.3	

Variables	English Language Arts (ELA) ^B						p-value *
	Eligible (n= 329,593)		Fail (n= 53,668)		Pass (n= 275,925)		
	No.	%	No.	%	No.	%	
Low birth weight							
Yes	21,682	6.6	5,126	9.6	16,556	6.0	<.001
No	307,911	93.4	48,542	90.5	259,369	94.0	
Small for gestational age							
Yes	37,622	11.4	8,476	15.8	29,146	10.6	<.001
No	291,971	88.6	45,192	84.2	246,779	89.4	
Live birth order							
1st	134,746	41.1	19,771	37.0	114,975	41.9	<.001
2-3	164,575	50.1	26,762	50.0	137,813	50.2	
4+	28,929	8.8	6,977	13.0	21,952	8.0	
Missing	1,343		158		1,185		
(Continuous Variables^C)	Mean	SD	Mean	SD	Mean	SD	p-value *
Maternal							
Maternal age, years	26.08	6.06	24.43	5.85	26.40	6.05	<.001
Last grade mother completed	12.51	2.66	11.20	2.52	12.76	2.61	<.001
Mother's # of cigs smoked/day	0.958	3.700	1.192	4.157	0.912	3.602	<.001
Mother's # of alcohol drinks/week	0.013	0.296	0.016	0.369	0.012	0.279	0.027
# of prenatal care visit	12.04	4.08	11.41	4.36	12.16	4.01	<.001
Father's age, years	29.28	6.72	27.88	6.75	29.51	6.69	<.001
Children							
Infant's birth weight, in grams	3,307	557	3,208	597	3,327	547	<.001
Gestational age, in weeks	38.72	2.08	38.53	2.38	38.75	2.02	<.001

^A 1,704 records were excluded due to missing values of maternal smoking status during pregnancy; a total of 329,952 left

^B 359 records were further excluded from 329,952 for missing values of Reading test.

^C Descriptive statistics were calculated for continuous variables, excluding missing values.

* p-values were calculated among students passing/failing CRCT ELA test, using χ^2 tests or t-tests.

Table 2c Characteristics of Georgia, singleton, 1st Grade students by CRCT Math test Pass/Fail status based on the linked Birth-Education Data ^A

Variables	Math ^B						p-value *
	Eligible (n=329, 569)		Fail (n=41,945)		Pass (n=287,624)		
	No.	%	No.	%	No.	%	
Maternal							
Maternal smoking during pregnancy							
Yes	30,326	9.2	4,478	10.7	25,848	9.0	<.001
No	299,243	90.8	37,467	89.3	261,776	91.0	
Maternal age, 5 years group							
11-14	1,169	0.4	280	0.7	889	0.3	<.001
15-19	48,833	14.8	8,877	21.2	39,956	13.9	
20-24	94,885	28.8	14,889	35.5	79,996	27.8	
25-29	87,890	26.7	9,606	22.9	78,284	27.2	
30-34	63,509	19.3	5,314	12.7	58,195	20.2	
35-39	28,250	8.6	2,457	5.9	25,793	9.0	
40-44	4,866	1.5	500	1.2	4,366	1.5	
45-53	167	0.1	22	0.1	145	0.1	
Maternal alcohol consumption during pregnancy							
Yes	1,974	0.6	253	0.6	1,721	0.6	0.906
No	327,526	99.4	41,686	99.4	285,840	99.4	
Missing	69		6		63		
Mother's marital status							
Married	203,630	61.8	17,551	41.8	186,079	64.7	<.001
Unmarried	125,936	38.2	24,394	58.2	101,542	35.3	
Unknown	3		0		3		
Maternal education							
Less than 12 Grades	82,997	25.6	17,488	42.6	65,509	23.1	<.001
High School	112,979	34.8	15,986	38.9	96,993	34.2	

Variables	Math ^B						p-value *
	Eligible (n=329, 569)		Fail (n=41,945)		Pass (n=287,624)		
	No.	%	No.	%	No.	%	
Some College	65,465	20.2	5,589	13.6	59,876	21.1	
College Completed	63,240	19.5	2,038	5.0	61,202	21.6	
Missing	4,888		844		4,044		
Prenatal care							
Yes	316,521	99.4	39,777	98.8	276,744	99.4	<.001
No	2,012	0.6	466	1.2	1,546	0.6	
Unknown	11,036		1,702		9,334		
Delivery payor							
Medicaid	155,357	47.3	27,845	66.6	127,512	44.5	<.001
Not Medicaid	172,876	52.7	13,959	33.4	158,917	55.5	
Missing	1,336		141		1,195		
Whether have prior adverse birth outcomes							
Yes	1,973	0.6	243	0.6	1,730	0.6	0.583
No *	327,596	99.4	41,702	99.4	285,894	99.4	
Children							
Child's sex							
Female	162,784	49.4	18,536	44.2	144,248	50.2	<.001
Male	166,785	50.6	23,409	55.8	143,376	49.9	
Child's race/ethnicity							
White	163,012	49.5	11,727	28.0	151,285	52.6	<.001
Black	115,902	35.2	22,699	54.1	93,203	32.4	
Hispanic	33,809	10.3	6,140	14.6	27,669	9.6	
Other	16,846	5.1	1,379	3.3	15,467	5.4	
Preterm birth							
Yes	33,532	10.2	5,653	13.5	27,879	9.7	<.001
No	296,037	89.8	36,292	86.5	259,745	90.3	

Variables	Math ^B						p-value *
	Eligible (n=329, 569)		Fail (n=41,945)		Pass (n=287,624)		
	No.	%	No.	%	No.	%	
Low birth weight							
Yes	21,669	6.6	4,520	10.8	17,149	6.0	<.001
No	307,900	93.4	37,425	89.2	270,475	94.0	
Small for gestational age							
Yes	37,609	11.4	6,985	16.7	30,624	10.7	<.001
No	291,960	88.6	34,960	83.4	257,000	89.4	
Live birth order							
1st	134,737	41.1	15,871	38.0	118,866	41.5	<.001
2-3	164,559	50.1	20,486	49.0	144,073	50.3	
4+	28,932	8.8	5,447	13.0	23,485	8.2	
Missing	1,341		141		1,200		
(Continuous Variables ^C)	Mean	SD	Mean	SD	Mean	SD	p-value *
Maternal							
Maternal age, years	26.08	6.06	24.41	5.89	26.33	6.05	<.001
Last grade mother completed	12.51	2.66	11.25	2.45	12.69	2.64	<.001
Mother's # of cigs smoked/day	0.958	3.699	1.087	3.938	0.939	3.663	<.001
Mother's # of alcohol drinks/week	0.013	0.296	0.018	0.401	0.012	0.277	0.004
# of prenatal care visit	12.04	4.08	11.32	4.38	12.15	4.02	<.001
Father's age, years	29.28	6.72	27.94	6.85	29.44	6.69	<.001
Children							
Infant's birth weight, in grams	3307	557	3172	614	3327	545	<.001
Gestational age, in weeks	38.72	2.08	38.45	2.50	38.76	2.01	<.001

^A 1,704 records were excluded due to missing values of maternal smoking status during pregnancy; a total of 329,952 left

^B 359 records were further excluded from 329,952 for missing values of Reading test.

^C Descriptive statistics were calculated for continuous variables, excluding missing values.

* p-values were calculated among students passing/failing CRCT Math test, using χ^2 tests or t-tests.

Table 3 Unadjusted associations between maternal smoking status during pregnancy and study covariates^A

Variables	Smoking during pregnancy (n=30,365)	Not smoking during pregnancy (n=299,587)	OR	95% CI	
				Low limit	Upper limit
Maternal					
Maternal age, 5 years group					
11-14	37	1,134	0.38	0.27	0.52
15-19	5,596	43,311	1.50	1.44	1.55
20-24	10,685	84,330	1.47	1.42	1.51
25-29 *	6,994	80,984	1.00		
30-34	4,146	59,418	0.81	0.78	0.84
35-39	2,412	25,867	1.08	1.03	1.13
40-44	482	4,389	1.27	1.15	1.40
45-53	13	154	0.98	0.55	1.72
Maternal alcohol consumption during pregnancy					
Yes	893	1,082	8.37	7.65	9.15
No *	29,432	298,476	1.00		
Missing	40	29			
Mother's marital status					
Married	15,297	188,545	0.60	0.58	0.61
Unmarried *	15,067	111,040	1.00		
Unknown	1	2			
Maternal education					
Less than 12 Grades *	13,779	69,353	1.00		
High School	11,471	101,638	0.57	0.55	0.58
Some College	4,027	61,486	0.33	0.32	0.34
College Completed	823	62,480	0.07	0.06	0.07
Missing	265	4,630	0.29	0.25	0.33
Prenatal care					
Yes	28,901	287,991	0.52	0.46	0.58
No *	326	1,686	1.00		
Unknown	1,138	9,910	0.59	0.52	0.68
Delivery payor					
Medicaid	40	29	2.76	2.69	2.83
Not Medicaid *	15,297	188,545	1.00		
Missing	15,067	111,040	2.35	1.99	2.78

Variables	Smoking during pregnancy (n=30,365)	Not smoking during pregnancy (n=299,587)	OR	95% CI	
				Low limit	Upper limit
Whether have prior adverse birth outcomes					
Yes	289	1,685	1.70	1.50	1.93
No *	30,076	297,902	1.00		
Children					
Child's sex					
Female	14,928	148,033	0.99	0.97	1.01
Male *	15,437	151,554	1.00		
Child's race/ethnicity					
White *	22,828	140,346	1.00		
Black	5,405	110,646	0.30	0.29	0.31
Hispanic	694	33,163	0.13	0.12	0.14
Other	1,438	15,432	0.57	0.54	0.61
Preterm birth					
Yes	3,733	29,846	1.27	1.22	1.31
No *	26,632	269,741	1.00		
Low birth weight					
Yes	3,127	18,578	1.74	1.67	1.81
No *	27,238	281,009	1.00		
Small for gestational age					
Yes	5,546	32,114	1.86	1.80	1.92
No *	24,819	267,473	1.00		
Live birth order					
1st *	9,942	124,963	1.00		
2-3	16,268	148,463	1.38	1.34	1.41
4+	3,997	24,975	2.01	1.93	2.09
Missing	158	1,186	1.67	1.42	1.98

^A 1,704 records are excluded due to missing values of maternal smoking status during pregnancy; a total of 329,952 left

* Reference group

Table 4a Unadjusted estimated odds ratios (OR), and 95% confidence intervals (CI) for the odds of failing on CRCT Reading test for the cohort of Georgia, singleton, 1st Grade students based on the linked Birth-Education Data ^A

Variables	Fail (n=31,499)	Eligible (n=329,625)	OR	95% CI	
				Low limit	Upper limit
Maternal					
Maternal smoking during pregnancy					
Yes	3,549	30,339	1.29	1.24	1.33
No *	27,950	299,286	1.00		
Maternal age, 5 years group					
11-14	213	1,169	2.48	2.13	2.88
15-19	6,706	48,836	1.77	1.71	1.83
20-24	11,276	94,908	1.50	1.45	1.55
25-29 *	7,248	87,895	1.00		
30-34	3,890	63,522	0.73	0.70	0.76
35-39	1,780	28,262	0.75	0.71	0.79
40-44	367	4,866	0.91	0.81	1.01
45-53	19	167	1.43	0.89	2.30
Maternal alcohol consumption during pregnancy					
Yes	184	1,974	0.97	0.84	1.13
No*	31,306	327,582	1.00		
Missing	9	69			
Mother's marital status					
Married	13,486	203,676	0.42	0.41	0.43
Unmarried *	18,016	125,946	1.00		
Unknown	0	3			
Maternal education					
Less than 12 Grades *	13,782	82,975	1.00		
High School	11,723	113,015	0.58	0.57	0.60
Some College	3,889	65,477	0.32	0.31	0.33
College Completed	1,362	63,276	0.11	0.10	0.12
Missing	743	4,882	0.90	0.83	0.98
Prenatal care					
Yes	29,802	316,581	0.50	0.44	0.56
No *	347	2,008	1.00		
Unknown	1,350	11,036	0.67	0.59	0.76
Delivery payor					
Medicaid	20,882	155,362	2.40	2.34	2.46
Not Medicaid *	10,521	172,924	1.00		
Missing	96	1,339	1.19	0.97	1.47

Variables	Fail (n=31,499)	Eligible (n=329,625)	OR	95% CI	
				Low limit	Upper limit
Whether have prior adverse birth outcomes					
Yes	183	1,971	0.97	0.83	1.13
No *	31,316	327,654	1.00		
Children					
Child's sex					
Female	11,594	162,830	0.57	0.55	0.58
Male *	19,905	166,795	1.00		
Child's race/ethnicity					
White *	8,980	163,091	1.00		
Black	15,988	115,940	2.74	2.67	2.82
Hispanic	5,434	33,745	3.29	3.18	3.41
Other	1,097	16,849	1.20	1.12	1.28
Preterm birth					
Yes	4,101	33,550	1.37	1.32	1.41
No *	27,398	296,075	1.00		
Low birth weight					
Yes	3,188	21,678	1.70	1.64	1.77
No *	28,311	307,947	1.00		
Small for gestational age					
Yes	5,238	37,620	1.64	1.59	1.69
No *	26,261	292,005	1.00		
Live birth order					
1st *	11,497	134,758	1.00		
2-3	15,498	164,588	1.11	1.09	1.14
4+	4,408	28,935	1.93	1.86	2.00
Missing	96	1,344	0.82	0.67	1.02

^A 329,625 records were analyzed for the Reading test results, which excludes missing values for maternal smoking status and Reading test result from Birth record-Education Dataset.

* Reference group

Table 4b Unadjusted estimated OR and 95% CI for the odds of failing on CRCT ELA test for the cohort of Georgia, singleton, 1st Grade students based on the linked Birth-Education Data ^A

Variables	Fail (n=53,668)	Eligible (n=329,593)	OR	95% CI	
				Low limit	Upper limit
Maternal					
Maternal smoking during pregnancy					
Yes	6,080	30,334	1.33	1.29	1.37
No *	47,588	299,259	1.00		
Maternal age, 5 years group					
11-14	328	1,169	2.35	2.06	2.67
15-19	11,263	48,826	1.80	1.75	1.85
20-24	18,989	94,903	1.50	1.47	1.54
25-29 *	12,531	87,887	1.00		
30-34	6,854	63,523	0.73	0.70	0.75
35-39	3,083	28,253	0.74	0.71	0.77
40-44	592	4,865	0.83	0.76	0.91
45-53	28	167	1.21	0.81	1.82
Maternal alcohol consumption during pregnancy					
Yes	311	1,974	0.96	0.85	1.09
No*	53,347	327,550	1.00		
Missing	10	69			
Mother's marital status					
Married	24,234	203,661	0.44	0.43	0.45
Unmarried *	29,434	125,929	1.00		
Unknown	0	3			
Maternal education					
Less than 12 Grades *	22,635	82,968	1.00		
High School	20,040	113,009	0.57	0.56	0.59
Some College	7,088	65,470	0.32	0.31	0.33
College Completed	2,706	63,262	0.12	0.11	0.12
Missing	1,199	4,884	0.87	0.81	0.93
Prenatal care					
Yes	50,961	316,549	0.47	0.43	0.52
No *	582	2,009	1.00		
Unknown	2,125	11,035	0.58	0.53	0.65
Delivery payor					
Medicaid	34,746	155,352	2.37	2.32	2.41
Not Medicaid *	18,764	172,903	1.00		
Missing	158	1,338	1.10	0.93	1.30

Variables	Fail (n=53,668)	Eligible (n=329,593)	OR	95% CI	
				Low limit	Upper limit
Whether have prior adverse birth outcomes					
Yes	317	1,972	0.98	0.87	1.11
No *	53,351	327,621	1.00		
Children					
Child's sex					
Female	20,627	162,802	0.59	0.58	0.60
Male *	33,041	166,791	1.00		
Child's race/ethnicity					
White *	17,359	163,073	1.00		
Black	25,344	115,925	2.35	2.30	2.40
Hispanic	9,015	33,745	3.06	2.97	3.15
Other	1,950	16,850	1.10	1.05	1.15
Preterm birth					
Yes	6,800	33,551	1.35	1.31	1.39
No *	46,868	296,042	1.00		
Low birth weight					
Yes	5,126	21,682	1.65	1.60	1.71
No *	48,542	307,911	1.00		
Small for gestational age					
Yes	8,476	37,622	1.59	1.55	1.63
No *	45,192	291,971	1.00		
Live birth order					
1st *	19,771	134,746	1.00		
2-3	26,762	164,575	1.13	1.11	1.15
4+	6,977	28,929	1.85	1.79	1.91
Missing	158	1,343	0.78	0.66	0.92

^A 329,593 records were analyzed for the ELA test results, which excludes missing values for maternal smoking status and ELA test result from Birth record-Education Dataset.

* Reference group

Table 4c Unadjusted estimated OR and 95% CI for the odds of failing on CRCT Math test for the cohort of Georgia, singleton, 1st Grade students based on the linked Birth-Education Data ^A

Variables	Fail (n=41,945)	Eligible (n=329,569)	OR	95% CI	
				Low limit	Upper limit
Maternal					
Maternal smoking during pregnancy					
Yes	4,478	30,326	1.21	1.17	1.25
No *	37,467	299,243	1.00		
Maternal age, 5 years group					
11-14	280	1,169	2.57	2.24	2.94
15-19	8,877	48,833	1.81	1.75	1.87
20-24	14,889	94,885	1.52	1.48	1.56
25-29 *	9,606	87,890	1.00		
30-34	5,314	63,509	0.74	0.72	0.77
35-39	2,457	28,250	0.78	0.74	0.81
40-44	500	4,866	0.93	0.85	1.03
45-53	22	167	1.24	0.79	1.94
Maternal alcohol consumption during pregnancy					
Yes	253	1,974	1.01	0.88	1.15
No*	41,686	327,526	1.00		
Missing	6	69			
Mother's marital status					
Married	17,551	203,630	0.39	0.38	0.40
Unmarried *	24,394	125,936	1.00		
Unknown	0	3			
Maternal education					
Less than 12 Grades *	17,488	82,997	1.00		
High School	15,986	112,979	0.62	0.60	0.63
Some College	5,589	65,465	0.35	0.34	0.36
College Completed	2,038	63,240	0.12	0.12	0.13
Missing	844	4,888	0.78	0.72	0.84
Prenatal care					
Yes	39,777	316,521	0.48	0.43	0.53
No *	466	2,012	1.00		
Unknown	1,702	11,036	0.60	0.54	0.68
Delivery payor					
Medicaid	27,845	155,357	2.49	2.43	2.54
Not Medicaid *	13,959	172,876	1.00		
Missing	141	1,336	1.34	1.13	1.60

Variables	Fail (n=41,945)	Eligible (n=329,569)	OR	95% CI	
				Low limit	Upper limit
Whether have prior adverse birth outcomes					
Yes	243	1,973	0.96	0.84	1.10
No *	41,702	327,596	1.00		
Children					
Child's sex					
Female	18,536	162,784	0.79	0.77	0.80
Male *	23,409	166,785	1.00		
Child's race/ethnicity					
White *	11,727	163,012	1.00		
Black	22,699	115,902	3.14	3.07	3.22
Hispanic	6,140	33,809	2.86	2.77	2.96
Other	1,379	16,846	1.15	1.09	1.22
Preterm birth					
Yes	5,653	33,532	1.45	1.41	1.50
No *	36,292	296,037	1.00		
Low birth weight					
Yes	4,520	21,669	1.90	1.84	1.97
No *	37,425	307,900	1.00		
Small for gestational age					
Yes	6,985	37,609	1.68	1.63	1.72
No *	34,960	291,960	1.00		
Live birth order					
1st *	15,871	134,737	1.00		
2-3	20,486	164,559	1.06	1.04	1.09
4+	5,447	28,932	1.74	1.68	1.80
Missing	141	1,341	0.88	0.74	1.05

^A 329,569 records were analyzed for the Math test results, which excludes missing values for maternal smoking status and Math test result from Birth record-Education Dataset.

* Reference group

Table 5a Risk/Odds Ratios (RR/OR) of failing on CRCT Reading test within each stratum of child's race, controlling for all maternal and child characteristics

Child's race	Maternal smoking during pregnancy	Fail	Eligible	Crude			Adjusted ^A			Adjusted ^A		
				RR	Lower	Upper	RR	Lower	Upper	OR	Lower	Upper
White	Yes	2,276	22,814	2.09	1.99	2.18	1.26	1.20	1.32	1.27	1.21	1.34
	No *	6,704	140,277	1.00			1.00			1.00		
Black	Yes	1,020	5,398	1.40	1.32	1.48	1.08	1.02	1.14	1.11	1.03	1.19
	No *	14,968	110,542	1.00			1.00			1.00		
Hispanic	Yes	96	692	0.86	0.71	1.04	0.80	0.67	0.97	0.77	0.62	0.96
	No *	5,338	33,053	1.00			1.00			1.00		
Other	Yes	157	1,435	1.79	1.53	2.11	1.18	1.00	1.38	1.19	0.99	1.42
	No *	940	15,414	1.00			1.00			1.00		

^A Gold Standard model, before assessing confounding, which controlled for all maternal and child characteristics

Table 5b RR/OR of failing on CRCT ELA test within each stratum of child's race, controlling for all maternal and child characteristics

Child's race	Maternal smoking during pregnancy	Fail	Eligible	Crude			Adjusted ^A			Adjusted ^A		
				RR	Lower	Upper	RR	Lower	Upper	OR	Lower	Upper
White	Yes	4,138	22,809	2.13	2.05	2.21	1.20	1.16	1.24	1.22	1.17	1.27
	No *	13,221	140,264	1.00			1.00			1.00		
Black	Yes	1,528	5,397	1.44	1.35	1.53	1.04	0.99	1.09	1.07	1.00	1.14
	No *	23,816	110,528	1.00			1.00			1.00		
Hispanic	Yes	162	691	0.84	0.70	1.00	0.81	0.71	0.93	0.76	0.63	0.91
	No *	8,853	33,054	1.00			1.00			1.00		
Other	Yes	252	1,437	1.72	1.49	1.99	1.07	0.95	1.20	1.06	0.91	1.23
	No *	1,698	15,413	1.00			1.00			1.00		

^A Gold Standard model, before assessing confounding, which controlled for all maternal and child characteristics

Table 5c RR/OR of failing on CRCT Math test within each stratum of child's race, controlling for all maternal and child characteristics

Child's race	Maternal smoking during pregnancy	Fail	Eligible	Crude			Adjusted ^A			Adjusted ^A		
				RR	Lower	Upper	RR	Lower	Upper	OR	Lower	Upper
White	Yes	2,777	22,803	2.03	1.94	2.13	1.21	1.16	1.26	1.21	1.15	1.26
	No *	8,950	140,209	1.00			1.00			1.00		
Black	Yes	1,394	5,398	1.46	1.37	1.55	1.06	1.01	1.11	1.10	1.03	1.17
	No *	21,305	110,504	1.00			1.00			1.00		
Hispanic	Yes	112	690	0.87	0.71	1.07	0.85	0.72	1.01	0.82	0.66	1.01
	No *	6,028	33,119	1.00			1.00			1.00		
Other	Yes	195	1,435	1.89	1.61	2.22	1.20	1.04	1.38	1.21	1.03	1.43
	No *	1,184	15,411	1.00			1.00			1.00		

^A Gold Standard model, before assessing confounding, which controlled for all maternal and child characteristics

Table 6a Modification of the effect of maternal smoking during pregnancy on CRCT Reading test by child's race, controlling for all maternal and child characteristics^A

Child's race	Smokers					Non-smokers				
	Fail	Pass	RR	Lower Limit	Upper Limit	Fail	Pass	RR	Lower Limit	Upper Limit
White	2,276	20,538	1.26	1.20	1.32	6,704	133,573	1.00	--	--
Black	1,020	4,378	2.09	1.96	2.23	14,968	95,574	1.94	1.88	2.00
Hispanic	96	596	1.59	1.32	1.92	5,338	27,715	1.98	1.91	2.06
Other	157	1,278	1.30	1.12	1.51	940	14,474	1.11	1.04	1.18

^A Gold Standard model, before assessing confounding, which controlled for all maternal and child characteristics

Table 6b Modification of the effect of maternal smoking during pregnancy on CRCT ELA test by child's race, controlling for all maternal and child characteristics ^A

Child's race	Smokers					Non-smokers				
	Fail	Pass	RR	Lower Limit	Upper Limit	Fail	Pass	RR	Lower Limit	Upper Limit
White	4,138	18,671	1.20	1.16	1.24	13,221	127,043	1.00	--	--
Black	1,528	3,869	1.66	1.58	1.74	23,816	86,712	1.60	1.56	1.64
Hispanic	162	529	1.42	1.24	1.63	8,853	24,201	1.74	1.70	1.79
Other	252	1,185	1.10	0.98	1.23	1,698	13,715	1.03	0.98	1.08

^A Gold Standard model, before assessing confounding, which controlled for all maternal and child characteristics

Table 6c Modification of the effect of maternal smoking during pregnancy on CRCT Math test by child's race, controlling for all maternal and child characteristics ^A

Child's race	Smokers					Non-smokers				
	Fail	Pass	RR	Lower Limit	Upper Limit	Fail	Pass	RR	Lower Limit	Upper Limit
White	2,777	20,026	1.21	1.16	1.26	8,950	131,259	1.00	--	--
Black	1,394	4,004	2.24	2.12	2.36	21,305	89,199	2.12	2.06	2.17
Hispanic	112	578	1.44	1.21	1.71	6,028	27,091	1.69	1.64	1.75
Other	195	1,240	1.25	1.09	1.43	1,184	14,227	1.04	0.98	1.10

^A Gold Standard model, before assessing confounding, which controlled for all maternal and child characteristics

Table 7a Adjusted estimated OR/RR and 95% CI for failing on CRCT Reading test for the gold standard model controlling for all maternal and child characteristics, with no interaction term of the main exposure with child's race ^A

Variables	aOR	95% CI		aRR	95% CI	
		Low limit	Upper limit		Low limit	Upper limit
Maternal						
Maternal smoking during pregnancy						
Yes	1.19	1.14	1.24	1.17	1.13	1.21
No *	1.00			1.00		
Maternal age, 5 years group						
11-14	1.05	0.90	1.23	1.04	0.92	1.19
15-19	0.96	0.92	1.00	0.97	0.94	1.01
20-24	1.04	1.01	1.08	1.04	1.01	1.07
25-29 *	1.00			1.00		
30-34	0.93	0.89	0.97	0.93	0.90	0.97
35-39	0.93	0.88	0.99	0.94	0.90	0.99
40-44	1.03	0.92	1.16	1.03	0.94	1.14
45-53	1.60	0.97	2.64	1.49	0.97	2.28
Maternal alcohol consumption during pregnancy						
Yes	0.91	0.77	1.06	0.91	0.80	1.04
No*	1.00			1.00		
Mother's marital status						
Married	0.84	0.82	0.87	0.86	0.84	0.89
Unmarried *	1.00			1.00		
Maternal education						
Less than 12 Grades *	1.00			1.00		
High School	0.67	0.65	0.69	0.71	0.69	0.73
Some College	0.41	0.39	0.42	0.46	0.44	0.47
College Completed	0.19	0.18	0.21	0.22	0.21	0.23
Missing ^B	0.93	0.86	1.01	0.95	0.89	1.02
Prenatal care						
Yes	0.90	0.79	1.01	0.92	0.83	1.01
No *	1.00			1.00		
Unknown ^B	0.99	0.87	1.13	1.00	0.90	1.11
Delivery payor						
Medicaid	1.23	1.19	1.27	1.20	1.17	1.23
Not Medicaid *	1.00			1.00		

Variables	aOR	95% CI		aRR	95% CI	
		Low limit	Upper limit		Low limit	Upper limit
Whether have prior adverse birth outcomes						
Yes	1.02	0.87	1.19	1.02	0.89	1.16
No *	1.00			1.00		
Children						
Child's sex						
Female	0.54	0.53	0.56	0.59	0.58	0.61
Male *	1.00			1.00		
Child's race/ethnicity						
White *	1.00			1.00		
Black	2.06	1.99	2.13	1.89	1.84	1.95
Hispanic	2.10	2.02	2.19	1.93	1.86	1.99
Other	1.09	1.02	1.16	1.09	1.02	1.15
Live birth order						
1st *	1.00			1.00		
2-3	1.17	1.14	1.20	1.15	1.12	1.17
4+	1.49	1.43	1.56	1.39	1.34	1.45
School year CRCT test taken						
2005	0.87	0.83	0.91	0.89	0.85	0.92
2006	1.30	1.25	1.34	1.24	1.21	1.28
2007 *	1.00			1.00		
2008	0.97	0.93	1.00	0.97	0.94	1.00
2009	0.94	0.90	0.98	0.95	0.92	0.98
Continuous variable						
	Exp(β)	Low limit	Upper limit	Exp(β)	Low limit	Upper limit
Child's age	0.97	0.94	0.99	0.97	0.95	0.99

^A Golden standard model which controlled for maternal and child characteristics, not including interaction term with child's race.

^B Missing or unknown category was put into the model as dummy variable.

* Reference group

Table 7b Adjusted estimated OR/RR and 95% CI for failing on CRCT ELA test for the gold standard model controlling for all maternal and child characteristics, with no interaction term of the main exposure with child's race^A

Variables	aOR	95% CI		aRR	95% CI	
		Low limit	Upper limit		Low limit	Upper limit
Maternal						
Maternal smoking during pregnancy						
Yes	1.15	1.11	1.19	1.13	1.10	1.16
No *	1.00			1.00		
Maternal age, 5 years group						
11-14	1.02	0.89	1.17	1.02	0.93	1.12
15-19	0.99	0.95	1.02	1.00	0.97	1.02
20-24	1.05	1.02	1.08	1.04	1.02	1.06
25-29 *	1.00			1.00		
30-34	0.92	0.89	0.95	0.93	0.91	0.96
35-39	0.92	0.88	0.96	0.93	0.90	0.97
40-44	0.95	0.87	1.04	0.97	0.90	1.04
45-53	1.38	0.90	2.12	1.29	0.92	1.80
Maternal alcohol consumption during pregnancy						
Yes	0.95	0.83	1.08	0.95	0.86	1.05
No*	1.00			1.00		
Mother's marital status						
Married	0.84	0.82	0.86	0.87	0.86	0.89
Unmarried *	1.00			1.00		
Maternal education						
Less than 12 Grades *	1.00			1.00		
High School	0.66	0.65	0.68	0.74	0.72	0.75
Some College	0.42	0.40	0.43	0.50	0.49	0.51
College Completed	0.20	0.19	0.21	0.25	0.24	0.26
Missing ^B	0.90	0.84	0.96	0.93	0.88	0.98
Prenatal care						
Yes	0.82	0.75	0.91	0.88	0.82	0.94
No *	1.00			1.00		
Unknown ^B	0.85	0.76	0.95	0.90	0.84	0.98
Delivery payor						
Medicaid	1.24	1.22	1.27	1.19	1.17	1.22
Not Medicaid *	1.00			1.00		
Whether have prior adverse birth outcomes						
Yes	1.04	0.91	1.18	1.03	0.94	1.13
No *	1.00			1.00		

Variables	aOR	95% CI		aRR	95% CI	
		Low limit	Upper limit		Low limit	Upper limit
Children						
Child's sex						
Female	0.56	0.55	0.57	0.64	0.63	0.65
Male *	1.00			1.00		
Child's race/ethnicity						
White *	1.00			1.00		
Black	1.75	1.70	1.79	1.57	1.53	1.60
Hispanic	1.95	1.89	2.02	1.70	1.66	1.75
Other	1.00	0.95	1.05	1.01	0.96	1.05
Live birth order						
1st *	1.00			1.00		
2-3	1.20	1.17	1.23	1.15	1.13	1.18
4+	1.49	1.44	1.54	1.35	1.31	1.38
School year CRCT test taken						
2005	0.82	0.79	0.85	0.85	0.83	0.88
2006	1.20	1.17	1.23	1.15	1.12	1.17
2007 *	1.00			1.00		
2008	0.84	0.81	0.86	0.87	0.85	0.89
2009	0.89	0.86	0.92	0.91	0.89	0.94
Continuous variable	Exp(β)	Low limit	Upper limit	Exp(β)	Low limit	Upper limit
Child's age	0.98	0.96	1.00	0.99	0.97	1.00

^A Golden standard model which controlled for maternal and child characteristics, not including interaction term with child's race.

^B Missing or unknown category was put into the model as dummy variable.

* Reference group

Table 7c Adjusted estimated OR/RR and 95% CI for failing on CRCT Math test for the gold standard model controlling for all maternal and child characteristics, with no interaction term of the main exposure with child's race^A

Variables	aOR	95% CI		aRR	95% CI	
		Low limit	Upper limit		Low limit	Upper limit
Maternal						
Maternal smoking during pregnancy						
Yes	1.15	1.11	1.20	1.14	1.10	1.17
No *	1.00			1.00		
Maternal age, 5 years group						
11-14	0.92	0.80	1.06	0.94	0.84	1.04
15-19	0.90	0.86	0.93	0.92	0.89	0.95
20-24	1.01	0.98	1.04	1.01	0.98	1.03
25-29 *	1.00			1.00		
30-34	0.95	0.92	0.99	0.96	0.93	0.99
35-39	0.98	0.93	1.03	0.98	0.94	1.02
40-44	1.08	0.98	1.19	1.07	0.99	1.16
45-53	1.40	0.87	2.24	1.32	0.91	1.91
Maternal alcohol consumption during pregnancy						
Yes	0.93	0.80	1.07	0.92	0.83	1.03
No*	1.00			1.00		
Mother's marital status						
Married	0.83	0.81	0.86	0.86	0.84	0.88
Unmarried *	1.00			1.00		
Maternal education						
Less than 12 Grades *	1.00			1.00		
	0.67	0.65	0.69	0.73	0.71	0.75
Some College	0.42	0.40	0.43	0.48	0.47	0.50
College Completed	0.20	0.19	0.21	0.24	0.23	0.25
Missing ^B	0.87	0.80	0.94	0.90	0.85	0.96
Prenatal care						
Yes	0.83	0.75	0.93	0.87	0.81	0.94
No *	1.00			1.00		
Unknown ^B	0.86	0.76	0.97	0.89	0.82	0.98
Delivery payor						
Medicaid	1.25	1.22	1.28	1.21	1.18	1.24
Not Medicaid *	1.00			1.00		
Whether have prior adverse birth outcomes						
Yes	1.03	0.90	1.19	1.03	0.92	1.15
No *	1.00			1.00		

Variables	aOR	95% CI		aRR	95% CI	
		Low limit	Upper limit		Low limit	Upper limit
Children						
Child's sex						
Female	0.76	0.75	0.78	0.80	0.79	0.82
Male *	1.00			1.00		
Child's race/ethnicity						
White *	1.00			1.00		
Black	2.37	2.31	2.44	2.08	2.03	2.13
Hispanic	1.77	1.71	1.84	1.66	1.61	1.71
Other	1.03	0.97	1.09	1.03	0.98	1.09
Live birth order						
1st *	1.00			1.00		
2-3	1.08	1.06	1.11	1.07	1.05	1.09
4+	1.26	1.21	1.31	1.20	1.16	1.24
School year CRCT test taken						
2005	0.58	0.56	0.60	0.65	0.63	0.67
2006	0.47	0.46	0.49	0.54	0.53	0.56
2007 *	1.00			1.00		
2008	0.72	0.69	0.74	0.77	0.75	0.79
2009	0.69	0.67	0.71	0.75	0.73	0.77
Continuous variable	Exp(β)	Low limit	Upper limit	Exp(β)	Low limit	Upper limit
Child's age	0.95	0.93	0.98	0.96	0.95	0.98

^A Golden standard model which controlled for maternal and child characteristics, not including interaction term with child's race.

^B Missing or unknown category was put into the model as dummy variable.

* Reference group

Table 8a Adjusted estimated OR/RR and 95% CI for failing on CRCT Reading test for the most parsimonious model ^A

Variables	aOR	95% CI		aRR	95% CI	
		Low limit	Upper limit		Low limit	Upper limit
Maternal						
Maternal smoking during pregnancy						
Yes	1.26	1.21	1.31	1.23	1.18	1.27
No *	1.00			1.00		
Maternal education						
Less than 12 Grades *	1.00			1.00		
High School	0.66	0.64	0.68	0.71	0.69	0.72
Some College	0.39	0.38	0.41	0.44	0.42	0.45
College Completed	0.18	0.17	0.19	0.20	0.19	0.21
Missing ^B	0.95	0.87	1.03	0.96	0.89	1.02
Delivery payor						
Medicaid	1.26	1.23	1.30	1.23	1.20	1.26
Not Medicaid *	1.00			1.00		
Children						
Child's race/ethnicity						
White *	1.00			1.00		
Black	2.26	2.20	2.33	2.07	2.01	2.12
Hispanic	2.14	2.06	2.23	1.97	1.90	2.04
Other	1.12	1.05	1.19	1.11	1.05	1.18

^A Most parsimonious model only controlled for maternal education, delivery payor, and child's race.

^B Missing or unknown category was put into the model as dummy variable.

* Reference group

Table 8b Adjusted estimated OR/RR and 95% CI for failing on CRCT ELA test for the most parsimonious model^A

Variables	aOR	95% CI		aRR	95% CI	
		Low limit	Upper limit		Low limit	Upper limit
Maternal						
Maternal smoking during pregnancy						
Yes	1.21	1.17	1.25	1.17	1.14	1.20
No *	1.00			1.00		
Maternal education						
Less than 12 Grades *	1.00			1.00		
High School	0.66	0.64	0.67	0.73	0.71	0.74
Some College	0.40	0.39	0.41	0.48	0.47	0.49
College Completed	0.18	0.18	0.19	0.23	0.22	0.24
Missing ^B	0.90	0.85	0.97	0.93	0.89	0.98
Delivery payor						
Medicaid	1.28	1.25	1.31	1.22	1.20	1.25
Not Medicaid *	1.00			1.00		
Children						
Child's race/ethnicity						
White *	1.00			1.00		
Black	1.92	1.88	1.96	1.70	1.67	1.73
Hispanic	1.97	1.91	2.03	1.73	1.68	1.77
Other	1.02	0.97	1.08	1.02	0.98	1.07

^A Most parsimonious model only controlled for maternal education, delivery payor, and child's race.

^B Missing or unknown category was put into the model as dummy variable.

* Reference group

Table 8c Adjusted estimated OR/RR and 95% CI for failing on CRCT Math test for the most parsimonious model ^A

Variables	aOR	95% CI		aRR	95% CI	
		Low limit	Upper limit		Low limit	Upper limit
Maternal						
Maternal smoking during pregnancy						
Yes	1.20	1.16	1.24	1.17	1.14	1.21
No *	1.00			1.00		
Maternal education						
Less than 12 Grades *	1.00			1.00		
High School	0.68	0.66	0.70	0.74	0.72	0.75
Some College	0.42	0.40	0.43	0.48	0.47	0.50
College Completed	0.20	0.19	0.21	0.23	0.22	0.24
Missing ^B	0.87	0.80	0.94	0.90	0.84	0.96
Delivery payor						
Medicaid	1.30	1.27	1.33	1.25	1.22	1.28
Not Medicaid *	1.00			1.00		
Children						
Child's race/ethnicity						
White *	1.00			1.00		
Black	2.59	2.52	2.65	2.25	2.20	2.30
Hispanic	1.88	1.81	1.95	1.75	1.69	1.80
Other	1.07	1.01	1.14	1.07	1.02	1.13

^A Most parsimonious model only controlled for maternal education, delivery payor, and child's race.

^B Missing or unknown category was put into the model as dummy variable.

* Reference group

Table 9a Adjusted estimated OR/RR and 95% CI for failing on CRCT Reading test for the gold standard model controlling for all maternal and child characteristics, and birth outcomes, with no interaction term of the main exposure with child's race^A

Variables	aOR	95% CI		aRR	95% CI	
		Low limit	Upper limit		Low limit	Upper limit
Maternal						
Maternal smoking during pregnancy						
Yes	1.15	1.11	1.20	1.14	1.10	1.18
No *	1.00			1.00		
Maternal age, 5 years group						
11-14	1.04	0.89	1.22	1.03	0.91	1.17
15-19	0.96	0.92	1.00	0.97	0.93	1.01
20-24	1.04	1.01	1.08	1.04	1.01	1.07
25-29 *	1.00			1.00		
30-34	0.92	0.88	0.96	0.93	0.90	0.97
35-39	0.92	0.87	0.97	0.93	0.89	0.98
40-44	1.01	0.90	1.13	1.01	0.92	1.12
45-53	1.55	0.94	2.56	1.45	0.95	2.23
Maternal alcohol consumption during pregnancy						
Yes	0.88	0.74	1.03	0.88	0.77	1.01
No*	1.00			1.00		
Mother's marital status						
Married	0.85	0.82	0.87	0.87	0.85	0.89
Unmarried *	1.00			1.00		
Maternal education						
Less than 12 Grades *	1.00			1.00		
High School	0.67	0.65	0.69	0.72	0.70	0.73
Some College	0.41	0.39	0.43	0.46	0.44	0.48
College Completed	0.20	0.18	0.21	0.22	0.21	0.24
Missing ^B	0.94	0.86	1.02	0.95	0.89	1.02
Prenatal care						
Yes	0.94	0.84	1.06	0.96	0.87	1.05
No *	1.00			1.00		
Unknown ^B	1.03	0.90	1.17	1.03	0.93	1.15
Delivery payor						
Medicaid	1.23	1.19	1.26	1.20	1.17	1.23
Not Medicaid *	1.00			1.00		
Whether have prior adverse birth outcomes						
Yes	0.91	0.78	1.07	0.93	0.81	1.06
No *	1.00			1.00		

Variables	aOR	95% CI		aRR	95% CI	
		Low limit	Upper limit		Low limit	Upper limit
Children						
Child's sex						
Female	0.54	0.53	0.56	0.59	0.58	0.60
Male *	1.00			1.00		
Child's race/ethnicity						
White *	1.00			1.00		
Black	1.99	1.93	2.06	1.84	1.78	1.89
Hispanic	2.10	2.02	2.19	1.93	1.86	2.00
Other	1.08	1.01	1.15	1.08	1.01	1.14
Preterm birth						
Yes	1.11	1.06	1.16	1.09	1.05	1.13
No *	1.00			1.00		
Low birth weight						
Yes	1.26	1.20	1.33	1.21	1.16	1.26
No *	1.00			1.00		
Small for gestational age						
Yes	1.24	1.19	1.28	1.19	1.16	1.23
No *	1.00			1.00		
Live birth order						
1st *	1.00			1.00		
2-3	1.19	1.16	1.23	1.16	1.13	1.19
4+	1.52	1.46	1.59	1.42	1.37	1.47
School year CRCT test taken						
2005	0.87	0.83	0.91	0.89	0.85	0.92
2006	1.30	1.25	1.35	1.25	1.21	1.28
2007 *	1.00			1.00		
2008	0.97	0.94	1.01	0.97	0.94	1.00
2009	0.94	0.90	0.97	0.95	0.92	0.98
Continuous variable	Exp(β)	Low limit	Upper limit	Exp(β)	Low limit	Upper limit
Child's age	0.96	0.94	0.98	0.97	0.95	0.99

^A Model controlled for maternal and child characteristics, as well as birth outcomes.

^B Missing or unknown category was put into the model as dummy variable.

* Reference group.

Table 9b Adjusted estimated OR/RR and 95% CI for failing on CRCT ELA test for the gold standard model controlling for all maternal and child characteristics, and birth outcomes, with no interaction term of the main exposure with child's race^A

Variables	aOR	95% CI		aRR	95% CI	
		Low limit	Upper limit		Low limit	Upper limit
Maternal						
Maternal smoking during pregnancy						
Yes	1.12	1.08	1.15	1.10	1.07	1.13
No *	1.00			1.00		
Maternal age, 5 years group						
11-14	1.01	0.88	1.16	1.01	0.92	1.11
15-19	0.98	0.95	1.02	0.99	0.97	1.02
20-24	1.05	1.02	1.08	1.04	1.02	1.06
25-29 *	1.00			1.00		
30-34	0.92	0.89	0.95	0.93	0.91	0.96
35-39	0.90	0.86	0.94	0.92	0.89	0.96
40-44	0.93	0.85	1.02	0.95	0.88	1.02
45-53	1.33	0.87	2.05	1.26	0.90	1.76
Maternal alcohol consumption during pregnancy						
Yes	0.92	0.81	1.05	0.92	0.84	1.02
No*	1.00			1.00		
Mother's marital status						
Married	0.84	0.82	0.86	0.88	0.86	0.89
Unmarried *	1.00			1.00		
Maternal education						
Less than 12 Grades *	1.00			1.00		
High School	0.67	0.65	0.68	0.74	0.73	0.75
Some College	0.42	0.41	0.44	0.50	0.49	0.52
College Completed	0.21	0.20	0.22	0.25	0.24	0.26
Missing ^B	0.90	0.84	0.97	0.93	0.89	0.98
Prenatal care						
Yes	0.87	0.78	0.96	0.91	0.85	0.98
No *	1.00			1.00		
Unknown ^B	0.89	0.79	0.99	0.93	0.86	1.00
Delivery payor						
Medicaid	1.24	1.21	1.27	1.19	1.17	1.21
Not Medicaid *	1.00			1.00		
Whether have prior adverse birth outcomes						
Yes	0.93	0.82	1.06	0.95	0.86	1.05
No *	1.00			1.00		

Variables	aOR	95% CI		aRR	95% CI	
		Low limit	Upper limit		Low limit	Upper limit
Child's sex						
Female	0.56	0.55	0.57	0.64	0.63	0.65
Male *	1.00			1.00		
Child's race/ethnicity						
White *	1.00			1.00		
Black	1.69	1.65	1.73	1.53	1.50	1.56
Hispanic	1.96	1.89	2.02	1.70	1.66	1.75
Other	0.99	0.94	1.04	1.00	0.96	1.04
Preterm birth						
Yes	1.12	1.08	1.16	1.09	1.06	1.12
No *	1.00			1.00		
Low birth weight						
Yes	1.25	1.20	1.31	1.18	1.14	1.22
No *	1.00			1.00		
Small for gestational age						
Yes	1.23	1.19	1.27	1.17	1.14	1.19
No *	1.00			1.00		
Live birth order						
1st *	1.00			1.00		
2-3	1.22	1.19	1.25	1.17	1.15	1.19
4+	1.52	1.46	1.57	1.36	1.33	1.40
School year CRCT test taken						
2005	0.82	0.79	0.85	0.85	0.83	0.88
2006	1.20	1.17	1.24	1.15	1.12	1.17
2007 *	1.00			1.00		
2008	0.84	0.81	0.86	0.87	0.85	0.89
2009	0.89	0.86	0.92	0.91	0.89	0.93
Continuous variable	Exp(β)	Low limit	Upper limit	Exp(β)	Low limit	Upper limit
Child's age	0.98	0.96	0.99	0.98	0.97	1.00

^A Model controlled for maternal and child characteristics, as well as birth outcomes.

^B Missing or unknown category was put into the model as dummy variable.

* Reference group.

Table 9c Adjusted estimated OR/RR and 95% CI for failing on CRCT Math test for the gold standard model controlling for all maternal and child characteristics, and birth outcomes, with no interaction term of the main exposure with child's race^A

Variables	aOR	95% CI		aRR	95% CI	
		Low limit	Upper limit		Low limit	Upper limit
Maternal						
Maternal smoking during pregnancy						
Yes	1.11	1.07	1.16	1.11	1.07	1.14
No *	1.00			1.00		
Maternal age, 5 years group						
11-14	0.91	0.79	1.05	0.93	0.83	1.03
15-19	0.89	0.86	0.93	0.92	0.89	0.95
20-24	1.01	0.98	1.04	1.01	0.98	1.03
25-29 *	1.00			1.00		
30-34	0.95	0.91	0.98	0.96	0.93	0.99
35-39	0.96	0.91	1.01	0.97	0.93	1.01
40-44	1.05	0.95	1.16	1.05	0.97	1.14
45-53	1.34	0.84	2.15	1.28	0.88	1.85
Maternal alcohol consumption during pregnancy						
Yes	0.89	0.78	1.03	0.90	0.80	1.00
No*	1.00			1.00		
Mother's marital status						
Married	0.84	0.82	0.86	0.87	0.85	0.89
Unmarried *	1.00			1.00		
Maternal education						
Less than 12 Grades *	1.00			1.00		
High School	0.67	0.65	0.69			
Some College	0.42	0.40	0.44	0.49	0.47	0.50
College Completed	0.21	0.19	0.22	0.24	0.23	0.26
Missing ^B	0.88	0.81	0.95	0.91	0.85	0.96
Prenatal care						
Yes	0.88	0.79	0.98	0.91	0.84	0.99
No *	1.00			1.00		
Unknown ^B	0.89	0.79	1.01	0.92	0.84	1.01
Delivery payor						
Medicaid	1.25	1.22	1.28	1.21	1.18	1.24
Not Medicaid *	1.00			1.00		
Whether have prior adverse birth outcomes						
Yes	0.91	0.79	1.05	0.93	0.83	1.04
No *	1.00			1.00		

Variables	aOR	95% CI		aRR	95% CI	
		Low limit	Upper limit		Low limit	Upper limit
Child's sex						
Female	0.76	0.74	0.78	0.80	0.79	0.81
Male *	1.00			1.00		
Child's race/ethnicity						
White *	1.00			1.00		
Black	2.29	2.22	2.35	2.01	1.96	2.06
Hispanic	1.78	1.71	1.84	1.66	1.61	1.71
Other	1.02	0.96	1.08	1.02	0.97	1.08
Preterm birth						
Yes	1.13	1.09	1.18	1.11	1.07	1.14
No *	1.00			1.00		
Low birth weight						
Yes	1.33	1.27	1.40	1.24	1.20	1.29
No *	1.00			1.00		
Small for gestational age						
Yes	1.22	1.18	1.26	1.17	1.14	1.20
No *	1.00			1.00		
Live birth order						
1st *	1.00			1.00		
2-3	1.10	1.08	1.13	1.08	1.06	1.11
4+	1.29	1.24	1.34	1.22	1.18	1.26
School year CRCT test taken						
2005	0.58	0.56	0.60	0.65	0.63	0.67
2006	0.47	0.46	0.49	0.54	0.53	0.56
2007 *	1.00			1.00		
2008	0.72	0.69	0.74	0.77	0.75	0.79
2009	0.69	0.67	0.71	0.75	0.73	0.76
Continuous variable	Exp(β)	Low limit	Upper limit	Exp(β)	Low limit	Upper limit
Child's age	0.94	0.92	0.96	0.95	0.93	0.97

^A Model controlled for maternal and child characteristics, as well as birth outcomes.

^B Missing or unknown category was put into the model as dummy variable.

* Reference group.

Table 10 Characteristics of Georgia, singleton, 1st Grade students by ordinal maternal smoking categories based on the linked Birth-Education Data ^A

Variables	Non-smokers		Moderate smokers		Heavy smokers		Very heavy smokers		p-value *
	0 cigs/day (n= 298,407 91.00%)		1-9 cigs/day (n=11,421 3.48%)		10-19 cigs/day (n=11,669 3.56%)		≥ 20 cigs/day (n=6,437 1.96%)		
	No.	%	No.	%	No.	%	No.	%	
Outcomes									
Reading									
Fail	27,876	9.35	1,338	11.73	1,288	11.05	797	12.39	<.0001
Pass	270,230	90.65	10,070	88.27	10,372	88.95	5,636	87.61	
Missing	301		13		9		4		
English/Language Arts									
Fail	47,461	15.92	2,269	19.88	2,265	19.43	1,356	21.09	<.0001
Pass	250,619	84.08	9,142	80.12	9,391	80.57	5,074	78.91	
Missing	327		10		13		7		
Math									
Fail	37,348	12.53	1,773	15.55	1,601	13.73	959	14.92	<.0001
Pass	260,718	87.47	9,626	84.45	10,061	86.27	5,468	85.08	
Missing	341		22		7		10		
Maternal									
Maternal age, 5 years group									
11-14	1,129	0.38	1,129	0.38	20	0.18	13	0.11	<.0001
15-19	43,191	14.47	43,193	14.47	2,425	21.23	2,150	18.42	
20-24	83,939	28.13	83,948	28.13	4,055	35.50	4,183	35.85	
25-29	80,604	27.01	80,612	27.01	2,433	21.30	2,693	23.08	

Variables	Non-smokers		Moderate smokers		Heavy smokers		Very heavy smokers		p-value *
	0 cigs/day (n= 298,407 91.00%)		1-9 cigs/day (n=11,421 3.48%)		10-19 cigs/day (n=11,669 3.56%)		≥ 20 cigs/day (n=6,437 1.96%)		
	No.	%	No.	%	No.	%	No.	%	
30-34	59,210	19.84	59,215	19.84	1,417	12.41	1,590	13.63	
35-39	25,796	8.64	25,798	8.64	888	7.78	878	7.52	
40-44	4,384	1.47	4,384	1.47	181	1.58	158	1.35	
45-53	154	0.05	154	0.05	2	0.02	4	0.03	
Maternal alcohol consumption during pregnancy									
Yes	953	0.32	375	3.30	224	1.93	106	1.66	<.0001
No	297,297	99.68	10,997	96.70	11,397	98.07	6,287	98.34	
Missing	157		49		48		44		
Mother's marital status									
Married	187,663	62.89	5,049	44.21	6,219	53.30	3,606	56.02	<.0001
Unmarried	110,742	37.11	6,372	55.79	5,449	46.70	2,831	43.98	
Unknown	2		0		1		0		
Maternal education									
Less than 12 Grades	69,202	23.56	4,789	42.30	5,395	46.56	3,260	51.19	<.0001
High School	101,239	34.46	4,360	38.51	4,439	38.31	2,349	36.88	
Some College	61,137	20.81	1,721	15.20	1,500	12.94	663	10.41	
College Completed	62,201	21.17	451	3.98	254	2.19	97	1.52	
Missing	4,628		100		81		68		
Prenatal care									
Yes	287,995	99.42	10,907	98.74	11,247	99.16	6,145	98.71	<.0001
No	1,685	0.58	139	1.26	95	0.84	80	1.29	
Unknown	8,727		375		327		212		

Variables	Non-smokers		Moderate smokers		Heavy smokers		Very heavy smokers		p-value *
	0 cigs/day (n= 298,407 91.00%)		1-9 cigs/day (n=11,421 3.48%)		10-19 cigs/day (n=11,669 3.56%)		≥ 20 cigs/day (n=6,437 1.96%)		
	No.	%	No.	%	No.	%	No.	%	
Delivery payor									
Medicaid	134,605	45.11	7,871	68.92	8,087	69.30	4,549	70.67	<.0001
Not Medicaid	163,802	54.89	3,550	31.08	3,582	30.70	1,888	29.33	
Missing									
Whether have prior adverse birth outcomes									
Yes	1,681	0.56	96	0.84	113	0.97	73	1.13	<.0001
No	296,726	99.44	11,325	99.16	11,556	99.03	6,364	98.87	
Children									
Child's sex									
Female	147,458	49.41	5,573	48.80	5,775	49.49	3,170	49.25	0.6184
Male	150,949	50.59	5,848	51.20	5,894	50.51	3,267	50.75	
Child's race/ethnicity									
White	139,596	46.78	7,103	62.19	9,608	82.34	5,532	85.94	<.0001
Black	110,314	36.97	3,451	30.22	1,280	10.97	480	7.46	
Hispanic	33,124	11.10	282	2.47	243	2.08	141	2.19	
Other	15,373	5.15	585	5.12	538	4.61	284	4.41	
Preterm birth									
Yes	29,717	9.96	1,443	12.63	1,416	12.13	755	11.73	<.0001
No	268,690	90.04	9,978	87.37	10,253	87.87	5,682	88.27	
Low birth weight									
Yes	18,494	6.20	1,141	9.99	1,230	10.54	672	10.44	
No	279,913	93.80	10,280	90.01	10,439	89.46	5,765	89.56	

Variables	Non-smokers		Moderate smokers		Heavy smokers		Very heavy smokers		p-value*
	0 cigs/day (n= 298,407 91.00%)		1-9 cigs/day (n=11,421 3.48%)		10-19 cigs/day (n=11,669 3.56%)		≥ 20 cigs/day (n=6,437 1.96%)		
	No.	%	No.	%	No.	%	No.	%	
Small for gestational age									
Yes	31,997	10.72	1,919	16.80	2,244	19.23	1,251	19.43	<.0001
No	266,410	89.28	9,502	83.20	9,425	80.77	5,186	80.57	
Live birth order									
1st	124,964	41.88	4,344	38.04	3,761	32.23	1,571	24.41	<.0001
2-3	148,464	49.75	5,649	49.47	6,495	55.66	3,810	59.19	
4+	24,975	8.37	1,427	12.50	1,413	12.11	1,056	16.41	
Missing	4		1		0		0		

^A A total of 327,934 1st Grade students born between the 1998 to 2002 in Georgia were included into this analysis.

* p-values were calculated among students with maternal smoking status during pregnancy, using χ^2 tests.

Table 11a Adjusted estimated OR/RR and 95% CI for failing on CRCT Reading test for the gold standard model controlling for all maternal and child characteristics, using ordinal maternal smoking categories ^A

Variables	aOR	95% CI		aRR	95% CI	
		Low limit	Upper limit		Low limit	Upper limit
Maternal						
Maternal smoking during pregnancy †						
Non-smokers *	1.00			1.00		
Moderate smokers	1.10	1.03	1.17	1.09	1.03	1.14
Heavy smokers	1.19	1.12	1.27	1.17	1.11	1.24
Very heavy smokers	1.33	1.22	1.44	1.29	1.21	1.38
Maternal age, 5 years group						
11-14	1.05	0.90	1.23	1.04	0.92	1.19
15-19	0.96	0.92	1.01	0.97	0.94	1.01
20-24	1.05	1.01	1.08	1.04	1.01	1.07
25-29 *	1.00			1.00		
30-34	0.92	0.89	0.96	0.93	0.90	0.97
35-39	0.93	0.88	0.99	0.94	0.90	0.99
40-44	1.03	0.92	1.16	1.03	0.94	1.14
45-53	1.59	0.96	2.63	1.48	0.97	2.27
Maternal alcohol consumption during pregnancy						
Yes	0.93	0.79	1.09	0.93	0.81	1.06
No*	1.00			1.00		
Mother's marital status						
Married	0.84	0.82	0.87	0.86	0.84	0.89
Unmarried *	1.00			1.00		
Maternal education						
Less than 12 Grades *	1.00			1.00		
High School	0.67	0.65	0.69	0.71	0.69	0.73
Some College	0.41	0.39	0.42	0.46	0.44	0.47
College Completed	0.19	0.18	0.21	0.22	0.21	0.23
Missing ^B	0.93	0.86	1.01	0.95	0.89	1.01
Prenatal care						
Yes	0.90	0.79	1.01	0.92	0.83	1.01
No *	1.00			1.00		
Unknown ^B	0.99	0.87	1.13	1.00	0.90	1.11
Delivery payor						
Medicaid	1.23	1.19	1.26	1.20	1.17	1.23
Not Medicaid *	1.00			1.00		

Variables	aOR	95% CI		aRR	95% CI	
		Low limit	Upper limit		Low limit	Upper limit
Whether have prior adverse birth outcomes						
Yes	1.02	0.87	1.19	1.01	0.89	1.16
No *	1.00			1.00		
Children						
Child's sex						
Female	0.54	0.53	0.56	0.59	0.58	0.61
Male *	1.00			1.00		
Child's race/ethnicity						
White *	1.00			1.00		
Black	2.06	2.00	2.13	1.90	1.84	1.95
Hispanic	2.10	2.02	2.19	1.93	1.86	2.00
Other	1.09	1.02	1.17	1.09	1.02	1.16
Live birth order						
1st *	1.00			1.00		
2-3	1.17	1.14	1.20	1.14	1.12	1.17
4+	1.49	1.43	1.56	1.39	1.34	1.45
School year CRCT test taken						
2005	0.87	0.83	0.91	0.88	0.85	0.92
2006	1.30	1.25	1.34	1.24	1.21	1.28
2007 *	1.00			1.00		
2008	0.97	0.93	1.00	0.97	0.94	1.00
2009	0.94	0.91	0.98	0.95	0.92	0.98
Continuous variable						
	Exp(β)	Low limit	Upper limit	Exp(β)	Low limit	Upper limit
Child's age	0.97	0.94	0.99	0.97	0.95	0.99

^A Model controlled for maternal and child characteristics.

^B Missing or unknown category was put into the model as dummy variable.

† The p-values for test of trend were <0.001 for both logistic and log-binomial models.

* Reference group

Table 11b Adjusted estimated OR/RR and 95% CI for failing on CRCT ELA test for the gold standard model controlling for all maternal and child characteristics, using ordinal maternal smoking categories ^A

Variables	aOR	95% CI		aRR	95% CI	
		Low limit	Upper limit		Low limit	Upper limit
Maternal						
Maternal smoking during pregnancy †						
Non-smokers *	1.00			1.00		
Moderate smokers	1.08	1.03	1.13	1.07	1.03	1.11
Heavy smokers	1.16	1.10	1.22	1.14	1.09	1.18
Very heavy smokers	1.24	1.16	1.32	1.20	1.15	1.26
Maternal age, 5 years group						
11-14	1.02	0.89	1.17	1.02	0.93	1.12
15-19	0.99	0.95	1.02	1.00	0.97	1.02
20-24	1.05	1.02	1.08	1.04	1.02	1.06
25-29 *	1.00			1.00		
30-34	0.92	0.89	0.95	0.93	0.91	0.96
35-39	0.92	0.88	0.96	0.93	0.90	0.97
40-44	0.95	0.87	1.04	0.96	0.90	1.04
45-53	1.37	0.89	2.11	1.28	0.92	1.79
Maternal alcohol consumption during pregnancy						
Yes	0.96	0.85	1.10	0.96	0.87	1.06
No*	1.00			1.00		
Mother's marital status						
Married	0.84	0.82	0.86	0.87	0.85	0.89
Unmarried *	1.00			1.00		
Maternal education						
Less than 12 Grades *	1.00			1.00		
High School	0.66	0.65	0.68	0.74	0.72	0.75
Some College	0.42	0.40	0.43	0.50	0.49	0.51
College Completed	0.20	0.19	0.21	0.25	0.24	0.26
Missing ^B	0.90	0.84	0.96	0.93	0.88	0.98
Prenatal care						
Yes	0.82	0.75	0.91	0.88	0.82	0.94
No *	1.00			1.00		
Unknown ^B	0.85	0.76	0.95	0.90	0.84	0.98
Delivery payor						
Medicaid	1.24	1.22	1.27	1.19	1.17	1.21
Not Medicaid *	1.00			1.00		

Variables	aOR	95% CI		aRR	95% CI	
		Low limit	Upper limit		Low limit	Upper limit
Whether have prior adverse birth outcomes						
Yes	1.04	0.92	1.18	1.03	0.94	1.14
No *	1.00			1.00		
Children						
Child's sex						
Female	0.56	0.55	0.57	0.64	0.63	0.65
Male *	1.00			1.00		
Child's race/ethnicity						
White *	1.00			1.00		
Black	1.75	1.70	1.79	1.57	1.54	1.60
Hispanic	1.95	1.89	2.02	1.70	1.66	1.75
Other	1.00	0.95	1.05	1.01	0.96	1.05
Live birth order						
1st *	1.00			1.00		
2-3	1.20	1.17	1.23	1.15	1.13	1.17
4+	1.49	1.43	1.54	1.35	1.31	1.38
School year CRCT test taken						
2005	0.82	0.79	0.84	0.85	0.83	0.88
2006	1.20	1.17	1.23	1.15	1.12	1.17
2007 *	1.00			1.00		
2008	0.84	0.81	0.86	0.87	0.85	0.89
2009	0.89	0.87	0.92	0.91	0.89	0.94
Continuous variable						
	Exp(β)	Low limit	Upper limit	Exp(β)	Low limit	Upper limit
Child's age	0.98	0.96	1.00	0.99	0.97	1.00

^A Model controlled for maternal and child characteristics.

^B Missing or unknown category was put into the model as dummy variable.

† The p-values for test of trend were <0.001 for both logistic and log-binomial models.

* Reference group

Table 11c Adjusted estimated OR/RR and 95% CI for the failing on CRCT Math test for the gold standard model controlling for all maternal and child characteristics, using ordinal maternal smoking categories ^A

Variables	aOR	95% CI		aRR	95% CI	
		Low limit	Upper limit		Low limit	Upper limit
Maternal						
Maternal smoking during pregnancy †						
Non-smokers *	1.00			1.00		
Moderate smokers	1.09	1.03	1.15	1.07	1.03	1.12
Heavy smokers	1.14	1.08	1.21	1.13	1.08	1.19
Very heavy smokers	1.26	1.17	1.36	1.24	1.17	1.32
Maternal age, 5 years group						
11-14	0.92	0.80	1.06	0.94	0.84	1.04
15-19	0.90	0.86	0.93	0.92	0.89	0.95
20-24	1.01	0.98	1.04	1.01	0.98	1.03
25-29 *	1.00			1.00		
30-34	0.95	0.92	0.99	0.96	0.93	0.99
35-39	0.98	0.93	1.03	0.98	0.94	1.02
40-44	1.08	0.98	1.19	1.07	0.99	1.16
45-53	1.39	0.87	2.24	1.32	0.91	1.91
Maternal alcohol consumption during pregnancy						
Yes	0.94	0.82	1.09	0.94	0.84	1.05
No*	1.00			1.00		
Mother's marital status						
Married	0.83	0.81	0.86	0.86	0.84	0.88
Unmarried *	1.00			1.00		
Maternal education						
Less than 12 Grades *	1.00			1.00		
High School	0.67	0.65	0.69	0.73	0.71	0.75
Some College	0.42	0.40	0.43	0.48	0.47	0.50
College Completed	0.20	0.19	0.21	0.24	0.23	0.25
Missing ^B	0.87	0.80	0.94	0.90	0.85	0.96
Prenatal care						
Yes	0.83	0.75	0.93	0.87	0.81	0.94
No *	1.00			1.00		
Unknown ^B	0.86	0.76	0.97	0.89	0.82	0.98
Delivery payor						
Medicaid	1.25	1.22	1.28	1.21	1.18	1.24
Not Medicaid *	1.00			1.00		

Variables	aOR	95% CI		aRR	95% CI	
		Low limit	Upper limit		Low limit	Upper limit
Whether have prior adverse birth outcomes						
Yes	1.03	0.90	1.19	1.03	0.92	1.15
No *	1.00			1.00		
Children						
Child's sex						
Female	0.76	0.75	0.78	0.80	0.79	0.82
Male *	1.00			1.00		
Child's race/ethnicity						
White *	1.00			1.00		
Black	2.38	2.31	2.44	2.08	2.03	2.13
Hispanic	1.77	1.71	1.84	1.66	1.61	1.71
Other	1.03	0.97	1.09	1.03	0.98	1.09
Live birth order						
1st *	1.00			1.00		
2-3	1.08	1.06	1.11	1.07	1.05	1.09
4+	1.26	1.21	1.31	1.20	1.16	1.24
School year CRCT test taken						
2005	0.58	0.56	0.60	0.65	0.63	0.67
2006	0.47	0.46	0.49	0.54	0.53	0.56
2007 *	1.00			1.00		
2008	0.72	0.69	0.74	0.77	0.75	0.79
2009	0.69	0.67	0.71	0.75	0.73	0.77
Continuous variable						
	Exp(β)	Low limit	Upper limit	Exp(β)	Low limit	Upper limit
Child's age	0.95	0.93	0.97	0.96	0.94	0.97

^A Model controlled for maternal and child characteristics.

^B Missing or unknown category was put into the model as dummy variable.

† The p-values for test of trend were <0.001 for both logistic and log-binomial models.

* Reference group

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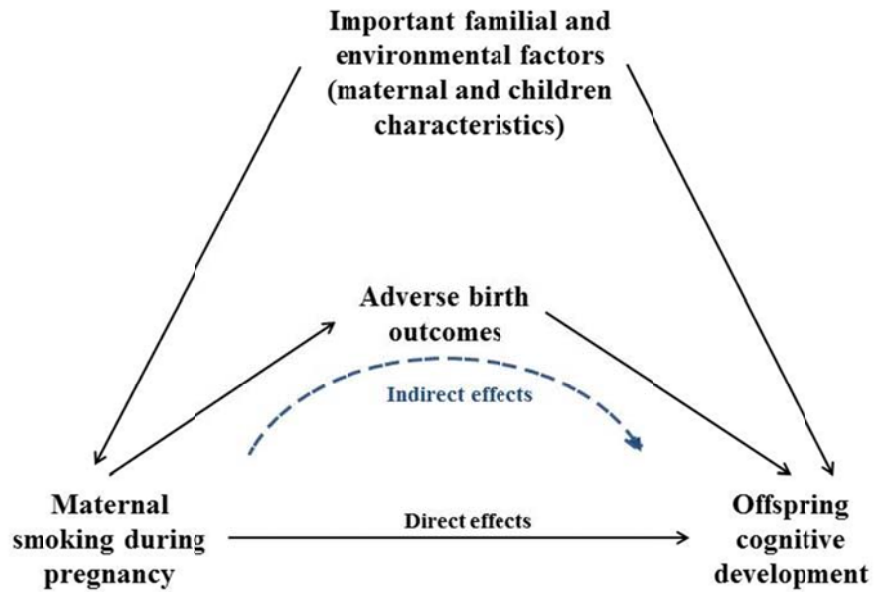


Figure 1 Causal DAG of the two-stage analyses hypotheses

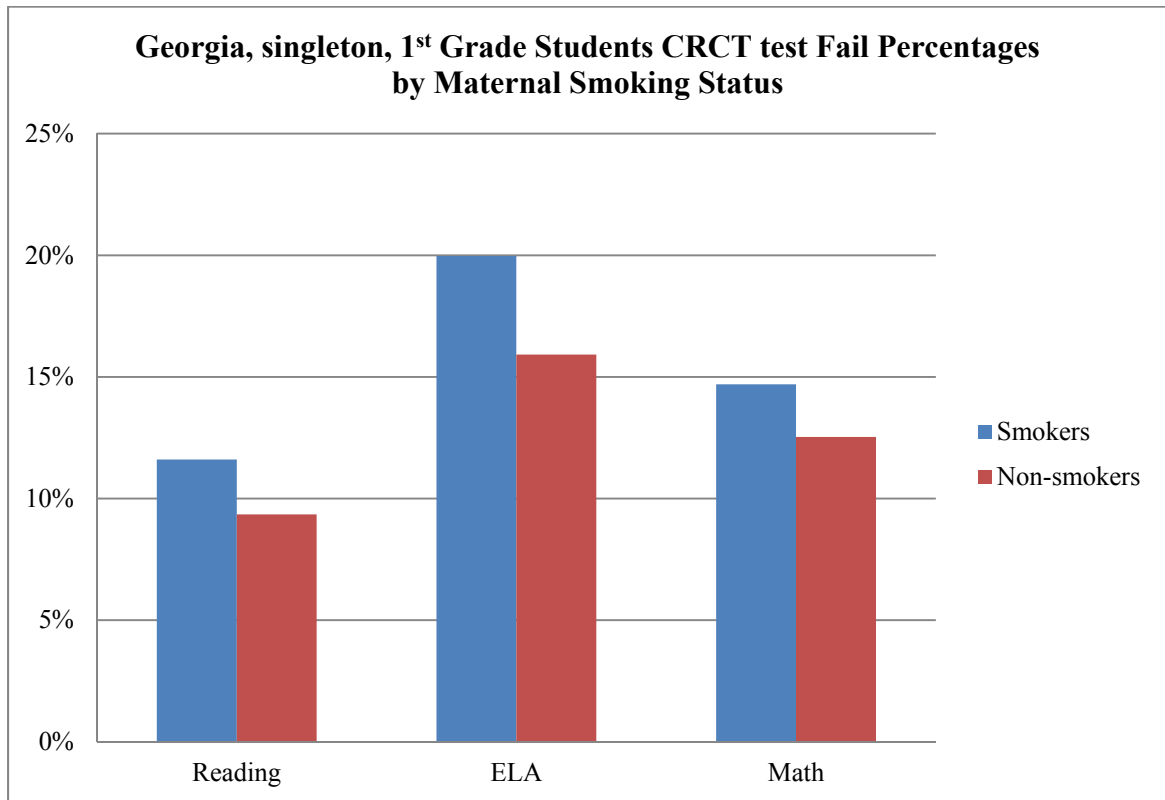


Figure 2 Georgia, singleton, 1st Grade students CRCT test failing percentages by maternal smoking status

APPENDIX A – IRB APPROVAL



EMORY
UNIVERSITY

Institutional Review Board

TO: Bryan Williams
Principal Investigator

CC: Dunlop Anne SOM: F&P PREV MED
Jain Lucky Neonatolog

DATE: August 19, 2010

RE: **Notification of Expedited Approval**
IRB00044043
Late Term Prematurity and Early School Performance

This is your notification that your above referenced study was reviewed and APPROVED under the Expedited review process per 45 CFR 46.110 (5), 45 CFR Part 46 subpart D section 46.404, and 21 CFR 56.110. In addition, a complete HIPAA waiver, a waiver of informed consent, and a waiver of assent have been granted for this study. The approval is valid from **8/18/2010 until 8/17/2011**. Thereafter, continued approval is contingent upon the submission of a continuing review request that must be reviewed and approved by the IRB prior to the expiration date of this study.

Any reportable events (serious adverse events, breaches of confidentiality, protocol deviation or protocol violations) or issues resulting from this study should be reported immediately to the IRB and to the sponsoring agency (if any). Any amendments (changes to any portion of this research study including but not limited to protocol or informed consent changes) must have IRB approval before being implemented.

All correspondence and inquiries concerning this research study must include the IRB ID, the name of the Principal Investigator and the Study Title.

Sincerely,

LaShawn Martin
Research Protocol Analyst
Emory University Institutional Review Board
This letter has been digitally signed