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:

Agasha K. Katabarwa

Date

EVALUATING THE ASSOCIATION BETWEEN MATERNAL SMOKING THREE MONTHS BEFORE PREGNANCY AND INFANT

ADMISSION INTO A NEONATAL INTENSIVE CARE UNIT AMONG AMERICAN INDIAN AND ALASKAN NATIVES IN 8 STATES

Ву

Agasha Katabarwa

MPH

Epidemiology

Dr. Carol Hogue, PhD, MPH

Committee Chair

Cheryl Raskind-Hood MPH, MS

Committee Member

EVALUATING THE ASSOCIATION BETWEEN MATERNAL SMOKING THREE MONTHS BEFORE PREGNANCY AND INFANT

ADMISSION INTO A NEONATAL INTENSIVE CARE UNIT AMONG AMERICAN INDIAN AND ALASKAN NATIVES IN 8 STATES

By

Agasha K. Katabarwa

Emory University

2012

Thesis Committee Chair: Carol Hogue, 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

Abstract

EVALUATING THE ASSOCIATION BETWEEN MATERNAL SMOKING THREE MONTHS BEFORE PREGNANCY AND

INFANT ADMISSION INTO A NEONATAL INTENSIVE CARE UNIT

AMONG AMERICAN INDIAN AND ALASKAN NATIVES IN 8 STATES

By Agasha K. Katabarwa

Purpose: Maternal smoking is one of the preventable risk factors for adverse infant outcomes. The aim of this study was to assess the association between maternal smoking three months before pregnancy and infant Neonatal Intensive Care Unit (NICU) admission among American Indian and Alaskan Native women in AK, MN, NE, NNM, OK, OR, UT and WA. It was hypothesized that infants born to women who smoked three months before pregnancy would more likely be admitted into the NICU.

Methods. PRAMS surveillance data from 2004 through 2011 from the PRAMS from Phases 5 and 6 were obtained from the CDC. Of the 95,428 mothers, analyses were conducted on 12,448 American Indian/Alaskan native mothers who had singleton births born in a hospital setting with no births defects. To assess the association between maternal smoking three months before pregnancy and infant NICU admission, odds ratios were calculated using multiple logistic regression controlling for covariates.

Results: There was no association for pre-pregnancy smoking and infant's NICU admission. Even when the association of heavy maternal smoking pre-pregnancy and infant NICU admission was assessed, no statistically significant association was revealed, (OR: 1.39, 95% CI: 0.67, 2.86). Only SGA was statistically associated with infant NICU admission, with SGA infants having a 2.02 higher odds of admission into the NICU compared to those who were not SGA (95% CI: 1.38, 2.96).

Conclusion: Although AI/AN women have the highest smoking prevalence compared with other racial/ethnic groups, prepregnancy smoking among this cohort of AI/AN pregnant women did not predict infant admission into a NICU. To end tobacco usage among AI/AN, tribes need to address prevention and treatment programs. For example, cessation programs need to be fully funded, the price of tobacco products should be increased, more smoke-free policies should be adopted, a reduction in tobacco advertising and promotion must occur, and more anti-tobacco media campaigns need to be promoted. Primary care and obstetric clinicians need to be trained to advise patients to quit smoking, and more counseling and cessation referral services must be established.

Key Words: Maternal Smoking, Pre-Pregnancy, American Indian, Alaskan Native, NICU, Maternal Health

List of Abbreviations

ACA:	Affordable Care Act
AI/AN:	American Indian/Alaskan Native
ASD:	Atrial septal defects
BMI:	Body Mass Index
CDC:	Centers for Disease Control and Prevention
FPL:	Federal Poverty Level
LBW:	Low Birth Weight
LOS:	Length of Stay
NICU:	Neonatal Intensive Care Unit
PNC:	Prenatal Care
SGA:	Small for Gestational Age
VSD:	Ventricular septal defects

ACKNOWLEDGMENTS

I would like to thank Ms. Cheryl Raskind-Hood whose thorough editing, knowledge and kind heart encouraged me to keep on going and to Dr. Hogue whose guidance inspired me to think more critically about my work.

TABLE OF CONTENTS

TABLE OF CONTENTS	7
CHAPTER I: Background/Literature Review	
Historical Overview of American Indians and Alaskan Natives	
Overview of present day American Indians and Alaskan Natives	
Summary of American Indian Tribes and Alaskan Natives in the 8 states (Alaska, Minnesota, Nebraska, Utah and Washington)	
State of American Indian and Alaskan Native Health	
Tobacco a Sacred Commodity	
Cigarette Smoking	
Tobacco Industry in AI/AN communities	
Maternal Smoking Pre-Pregnancy	
Adverse Infant Outcomes of Cigarette Smoking	
Maternal Smoking and Fetal Exposure to Lead	
Maternal Smoking, Low-Birth Weight and Preterm Birth	
Maternal Smoking and Birth Defects	
Maternal Smoking and NICU Admission	
Maternal Smoking and Social Economic Status	24
Smoking and the Affordable Care Act (ACA)	24
Objective	
CHAPTER II: MANUSCRIPT	
INTRODUCTION	25
METHODS	
Specific Aim	
Hypothesis	
Study Design	
Measures	
Analyses	
RESULTS	
Sample Characteristics	

Descriptive Statistics
Bivariate Logistic Regression
Logistic Regression Analysis
Analysis in the Appendix
DISCUSSION
APTER III: PUBLIC HEALTH IMPLICATIONS AND FUTURE DIRECTION
FERENCES
FIGURES
FIGURE 1. Study Sample
FIGURE 2. Causal DAG (Directed Acyclic Graph)51

5	1
Figure 4. Trends in Current Cigarette Smoking Among High School Students and Adults, United States, 1965-2011 (38)5	3

Table 1. Distributi	of Pre-Pregnancy Smoking (Exposure) and NICU Admission (Outcome) Pooled across Covariates for AI/AN wor
PRAMS 2004-2011	
Table 2. The Unad	ted Association between Infant Admission into the NICU and Pre-pregnancy Smoking Pooled Across 8 States –
PRAMS 2004-2011	
	sted Association between Infant Admission into the NICU and Maternal and Infant Characteristics Pooled Acro
States - PRAMS 20	-2011
	usted Association for AI/AN Women Who Smoked Three Months Before Pregnancy and Maternal and Infant d Across 8 States, PRAMS 2004 – 2011
	r of Cigarettes Smoked Three Months before Pregnancy Among AI/AN Women Across 8 States, PRAMS 2004 –
	n between Infant Admission into the NICU and Number of Cigarettes Smoked per Day Among AI/AN Women A
	· 2011
	isted Association between Infant Admission into the NICU and Pre-Pregnancy Smoking Pooled Across 8 States
	ISTIC REGRESSION MODEL: Adjusted Odd Ratios for Maternal Characteristics and the Risk of Infant NICU Admis ive Births, PRAMS 2004-2011 [*]
	STIC REGRESION MODEL: Adjusted Odd Ratios for Maternal Characteristics and the Risk of Infant NICU Admiss gleton Live Births, PRAMS 2004-2011 [*]
	D INITIAL LOGISTIC MODEL: Association between Number of Cigarettes Smoked per day for Heavy and Light Pr nd Infant NICU Admission.
	STIC MODEL: Association between the number of cigarettes smoked per day for Heavy and Light Pre-Pregnanc
PENDIX	
-	fic Summary Statistics of AI/AN Women Who Smoked Three Months before Pregnancy by 8 States, PRAMS 200
•	fic Summary Characteristics of AI/AN Women Whose Infant Was Admitted into the NICU by 8 States, PRAMS 2
SAS CODE TO CAL	ATE FEDERAL POVERTY LEVEL

CHAPTER I: Background/Literature Review

Historical Overview of American Indians and Alaskan Natives

The Native American way has long been immersed in a search of balance: balance in mind, body and spirit. As European settlers came to the "New World" fleeing religious persecution and seeking economic opportunities, the balance shifted to the side of imminent calamity for the native peoples. The first wave of Pilgrim immigration in 1620 shook the fabric of the Native American way of life with Indigenous communities paying a steep price (1). Starting almost 400 years ago, cultural trauma, displacement and high rates of poverty took a toll on the way of life of native peoples.

Although Christopher Columbus was said to be the first European to arrive in the "New World" in 1492, the Vikings had preceded him 500 years before, and the first human beings to arrive on North American soil were the American Indians, Eskimos, and Aleuts (2). 1492 marked a significant time for the indigenous populations, and as the number of European immigrants increased, settlements were built in areas where native buffalos grazed, disrupting the ecosystem. In addition, new diseases were introduced to the Native Americans among other changes (3). The most significant changes were due to the arrival of European settlers over land conflicts. From 1778 to 1871, various treaties were signed between the United States federal government and the native tribes. These were formal agreements between two sovereign nations, making the Native American people citizens of their tribe living within the boundaries of the United States (4). The treaties were negotiated by the executive branch of the U.S. and the tribes stated that the tribes would give up their rights to hunt and live on huge territories of land in exchange for trade and yearly payments. Recognizing that the American Native way of life would be hard to confine to small strips of land, the reservation system was formed and designed to encourage American Indians to live within clear defined zones (4). In 1887, the Dawes Act was signed into law by President Cleveland. This Act split up reservation lands held by Native Americans and distributed them to individuals within the tribe (5). The purpose was to integrate the Indians into agrarian culture. Under the Dawes Act, Native American land holdings were reduced 44% from 138 million acres to 78 million (5). This law also created boarding schools to assimilate Native American children into white society. Here, children were punished for speaking their native language or

performing native rituals. In 1934, the Dawes Act was abolished by President Franklin Roosevelt (5). Roughly, 325 reservations exist in the United States today (6). Unfortunately, these reservations are home to some of the nation's poorest citizens, although many Indian reservations have built up an economic system for themselves through legal gambling and casinos (7).

Overview of present day American Indians and Alaskan Natives

Presently, the Centers for Disease Control and Prevention (CDC) defines American Indians and Alaskan Natives (Al/AN) as people having origins in North and South America who maintain tribal affiliation or community attachment (8). These people are those who are self-reported to be American Indian or Alaskan Native or report being members of the Navajo, Blackfeet, Inupiat, Yup'ik or Central and South American Indian groups (8, 9). Today, there are 565 federally recognized tribes with whom the United States government has a unique legal and political relationship (10). Although these tribes are usually lumped together, probably due to their small populations, each tribe has its own culture, beliefs and practices. According to the 2012 American Community Survey, there are approximately 5.2 million American Indians and Alaskan Natives, including those of more than one race, comprising 2% of the total U.S. population (11). Of these, 49% are American Indian and Alaskan Native only, and 51% are American Indian and Alaskan Native in combination with one or more other races (11).

Summary of American Indian Tribes and Alaskan Natives in the 8 states (Alaska, Minnesota, Nebraska, New Mexico, Oklahoma, Oregon, Utah and Washington)

According to the 2010 U.S. Census, the top ten largest American Indian and Alaskan Native tribes in the United States are the Navajo, Cherokee, Sioux, Chippewa, Choctaw, Apache, Pueblo, Iroquois, Creek and Blackfeet in order of decreasing population (12).

The Navajo

The largest American Indian tribe in the United States, the Navajo, primarily resides in New Mexico and consists of 21 other Native Indian Tribes (13). The original habitants of the area that is now New Mexico were the Apache, Comanche, Jacome, Jano, Pueblo, Navajo, Ute and Zune tribes. The Navajo Nation, one of the largest American Indian tribes in the United States, expands 27,000 square miles extending into Utah, Arizona and New Mexico (14). The Navajo date back to prehistoric times (15). The tribe largely consisted of hunters and gatherers until they came in contact with the Puebloans and Spanish, and adopted crop farming, herding and weaving (15). The tribe did not officially make contact with the United States government, but rather was invaded during the Mexican American War of 1846 (16). After the Mexican American War, the Treaty of Guadalupe Hidalgo was signed in 1848 where Mexico relinquished the land in New Mexico and California. This territory now includes California, Nevada, Utah, parts of Arizona, New Mexico, Oklahoma, Colorado and Wyoming (17). Today, the Navajo Nation is marked by national monuments, tribal parks and historical sites, some of which are the Anasazi ancient ruins, the Chaco Culture National Historical Park and the majestic red sandstone walls (18).

The Cherokee Nation

According to the 2010 Census Brief on American Indian and Alaskan Native people, the Cherokee Nation is the second largest tribe with a population of 286,000 people who identify themselves as solely American Indian (8). The tribe lived in the mountain region of the south Alleghenies, in southwest Virginia, western North Carolina and South Carolina, north Georgia, east Tennessee, and northeast Alabama (19). Before the Trail of Tears, where the U.S. government forcibly removed the Cherokee nation from its land when gold was discovered there, the Cherokee had had dealings with European settlers. Their first encounter was with De Soto in 1540, and later, in 1736 with Christian Priber (19). The Cherokee had wars with the English of Carolina and during the revolution, the Cherokee fought against the Americans (19). At the end of the Trail of Tears in 1839, most of the Cherokee had been moved to Oklahoma (20).

The Sioux Nation

The Sioux Indians, the third largest group of American Indians, primarily reside in the states of Minnesota, Wisconsin, North and South Dakota, Nebraska, Illinois and Montana (21). The Mdewakanton, Sisseton, Tenton, Wahpekute, Wahpeton, Yankton and Yanktonai tribes comprise the Sioux Indians. Originally, these people were farmers, hunters and gatherers. When they had access to horses for hunting, their diet was predominantly buffalo meat. They occupied the vast lands from the Arkansas River in

the south to the western tributary of Lake Winnipeg in the north, and westward to the eastern slopes of the Rocky Mountains (22). The Sioux are known for their famous Indian chiefs in history. For example, Sioux Chief Sitting Bull, a holy man and a great leader, was known for his bravery after going to war at the age of 14, and later, he led his people to defeat Custer in the Battle of Little Big Horn in 1876 (21). The Sioux are known for fighting in The War of 1812 where they sided with the British, The Battle of Little Big Horn (Custer's Last Stand) in 1876, and The Battle of Wounded Knee in 1890 (22).

Alaskan Natives

More than half of Alaskan Natives are Eskimo (23). Alaska's indigenous peoples can be divided into five major groups based on broad cultural and linguistic similarities: Aleuts, Northern Eskimos (Inupiat), Southern Eskimos (Yuit), Interior Indians (Athabascans) and Southeast Coastal Indians (Tlingit and Haida) (23). In the mid-18th century, Alaska had approximately 80,000 indigenous people (24). The Aleuts, who reside in the coastal villages from Kodiak to the Aleutian Islands off Attu, are known for their expert maritime skills navigating, sailing, and sea hunting in the cold archipelago (24). When Europeans first arrived to the Americas, the Aleut population occupied the major Aleutian Islands, the Alaska Peninsula to Port Moller, and the Shumagin Islands (24). The Inupiat lived and still live in the north and northwestern parts of Alaska, and the Yupit in the southwestern parts. Along the northern coast of Alaska, Eskimos hunt beluga whales, walrus and seal. In the northwest, Eskimos reside on the river banks that flow into Kotzebue Sound where they rely more on hunting land mammals and fishing and less on hunting sea mammals. The most southern Eskimos live along the rivers leading to the Bering Sea and along the Bering Sea coast (23).

State of American Indian and Alaskan Native Health

The American Indian/Alaskan Native (AI/AN) population is riddled with adversity with respect to health equity. Cardiovascular disease, cancer, unintentional injuries, diabetes, obesity, alcoholism, chronic liver disease and cirrhosis, chronic lower respiratory diseases, stroke and suicide are some of the main causes of morbidity and mortality in these communities (8). American Indians live in adverse social and physical environments that place them at a higher risk for exposure to traumatic experiences (25). Mason et al. found that the lifetime exposure rate to at least one trauma was equal for both males and females

ranging from 62.4% to 69.8% (25). Violence and gang involvement among American Indian youth is associated with high risk behaviors such as alcohol and drug use, vandalism, theft and suicide attempts (26). The National Injury Mortality Study observed that AI/AN children were at a higher risk of death by vehicular accidents, suicide and drowning compared to their white counterparts (27).

There is also a large disparity in access to health care in communities compared to the general public (28). Through a network of hospitals and outpatient health care services, the Indian Health Service (IHS), a federal health system, provides medical care to approximately 2 million AI/AN (28). The 3.2 million that are not served by the IHS are presumed to receive care from the private sector or other public systems such as Medicaid and Medicare (28). However, in 2010, 29.2% of AI/AN were reported to lack health insurance (8). From 2009 IHS medical records, 51% were receiving an annual LDL cholesterol check, 48% were getting screened for domestic violence, 45% were screened for breast cancer and 59% for cervical cancer, 44% had depression screening, and 52% were receiving alcohol misuse screening (28).

Tobacco a Sacred Commodity

In 2009, both AI/AN youths aged 12-17 years and AI/AN adults aged 18 and older had the highest prevalence of current smoking compared with other racial/ethnic populations (29). Tobacco is a sacred plant in AI/AN culture, playing an important role in social and spiritual rituals (29). Historically, tobacco was used in its natural form for ceremonial and cleansing purposes by indigenous communities, and today, it is used for religious, medical, guidance and ceremonial purposes. Some believe that if it is used in a positive way, it has the power to heal and to protect; but if abused, it has the power to harm and take away (30). Spiritually, tobacco smoke in prayer represents receiving the breath of the creator (31). As prayers are said, the exhalation of the smoke represents ascension of prayers to the heavens (31). However, since tobacco is an important cultural element in AI/AN communities, it is not surprising that lung cancer is one of the leading causes of cancer death among AI/AN with 33.5 per 100,000 deaths in men, and 18.4 per 100,000 deaths in women attributed to cigarette smoking(32).

Cigarette Smoking

Unfortunately, commercial tobacco in the form of cigarettes is used as a substitute for the traditional plant, and AI/AN have the highest cigarette smoking rates of any group in the United States (33). Research has shown that there is no safe level of exposure to tobacco smoke (34). Tobacco smoke contains approximately 7000 compounds, most of which are toxic with 69 reported to cause cancer (34). Low levels of smoke exposure, including secondhand tobacco smoke, cause dysfunction and inflammation of the lining of the blood vessels (34). Crucial carcinogens in tobacco smoke are polycyclic aromatic hydrocarbons (PAHs), arylamines and N-nitrosamines (35). According the 30th Tobacco-related Surgeon General's Report, some chemicals in tobacco smoke are believed to interfere with a female's fallopian tubes increasing the risk for detrimental pregnancy outcomes such as ectopic pregnancy, miscarriage, and restrictive fetal growth (35). Furthermore, Levy et al. assert that there is a doseresponse associated with cigarette smoking and adverse health outcomes, such as respiratory tuberculosis, cancer of the mouth and larynx, chronic bronchitis, emphysema and various cancers especially lung cancer (36, 37).

Although surveillance systems and epidemiological studies show that smoking prevalence is decreasing at a steady rate, the percentage of cigarette smoking is still relatively high (38). As of 2011, the CDC estimated 18.1 percent of students, and 19 percent of adults are current smokers (38). According to the September 2011 issue of the CDC's Mortality and Morbidity (MMWR), in 2010, of the current adult smokers (45.3 million), 78.2% (35.4 million) smoked every day, and 21.8% (9.9 million) smoked some days. More men smoke than women with a prevalence of 21.5% and 17.3%, respectively (38). Non-Hispanic Al/AN had the highest prevalence of cigarette smoking at 31.4%, a prevalence that matches rates of the 1980s which was 33.2% according the CDC (38). Comparing smoking rates between low and high social economic status (SES), the prevalence of smoking was higher among those with a low rather than high SES (39). Amongst all the states, the Midwest had the highest prevalence of smoking, and Utah had the lowest smoking rates (39).

The literature typically categorizes smoking behaviors as very light, light, occasional or heavy (37). Levy et al. researched these categories across demographic characteristics in Massachusetts (37). Light smoking was defined as smoking 10 cigarettes or

fewer per day (half a pack), and was found common among young smokers who might be developing a pattern of smoking. These persons were more educated, had higher incomes and were more likely to be non-White females (37). Very light non-daily smokers (less than five cigarettes) compared to very light daily smokers were better educated and had higher incomes, but did not differ significantly in gender or age. Levy et al. also found that one fifth of U.S. smokers were occasional smokers, defined as smoking on a non-daily basis (37).

Tobacco Industry in AI/AN communities

Tobacco companies have long known about the prevalent use of tobacco in Al/AN communities and have used this to their advantage. Understanding the use of tobacco in cultural ceremonies, tobacco companies have built their credibility and acceptance in these communities through funding social events such as powwows and rodeos (32). These companies' use of cultural symbols and designs that laud Al/AN culture further entice the population to buy their products. For example, tobacco companies have promoted cigarette use by using agreeable images of American Indians smoking a pipe or American Indian warriors endorsing the cigarette brand (32). In addition, tobacco control infrastructures are different in Al/AN communities. Báezconde-Garbanati et al. suggest that this is probably related to the historical and cultural role tobacco has had in these communities and the sovereignty of tribal nations (40). Furthermore, tobacco control policies may not necessarily be implemented in Al/AN tribal communities (40).

Consequently, cigarette sales are shifting from smoke shops and small-town markets to easily accessible and enticing internet websites. A study performed by the University of Minnesota found that cigarettes could be purchased on American Indian–owned Internet sites for one fifth of the price at grocery stores (41). This type of marketing and sales subverts public health policy efforts to mitigate smoking by raising prices. Thirty-five sites, 32% of the 109 sites offering ordering information, accepted non-credit card payments, and 49% of the 109 sites accepted credit cards only with thirteen sites offering other options like personal checks (42). In addition, multiple online retailers claim affiliation with Native American tribes and share in tribal taxfree status (41). Lower tobacco prices makes purchasing cigarettes from American Indian sites more convenient for those bound by the habit. Easy purchase of tobacco could be having an association with the high prevalence of cigarette smoking in AI/AN communities in both males and females in comparison to the general population (41). Unfortunately, cigarette advertising, sales and purchases in AI/AN communities have gone largely unnoticed. Few studies have examined internet cigarette sales and even fewer have examined the marketing tools utilized by American Indian cigarette sales entrepreneurs (41). Interestingly, sales of discounted cigarettes from both online vendors and stores have agitated non-Native retailers and have drawn the attention of state and federal governments due to losses in cigarette excise tax revenue (43). Access to cigarette and tobacco products is now more convenient for AI/AN buyers; they are lower priced, colorful, enticing and appeal to ethnic pride. Above all, cigarette sales are a significant source of income for some tribes and individuals (41).

Maternal Smoking Pre-Pregnancy

Prenatal smoking remains one of the most common preventable causes of poor pregnancy and infant outcomes (44). Tong et al. identified groups with the highest pre-pregnancy smoking prevalence, pre-pregnancy defined as three months before pregnancy (45). This study analyzed 2004 to 2008 data from 186,064 women with recent live births from 32 states and New York City using the Pregnancy Risk Assessment Monitoring System (PRAMS). Pre-pregnancy smoking was defined as self-reported smoking of any amount of cigarettes three months before pregnancy.(45). Tong et al, 2011., observed that among women aged 18 to 24, American Indians had the highest prevalence of pre-pregnancy smoking compared to all other races (55.6% (95% CI: 52.8-58.4)), followed by Alaskan Natives (46.9% (95% CI: 42.8-51.2)). For women 25 years or older, Alaskan Natives and American Indians still had the highest prevalence of pre-pregnancy smoking, 40.4 % (95% CI: 37.8-43.1) and 35.2% (31.5-39.0), respectively. Overall, 47.8% (95% CI: 45.9-49.8) of Alaskan Natives, and 40.45% (95% CI: 37.6-43.3) of American Indians smoked pre-pregnancy. Although pre-pregnancy prevalence estimates were highest for Al/AN women compared to other races, Al/AN did not have the highest proportion of cigarettes smoked per day (45). Tong et al. categorized the number of cigarettes smoked per day as less than 5, 6 to 20, and greater than 20. On average, Hispanic and Al/AN women smoked the most number cigarettes per day. Controlling for maternal education, Medicaid enrollment, parity, pregnancy intention, state of residence, and year of birth, AN, aged 18 to 24, were more likely to smoke three months before pregnancy compared to women 25 years or more (RR: 1.20, 95%CI: 1.09-1.32). Tong et al 2011., mention that their findings suggest that young women of non-Hispanic White, American Indian, or Alaskan Natives who become pregnancy tend to smoke more than those who do not become pregnant (45). This is of concern because women who are pregnant should be deterred from smoking, and these findings point either to a lack of adequate healthcare services to help women cope with pregnancy and the stress it entails or to other unknown factors.

Tong et al. also evaluated the prevalence of pre-pregnancy smoking between 2000 and 2005 in 16 PRAMS states (Alaska, Arkansas, Colorado, Florida, Hawaii, Illinois, Maine, Nebraska, New Mexico, New York [excluding New York City], North Carolina, Oklahoma, South Carolina, Utah, Washington, and West Virginia) (44). Pre-pregnancy smoking in this study was also defined as smoking three months before pregnancy. The study found that the prevalence of smoking during pregnancy varied greatly among states from 6.2% in Utah to 35.7% in West Virginia. Overall, pre-pregnancy smoking decreased between 2000 and 2005 from 22.3% to 21.5% although the change was not significant. In 2005, the prevalence of pre-pregnancy smoking was 29.5% in Alaska, 27.2% in Minnesota, 25.8% Nebraska, 18.8% in New Mexico, 31.6% in Oklahoma, 21.6% in Oregon, 10.2% in Utah and 18.6% in Washington (46).

Although the PRAMS data probably underestimate the prevalence of smoking since it is self-reported, the differences seen among smoking prevalence rates could be due to the varied levels of success of anti-smoking campaigns between states, differences in cigarette taxes, and/or differences in prices. For example, the current price of cigarettes in West Virginia is \$5.07 having increased by one dollar since 2011, while the current price of a pack of cigarettes in Utah is \$6.64 having decreased from \$6.88 since 2011 (47).

According to the 2011 PRAMS data from 24 states, approximately 10% of women reported smoking during the last three months of pregnancy. Of the women who self-reported to have smoked three months before pregnancy, 55% quit indicated that they quit during pregnancy. Among women who quit smoking during pregnancy, 40% relapsed within 6 months after delivery (48). Women

who smoke during pregnancy are less likely to quit, more likely to have a partner who smokes, and more likely to be nicotine dependent (49).

Adverse Infant Outcomes of Cigarette Smoking

Tobacco smoke contains approximately 7000 compounds and many of the toxins to which infants are exposed to in utero or passively have been linked to poor infant outcomes (35). In 1976, a study performed by Bergman and Wiesner observed that of the infants whose mortality was a result of sudden infant death syndrome (SIDS), mothers were more likely to have smoked cigarettes during pregnancy and fathers of SIDS victims were more likely to be smokers (50). In a New Zealand case control study, Michell et al. reported a 1.65 higher odds of SIDS in mothers who smoked compared to those who did not (95% CI: 1.20, 2.28) (51). As the number of smokers in the environment around the infant increased, so did the odds of SIDS (1 household smoker OR: 1.12, 95%CI: 0.77, 1.63; 2 household smokers OR: 1.75, 95% CI: 1.23, 2.48; and 3 or more household smokers OR: 2.07, 95%CI: 1.26, 3.41) (51). Adjusting for maternal age, education, marital status, parity, prenatal care, type of residence (urban/rural) and maternal risk factors such as diabetes, hypertension, preeclampsia and smoking during pregnancy, Hwang et al. found that the odds of having a preterm birth for Al/AN women compared to non-Hispanic, white women was 1.34 times higher (OR 95%CI: 1.25, 1.44) in Washington and Montana (52).

Researchers at King's College Hospital in London conducted a study where they evaluated the relationship between maternal smoking and its association with neonatal intensive care unit (NICU) admission (53). This study looked at Caucasian, Asian, Caribbean, African, Vietnamese-Filipino, and Chinese ethnic groups who gave birth in 2005. The exposure variable was smoking during pregnancy and the outcome variables were birth weight and infant NICU admission. The study showed that more Caucasian women, 34%, indicated that they smoked during pregnancy than any other racial or ethnic group, e.g., Caribbean, 28%, Asian, 7%, African, 5% (53). It was also found that gestational age (OR: 4.7, 95% CI 3.1, 7.3), birth weight (OR: 032. 95%CI: 0.2, 0.4) and parity (OR: 0.84, 95%CI: 0.7, 0.98) were significantly related to NICU admission, but not maternal ethnicity or maternal smoking (53).

Maternal Smoking and Fetal Exposure to Lead

Lead is a nonessential ubiquitous trace metal and cigarettes contain from 16 to 149 ng of lead (54). Possible effects of lead exposure on health include learning disabilities, reduced attention, reduced IQ, retarded growth, hearing implications, and behavioral problems (54). Daily cigarette smoking during pregnancy has been shown to raise lead in cord blood levels in a doseresponse way (55). Low doses of prenatal exposure to lead have shown to be toxic to the cognitive development of the fetus (55). Detrimental effects have been observed at blood lead levels as low as 0.5 to 0.75 µmol/liter (56). In the general population, lead exposure commonly happens from ingesting food, drinking water, through one's occupation and atmospheric contamination (55). In addition, prenatally, the burden of lead stored in maternal bone can be released during pregnancy and contribute to fetal lead exposure since there is no protective barrier between the mother's blood stream and the placenta (56).

Maternal Smoking, Low-Birth Weight and Preterm Birth

In addition to asthma, allergies, and cancer in mothers and infants attributable to smoking tobacco, epidemiological studies have linked maternal tobacco smoking to low birth weight, preterm delivery, congenital anomalies, and small for gestational age for weight (57-60). Investigators have also observed dose response gradients in relation to the number of cigarettes smoked and its association to prenatal adverse effects (60). A combination of these outcomes is closely associated to neonatal and long-term morbidity (61). For example, small for gestational age birth weight increases the risk of developing chronic diseases later in life such as type 2 diabetes, coronary heart disease, and hypertension (62).

In the United States, in 2012, 7.99% of infants were born with low-birth weight (LBW) defined as less than 2500g including 1.42% who were born at very low-birth weight (1500g or less) (63). Low birth weight has been linked to demographic and environmental factors (35); however, tobacco smoking remains the most modifiable risk factor for fetal growth delays or growth retardation. Maternal smoking during pregnancy for heavy smokers results in approximately a 200 gram reduction in the average weight of the infant after adjusting for social class, maternal age, parity and maternal height (64). In regards to a dose-response relationship, studies have shown increased risk of low birth weight and small for gestational age with heavier maternal smoking

(more than 10 cigarettes per day), as well as noting an increased risk for very preterm birth (less than 35 weeks) (65). Surprisingly, smoking 20 cigarettes or more per day has not shown any relation to risk of preterm birth overall (60). This could be due to an adverse effect threshold.

Although adverse health effects on birth weight occur primarily during the last three months of pregnancy, smoking after the fourth month of pregnancy has been reported to have a significant effect in lowering birth weight (62). Infant birth weight also was reported to be higher in mothers who quit smoking during pregnancy than those who did not (62), and has been shown to decrease as the mother's smoking increased, but the differences comparing less than half a pack (1 to 5 cigarettes) and half a pack (6 to 10 cigarettes) per day were not significant (64).

Maternal Smoking and Birth Defects

In addressing birth defects and smoking, much of the literature focuses on how maternal smoking during pregnancy results in fetal death, restricted fetal growth, and prematurity, and centers less on other complications. An altered in utero environment during critical windows in perinatal development influences the risk of later in life health and disease (66). DNA modifications especially by methyl group modifications to cytosine bases adjacent to guanines represent an important form of epigenomic variation during critical windows in development (66). There have been some reports showing changes in the levels of DNA methylation associated with maternal smoking behavior during pregnancy (67). Although the mechanisms are not yet fully understood, they are thought to include the vasoconstrictor action of nicotine causing reduced blood flow to the placenta, carbon monoxide binding to hemoglobin so that less oxygen is available for placental and fetal tissues leading to hypoxia, and disruption of vascular neogenesis (68). Since organ formation occurs at critical periods during small windows during pregnancy (68), the first trimester is an important period when extraneous toxic factors can lead to malformation development, especially of the limbs (69).

For families without a history of birth defects, there is a significant association between maternal smoking and the genotype for the risk of oral cleft palate (70). Hwang et al. found cases of cleft palates and oral cleft palates in mothers who

smoked 10 cigarettes per day (70). Casper et al., in 2013, observed an association between mothers who were exposed to cigarette smoke and higher odds of having infants with limb deficiencies (69). These deficiencies are characterized by the failure in formation or disruption of a portion of the entire upper or lower limbs or digits during fetal development. This process begins as early as four weeks after conception. While clefts and cleft palates are the most studied congenital malformations associated with maternal smoking during pregnancy, there are four other organ systems that could be affected: cardiovascular, muscular, diaphragm and gastrointestinal systems. A meta-analyses done at the University College of London with 173,687malformed cases and 11.7 million controls revealed a 1.09 greater odds for congenital heart defects (No. studies: 19, 95% Cl: 1.00, 2.18), a 1.16 increased risk for musculoskeletal defects (No. Studies: 25, 95% Cl: 1.05, .27) and 1.27 increased risk in gastrointestinal defects (No. Studies: 35, 95%Cl: 1.18, 1.36) among infants born to mothers who smoked during pregnancy compared to those who didn't smoke (68). Ventricular septal defects (VSD) (OR: 1.34, 95% Cl: 1.53, 2.57) and atrial septal defects (ASD) (OR: 1.98, 95% Cl 153, 2.57) showed the strongest association with maternal smoking (68, 71).

Maternal Smoking and NICU Admission

In the United States, 4 million babies are born each year with 15 percent of those born premature (72). Prematurity is defined as less than 37 weeks gestational age (73). Of these, 5 percent are born weighing less than 2 pounds with many requiring specialized care in a neonatal intensive care unit (NICU) (74). Daily NICU costs have been reported to exceed \$3,500 per infant (72). In a CDC MMWR report on state estimates of neonatal health care costs associated with maternal smoking found that smoking attributable neonatal expenditures (SAE) were \$366 million, an estimated \$704 per maternal smoker (75). In the same report, the SAE per maternal smoker for those receiving Medicaid or for those who were uninsured was more than those with private or other insurance (75). For those receiving Medicaid or who were uninsured, the SAE in Alaska was \$543, in Minnesota, it was \$714, in New Mexico, it was \$635, in Nevada, it was \$678, in Oklahoma, it was \$717, in Utah , it was \$587, and in Washington, it was \$610 (75). Adams et al. found that maternal smoking increased the relative risk of admission into a NICU by almost 20 percent, with maternal smoking adding over \$700 in neonatal costs (76).

Maternal Smoking and Social Economic Status

Maternal smoking has also been associated with low social economic status. Smoking during the last trimester of pregnancy has been reported to be exceptionally high for low income women and for women receiving WIC (77). Although infants with low birth weight do catch up to their peers within the first two years of life, growth retardation has shown to be a risk factor for overweight and metabolic syndrome later in life (57). Therefore, many have suggested that smoking cessation services should be integrated into health care settings where women at risk are likely to attend, such as family planning clinics (45). A significant number of smokers reported that their recent births were unintended compared to non-smokers illuminating the need for appropriate contraceptive counseling in addition to cessation services (45).

Smoking and the Affordable Care Act (ACA)

Although the Affordable Care Act (ACA) allows companies to charge tobacco users up to 50 percent more in health care insurance premiums, it does provide incentives to Medicare and Medicaid recipients to complete behavior modification programs (78). In 2004, smoking cost the United States over \$193 billion including \$97 billion in low productivity and \$96 billion in direct health care expenditures, or an average of \$4260 per adult smoker (78). The ACA requires Medicaid to provide coverage for tobacco cessation services for pregnant women (79).

Objective

Given that epidemiological studies have shown that maternal smoking has an association with adverse prenatal outcomes, and that smoking among AI/AN women compared to other racial/ethnic groups is more prevalent, this study aims to evaluate whether pre-pregnancy smoking -- smoking three months before pregnancy -- in AI/AN women is associated with infant admission into a NICU adjusting for maternal characteristics. Therefore, this study seeks to add to the literature addressing the adverse effects of maternal smoking in AI/AN women.

CHAPTER II: MANUSCRIPT

EVALUATING THE ASSOCIATION BETWEEN MATERNAL SMOKING THREE MONTHS BEFORE PREGNANCY AND INFANT ADMISSION INTO A NEONATAL INTENSIVE CARE UNIT AMONG AMERICAN INDIAN AND ALASKAN NATIVES IN 8 STATES

Agasha Katabarwa

INTRODUCTION

Prenatal smoking remains one of the most common preventable causes of poor pregnancy and infant outcomes (44). Although the prevalence of smoking has decreased over recent years, AI/AN women still have significantly higher rates of smoking than the general population (33). Compared to the general population, 29.6% (95 %CL: 27.1, 32.3) AI/AN women smoke during pregnancy as compared to 19.5% (95% CL: 19.3, 19.7) in the general population (33). Tobacco has been linked to adverse health outcomes in both adults and infants (35, 79). Exposure to cigarette toxins in utero has been linked to poor infant outcomes, including low birth weight, preterm delivery, congenital anomalies and small for gestational age, all of which typically lead to a neonatal intensive care unit (NICU) admission (57-60). In a study done by Butler et al. in 2000, maternal smoking during pregnancy for heavy smokers results in approximately a 200 gram reduction in the average weight of the infant after adjusting for social class, maternal age, parity and maternal height (64). Studies have shown increased risk of low birth weight and small for gestational age with heavier maternal smoking (more than 10 cigarettes per day), as well as noting an increased risk for very preterm birth (less than 35 weeks) (65). However, , in at least one study NICU admissions were not associated with maternal smoking (53). Researchers at King's College Hospital in London evaluated the association between maternal smoking and NICU admission among Caucasian, Asian, Caribbean, African, Vietnamese-Filipino and Chinese women. This study found that only gestational age (OR: 4.7, 95%CI 3.1, 7.3), birth weight (OR: 0.32, 95%CI: 0.2, 0.4), and parity (OR: 0.84, 95%CI: 0.7, 0.98) (53).

Women who smoke prior to pregnancy may continue to smoke during pregnancy. Tong et al. reported that approximately 1 in 2 women who smoked during the 3 months pre-pregnancy, aged 18 to 24 years of non-Hispanic white, American Indian or Alaskan Native ethnicity, continued to smoke during pregnancy (45). Given that maternal smoking during pregnancy has been

associated with poor infant outcomes, this study seeks to investigate the relationship between pre-pregnancy smoking among AI/AN women and infant admission into NICU in 8 U.S. states: Alaska, Minnesota, Nebraska, New Mexico, Oklahoma, Oregon, Utah and Washington.

METHODS

Specific Aim

The specific aim of this study is to evaluate the association between maternal smoking three months before pregnancy among American Indian and Alaskan Native (AI/AN) women and infant admission into a NICU using data from the Pregnancy Risk Assessment Monitoring System (PRAMS) during 2004-2011 in 8 states: Alaska, Minnesota, Nebraska, New Mexico, Oklahoma, Oregon, Utah and Washington during 2004 to 2011.

Hypothesis: AI/AN mothers from 8 states who smoked three months pre-pregnancy will be at greater risk for having an infant admitted into NICU.

H₀: Maternal pre-pregnancy smoking has no association with infant admission into a NICU.

H_A: Maternal pre-pregnancy smoking is associated with increased infant admission into a NICU.

Data

Data were obtained from the Centers for Disease Control and Prevention (CDC) Pregnancy Risk Assessment Monitoring System (PRAMS) from Phase 5 and 6 which include years 2004 through 2011. PRAMS is a population-based surveillance questionnaire of maternal behaviors and experiences before, during and after pregnancy in 40 currently participating states. It is conducted both at state and local health departments in collaboration with the CDC. Each participating state samples between 1300 and 3400 women per year. Women from smaller, higher risk populations are sampled at a higher rate. Monthly, stratified samples of 100 to 300 new mothers are selected systematically from recent birth certificates from each state, and mothers are sent a self-administered questionnaire to complete two- to three-months after the delivery of a live infant. Subjects who do not respond are sent two additional questionnaires of the same content. If they do not respond, they are telephoned to complete the survey. To minimize recall bias, efforts to contact the women ends at nine months after delivery. The weighted data represent all live births delivered in each respective site in the given year. Data from infant birth certificates are also linked to these data.

Study Design

A case-control design was employed in this study. The design used a cross-section of PRAMS data collected from 2004-2011 from a cohort of AI/AN women pooled across 8 states. Cases were singleton births without birth defects, born in a hospital setting and admitted to an NICU prior to hospital discharge. Controls were singleton births without birth defects who were not admitted to an NICU. The exposure was tobacco use three months before pregnancy and the outcome of interest was baby's NICU admission. The study sample included those states with a 5% or greater proportion of AI/AN births in the PRAMS sample for each year, 2004 through 2011 (80). These states included Alaska, Minnesota, Nebraska, New Mexico, Oklahoma, Oregon, Utah and Washington. For Minnesota, Nebraska, Oklahoma, Oregon, Utah and Washington, data were available for years 2004 to 2011. Alaska contributed years 2004 through 2010, and only years 2004, 2005, and 2011 were available for New Mexico. The total sample size was 95,428 individuals. After plural births (n = 3,301), infants not born in a hospital (n = 3,003), and those with birth defects (n = 1,509) were excluded, 84,166 individuals remained. The analytic sample was further constrained to include only the 10,941 Al/AN women (14.21%) of the 84,166. Of these Al/AN women, 4,971 (46.18%) smoked three months pre-pregnancy and 1,558 (14.38%) had an infant admitted into NICU (Figure 1).

Measures

Exposure: Maternal Smoking 3 months Pre-Pregnancy

Although maternal smoking status is included on both the birth certificate and in PRAMS, maternal smoking three months before pregnancy was ascertained from the PRAMS data only. Further, the number of cigarettes smoked three months before pregnancy was ascertained from the PRAMS questionnaire. Here, mothers responded 'Yes' or 'No' to whether they smoked cigarettes three months before pregnancy. If they responded 'Yes', they were directed to a question that asked how many cigarettes they smoked per day. Number of cigarettes smoked per day was grouped by pack size. The categorical grouping was: 41 or more cigarettes (more than 2 packs), 21 to 40 cigarettes (2 packs), 11 to 20 cigarettes (1 pack), 6 to 10 cigarettes (half a pack), 1 to 5 cigarettes (less than half a pack), and none. In addition, the number of cigarettes smoked per day was grouped into two categories, heavy smokers vs. light and non smokers. Those who smoked two packs or more a day were defined as heavy smokers and those who smoked less than half a pack to one pack a day were defined as light smokers. For this study, maternal smoking 3 months pre-pregnancy was defined in two ways; 1. Yes vs. No and 2. Heavy smokers vs. Light and non smokers.

Outcome: Infant Admission into the NICU

Admission into the NICU was obtained from the Morbidity section of the PRAMS survey which inquired whether the infant was placed in the intensive care unit after birth. Mothers indicated 'Yes', 'No' or 'I don't know'. Those who indicated 'I don't know' were coded as missing.

Covariates

Age

Based on preliminary examination of the data, maternal age categorized by <25 years and <u>></u>25 years was associated with NICU admission. Mothers younger than 25 years were the referent group.

Educational Level Obtained

Maternal education was defined dichotomously as college level or less (\leq 16 years) or greater than a college level education (> 16 years). According the literature, smoking differs with relation to educational level attained. Individuals with a college level or less, smoke more than those who have more than college level education (81). Mothers with an educational level greater than 16 years were the referent group.

Early Prenatal Care (PNC)

Early entry into prenatal care was also a dichotomized variable, defined as first prenatal care visit (PNC) at or before 5 months of pregnancy being early and first prenatal care visit after 5 months of pregnancy or no prenatal care as late. Those who had early PNC were the referent group.

Body Mass Index (BMI)

BMI is a measure of body fat based on height and weight. It is calculated by dividing weight by the square of the height.... The standard categorizations for body mass index (BMI) were used: less than 18.5 (Underweight), 18.5 to 24.9 (Normal weight), 25 to 29.9 (Overweight) and greater than 30 (Obese). BMI scores less than 12 or greater than 84 were considered implausible, and therefore, set to missing. In the analysis those who were underweight, were used as the reference group.

Income/Federal Poverty Level (FPL) and Family Size

Income level was defined as 138% above or below the federal poverty level. Income level was calculated using family size and median income for each state. Family size was calculated using the number of dependents plus the infant born. SUDAAN code to calculate federal poverty level was obtained from the CDC PRAMS office. To determine FPL, first, the family size was calculated using the number of income dependents plus the new infant. A midpoint was assigned to the income categories: less than \$10,000, \$10,000-\$14,999, \$15,000 to \$19,999, \$20,000 to \$24,999, \$25,000 to 34,999, \$35,000 to \$49,999, \$50,000 to \$74,999 and \$75,000 or more. The income midpoint was then used to calculate the poverty cutoff percentage by family size.

Prematurity

A clinical estimate of gestational age was used to classify whether an infant was preterm or not. Preterm is defined as less than 37 weeks gestation. Term births were defined as a birth between 37 and 42 weeks, and post-term births, those 43 weeks and after, were set to missing and omitted from the analysis. Infants with term births were the reference group.

Small for Gestational Age

Small for gestational age (SGA), which gauges whether an infant is the appropriate size for his/her gestational age, was determined using the 10th percentile guidelines (83). These guidelines do not make a distinction between babies who are naturally small and those who are small due to growth restriction (82). Infants that were not SGA were considered the reference group. Figure 3 in the Appendix illustrates the guidelines (83).

Infant Length of Stay (LOS)

Infant length of stay in the hospital was grouped into two categories: those who stayed less than or equal to two days and those who stayed for three days are more in the hospital. Infant length of stay less than or equal to two days was the reference group.

Directed Acyclic Graph (DAG)

A Directed Acyclic Graph (DAG) was constructed to evaluate the main hypothesis as well as the covariates on the effects of smoking three months pre-pregnancy among AI/AN women on having an infant admitted into a NICU. According to the literature, maternal age, race/ethnicity, prematurity and SGA are associated with both smoking during pregnancy and infant NICU admission (44, 76, 84-86). De Jongh et al, 2012, performed a study evaluating the differential effects of maternal age, race/ethnicity and insurance on neonatal intensive care unit admission rate. In this study, including 167,160 births, mothers who were 35 years to 49 years had the highest percentage of NICU admissions compared to those who were 14 to 34 years old (86). The percentage of NICU admissions also differed by race/ethnicity. Overall, African American / Black mothers had a higher percentage of NICU admissions and Hispanic mothers had the least percentage, with race/ethnicity categories being white/Non-Hispanic, Black/Non-Hispanic and Hispanic (86). In this study, having private insurance was a determining factor to whether and infant was in NICU or not. For those mothers who had private insurance, their infants were less likely to have an NICU Admission except for Black/Non-Hispanic mothers of whom ownership of private insurance increased the risk for NICU admission (86). The literature is also informative in regards to maternal education level and smoking. Fagan et al. 2009, in their article entitled, "Light and intermittent smoking: The road less traveled," speak of smoking habits differing by education level. Those with a higher level of education smoke less than those with a lesser level of education (81). Because smoking habits differ with respect to race/ethnicity, maternal age, education and income level which leads to poor infant outcomes such as prematurity and SGA which in turn have an association with NICU admission all these covariates were included as potential confounders (Figure 2).

Analyses

All analyses were conducted using SAS version 9.4 (SAS Institute, Inc. Cary, North Carolina) and SUDAAN version 11 (Research Triangle Institute, Research Triangle Park, North Carolina) to account for the complex survey design of PRAMS, and in all analyses, the alpha level of 0.05 was used to determine statistical significance.

Descriptive analysis was conducted to ascertain prevalence estimates of pre-pregnancy smoking and infant NICU admission in AI/AN women pooled across all 8 states (Alaska, Minnesota, Nebraska, New Mexico, Oklahoma, Oregon, Utah and Washington). In addition, summary statistics describing the number of cigarettes smoked by AI/AN women was performed. Additional statespecific descriptive analyses were run to enable a comparison of pre-pregnancy smoking and NICU admission among the states.

An unadjusted odds ratio (OR) was calculated using the Pearson's chi-square test to analyze the association of prepregnancy smoking (exposure) and infant NICU admission (outcome). Bivariate logistic regression analyses were used to test the association of NICU admission and selected covariates. The same procedure was employed to assess the association between the exposure, pre-pregnancy smoking and the selected covariates. Covariates that were statistically associated with both the outcome and the exposure were included in the logistic regression model except for education level, which strongly correlated to FPL and preterm birth which was correlated with SGA after running a Pearson correlation test. To assess whether the number of cigarettes smoked per day three months before pregnancy among AI/AN women was associated with infant NICU admission, additional bivariate analyses were performed to obtain unadjusted and adjusted odd ratios (ORs).

To obtain and better illustrate a logistic model, variable specification from the literature was used. Variables identified as confounders of the association between maternal smoking and NICU or maternal smoking and preterm birth were included in the DAG. In addition to a DAG (Directed Acyclic Graph), stratified analyses and backwards elimination methods were also used to identify potential confounders. Confounding was determined to be present if the covariates changed the association of smoking 3 months pregnancy and NICU admission by 10% or more. In addition, covariates that were associated with both the pre-pregnancy smoking (exposure) and infant NICU admission (outcome) through stratified analysis were determined confounders.

DAG was utilized to support the stratified analysis. Since income and educational level are often used to assess social economic status (SES), a Pearson correlation coefficient revealed that these two variables were moderately correlated (r = 0.45, p-value = <0.0001), and income was associated with both the exposure and the outcome, while education was only associated with the exposure, and therefore income level was retained in the model. The final logistic regression model was applied controlling for the following potential confounders to obtain adjusted estimates: maternal age, BMI, income level and SGA. An additional logistic regression model was run controlling for maternal age, BMI, FPL and SGA to obtain adjusted OR estimates assessing whether the amount of cigarettes smoked pre-pregnancy, dichotomized as heavy smokers vs. light and non smokers, was associated with NICU admission.

RESULTS

Sample Characteristics

Of the original 95,428 women in the PRAMS dataset from 2004 to 2011, 12,448 (14.22%) women self-identified themselves as AI/AN (14.21%). Of those, 1,507 women were excluded because they did not have an infant born in a hospital, or had an infant with a birth defect. One hundred seventy-six (176) AI/AN women were missing pre-pregnancy smoking data and 110 were missing infant NICU admission data, and were excluded from the analyses. After the exclusion criteria were applied, 10,941 women remained in the analytic sample. Figure 1 shows the sample construction.

Descriptive Statistics

The final sample is comprised of 10,941 Al/AN women who had a singleton birth in a hospital setting without any birth defect. Of those, 4,971 (43.89%) smoked three months before getting pregnant and 1,558 (9.59%) had an infant admitted to the NICU, while 5,812 (56.11%) did not smoke three months before pregnancy and 9,273 (90.41%) did not deliver an infant requiring NICU admission. Table 1 summarizes the descriptive statistics for the overall study population, for the covariates as well as by prepregnancy smoking status (exposure) and NICU admission (outcome). Overall, there was a higher percentage of Al/AN women who were 24 years and younger (51.45%), who had a lower than college level education (91.63%), who entered prenatal care 5 months or earlier (90.30%), were of normal BMI (42.23%), who lived 138% under the FPL (71.51%), and who did not have a preterm infant (91.30%), an SGA infant (91.83%) or an infant who stayed two days or less in the hospital (63.04%). Note that pregnancy smoking, maternal age, education, prematurity, SGA and Infant LOS were missing for less than 5% of the data while early entry into prenatal care (7.62%), BMI (5.33%), and FPL (8.92%)were missing for more than 5% of the data.

Bivariate Logistic Regression

Table 2 reports the crude OR and 95% CI for the main exposure, smoking three months pre-pregnancy and the outcome, NICU admission. Although there was no significant association for the exposure (pre-pregnancy smoking) and outcome (NICU

admission), the crude odds ratio (crude OR=1.12) indicates a slight trend that women who smoked pre-pregnancy were more likely to have an infant admitted into the NICU.

The Association between NICU Admission (Outcome) and Covariates

Table 2a summarizes the crude, unadjusted ORs and 95% CI for the NICU admission (outcome) and each independent variable. There were no significant associations in the odds of being admitted into a NICU for maternal age, BMI, education level, or early PNC. However, FPL under 138%, prematurity, SGA, and infant LOS revealed significant ORs. Mothers who were living 138% under the FPL were 1.31 times as likely to have an infant in the NICU (95% CI: 1.00, 1.72). In comparison to term births, preterm babies were 10.92 times as likely to be admitted (95% CI: 8.39, 14.17), and SGA infants were also more likely to be admitted into the NICU compared the non SGA infants (OR: 1.87, 95% CI: 1.32, 2.65). Infants who stayed three or more days in the hospital were 8.11 times as likely to be admitted in to the NICU compared to those who stayed two or less (95% CI: 5.80, 11.34).

The Association between Maternal Smoking Three Months before Pregnancy (Exposure) and Covariates

Table 2b summarizes the crude, unadjusted ORs and 95% CI for smoking three months pre-pregnancy (exposure) and each independent variable among AI/AN women. There were no significant associations in the odds of smoking three months pre-pregnancy for prematurity and SGA. However, all other covariates revealed significant ORs. Mothers who were 25 years of age or older were less likely to smoke three months pre-pregnancy (OR: 0.64, 95% CI: 0.54, 0.75). The association between maternal smoking three months before pregnancy and BMI was statistically significant for all BMI classifications. Mothers who were classified as normal, overweight and obese were less likely to smoke three months pre-pregnancy in comparison to those who were underweight (normal: OR: 0.47, 95% CI: 0.29, 0.76); (overweight: OR: 0.49, 95% CI: 0.30, 0.80); and (obese: OR: 0.45, 95% CI: 0.28, 0.73). Mothers who had an college education level or less were 5.60 as likely to smoke three months pre-pregnancy than those who had greater than a college level education (95% CI: 3.87, 8.10). Mothers living 138% below the federal poverty level (FPL) were 2.28 times as likely to smoke than those living 138% above the FPL (95% CI: 1.89, 2.75). Those who entered prenatal care after 5 months were also more likely to smoke three months pre-pregnancy (OR: 1.32, 95% CI: 1.01, 1.72) compared to those

who entered early (5 months or earlier). Lastly, infants who stayed three or more days in the hospital were 1.22 times as likely to have a mother who smoked three months before pregnancy compared to those who stayed 2 or less days (95% CI: 1.03, 1.43).

The Association between the Number of Cigarettes Smoked Three Months before Pregnancy (Exposure) in AI/AN

women and Infant Admission into the NICU (Outcome)

For those 4,971 women who reported the number of cigarettes smoked three months before pregnancy, 85.88% reported smoking 1 pack or less per day, while 8.65% reported smoking more than 1 pack/day (Table 3a). While there was no significant association in the odds of the number of cigarettes smoked per day among all categories (41 cigarettes or more, 21 to 40 cigarettes, 11 to 20 cigarettes, 6 to 10 cigarettes, 1 to 5 cigarettes and less than 1 cigarette) and NICU admission (Table 3b), the association of 3 months pre-pregnancy smoking in women who smoked more than one pack a day (21 cigarettes or more; i.e., heavy smokers) and NICU was 1.25 times that of those who smoked less than a pack a day, although this effect was not statistically significant (95% CI: 0.62, 2.52; p-value: 0.540) (Table 3c).

Logistic Regression Analysis

Two regressions models were performed to assess the relationship between maternal smoking three months prepregnancy and infant NICU admission. Table 4a and 4b show the initial and final logistic regression models, respectively, using smoking three months pre-pregnancy as the primary exposure. Another set of logistic regressions were also conducted using the number of cigarettes smoked per day, and these results are reported in Table 5a and 5b showing both initial and final logistic regression models. For both models, control variables included maternal age, maternal BMI, income level (FPL) and SGA.

Model 1 - Maternal Smoking Three Months Pre-Pregnancy as Primary Exposure Variable

Logistic Regression Model:

Initial Model: Table 4a describes the characteristics of the initial model for exposure (smoking three months pre-pregnancy) and outcome (NICU admission). The proportion of NICU admissions in the initial model was slightly higher among women who smoked three months pre-pregnancy although the result was not statistically significant [OR=1.09, 95%CI: (0.77, 1.53)]. The logistic

regression initial model assessed whether the NICU admission could be predicted from a set of independent potential factors including maternal age, BMI, education level, income level (FPL), early pre-natal care, prematurity and SGA. After controlling for a full set of variables, backward elimination was used to reduce the set of predictor variables to the minimum number necessary that accounts for nearly as much of the variance as was accounted for in the initial full model. However, backwards elimination removed all of the variables except prematurity and SGA, and so, a model based on the literature, the stratified analysis between exposure and outcome, supported by the DAG was constructed. A total of 8,197 Al/AN mothers were included in the initial logistic analysis resulting in 25% missing. The initial model retained 1,070 Al/AN women who smoked pre-pregnancy and 7,127 as non smokers. Only FPL, prematurity and SGA were found to be statistically associated with NICU admission.

Logit P (NICU) = -4.03 + 0.02 (Smoking three months before pregnancy) + 0.12 (Maternal Age) + 0.13 (Normal BMI) + 0.19

(Overweight BMI) + 0.29 (Obese BMI) - 0.37 (Education) + 0.38 (FPL) + 0.06 (Early PNC) + 2.10 (Prematurity) + 0.72 (SGA) **Final Model:** Table 4b describes the final model based on a total of 9,026 AI/AN women were included in the analysis: 1,174 smokers and 7,852 non smokers; 17.5% of the data was missing. Adjusting for maternal age, BMI, income level and SGA, the association between maternal smoking three months pre-pregnancy and infant NICU admission was not statistically significant (OR: 1.05, 95% CI: 0.79, 1.40) (Table 4b). The adjusted ORs for the relationship between maternal age, BMI and income level were not statistically significant. SGA was statistically associated with infant NICU admission. SGA infants had a 2.02 higher odds of admission into the NICU compared to those who were not SGA (95% CI: 1.38, 2.96).

Logit P (NICU) = -2.67 + 0.05 (Smoking three months pre-pregnancy) + 0.20 (Age) – 0.14 (Normal BMI) – 0.02 (Overweight BMI) – 0.02 (Obese BMI) + 0.32 (FPL) + 0.71 (SGA)
Model 2 – Heavy vs. Light and Non Smoking 3 months Pre-Pregnancy

Logistic Regression Model:

Initial Model: Table 5a describes the initial model based on a total of 3,967 AI/AN women included in the analysis: 557 smokers and 3,410 light and non smokers. Adjusting for maternal age, BMI, income level and SGA, the proportion of maternal heavy smoking three months pre-pregnancy and infant NICU admission was 1.31 times that of light and no maternal smoking three months pre-pregnancy, although the effect was not statistically significant (95% CI: 0.52, 3.29) (Table 5a). The adjusted ORs for the relationship between maternal age, BMI and income level, education and early prenatal care with infant NICU admission were not statistically significant. Nevertheless, preterm and SGA were significantly associated with infant NICU after controlling for all other covariates. Preterm infants were 7.53 times as likely to be admitted into the NICU than those that were term (95% CI: 4.69, 12.08). SGA infants had a 2.52 higher odds of admission into the NICU compared to those who were not SGA (95% CI: 1.31, 4.84).

Logit P (NICU) = -3.70 + 0.27 (heavy smokers) + 0.01 (Age) +0.80 (Normal BMI) + 0.72 (Overweight BMI) +0.60 (Obese BMI) + 0.25 (Education) + 0.18 (FPL) - 0.26 (Early Prenatal Care) + 2.02 (Preterm) + 0.92 (SGA)

Final Model: Table 5b describes the final model of heavy maternal smoking pre-pregnancy and infant NICU admission. This analysis included 4,391 observations. Adjusting for maternal age, BMI, income level and SGA, the association between heavy maternal smoking three months pre-pregnancy and infant NICU admission was not statistically significant (OR: 1.39, 95% CI: 0.67, 2.86) (Table 5b). The adjusted ORs for the relationship between maternal age, BMI and income level were not statistically significant. SGA was statistically associated with infant NICU admission. SGA infants had a 2.01 higher odds of admission into the NICU compared to those who were not SGA (95% CI: 1.13, 3.58).

Logit P (NICU) = - 2.76 + 0.33 (heavy smokers) + 0.08 (Age) + 0.47 (Normal BMI) +

0.35 (Overweight BMI) - 0.20 (Obese BMI) + 0.08 (FPL) + 0.70 (SGA)

Analysis in the Appendix

In the Appendix are state-specific descriptive analyses of smoking three months pre-pregnancy and Infant NICU admission with weighted percentages. Table 6a presents the summary statistics of three months pre-pregnancy smoking. Among the 4,971 AI/AN women who smoked pre-pregnancy, Alaska had the highest number of smokers (1432) and Utah the least (56). In all the states, mothers who didn't have an infant admitted into NICU, were 24 years or less, had sixteen years of education or less, lived 138% above the FPL, had early prenatal care, had a term birth, had a non SGA birth and had an infant who spent two days or less in the hospital had a higher prevalence of maternal smoking three months pre-pregnancy. In regards to BMI, in all states, mothers who were underweight (<18.5 BMI) smoked less than those who were of normal weight, overweight or obese. Mothers with a normal BMI (18.5 to 24.9 BMI) smoked more than all the other categories of BMI (AK: 41.94%, MN: 32.73%, NE: 42.91%, NM: 49.84%, OK: 43.84%, OR: 41.93%, UT: 38.68%, and WA: 41.42%).

Table 6b presents state-specific summary statistics of the 1,558 AI/AN women whose infants were admitted into the NICU. Alaska had the most number of infants admitted into the NICU (456), and New Mexico and Utah had the least (47 and 39, respectively). Mothers who smoked 3 months pre-pregnancy had a higher percentage of infant NICU admissions especially in New Mexico and Utah where mothers who smoked 3 months pre-pregnancy had fewer infant NICU admissions. In New Mexico, there were 10 mothers who smoked (24.51%) and had an infant admitted in the NICU and 36 mothers who did not smoke (75.49%) and whose infants were admitted into the NICU. In Utah 11 mothers smoked pre-pregnancy (26.45%) and had an infant admitted in the NICU and 27 did not smoke pre-pregnancy (73.55%) whose infants were admitted in the NICU. In all states, mothers who had 16 or less years of education, lived a 138% above the FPL, had early prenatal care, had term birth, had an SGA infant and had an infant who had stayed 3 days or more in the hospital had a higher prevalence of infant NICU admission than mothers who had more than 16 years of education, lived 138% under the FPL, had late entry into prenatal care, had preterm birth, a non SGA infant and an infant who had two days or less in the hospital.

DISCUSSION

Mothers who smoked three months pre-pregnancy were 1.12 times as likely to have their infant admitted into the NICU although this association was not statistically significant (Table 4b). When the number of cigarettes smoked pre-pregnancy per day was dichotomized into heavy smokers and light and non-smokers, mothers who were heavy smokers were 1.39 times as likely to have their infant admitted into the NICU, though this was not statistically significant (Table 5b). All covariates adjusted for in the models like maternal age, all categories of BMI and income level were not statistically associated with infant NICU admission. Only SGA was statistically associated with infant NICU. Interestingly, although maternal smoking is a known risk factor for preterm births and having a SGA infant (65), which contribute to infant NICU admission, pre-pregnancy smoking itself was not significantly associated with NICU admission.

These results are in congruency with Rao et al., 2008 who also found no association between maternal smoking and NICU admission, but found an association between maternal smoking and gestational age, birth weight and parity (OR: 4.7, 95% CI 3.1, 7.3, OR: 032. 95% CI: 0.2, 0.4, OR: 0.84, 95% CI: 0.7, 0.98 respectively) (53). Rao et al., suggest that their study subjects could have admitted to smoking less cigarettes than they actually do, weakening some of the associations between maternal smoking and adverse infant outcomes. This could be the case in this study, there were a significantly larger number of mothers who smoked less than two packs a day than those who smoked two or more packs a day. A lack of accurate self-reporting of the quantity of cigarettes smoked might be reflected in the weak association between pre-pregnancy smoking and NICU admission. The lack of a significant association between pre-pregnancy smoking and NICU admission (87, 88). Therefore, maybe if there were more mothers in the study who were 45 years or older, smoking pre-pregnancy might have compounded the association with NICU admission.

Although pre-pregnancy smoking was not significantly associated with NICU admission, smoking cessation and public health interventions targeting young mothers should still be funded. Younger mothers had a higher prevalence of pre-pregnancy

smoking than older mothers. Tong et al 2011, suggests that mothers who were pregnant were more likely to smoke than those who were not pregnant (45). This suggestion could be due to the fact that these mothers who were more likely to smoke were younger and therefore had more stress about pregnancy. These younger mothers could also have had a higher prevalence of unintended pregnancies, resulting in the lack of quitting smoking three months before pregnancy.

Tong, et al. notes that more pregnant smokers were identified on the PRAMS questionnaire than on the birth certificate, which is based on women reporting smoking to their health care provider (45). This suggests that women were more likely to report smoking through a confidential survey. Nevertheless, because PRAMS data is self-reported, it is subject to recall bias. Mothers might not have been able to accurately remember how many cigarettes they smoked three months before pregnancy, or when they started prenatal care. There might also have been error in accurately reporting SGA. This study also excluded mothers who did not give birth in a hospital, leading to selection bias. Mothers who did not give birth in a hospital, leading to selection bias. Mothers who did not give birth in a hospital could have a significant difference in prevalence of smoking and infant outcomes like preterm births and SGA. Also, because this study only included categorical variables and not continuous variables, associations between pre-pregnancy smoking and infant NICU admission could have been masked and might have been easily seen with covariates being continuous and pre-pregnancy smoking being denoted by the number of cigarettes smoked instead of number of packs. However, even when we tested the extremes in smoking, heavy vs. light, there was no significant association of pre-pregnancy smoking and NICU admission.

CHAPTER III: PUBLIC HEALTH IMPLICATIONS AND FUTURE DIRECTION

Preventing tobacco use is the single most preventable cause of death in the United States (89). According to Health People 2020, about 443,000 of deaths are attributable to tobacco-related illnesses. For each tobacco mortality death, 20 more people suffer with a morbidity caused by tobacco exposure. Although, maternal pre-pregnancy smoking was not significantly associated with infant NICU admission in Al/AN women in this study, it was significantly associated with SGA. Multiple interventions have been set in place to reduce tobacco exposure. Healthy people 2020 suggests that to end the tobacco use epidemic, tobacco control programs have to be fully funded, the price of tobacco products has to be increased, more smoke-free policies must be adopted, a reduction in tobacco advertising and promotion has to occur, and more anti-tobacco media campaigns in addition to more tobacco cessation programs assisting users to quit must be put into place (2). For Al/AN populations, these interventions are more difficult owing to the special circumstances of tribal laws. Observing the prevalence rates of smoking in this study and comparing them to the recent cigarette tax rates in the states, Alaska \$2.00, Nebraska, \$0.64, Minnesota \$2.83, Oregon \$ 1.31, Oklahoma \$1.03, New Mexico \$ 1.66, Utah \$1.70 and Washington \$3.025, cigarette tax rates are not proportional to prevalence rates. This suggests that cigarette tax rates are not solely enough to reduce smoking rates for Al/AN people who have access to untaxed, online purchases.

A study performed by Bock et al., evaluated smoking behavior and risk perception among the parents of infants in the NICU and found that although about half of the parents reported a health provider inquiry of their smoking status, only one-third were reported being advised to quit and a smaller percentage reported being offered assistance for quitting (90). Moving forward, the National Cancer Institute's 5As should be implemented; ASK, ADVISE, ASSESS, ASSIST and ARRANGE. Health care providers need to ask mothers about their smoking status, then education on the dangers of smoking and advantages of cessation should be clearly explained. It is also important to assess past and current levels of smoking and willingness to stop smoking or resistance to quitting. Counseling and/or referral should be offered following up with positive reinforcement and assessment of barriers to

successful smoking cessation (91). Low income smokers also have multiple stressors therefore need more social support services, not only for encouraging cessation, but also for maternal and infant outcomes (92).

Future studies should be performed including other risk factors for pre-pregnancy smoking like marital status, unintended pregnancy, first time mothers and enrollment in Medicaid and/or Women, Infants and Children Program (91). The analysis should also include continuous variables for covariates because categorizing continuous variables might mask associations.

REFERENCES

- 1. United States Immigration to 1965. In: History.com. <u>http://www.history.com/topics/united-states-immigration-to-1965</u>.
- 2. Thornton R. American Indian Holocaust and Survival: A Population History Since 1492: University of Oklahoma Press; 1987.
- 3. WHO | Broader impacts of household energy. In: WHO. <u>http://www.who.int/indoorair/impacts/en/</u>.
- 4. Long History of Treaties between Native Americans and the U.S.

http://www.nebraskastudies.org/0700/frameset_reset.html?http://www.nebraskastudies.org/0700/stories/0701_0143.html.

5. Cleveland signs devastating Dawes Act into law — History.com This Day in History — 2/8/1887. In: History.com.

http://www.history.com/this-day-in-history/cleveland-signs-devastating-dawes-act-into-law.

- 6. Bureau USC. American Indians: Census Facts | Infoplease.com. <u>http://www.infoplease.com/spot/aihmcensus1.html</u>.
- 7. The many Indian reservations across the US. <u>http://www.indians.org/articles/indian-reservations.html</u>.
- 8. Health CsOoM, Health E. CDC American Indian Alaska Native Populations Racial Ethnic Minorities Minority Health.

http://www.cdc.gov.proxy.library.emory.edu/minorityhealth/populations/REMP/aian.html.

9. Harrison RL, Veronneau J, Leroux B. Effectiveness of maternal counseling in reducing caries in Cree children. J. Dent. Res. 2012;

91(11):1032-7. doi:10.1177/0022034512459758

- 10. American Indians and Alaska Natives. In: U.S. Department of the Interior. <u>http://www.doi.gov/tribes/index.cfm</u>.
- 11. Information USCBP. Facts for Features: American Indian and Alaska Native Heritage Month: November 2013 Facts for Features &

Special Editions - Newsroom - U.S. Census Bureau.

http://www.census.gov/newsroom/releases/archives/facts_for_features_special_editions/cb13-ff26.html.

12. Fernald LCH, Gertler PJ, Neufeld LM. 10-year effect of Oportunidades, Mexico's conditional cash transfer programme, on child growth, cognition, language, and behaviour: a longitudinal follow-up study. Lancet. 2009; 374(9706):1997-2005. doi:10.1016/S0140-6736(09)61676-7

13. List of Federal and State Recognized Tribes. In: National Conference of State Legislatures. 2013. <u>http://www.ncsl.org/research/state-</u>

tribal-institute/list-of-federal-and-state-recognized-tribes.aspx#nm.

- 14. History. In: Official Site of the Navajo Nation. 2011. <u>http://www.navajo-nsn.gov/history.htm</u>.
- 15. Navajo Indian Tribe History. <u>http://www.navajoindian.net/navajo-indian-tribe-history/</u>.

- 16. Navajo I. Navajo Culture | Navajo Indian Culture and Traditions. 2014. <u>http://www.navajoindian.net/navajo-culture-and-traditions/</u>.
- 17. WGBH American Experience . U.S. Grant: Warrior | PBS. In: American Experience.

http://www.pbs.org/wgbh/americanexperience/features/general-article/grant-mexican-american-war/.

- 18. Discover Navajo Navajo Nation Culture, Tourism, Native American Information. <u>http://www.discovernavajo.com/</u>.
- 19. Hodge FW. Cherokee Tribe. In: The Handbook of American Indians North of Mexico. Burea of American Ethnology, Government Printing Office. 2012. http://www.accessgenealogy.com/native/cherokee-tribe.htm.
- 20. Cherokee Ancestry Search Cherokee Genealogy by City ePodunk.com. http://www.epodunk.com/ancestry/Cherokee.html.
- 21. SIOUX INDIAN TRIBE FACTS. http://native-american-indian-facts.com/Great-Plains-American-Indian-Facts/Sioux-Indian-Tribe-

Facts.shtml.

- 22. Sioux Indians. <u>http://www.sonofthesouth.net/union-generals/sioux-indians/sioux-indians.htm</u>.
- 23. Home | Alaska Native. http://www.alaskanative.net/.
- 24. Langdon S. PBS Harriman: Alaska Native Communities. <u>http://www.pbs.org/harriman/1899/native.html</u>.
- 25. Manson SM, Beals J, Klein SA, et al. Social epidemiology of trauma among 2 American Indian reservation populations. American journal

of public health. 2005; 95(5):851-9. doi:10.2105/AJPH.2004.054171

26. Potthoff SJ, Bearinger LH, Skay CL, et al. DImensions of risk behaviors among american indian youth. Arch Pediatr Adolesc Med. 1998;

152(2):157-63. doi:10.1001/archpedi.152.2.157

27. Centers for Disease C, Prevention. Injury mortality among American Indian and Alaska Native children and youth--United States, 1989-1998. MMWR. Morbidity and mortality weekly report. 2003; 52(30):697-701.

28. Sequist TD, Cullen T, Acton KJ. Indian health service innovations have helped reduce health disparities affecting american Indian and alaska native people. Health Aff (Millwood). 2011; 30(10):1965-73. doi:10.1377/hlthaff.2011.0630

29. Watt TT. Alcohol use and cigarette smoking during pregnancy among American Indians/Alaska Natives. J Ethn Subst Abuse. 2012;

11(3):262-75. doi:10.1080/15332640.2012.701570

- 30. What is Tobacco? <u>http://www.anbl.org/?q=node/9</u>.
- 31. Use of Sacred Tobacco 2012.

32. Meckel RA. Save the babies: American public health reform and the prevention of infant mortality, 1850–1929. Baltimore, MD: The Johns Hopkins University Press; 1990.

33. Castor ML, Smyser MS, Taualii MM, et al. A Nationwide Population-Based Study Identifying Health Disparities Between American Indians/Alaska Natives and the General Populations Living in Select Urban Counties. American Journal of Public Health. 2006; 96(8):1478-84. doi:10.2105/AJPH.2004.053942

10.2105/AJPH.2004.053942</div> </div> </div>

34. Office of the Surgeon G. A Report of the Surgeon General: How Tobacco Smoke Causes Disease.

http://www.surgeongeneral.gov/library/reports/tobaccosmoke/factsheet.html.

35. Wang X, Zuckerman B, Pearson C, et al. MAternal cigarette smoking, metabolic gene polymorphism, and infant birth weight. JAMA.

2002; 287(2):195-202. doi:10.1001/jama.287.2.195

36. DANGERS of cigarette-smoking. Br Med J. 1957; 1(5034):1518-20.

37. Levy DE, Biener L, Rigotti NA. The natural history of light smokers: A population-based cohort study. Nicotine Tob Res. 2009; 11(2):156-

63. doi:10.1093/ntr/ntp011

38. Smoking CDsOo, Health. Smoking and Tobacco Use; Data and Statistics; Tables, Charts, and Graphs; Trends in Current Cigarette Smoking. In: Smoking and Tobacco Use. http://www.cdc.gov/tobacco/data_statistics/tables/trends/cig_smoking/.

39. Centers for Disease C, Prevention. Vital signs: current cigarette smoking among adults aged ≥18 years--United States, 2005-2010.

MMWR. Morbidity and mortality weekly report. 2011; 60(35):1207-12.

40. Báezconde-Garbanati L, Beebe LA, Pérez-Stable EJ. Building capacity to address tobacco-related disparities among American Indian and Hispanic/Latino communities: conceptual and systemic considerations. Addiction. 2007; 102(s2):112-22.

41. Hodge FS, Cantrell BAG, Struthers R, et al. American Indian Internet Cigarette Sales: Another Avenue for Selling Tobacco Products.

American Journal of Public Health. 2004; 94(2).

42. Malone RE, Bero LA. Cigars, youth, and the Internet link. American Journal of Public Health. 2000; 90(5).

43. Stehr M. Cigarette tax avoidance and evasion. Journal of Health Economics. 2005; 24(2):277-97. doi:10.1016/j.jhealeco.2004.08.005

44. Dietz PM, England LJ, Shapiro-Mendoza CK, et al. Infant morbidity and mortality attributable to prenatal smoking in the U.S. American Journal of Preventive Medicine. 2010; 39(1):45-52. doi:10.1016/j.amepre.2010.03.009

45. Tong VT, Dietz PM, England LJ, et al. Age and racial/ethnic disparities in prepregnancy smoking among women who delivered live births. Prev Chronic Dis. 2011; 8(6).

46. Tong VT, Jones JR, Dietz PM, et al. Trends in smoking before, during, and after pregnancy - Pregnancy Risk Assessment Monitoring System (PRAMS), United States, 31 sites, 2000-2005. MMWR Surveill Summ. 2009; 58(4):1-29.

47. Jampel S. What A Pack Of Cigarettes Costs Now, State By State. The Awl2013.

48. CDC - Tobacco Use and Pregnancy - Reproductive Health.

http://www.cdc.gov.proxy.library.emory.edu/Reproductivehealth/TobaccoUsePregnancy/index.htm.

49. Knopik VS, Maccani MA, Francazio S, et al. The epigenetics of maternal cigarette smoking during pregnancy and effects on child development. Development and Psychopathology. 2012; 24(Special Issue 04):1377-90. doi:10.1017/S0954579412000776

50. Bergman AB, Wiesner LA. Relationship of passive cigarette-smoking to sudden infant death syndrome. Pediatrics. 1976; 58(5):665-8.

51. Mitchell EA, Ford RPK, Stewart AW, et al. Smoking and the sudden infant death syndrome. Pediatrics. 1993; 91(5):893-6.

52. Hwang M, Shrestha A, Yazzie S, et al. Preterm Birth Among American Indian/Alaskan Natives in Washington and Montana: Comparison

with Non-Hispanic Whites. Maternal and Child Health Journal.1-5. doi:10.1007/s10995-012-1215-4

53. Roa H, Donaldson N, Dobson P, et al. Maternal smoking and ethnic origin, association with birth weight and NICU admission

Archives of Medical Science. 2008; 4(3):310–4.

54. Nitsch A.; Kalcher K.; Greschonig H.; Pietsch R. Heavy metals in tobacco and tobacco smoke ii trace metals cadmium lead copper cobalt and nickel in austrian cigarettes and in particle phase and smoke gas. Beitraege Zur Tabakforschung International. 1991; 1(2):15.

55. Rhainds M, Levallois P. Effects of maternal cigarette smoking and alcohol consumption on blood lead levels of newborns. American journal of epidemiology. 1997; 145(3):250-7.

56. Bellinger D, Sloman J, Leviton A, et al. Low-level lead exposure and children's cognitive function in the preschool years. Pediatrics. 1991; 87(2):219-27.

57. Beyerlein A, Rückinger S, Toschke AM, et al. Is low birth weight in the causal pathway of the association between maternal smoking in pregnancy and higher BMI in the offspring? European journal of epidemiology. 2011; 26(5):413-20.

58. Cabacungan ET, Ngui EM, McGinley EL. Racial/Ethnic Disparities in Maternal Morbidities: A Statewide Study of Labor and Delivery Hospitalizations in Wisconsin. Maternal and Child Health Journal. 2012; 16(7):1455-67. doi:10.1007/s10995-011-0914-6

59. Baldwin L-M, Grossman DC, Casey S, et al. Perinatal and Infant Health Among Rural and Urban American Indians/Alaska Natives. American Journal of Public Health. 2002; 92(9):1491-7.

60. Danileviciute A, Grazuleviciene R, Paulauskas A, et al. Low level maternal smoking and infant birthweight reduction: genetic contributions of GSTT1 and GSTM1 polymorphisms. BMC Pregnancy Childbirth. 2012; 12. doi:10.1186/1471-2393-12-161

61. Clifford A, Lang L, Chen R. Effects of maternal cigarette smoking during pregnancy on cognitive parameters of children and young adults: A literature review. Neurotoxicology and Teratology. 2012; 34(6):560-70. doi:10.1016/j.ntt.2012.09.004

62. Chiolero A, Bovet P, Paccaud F. Association between maternal smoking and low birth weight in Switzerland: the EDEN study. Swiss medical weekly. 2005; 135(35-36):525-30.

63. Low Birth Weight, Child Health USA 2013. <u>http://mchb.hrsa.gov/chusa13/perinatal-health-status-indicators/p/low-birth-weight.html</u>.

64. Butler NR, Goldstein H, Ross EM. Cigarette smoking in pregnancy: its influence on birth weight and perinatal mortality. British Medical Journal. 1972; 2(5806).

65. Windham GC, Hopkins B, Fenster L, et al. Prenatal Active or Passive Tobacco Smoke Exposure and the Risk of Preterm Delivery or Low Birth Weight. Epidemiology. 2000; 11(4):427-33.

66. Suter M, Ma J, Harris AS, et al. Maternal tobacco use modestly alters correlated epigenome-wide placental DNA methylation and gene expression. Epigenetics. 2011; 6(11):1284-94. doi:10.4161/epi.6.11.17819

67. Breton CV, Byun H-M, Wenten M, et al. Prenatal tobacco smoke exposure affects global and gene-specific DNA methylation. Am. J. Respir. Crit. Care Med. 2009; 180(5):462-7. doi:10.1164/rccm.200901-0135OC

68. Hackshaw A, Rodeck C, Boniface S. Maternal smoking in pregnancy and birth defects: a systematic review based on 173 687 malformed cases and 11.7 million controls. Hum. Reprod. Update. 2011; 17(5):589-604. doi:10.1093/humupd/dmr022

69. Caspers KM, Romitti PA, Lin S, et al. Maternal periconceptional exposure to cigarette smoking and congenital limb deficiencies. Paediatric and perinatal epidemiology. 2013; 27(6):509-20. doi:10.1111/ppe.12075

70. Hwang S-J, Beaty TH, Panny SR, et al. Association Study of Transforming Growth Factor Alpha (TGFα) Taql Polymorphismand Oral Clefts: Indication of Gene-Environment Interaction in a Population-based Sample of Infants with Birth Defects. American Journal of Epidemiology. 1995; 141(7):629-36.

71. Malik S, Cleves MA, Honein MA, et al. Maternal smoking and congenital heart defects. Pediatrics. 2008; 121(4):e810-6. doi:10.1542/peds.2007-1519

72. Muraskas J, Parsi K. The Cost of Saving the Tiniest Lives: NICUs versus Prevention. Virtual Mentor. 2008; 10(10).

doi:10.1001/virtualmentor.2008.10.10.pfor1-0810

73. Cavalli AS, Tanaka T. Relationship between maternal physical activities and preterm birth. Environmental health and preventive medicine. 2001; 6(2):74-81. doi:10.1007/BF02897949

74. Catlin A. Extremely long hospitalizations of newborns in the United States: data, descriptions, dilemmas. Adv Neonatal Care. 2008; 8(2):125-32. doi:10.1097/01.ANC.0000317261.99072.e7

75. Centers for Disease C, Prevention. State estimates of neonatal health-care costs associated with maternal smoking--United States, 1996. MMWR. Morbidity and mortality weekly report. 2004; 53(39):915-7.

76. Adams EK, Miller VP, Ernst C, et al. Neonatal health care costs related to smoking during pregnancy. Health Econ. 2002; 11(3):193-206.

77. Centers for Disease C, Prevention. Cigarette smoking during the last 3 months of pregnancy among women who gave birth to live infants--Maine, 1988-1997. MMWR. Morbidity and mortality weekly report. 1999; 48(20):421-5.

78. Control CfD. Smoking-attributable mortality, years of potential life lost, and productivity losses–United States, 2000-2004. MMWR. Morbidity and mortality weekly report. 2008; 57(45).

79. Summary of the Affordable Care Act. 2013.

80. Kim SY, Tucker M, Danielson M, et al. How can PRAMS survey response rates be improved among American Indian mothers? Data from 10 states. Maternal and child health journal. 2008; 12 Suppl 1:119-25. doi:10.1007/s10995-008-0334-4

81. Fagan P, Rigotti NA. Light and intermittent smoking: The road less traveled. Nicotine Tob Res. 2009; 11(2):107-10.

doi:10.1093/ntr/ntn015

82. Battaglia FC, Lubchenco LO. A practical classification of newborn infants by weight and gestational age. J Pediatr. 1967; 71(2):159-63.

83. Peleg D, Kennedy CM, Hunter SK. Intrauterine growth restriction: identification and management. Am Fam Physician. 1998; 58(2):453-60, 66-7.

84. Mitchell EA, Thompson JM, Robinson E, et al. Smoking, nicotine and tar and risk of small for gestational age babies. Acta paediatrica. 2002; 91(3):323-8.

85. Ashford KB, Hahn E, Hall L, et al. The effects of prenatal secondhand smoke exposure on preterm birth and neonatal outcomes. J Obstet Gynecol Neonatal Nurs. 2010; 39(5):525-35. doi:10.1111/j.1552-6909.2010.01169.x

86. de Jongh BE, Locke R, Paul DA, et al. The differential effects of maternal age, race/ethnicity and insurance on neonatal intensive care unit admission rates. BMC pregnancy and childbirth. 2012; 12:97. doi:10.1186/1471-2393-12-97

87. Yuksel B, Greenough A, Dobson P, et al. Advanced maternal age and smoking: risk factors for admission to a neonatal intensive care unit. J Perinat Med. 1996; 24(4):397-403.

88. Laopaiboon M, Lumbiganon P, Intarut N, et al. Advanced maternal age and pregnancy outcomes: a multicountry assessment. BJOG : an international journal of obstetrics and gynaecology. 2014; 121 Suppl 1:49-56. doi:10.1111/1471-0528.12659

89. Hutchinson AB, Farnham PG, Dean HD, et al. The economic burden of HIV in the United States in the era of highly active antiretroviral therapy: evidence of continuing racial and ethnic differences. J. Acquir. Immune Defic. Syndr. 2006; 43(4):451-7.

doi:10.1097/01.qai.0000243090.32866.4e

90. Bock BC, Becker BM, Borrelli B. Smoking behavior and risk perception among the parents of infants in the neonatal intensive care unit. Nicotine Tob. Res. 2008; 10(1):47-54. doi:10.1080/14622200701767795

91. Phelan S. Smoking Cessation in Pregnancy. Obstet. Gynecol. Clin. North Am. 2014; 41(2):255-66. doi:10.1016/j.ogc.2014.02.007

92. Adams KE, Melvin CL, Raskind-Hood CL. Sociodemographic, insurance, and risk profiles of maternal smokers post the 1990s: how can we reach them? Nicotine Tob. Res. 2008; 10(7):1121-9. doi:10.1080/14622200802123278

FIGURES

FIGURE 1. Study Sample















Trends in Current Cigarette Smoking by High School Students* and Adults** - United States, 1965-2011

*Percentage of high school students who smoked cigarettes on 1 or more of the 30 days preceding the survey (Youth Fisk Behavior Survey, 1991-2011). **Percentage of adults who are current cigarette smokers (National Health Interview Survey, 1965-2011).

TABLES

Table 1. Distribution of Pre-Pregnancy Smoking (Exposure) and NICU Admission (Outcome) Pooled across
Covariates for AI/AN women, PRAMS 2004-2011

	<u>TOTAL</u>	<u>TOTAL</u> <u>EXPOSURE</u> Smoked Three Months Pre-Pregnancy		
	N=10,941 (%)	n=4,971 (%)	n=1,558 (%)	Missing (%)
Pre-Pregnancy Smoking				
Yes	4,971 (43.89)	4,971	749	1.44
No	5,812 (56.11)	-	787	
NICU admission				
Yes	1,558 (9.59)	749	1,558	1.01
No	9,273 (90.41)	4,179	-	
Maternal Age				
<=24 years	5,521 (51.45)	2,817 (57.84)	746 (48.88)	0.01
>=25 years	5,419 (48.55)	2,153 (42.16)	812 (51.12)	
Education				
≤16 years	9,909 (91.63)	4,751 (97.41)	1416 (91.59)	1.32
>16 years	888 (8.37)	149 (2.59)	129 (8.41)	
Early PNC				
5 months or earlier	9,209 (90.30)	4,129 (88.90)	1290 (89.66)	7.62
After 5 months	898 (9.70)	443 (11.10)	117 (10.34)	
BMI				
<18.5 (Underweight)	318 (3.54)	175 (5.00)	53 (3.74)	5.33
18.5 to 24.9 (Normal)	4,306 (42.23)	1954 (41.72)	582 (40.27)	
25 to 29.9 (Overweight)	2,736 (26.92)	1247 (27.19)	361 (27.37)	
>=30 (Obese)	2,998 (27.30)	1351 (26.09)	475 (28.62)	
FPL				
138% or under FPL	7,034 (71.51)	3601(80.58)	1032 (76.16)	8.92
Above 138% FPL	2,931 (28.49)	920 (19.42)	381 (23.84)	
Prematurity				
Preterm < 37 weeks	1,527 (8.70)	708 (9.42)	924 (61.44)	2.3
Not preterm >= 37 weeks	9,162 (91.30)	4161 (90.58)	614 (38.56)	
SGA				
Yes	988 (8.17)	518 (9.33)	241 (13.28)	3.03
No	9,621 (91.83)	4305 (90.67)	1133 (86.72)	
Infant LOS				
<= 2 days	6,481 (63.04)	2895 (60.46)	209 (20.43)	1.04
3+ days	4,346 (36.96)	2024 (39.54)	1296 (79.57)	

Table 2. The Unadjusted Association between Infant Admission into the NICU and Pre-pregnancy Smoking PooledAcross 8 States - PRAMS 2004-2011

	OR	95% CI	p-value
Pre-Pregnar			
No	1.00	Referent	
Yes	1.12	(0.88 <i>,</i> 1.43)	0.339

Table 2a. The Unadjusted Association between Infant Admission into the NICU and Maternal and InfantCharacteristics Pooled Across 8 States - PRAMS 2004-2011

	OR	95% CI	p-value
Maternal Age			
≤ 24 years	1.00	Referent	
≥ 25 years	1.11	(0.88, 1.41)	0.37
BMI			
<18.5 (Underweight)	1.00	Referent	
18.5 to 24.9 (Normal)	0.90	(0.48 <i>,</i> 1.69)	0.74
25 to 29.9 (Overweight)	0.96	(0.50 <i>,</i> 1.84)	0.91
>=30 (Obese)	1.00	(0.53 <i>,</i> 1.86)	0.99
Education			
≤16 years	1.00	(0.66, 1.52)	1.00
>16 years	1.00	Referent	
FPL			
Above 138% FPL	1.00	Referent	
138% or under FPL	1.31	(1.00, 1.72)	0.05
Early PNC			
5 months or earlier	1.00	Referent	
After 5 months	1.10	(0.77 <i>,</i> 1.59)	0.59
Prematurity			
Term	1.00	Referent	
Preterm	10.92	(8.39, 14.17)	<0.001
SGA			
No	1.00	Referent	
Yes	1.87	(1.32, 2.65)	<0.001
Infant LOS			
<= 2 days	1.00	Referent	
3+ days	8.11	(5.80, 11.34)	<0.001

	OR	95% CI	p-value
Maternal Age			
≤ 24 years	1.00	Referent	
≥ 25 years	0.64	(0.54, 0.75)	<0.001
BMI			
<18.5 (Underweight)	1.00	Referent	
18.5 to 24.9 (Normal)	0.47	(0.29, 0.76)	0.002
25 to 29.9 (Overweight)	0.49	(0.30, 0.80)	0.005
≥ 30 (Obese)	0.45	(0.28, 0.73)	0.001
Education			
≤16 years	5.60	(3.87, 8.10)	<0.001
>16 years	1.00	Referent	
FPL			
Above 138% FPL	1.00	Referent	
138% or under FPL	2.28	(1.89 <i>,</i> 2.75)	<0.001
Early PNC			
5 months or earlier	1.00	Referent	
After 5 months	1.32	(1.01, 1.72)	0.041
Prematurity			
Term	1.00	Referent	
Preterm	1.18	(0.94 <i>,</i> 1.49)	0.151
SGA			
No	1.00	Referent	
Yes	1.33	(1.00, 1.78)	0.054
Infant LOS			
≤ 2 days	1.00	Referent	
> 3 days	1.22	(1.03, 1.43)	0.019

Table 2b. The Unadjusted Association for AI/AN Women Who Smoked Three Months Before Pregnancy andMaternal and Infant Characteristics Pooled Across 8 States, PRAMS 2004 – 2011

Table 3a. The Number of Cigarettes Smoked Three Months before Pregnancy Among AI/AN Women Across 8 States, PRAMS 2004 – 2011

_	N (%)		
More than 1 pack per day (Heavy Smokers)			
41 Cigarettes or more	130 (2.40)		
21 to 40 Cigarettes	258 (6.25)		
1 pack or less per day			
11 to 20 Cigarettes	1044 (19.29)		
6 to 10 Cigarettes	1474 (29.31)		
1 to 5 Cigarettes	1730 (31.53)		
Less than 1 Cigarette	335 (5.75)		
None	263 (5.58)		

Table 3b: Association between Infant Admission into the NICU and Number of Cigarettes Smoked per Day AmongAI/AN Women Across 8 States, PRAMS 2004 - 2011

	OR	95% CI	p-value		
More than 1 pack per day (Heavy Smokers)					
41 Cigarettes or more	0.89	(0.25 <i>,</i> 3.14)	0.859		
21 to 40 Cigarettes	0.7	(0.20, 2.44)	0.575		
Less than 1 pack	Less than 1 pack per day (Light and Non Smokers)				
11 to 20 Cigarettes	0.47	(0.19 <i>,</i> 1.15)	0.098		
6 to 10 Cigarettes	0.58	(0.23 <i>,</i> 1.50)	0.262		
1 to 5 Cigarettes	0.62	(0.25 <i>,</i> 1.54)	0.302		
Less than 1 Cigarette	0.73	(0.28 <i>,</i> 1.86)	0.505		
None	1	Referent			

Table 3c. The Unadjusted Association between Infant Admission into the NICU and Pre-Pregnancy Smoking PooledAcross 8 States - PRAMS 2004-2011

	OR	95% CI	p-value
Pre-Pregnancy Smoking			
Light and Non Smokers	1.00	Referent	
Heavy Smokers	1.25	(0.62, 2.52)	0.540

	C	DR	95% CI	p-value
Pre-Pregnancy Smol	king			
No	1.00		Referent	
Yes	1.09		(0.77, 1.53)	0.628
Maternal Age				
≤ 24 years	1.00		Referent	
≥ 25 years	1.04		(0.72, 1.51)	0.817
BMI				
<18.5 (Underweight)	1.00		Referent	
18.5 to 24.9 (Normal)	1.17		(0.45, 3.04)	0.743
25 to 29.9 (Overweight)	1.34		(0.50, 3.56)	0.560
>=30 (Obese)	1.39		(0.54, 3.57)	0.499
Education				
≤16 years	0.73		(0.40, 1.32)	0.292
>16 years	1.00		Referent	
FPL				
Above 138% FPL	1.00		Referent	
138% or under FPL	1.54		(1.04, 2.27)	0.031
Early PNC				
5 months or earlier	1.00		Referent	
After 5 months	1.01		(0.61, 1.68)	0.966
Prematurity				
Term	1.00		Referent	
Preterm	10.65		(7.76, 14.63)	<0.001
SGA				
No		1.00	Referent	
Yes		2.37	(1.52, 3.68)	<0.001

Table 4a. INTIAL LOGISTIC REGRESSION MODEL: Adjusted Odd Ratios for Maternal Characteristics and the Risk of Infant NICU Admission for AI/AN Singleton Live Births, PRAMS 2004-2011*

*Observations used in the analysis = 8,197

	OR	95% CI	p-value
Pre-Pregnancy Smoking			
No	1.00	Referent	
Yes	1.05	(0.79, 1.40)	0.718
Age (years)			
≤ 24	1.00	Referent	
≥ 25	1.22	(0.91, 1.64)	0.190
BMI			
Under Weight	1.00	Referent	
Normal	0.87	(0.43, 1.77)	0.700
Overweight	0.98	(0.48, 2.03)	0.963
Obese	0.98	(0.49, 1.96)	0.950
FPL			
Above 138% FPL	1.00	Referent	
138% or under FPL	1.38	(1.00, 1.91)	0.052
SGA			
No	1.00	Referent	
Yes	2.02	(1.38, 2.96)	<0.001

Table 4b. FINAL LOGISTIC REGRESION MODEL: Adjusted Odd Ratios for Maternal Characteristics and the Risk of Infant NICU Admission in a Cohort of AI/AN Singleton Live Births, PRAMS 2004-2011*

*Observations analyzed in sample =9,026

	OR	95% CI	p-value
CRUDE ESTIMATE			
Pre-Pregnancy Smoking			
Light and Non Smokers	1.00	Referent	
Heavy Smokers	1.25	(0.62, 2.52)	0.540
INITIAL MODEL			
Pre-Pregnancy Smoking			
Light and Non Smokers	1.00	Referent	
Heavy Smokers	1.31	(0.52, 3.29)	0.628
Maternal Age			
≤ 24 years	1.00	Referent	
≥ 25 years	1.01	(0.59, 1.74)	0.561
BMI			
<18.5 (Underweight)	1.00	Referent	
18.5 to 24.9 (Normal)	2.22	(0.64, 7.67)	0.210
25 to 29.9 (Overweight)	2.05	(0.56, 7.47)	0.277
≥ 30 (Obese)	1.83	(0.52, 6.43)	0.348
Education			
≤16 years	1.28	(0.57, 2.86)	0.545
>16 years	1.00	Referent	
FPL			
Above 138% FPL	1.00	Referent	
138% or under FPL	1.19	(0.63, 2.23)	0.592
Early PNC			
5 months or earlier	1.00	Referent	
After 5 months	0.77	(0.39, 1.54)	0.465
Prematurity			
Term	1.00	Referent	
Preterm	7.53	(4.69, 12.08)	<0.001
SGA			
No	1.00	Referent	
Yes	2.52	(1.31, 4.84)	0.006

Table 5a. CRUDE AND INITIAL LOGISTIC MODEL: Association between Number of Cigarettes Smoked per day forHeavy and Light Pre-Pregnancy Smokers and Infant NICU Admission.

*Observations used in analysis = 3, 967

	OR	95% CI	p-value
Pre-Pregnancy Smoking			
Light and Non Smokers	1.00	Referent	
Heavy Smokers	1.39	(0.67, 2.86)	0.379
Age (years)			
≤ 24	1.00	Referent	
≥ 25	1.08	(0.69, 1.68)	0.732
BMI			
Under Weight	1.00	Referent	
Normal	1.61	(0.64, 4.06)	0.316
Overweight	1.42	(0.53, 3.79)	0.488
Obese	1.22	(0.48, 3.09)	0.679
FPL			
Above 138% FPL	1.00	Referent	
138% or under FPL	1.08	(0.63 <i>,</i> 1.85)	0.780
SGA			
No	1.00	Referent	
Yes	2.01	(1.13, 3.58)	0.018

Table 5b. FINAL LOGISTIC MODEL: Association between the number of cigarettes smoked per day for Heavy and Light Pre-Pregnancy Smokers and Infant NICU admission*

*Observations used in analysis = 4,391

APPENDIX

Table 6a. State-Specific Summary Statistics of AI/AN Women Who Smoked Three Months before Pregnancy by 8 States, PRAMS 2004 – 2011 (n =4,971)

		AK	MN	NE	NM	OK	OR	UT	WA
	Total	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
EXPOSURE									
Pre-Pregnancy Smoking									
Yes	4,971	1432	714	529	86	643	870	56	641
OUTCOME									
Infant NICU Admission									
Yes	749	242 (10.84)	61 (8.04)	68 (11.92)	10 (13.31)	204 (9.15)		11 (10.96)	68 (12.97)
No	4179	1168 (89.16)	650 (91.96)	458 (88.08)	74 (86.69)	434 (90.85)	780 (90.70)	45 (89.04)	570 (87.03)
VARIABLES									
Maternal Age									
≤ 24 years	2817	822 (59.30)	406 (59.14)		60 (69.39)		498 (57.26)		332 (54.00)
≥ 25 years	2153	610 (40.70)	308 (40.86)	227 (42.19)	26 (30.61)	279 (42.67)	372 (42.74)	23 (42.08)	308 (46.00)
BMI		/			- /	/	/		
<18.5 (Underweight)	175	33 (2.28)	24 (2.51)	24 (4.80)	2 (2.24)	48 (7.74)		1 (1.83)	19 (4.88)
18.5 - 24.9 (Normal)	1954	565 (41.94)	245 (32.73)	. ,	39 (49.34)		362 (41.93)	. ,	256 (41.42)
25 - 29.9 (Overweight)	1247	394 (29.76)		107 (22.82)	23 (26.26)		206 (24.38)		169 (29.67)
>=30 (Obese)	1351	348 (26.01)	225 (34.24)	139 (29.47)	18 (22.16)	189 (23.34)	250 (31.00)	14 (30.23)	168 (24.04)
Education									
≤16 years	4751	· · ·		. ,	83 (97.98)	, ,	843 (97.20)	,	,
>16 years	149	23 (1.61)	33 (2.88)	16 (2.82)	2 (2.02)	35 (3.38)	23 (2.80)	0 (0.00)	17 (1.73)
FPL	2001			412 (00 00)		477 (01 00)		44 /74 24)	101 (70 70)
Above 138% FPL	3601	948 (76.45)		413 (89.09)	71 (85.70)		645 (81.78)		
138% or under FPL	920	277 (23.55)	123 (13.41)	67 (10.91)	12 (14.30)	127 (19.00)	161 (18.22)	13 (28.09)	140 (23.25)
Early PNC 5 months or earlier	4129	1278 (91.26)	613 (90.93)	112 (97 90)	69 (84.95)	E 12 (07 21)	745 (91.38)	12 (02 01)	125 (00 22)
After 5 months	4129	118 (8.74)	68 (9.07)	413 (87.89) 45 (12.11)	10 (15.05)	60 (12.76)		43 (83.91)	423 (90.22) 61 (9.78)
Prematurity	445	110 (0.74)	08 (9.07)	45 (12.11)	10 (15.05)	00 (12.70)	70 (8.02)	11 (10.09)	01 (9.78)
Yes	708	228 (8.95)	50 (6.19)	48 (8.78)	8 (9.97)	239 (11.16)	66 (8.07)	12 (8.11)	57 (8.70)
No	4161		661 (93.81)		78 (90.03)		732 (91.93)	· · · ·	
SGA	4101	1103 (31.03)	JUL (JJ.01)	., 0 (31.22)	/0 (50.05)	102 (00.0 4)	, 52 (51.55)	, (51.05)	505 (51.50)
Yes	518	165 (7.53)	54 (11.12)	49 (10.13)	12 (13.18)	113 (9.33)	76 (9.20)	6 (5.40)	43 (9.73)
No	4305				72 (8682)		768 (90.80)		
Infant LOS	1505		551 (50.00)	.,, (05.07)	, 2 (0002)	107 (30.07)	, (50.00)	15 (54.00)	55. (50.27)
<= 2 days	2895	866 (67.58)	451 (57.16)	294 (55.40)	56 (65.04)	277 (60.00)	507 (58.79)	23 (52.99)	421 (58.78)
3+ days	2024	537 (32.42)		233 (44.60)	29 (34.96)		359 (41.21)		217 (41.22)

Table 6b. State-Specific Summary Characteristics of AI/AN Women Whose Infant Was Admitted into the NICU by 8 States, PRAMS 2004-2011 (n=1,558)

		AK	MN	NE	NM	ОК	OR	UT	WA
	Total	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
OUTCOME									
Infant NICU Admission									
Yes	1,558	456	109	126	47	432	191	39	158
EXPOSURE									
Pre-pregnancy Smoking									
Yes		242 (53.11)		. ,	. ,	204 (48.95)	. ,	. ,	68 (44.17)
No	788	211 (46.89)	44 (34.85)	57 (45.40)	36 (75.49)	223 (51.05)	101 (55.15)	27 (73.55)	89 (55.83)
VARIABLES									
Maternal Age		/	/		/		/	/	/
≤ 24 years		232 (54.29)	. ,			214 (48.65)			63 (52.31)
≥ 25 years	812	224 (45.71)	58 (46.38)	59 (46.07)	27 (60.15)	218 (51.55)	109 (57.49)	22 (65.65)	95 (47.69)
BMI			2 (4.05)	c (F aa)	0 (0 00)	27 (7 25)	2 (0.00)	2 (2 25)	c (2.20)
<18.5 (Underweight)	53	7 (1.15)	, ,			. ,	. ,	. ,	6 (2.39)
18.5 to 24.9 (Normal)		196 (45.01)	,	, ,	, ,	149 (38.49)	, ,	, ,	52 (46.57)
25 to 29.9 (Overweight)		107 (27.55)	. ,		14 (30.88)	. ,	49 (26.15)	. ,	42 (27.30)
>=30 (Obese)	475	110 (26.29)	43 (36.13)	39 (32.62)	15 (34.05)	146 (27.22)	63 (35.02)	10 (32.80)	49 (23.74)
Education	1/16	431 (95.90)	02 (00 02)	122 (00 02)	AE (06 22)	271 (OE 20)	160 (07 00)	26 (06 77)	116 (OC 9E)
≤16 years	1410		15 (11.07)		2 (3.68)		21 (12.92)		
>16 years	129	17 (4.10)	15 (11.07)	4 (1.96)	2 (5.00)	50 (14.02)	21 (12.92)	5 (5.25)	11 (3.15)
Above 138% FPL	1022	310 (77.23)	7/ (78/11)	02 (86 08)	22 (77 65)	280 (75.84)	118 (67 25)	27 (81 57)	99 (73.94)
138% or under FPL	381		30 (21.59)			127 (24.16)			49 (26.06)
Early PNC	501	15 (22.77)	50 (21.55)	15 (15.52)	5 (22.55)	127 (24.10)	57 (52.75)	11 (10.45)	45 (20.00)
5 months or earlier	1290	394 (88.81)	98 (94,88)	99 (90,10)	33 (72,86)	361 (89.62)	166 (93,11)	35 (92,63)	104 (94.05)
After 5 months	117	37 (11.19)			10 (27.14)				10 (5.95)
Prematurity	/	07 (11110)	/ (0)	, (0.00)	(_/)	01 (10100)	(0.00)	0 (1.07)	_0 (0.00)
Yes	924	272 (38.38)	40 (32.40)	59 (47.72)	17 (37.02)	366 (38.92)	80 (48.34)	25 (47.18)	65 (33.60)
No		182 (61.62)	. ,	. ,	30 (62.98)		96 (51.66)		93 (66.40)
SGA	-	- (/		()		- ()		(<i>)</i>	
Yes	1133	347 (88.39)	89 (89.93)	107 (91.03)	33 (69.18)	238 (89.40)	157 (83.69)	29 (88.17)	133 (86.67)
No	241					84 (10.60)			
Infant LOS		. ,	. ,	. ,	. ,	. ,	. ,	. /	. ,
≤ 2 days	209	63 (22.59)	15 (11.68)	17 (12.54)	9 (17.88)	29 (17.98)	28 (14.37)	5 (19.68)	43 (31.22)
≥ 3 days	1296	372 (77.41)	93 (88.32)	108 (87.46)	37 (82.12)	382 (82.02)	161 (85.63)	32 (80.32)	

SAS CODE TO CALCULATE FEDERAL POVERTY LEVEL

*find number of dependents;

if inc_ndep in (**.B**, **.N**) then fam_size=.; else fam size= inc ndep + **1**; *family size 12 months before baby plus 1 for baby born;

*assign midpoint to income categories;

if stateid in (1,7) then do; *Alaska & Utah; if income5 in(.B) then income_mid=.; else if income5 = 1 then income_mid=5000; else if income5 = 2 then income_mid=12500; else if income5 = 3 then income_mid=17500; else if income5 = 4 then income_mid=22500; else if income5 = 5 then income_mid=30000; else if income5 = 6 then income_mid=42500; else if income5 in (7,10) then income_mid=62500; else if income5 = 11 then income_mid=130000;

end;

else if stateid =4 then do; *New Mexico; if income5 in(.B) then income_mid=.; else if income5 = 1 then income_mid=5000; else if income5 = 2 then income_mid=12500; else if income5 = 3 then income_mid=17500; else if income5 = 4 then income_mid=22500; else if income5 = 5 then income_mid=30000; else if income5 = 6 then income_mid=42500; else if income5 = 7 then income_mid=62500; else if income5 = 14 then income_mid=57500; else if income5 = 19 then income_mid=70000; else if income5 = 11 then income_mid=130000; else if income5 = 11 then income_mid=130000;

else if stateid = 6 then do; *Oregon;

if income5 in(.B) then income_mid=.; else if income5 = 1 then income_mid=5000; else if income5 = 2 then income_mid=12500; else if income5 = 3 then income_mid=17500; else if income5 = 4 then income_mid=22500; else if income5 = 5 then income_mid=30000; else if income5 = 6 then income_mid=42500; else if income5 = 7 then income_mid=62500; else if income5 = 12 then income_mid=60000; else if income5 = 13 then income_mid=130000; end;

```
else do; *all other states- Oklahoma, Minnesota, Washington, Nebraska;
if income5 in(.B) then income_mid= .;
else if income5 = 1 then income_mid=5000;
else if income5 = 2 then income_mid=12500;
else if income5 = 3 then income_mid=17500;
else if income5 = 4 then income_mid=22500;
else if income5 = 5 then income_mid=30000;
else if income5 = 6 then income_mid=42500;
else if income5 = 7 then income_mid=62500;
end;
```

*2004 data- use 2003 poverty cut offs;

if yy4_dob = **2004** then do;

if stateid = 1 then do; *Alaksa;

if income_mid = . or fam_size = . then povcut=.; else if fam_size = 1 then povcut=income_mid/11210; else if fam_size = 2 then povcut=income_mid/15140; else if fam_size = 3 then povcut=income_mid/23000; else if fam_size = 4 then povcut=income_mid/23000; else if fam_size = 5 then povcut=income_mid/26930; else if fam_size = 6 then povcut=income_mid/30860; else if fam_size = 7 then povcut=income_mid/34790; else if fam_size = 8 then povcut=income_mid/38720; else if fam_size = 9 then povcut=income_mid/42650; else if fam_size = 10 then povcut=income_mid/46580; else if fam_size = 11 then povcut=income_mid/50510; else if fam_size = 12 then povcut=income_mid/58370;

end;

if stateid in (2,3,4,5,6,7,8) then do; *all rest;

if income_mid = . or fam_size = . then povcut=.;

```
else if fam_size = 1 then povcut=income_mid/8980;
else if fam_size = 2 then povcut=income_mid/12120;
else if fam_size = 3 then povcut=income_mid/15260;
else if fam_size = 4 then povcut=income_mid/18400;
else if fam_size = 5 then povcut=income_mid/21540;
else if fam_size = 6 then povcut=income_mid/24680;
else if fam_size = 7 then povcut=income_mid/27820;
else if fam_size = 8 then povcut=income_mid/30960;
else if fam_size = 9 then povcut=income_mid/34100;
else if fam_size = 10 then povcut=income_mid/37240;
```

```
else if fam_size = 11 then povcut=income_mid/40380;
else if fam_size = 12 then povcut=income_mid/43520;
else if fam_size >= 13 then povcut=income_mid/46660;
end:
```

end;

*2005 data- use 2004 levels;

if yy4_dob = **2005** then do;

if stateid = **1** then do; *Alaksa;

```
if income_mid = . or fam_size = . then povcut=.;
else if fam_size = 1 then povcut=income_mid/11630;
else if fam_size = 2 then povcut=income_mid/15610;
else if fam_size = 3 then povcut=income_mid/23570;
else if fam_size = 4 then povcut=income_mid/23570;
else if fam_size = 5 then povcut=income_mid/27550;
else if fam_size = 6 then povcut=income_mid/31530;
else if fam_size = 7 then povcut=income_mid/35510;
else if fam_size = 8 then povcut=income_mid/39490;
else if fam_size = 9 then povcut=income_mid/43470;
else if fam_size = 10 then povcut=income_mid/47450;
else if fam_size = 11 then povcut=income_mid/51430;
else if fam_size = 12 then povcut=income_mid/55410;
else if fam_size >= 13 then povcut=income_mid/59390;
```

end;

if stateid in (2,3,4,5,6,7,8) then do; *all rest;

```
if income_mid = . or fam_size = . then povcut=.;
else if fam_size = 1 then povcut=income_mid/9310;
else if fam_size = 2 then povcut=income_mid/12490;
else if fam_size = 3 then povcut=income_mid/15670;
else if fam_size = 4 then povcut=income_mid/18850;
else if fam_size = 5 then povcut=income_mid/22030;
else if fam_size = 6 then povcut=income_mid/25210;
else if fam_size = 7 then povcut=income_mid/28390;
else if fam_size = 8 then povcut=income_mid/31570;
else if fam_size = 9 then povcut=income_mid/34750;
else if fam_size = 10 then povcut=income_mid/37930;
else if fam_size = 11 then povcut=income_mid/41110;
else if fam_size = 12 then povcut=income_mid/44290;
else if fam_size >= 13 then povcut=income_mid/47470;
```

end;

end;

*2006 data- use 2005 levels; if yy4 dob = **2006** then do;

if stateid = 1 then do; *Alaksa;

```
if income_mid = . or fam_size = . then povcut=.;
else if fam_size = 1 then povcut=income_mid/11950;
else if fam_size = 2 then povcut=income_mid/16030;
else if fam_size = 3 then povcut=income_mid/20110;
else if fam_size = 4 then povcut=income_mid/24190;
else if fam_size = 5 then povcut=income_mid/28270;
else if fam_size = 6 then povcut=income_mid/32350;
else if fam_size = 7 then povcut=income_mid/36430;
else if fam_size = 8 then povcut=income_mid/40510;
else if fam_size = 9 then povcut=income_mid/44590;
else if fam_size = 10 then povcut=income_mid/48670;
else if fam_size = 11 then povcut=income_mid/56830;
else if fam_size = 12 then povcut=income_mid/56830;
else if fam_size >= 13 then povcut=income_mid/60910;
```

end;

if stateid in (2,3,4,5,6,7,8) then do; *all rest;

if income_mid = . or fam_size = . then povcut=.; else if fam_size = 1 then povcut=income_mid/9570; else if fam_size = 2 then povcut=income_mid/12830; else if fam_size = 3 then povcut=income_mid/16090; else if fam_size = 4 then povcut=income_mid/19350; else if fam_size = 5 then povcut=income_mid/22610; else if fam_size = 6 then povcut=income_mid/25870; else if fam_size = 7 then povcut=income_mid/29130; else if fam_size = 8 then povcut=income_mid/32390; else if fam_size = 9 then povcut=income_mid/35650; else if fam_size = 10 then povcut=income_mid/38910; else if fam_size = 12 then povcut=income_mid/42170; else if fam_size = 13 then povcut=income_mid/48690;

end;

end;

*2007 data- use 2006 levels;

```
if yy4 dob = 2007 then do;
```

if stateid = 1 then do; *Alaksa;

if income_mid = . or fam_size = . then povcut=.; else if fam_size = 1 then povcut=income_mid/12250; else if fam_size = 2 then povcut=income_mid/16500; else if fam_size = 3 then povcut=income_mid/20750; else if fam_size = 4 then povcut=income_mid/25000; else if fam_size = 5 then povcut=income_mid/29250; else if fam_size = 6 then povcut=income_mid/33500;

```
else if fam size = 7 then povcut=income mid/37750;
       else if fam size = 8 then povcut=income mid/42000;
       else if fam size = 9 then povcut=income mid/46250;
       else if fam size = 10 then povcut=income mid/50500;
       else if fam size = 11 then povcut=income mid/54750;
       else if fam size = 12 then povcut=income mid/59000;
       else if fam size >= 13 then povcut=income mid/63250;
end;
if stateid in (2,3,4,5,6,7,8) then do; *all rest;
       if income mid = . or fam size = . then povcut=.;
       else if fam size = 1 then povcut=income mid/9800;
       else if fam size = 2 then povcut=income mid/13200;
       else if fam size = 3 then povcut=income mid/16600;
       else if fam size = 4 then povcut=income mid/20000;
       else if fam size = 5 then povcut=income mid/23400;
       else if fam size = 6 then povcut=income mid/26800;
       else if fam size = 7 then povcut=income mid/30200;
       else if fam size = 8 then povcut=income mid/33600;
       else if fam size = 9 then povcut=income mid/37000;
       else if fam size = 10 then povcut=income mid/40400;
       else if fam size = 11 then povcut=income mid/43800;
       else if fam size = 12 then povcut=income mid/47200;
       else if fam size >= 13 then povcut=income mid/50600;
end;
```

end;

```
*2008 data- use 2007 levels;
if yy4 dob = 2008 then do;
       if stateid = 1 then do; *Alaksa;
              if income_mid = . or fam_size = . then povcut=.;
              else if fam size = 1 then povcut=income mid/12770;
              else if fam size = 2 then povcut=income mid/17120;
              else if fam size = 3 then povcut=income mid/21470;
              else if fam size = 4 then povcut=income mid/25820;
              else if fam size = 5 then povcut=income mid/30170;
              else if fam size = 6 then povcut=income mid/34520;
              else if fam size = 7 then povcut=income mid/38870;
              else if fam size = 8 then povcut=income mid/43220;
              else if fam size = 9 then povcut=income mid/47570;
              else if fam size = 10 then povcut=income mid/51920;
              else if fam size = 11 then povcut=income mid/56270;
              else if fam size = 12 then povcut=income mid/60620;
              else if fam size >= 13 then povcut=income mid/64970;
```

if stateid in (2,3,4,5,6,7,8) then do; *all rest;

```
if income_mid = . or fam_size = . then povcut=.;
else if fam_size = 1 then povcut=income_mid/10210;
else if fam_size = 2 then povcut=income_mid/13690;
else if fam_size = 3 then povcut=income_mid/21650;
else if fam_size = 4 then povcut=income_mid/21650;
else if fam_size = 5 then povcut=income_mid/24130;
else if fam_size = 6 then povcut=income_mid/27610;
else if fam_size = 7 then povcut=income_mid/31090;
else if fam_size = 8 then povcut=income_mid/34570;
else if fam_size = 9 then povcut=income_mid/38050;
else if fam_size = 10 then povcut=income_mid/41530;
else if fam_size = 11 then povcut=income_mid/45010;
else if fam_size = 12 then povcut=income_mid/48490;
else if fam_size >= 13 then povcut=income_mid/51970;
```

end;

*2009 data- use 2008 levels;

end;

```
if yy4 dob = 2009 then do;
       if stateid = 1 then do; *Alaksa;
              if income mid = . or fam size = . then povcut=.;
              else if fam size = 1 then povcut=income mid/13000;
              else if fam size = 2 then povcut=income mid/17500;
              else if fam size = 3 then povcut=income mid/22000;
              else if fam size = 4 then povcut=income mid/26500;
              else if fam size = 5 then povcut=income mid/31000;
              else if fam size = 6 then povcut=income mid/35500;
              else if fam size = 7 then povcut=income mid/40000;
              else if fam size = 8 then povcut=income mid/44500;
              else if fam size = 9 then povcut=income mid/49000;
              else if fam size = 10 then povcut=income mid/53500;
              else if fam size = 11 then povcut=income mid/58000;
              else if fam size = 12 then povcut=income mid/62500;
              else if fam size >= 13 then povcut=income mid/67000;
       end;
       if stateid in (2,3,4,5,6,7,8) then do; *all rest;
              if income mid = . or fam size = . then povcut=.;
              else if fam size = 1 then povcut=income mid/10400;
              else if fam size = 2 then povcut=income mid/14000;
              else if fam size = 3 then povcut=income mid/17600;
```

```
else if fam_size = 4 then povcut=income_mid/21200;
```

```
else if fam_size = 5 then povcut=income_mid/24800;
else if fam_size = 6 then povcut=income_mid/28400;
```

```
else if fam_size = 7 then povcut=income_mid/32000;
else if fam_size = 8 then povcut=income_mid/35600;
else if fam_size = 9 then povcut=income_mid/39200;
else if fam_size = 10 then povcut=income_mid/42800;
else if fam_size = 11 then povcut=income_mid/46400;
else if fam_size = 12 then povcut=income_mid/50000;
else if fam_size >= 13 then povcut=income_mid/53600;
end;
```

.

```
end;
```

```
*2010/11 data- use 2009/10 levels;
```

if yy4_dob in (**2010**, **2011**) then do;

if stateid = 1 then do; *Alaksa;

if income_mid = . or fam_size = . then povcut=.; else if fam_size = 1 then povcut=income_mid/13530; else if fam_size = 2 then povcut=income_mid/18210; else if fam_size = 3 then povcut=income_mid/22890; else if fam_size = 4 then povcut=income_mid/27570; else if fam_size = 5 then povcut=income_mid/32250; else if fam_size = 6 then povcut=income_mid/36930; else if fam_size = 7 then povcut=income_mid/41610; else if fam_size = 8 then povcut=income_mid/46290; else if fam_size = 9 then povcut=income_mid/50970; else if fam_size = 10 then povcut=income_mid/55650; else if fam_size = 11 then povcut=income_mid/60330; else if fam_size = 12 then povcut=income_mid/69390;

end;

if stateid in (2,3,4,5,6,7,8) then do; *all rest;

```
if income_mid = . or fam_size = . then povcut=.;
else if fam_size = 1 then povcut=income_mid/10830;
else if fam_size = 2 then povcut=income_mid/14570;
else if fam_size = 3 then povcut=income_mid/22050;
else if fam_size = 4 then povcut=income_mid/25790;
else if fam_size = 5 then povcut=income_mid/29530;
else if fam_size = 6 then povcut=income_mid/29530;
else if fam_size = 7 then povcut=income_mid/33270;
else if fam_size = 8 then povcut=income_mid/37010;
else if fam_size = 9 then povcut=income_mid/40750;
else if fam_size = 10 then povcut=income_mid/44490;
else if fam_size = 12 then povcut=income_mid/51970;
else if fam_size = 13 then povcut=income_mid/55710;
```

end;

*create federal poverty percent and categories; if povcut = . then FPL=. ; else FPL = povcut * 100; if FPL = . then fpl_cat=.; else if FPL <= 138 then fpl_cat=1; * 138% or under FPL; else if FPL > 138 then fpl_cat=2; *above 138% FPL;