Distribution Agreement

In presenting this thesis or dissertation as a partial fulfillment of the requirements for an advanced degree from Emory University, I hereby grant to Emory University and its agents the non-exclusive license to archive, make accessible, and display my thesis or dissertation in whole or in part in all forms of media, now or hereafter known, including display on the world wide web. I understand that I may select some access restrictions as part of the online submission of this thesis or dissertation. I retain all ownership rights to the copyright of the thesis or dissertation. I also retain the right to use in future works (such as articles or books) all or part of this thesis or dissertation.

Signature:

_____ _____

Shannon Pruitt Date

The effect of maternal alcohol consumption on the diagnosis of reactive airway disease in early childhood: Data from the Fetal Growth and Development Study (FGDS) and the Follow-Up of Development and Growth Experiences Study (FUDGE)

By

Shannon Pruitt
Master of Public Health

Epidemiology

Carolyn Drews-Botsch, PhD, MPH
Committee Chair

The effect of maternal alcohol consumption on the diagnosis of reactive airway disease in early childhood: Data from the Fetal Growth and Development Study (FGDS) and the Follow-Up of Development and Growth Experiences Study (FUDGE)

By

Shannon Pruitt

B.A., Westminster College, 2015

Thesis Committee Chair: Carolyn Drews-Botsch, PhD, MPH

An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
in partial fulfillment of the requirements for the degree of
Master of Public Health
in Epidemiology
2017

Abstract

The effect of maternal alcohol consumption on the diagnosis of reactive airway disease in early childhood: Data from the Fetal Growth and Development Study (FGDS) and the Follow-Up of Development and Growth Experiences Study (FUDGE)

By Shannon Pruitt

Asthma is a major cause of morbidity and hospitalization in young children. However, little is known about the etiology of asthma. Alcohol consumption during pregnancy could be a factor involved in the development of childhood asthma. The aims of this analysis were to examine the relationship between differing levels of maternal alcohol consumption and diagnosis of asthma during early childhood. Data for this analysis were obtained from the Fetal Growth and Development Study (FGDS) and the Follow-up of Development and Growth Experiences Study (FUDGE). FGDS was a case control study of risk factors for infants born small-for-gestational age in two metropolitan Atlanta hospitals in 1993 and 1994. FUDGE was a follow-up to FGDS and included a proportion of participants at age four and a half years. Multivariable logistic regression was used to examine the effect of any alcohol consumption, moderate alcohol consumption, heavy alcohol consumption, and binge drinking on the development of childhood reactive airway disease. In unadjusted models, differing levels of maternal alcohol use showed no association with diagnosis of reactive airway disease unaffected by adjustment. While unadjusted models showed an inverse association, this effect was not present after controlling for education, small for gestational age, income, and smoking. Although imprecise, these data provide evidence that prenatal exposure to alcohol is not associated with diagnosis of reactive airway disease. These findings suggest that future research should examine other factors outside of maternal alcohol consumption to understand the large prevalence of asthmatic disease in children.

The effect of maternal alcohol consumption on the diagnosis of reactive airway disease in early childhood: Data from the Fetal Growth and Development Study (FGDS) and the Follow-Up of Development and Growth Experiences Study (FUDGE)

By

Shannon Pruitt

B.A., Westminster College, 2015

Thesis Committee Chair: Carolyn Drews-Botsch, PhD, MPH

A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
In partial fulfillment of the requirements for the degree of
Master of Public Health
in Epidemiology
2017

TABLE OF CONTENTS

CHAPTER 1: BACKGROUND AND LITERATURE REVIEW

Burden of Disease:

Childhood asthma is one of the most common respiratory disorders worldwide (1). The World Health Organization estimates that approximately 235 million people suffer from asthma around the world and in the United States more than 7.1 million children have been diagnosed with asthma (1). Asthma is considered the most common chronic condition among children and the burden due to asthma is a significant public health problem in the United States (1, 2). According to the 2014 Global Asthma Report, asthma is the 14th most important disorder in terms of disability (3). According to the NHIS, 1.4% of children in the United States experienced some degree of disability due to asthma in 1993 and 1995 (4). This disability ranged from children who were unable to attend school (0.2% of all children), who were limited in the amount or type of play (0.5% of all children), and children who were limited in other activities such as school sports (0.7% of all children) (4) An increased prevalence of asthma is seen in Western and Industrialized countries where asthmatic disease inflicts a high economic burden (1).

The high prevalence of asthma leads to thousands of annual hospitalizations in children under the age of 15 (1). Not only does this result in an increased economic burden, but also 10 million missed school days per year (1). In the United States the estimated cost of health care expenditures for asthma are more than $50.1 billion per year (1). Globally, the estimated economic cost for asthma in the United Kingdom is 1.8 billion and 460 million in Australia (1).

The etiology of asthma is poorly understood (5). Risk factors have not been identified that can account for the rapidly increasing incidence of childhood asthma during the last two decades (1). Despite previous research, the cause of asthma remains unclear (2).

While many environmental exposures during childhood have been investigated in regards to asthma, the environment in utero could have an effect on the developing fetal lung. Overall, exposures during the prenatal period and their potential relationship to childhood asthma are not well understood (1).

Epidemiology

Asthma has many complex risk factors that include genetic, environmental, and behavioral risk factors and many of these are currently underexplored (3). Established risk factors for the development of asthma include parental asthma, prenatal environmental tobacco smoke, and prematurity (6). Other risk factors, such as maternal smoking and obesity, have been shown to increase childhood vulnerability to lung disease (1).

It has been demonstrated that males are more susceptible to asthma in early childhood than females (1,2). Male preterm infants are also shown to have higher rates of asthma incidence and chronic lung disease than female preterm infants (1). While gender appears to have a strong effect, asthma is also more prevalent in African American children than in other populations (1,2).

Maternal exposures during pregnancy have also been demonstrated as a means of influencing future asthmatic disease in infants. Children of allergic mothers are more likely to develop asthma than children of asthmatic fathers (8). This relationship suggests

that maternal programming of the growing fetus has an effect on the development of childhood asthma separately from genetic risk factors.

Potentially modifiable risk factors for asthma have been identified. There is a mild to moderate effect of maternal obesity on childhood asthma (6). A direct relationship has been identified between the duration of breastfeeding and asthma protection in the infant (1). Other risk factors that could affect the development of the fetal lung include maternal smoking and low gestational age (8).

Despite known risk factors, no single factor can account for the rapidly increasing incidence of childhood asthma (1). The rapidly increasing prevalence of asthma suggests that it may be attributable to environmental factors rather than genetics (7). More research needs to be conducted to understand the etiology of asthma.

Biological Effects

The environment in utero can affect the development of the fetal lung (8). There is increasing evidence that mothers have an important role to play in the development of infant immune response during gestation (9). It has been hypothesized that avoiding certain environmental exposures during pregnancy could prevent the development of asthma (9). Further providing evidence of in utero immune programming, pre-eclampisa is a prenatal risk factor for multiple allergic diseases and maternal use of antibiotics during pregnancy has been found to increase the risk of asthma in offspring (10, 11).

Early pregnancy has been shown to have a crucial effect on future embryonic development (11). Both the mother and the placenta play important roles in the development of allergic responses (9). There is very compelling evidence that there are in utero development of fetal immune responses to allergens (9).

Alcohol

According to the Centers for Disease Control and Prevention (CDC), prenatal alcohol exposure is the leading preventable cause of birth defects, developmental disabilities, and mental retardation in the United States (12). The National Birth Defects Prevention Study (NBDPS) reports that 30% of women drink during their pregnancy and around 8% binge drink (more than 5 drinks in one sitting) (13). As nearly 50% of pregnancies are unplanned, binge drinking during early pregnancy is a significant problem (12). Approximately 1 in 33 pregnant women consume alcohol at levels shown to increase the risk of having a baby with fetal alcohol spectrum disorder (12).

Fetal alcohol has been suggested to promote toxicity to the developing fetal lungs (12,13). In utero alcohol induces significant alterations in oxidant stress, but the effect of alcohol on the developing lung is not fully understood (12). It has been hypothesized that fetal alcohol exposure could result in altered pulmonary dynamics and increase the risk of lung scarring lesions (13). Animal models suggest that in utero alcohol exposure damages the immune defense in the developing lung (12). Other animal studies have also shown that prenatal alcohol exposure leads to smaller, less developed lungs (14).

It is not known if prenatal alcohol exposure plays a role in childhood asthma (15). Studies are limited based on the inability to accurately identify newborns that are exposed to alcohol (13). Under reporting of alcohol consumption is common (16). Alcohol is a prenatal-perinatal risk factor that has been suggested to increase the risk of some pediatric allergic disease including asthma (17). In utero alcohol exposure dramatically increases the risk of premature delivery and prematurity has been associated with an increased risk of asthmatic disease (12, 7).

Few studies have been conducted examining the effect of maternal alcohol use on the development of childhood asthma and many show contradictory results. A study by Patra showed that BMI, smoking, and drinking in combination are associated with a two or three fold increased risk of developing asthma (3). Other studies, however, show a non-significant effect of the effect of alcohol on the future development of asthma (13). Paradoxically, others have shown that low-dose prenatal alcohol exposure shows a significant inverse association with current asthma (14).

More research needs to be conducted to understand the etiology behind childhood asthma. Alcohol has been suggested to have an effect on fetal lung development, but few studies have investigated the link between prenatal alcohol exposure and subsequent development of childhood asthma. This study will help to further investigate the connection between maternal alcohol consumption and childhood asthma.

CHAPTER II: MANUSCRIPT

INTRODUCTION

Asthma is a major cause of morbidity and hospitalization in young children (8). It is estimated that 300 million people globally were affected by asthma in 2001 and that between 250,000 and 345,000 people die from asthma related complications each year (11). Childhood asthma is one of the most common respiratory disorders worldwide and asthma prevalence is higher among children than adults (11,18). An increased prevalence of Asthma has been seen in Western industrialized societies where asthmatic disease inflicts a high economic burden (11, 1). It has been estimated that 7.1 million children had asthma in the United States in 2011 (1).

The etiology of asthma is poorly understood (5). While many environmental exposures during childhood have been investigated in regards to asthma, the environment *in utero* could have an effect on the developing fetal lung. It has been demonstrated that maternal exposures during pregnancy, such as maternal smoking and obesity, increase childhood vulnerability to lung diseases (1). Overall, exposures during the prenatal period and their potential relationship to childhood asthma are not well understood (1). Alcohol consumption during pregnancy could be an environmental factor involved in the development of childhood asthma.

Current health recommendations state that there is no safe level of alcohol consumption during pregnancy. Despite this recommendation, it has been estimated that 30% of women drink during their pregnancy and 8.3% reported binge drinking (more than 5 drinks per sitting) (13). True numbers, however, are difficult to estimate as

maternal self-report of alcohol consumption often results in an under-representation (19, 13). It has been estimated that the average prevalence estimates of prenatal alcohol exposure will be four times higher using meconium testing as compared to maternal self-report (19). Drinking during pregnancy has been shown to cause a number of ailments in the developing fetus including fetal alcohol spectrum disorder, birth defects, and adverse birth outcomes (14, 12, 20). A link between maternal consumption of alcohol and the development of asthma during childhood has not been established.

However, animal studies have suggested that alcohol exposure during the prenatal period alters lung development (13). Other models involving animals have indicated that fetal exposure to alcohol can lead to numerous respiratory problems such as less developed lungs, increased oxidative stress, and increased risk of respiratory distress (14). Fetal alcohol has been suggested to promote toxicity to the developing lungs (12, 13). It has been hypothesized that fetal alcohol exposure could result in altered pulmonary dynamics and increase the risk of lung-scarring lesions (13). Clinical studies investigating the effect of alcohol on the developing human fetus, however, have been limited (13). Studies conducted looking at the effect of alcohol consumption on development of asthma have had conflicting results with some showing a dose-based response and others showing an inverse association (3, 14). This analysis will help to further investigate the connection between maternal alcohol consumption and diagnosis of childhood asthma.

METHODS

Data Sources:

Data for this analysis were obtained from the Fetal Growth and Development Study (FGDS) and the Follow-up of Development and Growth Experiences Study

(FUDGE). FGDS was a case-control study of risk factors for infants born small-for-gestational age (SGA) in two metropolitan Atlanta hospitals in 1993 and 1994. These two hospitals account for more than one-third of all deliveries in the five central counties of metropolitan Atlanta (21). FUDGE was a follow-up to the FGDS and included a proportion of participants at age four and a half years. The key exposure in these studies was maternal alcohol consumption.

Participants for the FGDS selected from deliveries at two large hospitals in metropolitan Atlanta between February 1993 and December 1994. One of hospital was private and located in a northern Atlanta suburb serving patients of a generally mid to high socioeconomic class. The second hospital was a public, teaching hospital located in an urban area serving patients of a mostly lower socioeconomic status. Interviews were conducted post-partum and study personnel were randomly assigned to one of the hospitals each week. This random assignment was blocked in groups of four weeks to ensure similarity in the seasonal distribution of deliveries. Criteria for inclusion was based on race (white or black) and gestational age (32 to 42 weeks). Infants were categorized as small for gestational age (SGA) if their birth weight was less than the 10^{th} percentile for gestational age, race and sex using data from US births. Infants were categorized as appropriate for gestational age (AGA) if their birth weight was above the 10^{th} percentile. All SGA infants and a three percent random sample of AGA infants were invited to participate in the study.

The FUDGE study included a proportion of those births included in the FGDS study. The participants included all children who had previously been categorized as AGA, all children who had been categorized as SGA whose mothers reported any alcohol

use in pregnancy, and a 50% random sample of SGA children whose mothers did not consume alcohol during their pregnancy. Of the 760 selected for follow-up, 510 participated in FUDGE. After excluding those who had had missing data for the outcome or exposure, the final sample size for this analysis was 497.

Questionnaire:

Written informed consent for the FGDS maternal interview was administered in the hospital, usually within 18 to 36 hours after delivery. The interview included questions on demographic factors, health history, and pregnancy behaviors. The FUGDE study was conducted when the children were 4 ½ years old. The mothers completed an interview including questions on household demographics and health outcomes of the child.

Informed consent was required for inclusion in the study. Both the FUDGE and the FGDS were approved by the institutional review boards at Emory University and the Centers for Disease Control and Prevention.

Analysis:

The outcome for this study is a maternal report that the child had received a diagnosis of reactive airway disease by age 4 ½ years of age. The primary exposure of interest, self-reported drinking during pregnancy, was reported post-partum. Questions about alcohol consumption during pregnancy were included on the FGDS interview and included four separate time periods: 3 months before conception, the first trimester (2-13 weeks), the second trimester (14-24 weeks), and the third trimester (25 weeks to delivery). For this analysis drinking during the preconception period was excluded from analysis. These questions allowed for the calculation of the average number of drinks per week during these time periods. For the purposes of this analysis, moderate drinking was

defined as 7-13 drinks per week, heavy drinking was defined as greater than or equal to 14 drinks per week, and binge drinking was defined as more than 5 alcoholic drinks in one day.

Analysis techniques included descriptive statistics and logistic regression to estimate the associations between different levels of alcohol consumption and diagnosis of reactive airway disease in early childhood. Frequency distributions were used to examine proportion of predictors and diagnosis of reactive airway disease. Chi-square statistics were used to test the significance of differences in risk factors. Multivariable logistic regression was used to examine the effect of any alcohol consumption, moderate alcohol consumption, heavy alcohol consumption, and binge drinking on the development of childhood reactive airway disease. All analyses were conducted using SAS V9.4.

RESULTS

Mothers who reported that their child received a diagnosis of reactive airway disease were more likely to be black than white, have less than a high school education, have insurance other than private, and have an income less than $25,000 (Table 1). Children who were diagnosed with reactive airway disease were more likely to be born small for gestational age (< 10^{th} percentile) and to born at the public hospital. There does not appear to be a significant association between maternal age, hospital at birth, or maternal smoking on diagnosis of reactive airway disease.

In unadjusted models, differing levels of maternal alcohol use showed no association with diagnosis of reactive airway disease unaffected by adjustments (Table

2). Report of any alcohol use during pregnancy showed the smallest inverse association (OR=0.85, 95% CI, 0.54, 1.32). Report of any alcohol use in the 2nd and 3rd trimesters showed the largest inverse association (OR=0.63, 95% CI, 0.36, 1.06) followed by moderate alcohol use (OR=0.71, 95% CI, 0.26, 1.73), binge drinking (OR=0.81, 95% CI, 0.37, 1.69), and heavy alcohol use (OR=0.84, 95% CI, 0.15, 3.23).

When stratifying by sex of the child, hospital at birth, and parity no significant effect measure modification was found. Confounding was assessed for education, maternal age, smoking, income, and small for gestational age. Confounding resulting a greater than 10% change in odds ratio estimate was found by education, small for gestational age, income, and smoking.

Adjusted models (Table 3) controlling for education, small for gestational age, income, and smoking showed no significant association between maternal drinking during pregnancy and diagnosis of reactive airway disease. Similarly to the unadjusted analysis, binge drinking showed an inverse association (OR=0.90, 95% CI, 0.34, 2.37) as well as heavy alcohol use (OR=0.93, 95% CI, 0.19, 4.42). Additional measures of maternal alcohol use, however, showed increased odds of diagnosis of reactive airway disease. This increased odds was highest among those using any alcohol during the second and third trimester (OR=1.45; 95% CI, 0.79, 2.66) followed by moderate alcohol use (OR=1.22, 95% CI, 0.41, 3.62) All of the estimates calculated with the adjusted model were non-significant.

Overall, this analysis suggests that there is no evidence of an association between differing levels of maternal alcohol consumption and diagnosis of childhood asthma.

While the observed effect for the unadjusted and adjusted models were non-significant, the inverse association in the unadjusted model appears to be the result of confounding.

DISCUSSION:

Although imprecise, these data provide no evidence that prenatal exposure to alcohol is associated with diagnosis of reactive airway disease. While unadjusted models were suggestive of an inverse association between maternal alcohol use across the levels of drinking (any, moderate, heavy, and binge drinking) and risk of asthma, this appears likely due to confounding by a variety of sociodemographic characteristics since there was no association observed in models that adjusted for education, SGA, income, and maternal age.

The results of this study were similar to previous studies where alcohol exposure resulted in a protective effect on the development of asthma. Magnus et al. also did not observe a significant association between maternal alcohol intake during pregnancy and current asthma at either 35 months or 7 years (14). Similarly, a study of prenatal alcohol exposure and childhood atopic disease suggested that maternal drinking in late pregnancy was associated with a lower risk of childhood asthma (16). Conversely, Patra et al. found that, together, BMI, smoking, drinking, and solid fuel use were associated with a more than doubling of the risk of developing asthma (3).

Strengths of the current study included the sampling design, which allowed for a large sample of women who reported alcohol drinking during pregnancy. Additionally, as data on prenatal drinking was collected shortly after birth before questions regarding asthma diagnosis there is no chance of recall bias. Because of the sampling design for the FGDS and FUDGE, there were a larger proportion of children that were born SGA as

compared to the general population. Despite this robust sample, numbers were too sparse to examine effects of differing levels of alcohol use across trimesters individually. The power of the analysis was further constrained by the small number of women who reported drinking during pregnancy and this could have contributed to the imprecision of the analysis.

Another potential limitation is that much of the data were self-reported. This self-report could have led to unknown levels of measurement error. The validity of the study depends on the quality of the self-reported alcohol use. It has been estimated that the average prevalence estimates of prenatal alcohol exposure will be four times higher using meconium testing as compared to maternal self-report (19). Under-reporting of maternal alcohol use may differ by unknown variables and this study did not confirm alcohol use biochemically.

Data collected for both maternal drinking and asthma diagnosis were self-reported. While the self-reported data could have lead to some inaccuracies, data collected pertaining to maternal drinking appear to be of a high quality as the estimates are similar to other reports (22). The observed prevalence of asthma in this study (25.4%), however, is higher than the prevalence reported by 2008 BRFSS data for children in Georgia between the age of 0 and 4 (11.0%) (23). Both data sources rely on self-report of diagnosis, however BRFSS asks solely for asthma diagnosis while FUDGE asked for asthma or reactive airway disease diagnosis. The high prevalence of asthma seen in this data could also be due to location as participants were living in a large metropolitan area with perhaps greater risk factors (e.g. air pollution).

Low participation rates could be an additional limitation in this analysis. At the public hospital 88% of selected mothers were interviewed while only 69% of selected mothers were interviewed at the private hospital (21). This analysis did not show a significant difference between effects when stratifying on hospital at birth. While this study included a diverse population of mothers in metropolitan Atlanta, additional studies would be needed to establish if results are generalizable to the overall U.S. population.

The results of this study suggest that there is no effect of maternal alcohol consumption during pregnancy on the diagnosis of childhood asthma. These findings suggest that future research should examine other factors outside of maternal alcohol consumption to understand the large incidence of asthmatic disease in children. This analysis does not, however, contradict the other potential negative consequences of maternal alcohol consumption during pregnancy. Further investigations into the etiology behind asthmatic disease are warranted.

REFERENCES

1. Noutsios GT, Floros J. Childhood asthma: causes, risks, and protective factors; a role of innate immunity. *Swiss medical weekly* 2014;144:w14036.
2. Akinbami L. The State of Childhood Asthma, United States, 1980-2005. *Advance data from vital and health statistics* 2006 (381).
3. Patra J, Maher YI, Mishra S, et al. Effects of body mass index, tobacco smoking, alcohol drinking and solid fuel use on the risk of asthma: Individual Participant Data (IPD) meta-analysis of 175 000 individuals from 51 nationally representative surveys. *BMJ open respiratory research* 2016;3(1):e000121.
4. Newacheck PHN. Prevalence, Impact, and Trends in Childhood Disability Due to Asthma *Arch pediatr adolesc med* 2000;154:287-93.
5. Martinez FD, Wright AL, Taussig LM, et al. Asthma and wheezing in the first six years of life. The Group Health Medical Associates. *The New England journal of medicine* 1995;332(3):133-8.
6. Castro-Rodriguez JA, Forno E, Rodriguez-Martinez CE, et al. Risk and Protective Factors for Childhood Asthma: What Is the Evidence? *The journal of allergy and clinical immunology In practice* 2016.
7. Yuan Wei BO, Sorensen Henrick T, and Jorn Olsen. Fetal growth and hospitalization with asthma during early childhood: a follow-up study in Denmark. *International Journal of Epidemiology* 2002;31:1240-5.
8. Braback L OB, G Nordahl. Early determinates of first hospital admissions for asthma and acute bronchitis among Swedish children. *Acta Paediatrica* 2003;92:27-33.
9. Warner JA JC, Williams TJ, Warner JO. Materna programming in asthma and allergy

Clinical and Experimental Allergy 1998;28(5):35-8.

10. Stokholm J, Sevelsted A, Anderson UD, et al. Preeclampsia Associates with Asthma, Allergy and Eczema in Childhood. *American journal of respiratory and critical care medicine* 2016.
11. Chu S, Yu H, Chen Y, et al. Periconceptional and Gestational Exposure to Antibiotics and Childhood Asthma. *PloS one* 2015;10(10):e0140443.
12. Giliberti D, Mohan SS, Brown LA, et al. Perinatal exposure to alcohol: implications for lung development and disease. *Paediatric respiratory reviews* 2013;14(1):17-21.
13. Gauthier TW, Brown LA. In utero alcohol effects on foetal, neonatal and childhood lung disease. *Paediatric respiratory reviews* 2016.
14. Magnus MC, DeRoo LA, Haberg SE, et al. Prospective study of maternal alcohol intake during pregnancy or lactation and risk of childhood asthma: the Norwegian Mother and Child Cohort Study. *Alcohol Clin Exp Res* 2014;38(4):1002-11.
15. Yuan W, Sørensen HT, Basso O, et al. Prenatal Maternal Alcohol Consumption and Hospitalization With Asthma in Childhood: A Population-Based Follow-Up Study. *Alcoholism: Clinical and Experimental Research* 2004;28(5):765-8.
16. Shaheen SO, Rutterford C, Zuccolo L, et al. Prenatal alcohol exposure and childhood atopic disease: a Mendelian randomization approach. *The Journal of allergy and clinical immunology* 2014;133(1):225-32.e1-5.
17. Dietert RR, Zelikoff JT. Early-life environment, developmental immunotoxicology, and the risk of pediatric allergic disease including asthma. *Birth defects research Part B, Developmental and reproductive toxicology* 2008;83(6):547-60.
18. Akinbami, LJ; Moorman, JE; Bailey, C; et al. Trends in asthma prevalence, health care

use, and mortality in the United States, 2001-2010. *NCHS data brief, no 94. Hyattsville MD: National Center for Health Statistics*. 2012.

19. Lange SS, K; Koren, G; Rehm, J; and Popova, S. A comparison of the prevalnce of prenatal alcohol exposure obtained via maternal self-reports versus meconium testing: a systematic literature review and meta-analysis *BMC Pregnancy and Childbirth* 2014 (14):127.
20. Nykjaer CANG, DC; Simpson NAB, Hay AWM, White KLM, Cade JE. Maternal alcohol intake prior to and during pregnancy and risk of adverse birth outcomes: evidence from a British cohort *Journal Epidemiology Community Health* 2013(68):542-9.
21. Drews CD, Coles CD, Floyd RL, et al. Prevalence of prenatal drinking assessed at an urban public hospital and a suburban private hospital. *The journal of maternal-fetal & neonatal medicine : the official journal of the European Association of Perinatal Medicine, the Federation of Asia and Oceania Perinatal Societies, the International Society of Perinatal Obstet* 2003;13(2):85-93.
22. Bhuvaneswar CG, Chang G, Epstein LA, et al. Alcohol Use During Pregnancy: Prevalence and Impact. *Primary Care Companion to The Journal of Clinical Psychiatry* 2007;9(6):455-60.
23. Asthma in Georgia. *CDC's National Asthma Control Program.* Retrieved from https://www.cdc.gov/asthma/stateprofiles/asthma_in_ga.pdf

TABLES

Table 1. Diagnosis of reactive airway disease by selected characteristics, Fetal Growth and Development Study (FGDS) and the Follow-up of Development and Growth Experiences Study (FUDGE)

	Diagnosis of Reactive Airway Disease		
	Yes	No	OR (95% CI)
Race[1]			
White	32 (14.6%)	188 (85.4%)	1.00 (referent)
Black	66 (24.6%)	202 (75.4%)	1.92 (1.20, 3.06)
Education			
< High School Graduate	30 (25.0%)	90 (75.0%)	1.92 (1.20, 3.06)
High School Graduate	26 (23.2%)	86 (76.8%)	1.00 (referent)
Some College	21 (18.4%)	93 (81.6%)	1.10 (0.60, 2.01)
College Graduate	23 (15.23%)	128 (84.8%)	0.75 (0.39, 1.42)
Income[2]			
< 10,000	34 (25.2%)	101 (74.8%)	2.45 (1.30, 4.65)
10,000-24,999	21 (27.3%)	56 (72.7%)	2.74 (1.34, 5.58)
25,000-54,999	22 (18.5%)	97 (81.5%)	1.65 (0.83, 3.29)
≥ 55,000	17 (12.1%)	124 (87.9%)	1.00 (referent)
Maternal Age			
< 20	21 (28.0%)	54 (72.0%)	1.69 (0.96, 2.98)
20-34	69 (18.7%)	300 (81.3%)	1.00 (referent)
≥ 35	10 (18.9%)	43 (81.1%)	1.01 (0.48, 2.11)
Marital Status[3]			
Married	46 (17.5%)	217 (82.5%)	1.00 (referent)
Single	53 (22.8%)	180 (77.3%)	1.39 (0.89, 2.16)
Insurance			
Other[4]	61 (25.0%)	183 (75.0%)	1.83 (1.17, 2.88)
Private	39 (15.4%)	214 (84.6%)	1.00 (referent)
SGA			
Yes (< 10^{th} percentile)	35 (20.0%)	140 (80.0%)	1.95 (1.24, 3.06)
No (≥ 10^{th} percentile)	65 (20.2%)	257 (79.8%)	1.00 (referent)
Hospital			
Public	60 (25.3%)	117 (74.7%)	2.81 (1.78, 4.48)
Private	40 (15.4%)	220 (84.6%)	1.00 (referent)
Smoking			
Yes	26 (18.7%)	113 (81.3%)	0.88 (0.53, 1.44)
No	74 (20.7%)	284 (79.3%)	1.00 (referent)

[1] missing 9 observations; [2]missing 25 observations; [3]missing 3 observations; [4] self-pay and Medicaid

Table 2. Diagnosis of reactive airway disease by levels of maternal alcohol use, Fetal Growth and Development Study (FGDS) and the Follow-up of Development and Growth Experiences Study (FUDGE)

	Diagnosis of Reactive Airway Disease			
	Yes	No	OR (95% CI)	aOR[1] (95% CI)
Any Alcohol	48 (18.8%)	207 (81.2%)	0.85 (0.54, 1.32)	1.00 (0.60, 1.68)
2nd and 3rd trimesters	21 (15.1%)	118 (84.9%)	0.63 (0.36, 1.06)	1.45 (0.79, 2.66)
Moderate Alcohol	6 (16.2%)	31 (83.8 %)	0.71 (0.26, 1.73)	1.22 (0.41, 3.62)
Heavy Alcohol	3 (18.6%)	13 (81.3%)	0.84 (0.15, 3.23)[2]	0.93 (0.19, 4.42)
Binge Drinking	10 (1.8%)	45 (81.2%)	0.81 (0.37, 1.69)	0.90 (0.34, 2.37)
Abstained from Alcohol	52 (21.5%)	190 (78.5%)	1.00 (referent)	1.00 (referent)

Referent-asthma; Alcohol use includes all trimesters unless otherwise stated;[1] Adjusted for education, small for gestational age, income, and smoking; [2] Fisher's exact

CHAPTER III: SUMMARY, PUBLIC HEALTH IMPLICATIONS, POSSIBLE FUTURE DIRECTIONS

Asthma is one of the main causes of morbidity and hospitalization in young children and the etiology of the disease is poorly understood (Braback, 2003; Martinez, 1995). Alcohol consumption during pregnancy is one proposed environmental factor that could be involved in the development of childhood asthma. Data for this analysis were obtained from the Fetal Growth and Development Study (FGDS) and the Follow-up of Development and Growth Experiences Study (FUGDE). These studies included births from two metropolitan hospitals in Atlanta in 1993 and 1994 along with a follow-up with a portion of participations at age four and a half. The exposures for this analysis included any reported drinking during the first trimester (2-13 weeks), the second trimester (15-24 weeks), and the third trimester (25 weeks to delivery). Levels of drinking were defined as any report of alcohol consumption, any alcohol consumption during the second or third trimester, moderate drinking (7-13 drinks per week), heavy drinking (greater than or equal to 14 drinks per week), and binge drinking (more than 5 alcoholic drinks in one day). Unadjusted models showed a non-significant inverse effect of each level of alcohol consumption on the diagnosis of asthma or reactive airway disease. After adjusting for education, small for gestational age, income, and smoking this non-significant inverse effect was only seen for mothers who reported binge drinking. Any alcohol consumption during the 2nd and 3rd trimester, moderate alcohol consumption, and heavy alcohol consumption showed non-significant increased odds of diagnosis of asthma or reactive airway disease in childhood. This analysis suggests that there may not be an effect of

maternal alcohol consumption during pregnancy on the diagnosis of childhood asthma before the age of five.

These findings, along with previous studies, suggest that future research should examine other factors outside of maternal alcohol consumption to understand the large prevalence of asthmatic disease in children. These findings, however, do not contradict the potential risk of other negative birth outcomes and defects associated with maternal alcohol consumption such as Fetal Alcohol Spectrum disorder.

More research needs to be conducted to understand the etiology behind childhood asthma. While this study suggests that maternal alcohol consumption may not have a negative effect on fetal development that leads to reactive airway disease, other prenatal exposures may have an association that is currently unknown. It would be interesting to examine maternal exposure to other environmental factors in combination with maternal alcohol drinking to see if this contributes to the development of asthmatic disease. More research is required to understand if the cause of asthma is related to fetal lung development, environmental exposures postnatally, or some combination of both factors.