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The Associations of Hypertensive Disorders in Pregnancy with Maternal and Neonatal Outcomes in Haiti

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Abstract

The Associations of Hypertensive Disorders in Pregnancy with Maternal and Neonatal Outcomes in Haiti

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Abstract

Objective: The objective of this study was to determine reported prevalence of hypertensive disorders in pregnancy (HDP) and maternal and neonatal outcomes associated with these disorders among women delivering at selected hospitals across Haiti.

Methods: A retrospective review of 8,822 singleton deliveries between January 2012 and December 2014 was conducted at four hospitals in separate Departments throughout Haiti. Researchers examined the proportion of women with reported HDP (hypertension, preeclampsia, eclampsia) in 4 hospitals and the association between women with HDP and three neonatal outcomes: low birth weight (<2500 grams), preterm birth (<37 weeks' gestation), and stillbirths; and two maternal outcomes: placental abruption and maternal death (prior to hospital discharge) in Hôpital Albert Schweitzer (HAS). Odds ratios for associations between HDP and perinatal outcomes were assessed using logistic regression, adjusting for potential confounders.

Results: Of the 8,822 singleton births included in the study, 510 (5.8%) had a reported HDP (including 285 (55.9%) were preeclamptic, 119 (23.3%) eclamptic, and 106 (20.8%) hypertensive diagnoses). Prevalence of HDP among each hospital was: HAS (13.5%), HIC (3.2%), Fort Liberté (4.3%), and HSC (3.0%). Among women at HAS with HDP, the adjusted odds of having a low birth weight baby was four times that of women without HDP (aOR 4.17, 95% CI 3.19-5.45), more than three times that for stillbirths (aOR 3.51, 95% CI 2.43-5.06), and five times as likely to result in maternal death (aOR 5.13, 95% CI 1.53-17.25). Among the 3 types of HDP, eclampsia was associated with the greatest odds of adverse events with five times the odds of having a low birth weight baby (aOR 5.00, 95% CI 2.84), six times the odds for stillbirths (aOR 6.34, 95% CI 3.40-11.82), and more than twelve times as likely to result in maternal death (aOR 12.70, 95% CI 2.33-69.31).

Conclusions: HDP was associated with higher rates of adverse maternal and neonatal outcomes in one hospital with possibly better reporting of maternal complications than other hospitals in Haiti. This finding is comparable to studies of HDP conducted in high-income countries.

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Glossary

ePOSS	Enhanced Routine Pregnancy Outcome Surveillance System
HAS	Hôpital Albert Schweitzer
HDP	Hypertensive Disorders in Pregnancy
HIC	Hôpital Immaculée Conception des Cayes
HSC	Hôpital Sacré Coeur de Milot
LMIC	Low and middle-income countries
MDG	Millennium Development Goals
MMR	Maternal mortality ratio
NGO	Non-governmental organizations
SDG	Sustainable Development Goals
SOG	Soins Obstetricaux Gratuits
WHO	World Health Organization

Chapter I: Literature Review

Hypertensive disorders in pregnancy (HDP) are one of the leading causes of maternal and infant mortality.[1] HDP includes pregnancy-induced hypertension, chronic hypertension, preeclampsia, and eclampsia.[2] High blood pressure, or hypertension, affects about 10% of all pregnancies.[3] Preeclampsia is a pregnancy-specific medical condition involving high blood pressure and the presence of proteinuria.[4] Globally, preeclampsia affects 3-5% of all pregnancies, and is known to drastically increase the likelihood of adverse fetal outcomes and maternal complications.[4] Eclampsia, a more severe hypertensive disorder, is characterized by hypertension, proteinuria, and seizures. Because delivery is the only known treatment once a woman has preeclampsia, over half of all mothers with preeclampsia or eclampsia deliver preterm, which too can lead to negative outcomes.[2]

To better understand the associations of HDP with maternal and neonatal outcomes, this literature review begins with an overview of the global impact of this public health issue along with a summary of the published research conducted in the developed world. The current health system in Haiti will be described along with an overview of the limited published research on this topic within the country. This literature review will display a gap in the current available research in Haiti and will exemplify how this study can add to other published studies by examining the association of maternal hypertensive disorders and certain maternal and neonatal outcomes within the population of women delivering in one hospital with presumably better reporting of maternal complications in the lower socioeconomic status areas of Haiti.

Hypertensive Disorders in Pregnancy: A Global Problem

Maternal and infant mortality are global issues, particularly in low and middle-income countries (LMIC). Worldwide, over 300,000 women die annually due to complications during pregnancy.[1] The World Health Organization (WHO) approximates that 830 women die each day from preventable causes related to pregnancy and childbirth.[1] Alarmingly, 99% of these maternal deaths occur in LMIC.[1; 3; 5] Infant mortality is also alarming as 4.5 million children die within the first year of life.[6] The rates of infant mortality are four to five times higher in underdeveloped countries in comparison with the United States and the developed European countries.[6] Additionally, stillbirths are abnormally high in the underdeveloped world. Of the 2.6 millions third trimester stillbirths that occur throughout the world every year, 98% of them occur in LMIC.[7; 8]

Maternal mortality ratio (MMR) is defined at the "number of women who die from pregnancy-related causes while pregnant or within 42 days of pregnancy termination per 100,000 live births".[9; 10] During the last 25 years, the world-wide MMR has dropped 44% from an estimated 385 deaths per 100,000 live births in 1990 to 216 maternal deaths per 100,000 live births in 2015.[1] Infant mortality rate is defined as the "number of infants dying before reaching one year of age, per 1,000 live births in a given year".[11] The global infant mortality rate has declined from an estimated 63 deaths per 1,000 live births in 1990 to 32 deaths per 1,000 live births in 2015.[6] Neonatal mortality rate is defined as the "number of neonates dying before reaching 28 days of age, per 1,000 live births in a given year".[12] During the last 25 years, the global neonatal mortality rate has dropped from an estimated 26 deaths per 1,000 live births in 1990 to 19 deaths per 1,000 live births in

2015.[13] Stillbirth rate is defined as the number of babies born with no signs of life at or after 28 weeks' gestation, per 1,000 live births in a given year.[7] From 2000 to 2015, the number of stillbirths has declined by 19.4% (an annual percentage rate of reduction of 2%).[7] Despite the reduction of mortality to 4.5 million infant deaths, 5.1 million neonatal deaths, and 2.6 million stillbirths per year, most of the improvement has concentrated in high-income countries.[2; 6; 7; 13] Most poor and underdeveloped countries have seen only slight improvement in this area. While progress has been made globally on reducing maternal and infant mortality, neonatal mortality has not been going down substantially and thus represents a greater percent of infant mortality overall.[13]

These mortality issues have come to the international attention, resulting in the creation of the 2015 Millennium Development Goals (MDGs) 4 and 5, which aim to reduce mortality rates and improve maternal health.[14; 15] MDG 4.2 specifically called for a reduction by two-thirds, between 1990 and 2015, in the under-five mortality rate.[15] MDG 5A called for a reduction by three-quarters in the maternal mortality ratio during that same time period.[14; 15] In 2016, the United Nations updated these recommendations and proposed the 2030 Sustainable Development Goals (SDG), which are "17 goals to transform our world".[16] SDG 3 focuses on ensuring healthy lives and promoting well-being for all ages. Included in this goal is the target of reducing the global maternal mortality ratio to less than 70 deaths per 100,000 live births by 2030.[16] Also included in SDG 3 is the target of "ending preventable deaths of newborns and children under 5 years of age, with all countries aiming to reduce neonatal mortality to at least as low as 12 per 1,000 live births and under-5 mortality to at least as low as 25 per 1,000 live births".[16]

According to the WHO, Haiti made no progress towards MDG 5A.[17] Haiti's estimated MMR in 1990 was 625 deaths per 100,000 live births and in 2015 their MMR was 359 deaths per 100,000 live births.[17] While it is a decline, the 2.2% annual percent change is much lower than most other countries.[17] In 2012, the estimated infant mortality rate in Haiti was 56.5 deaths per 1,000 live births, which translates to almost 15,000 annual infant deaths.[18] The estimated neonatal mortality rate is 25.4 deaths per 1,000 live births, resulting in 6,745 neonatal deaths.[18] The estimated stillbirth rate is 15.5 deaths per 1,000 live births, resulting in 4,300 stillbirths per year.[8] All of these statistics are abnormally high compared to the global statistics; thus further research is needed to understand these disparities.[1; 17; 18]

There are several causes of maternal and neonatal mortality, of which most are preventable.[1] Approximately 75% of maternal deaths can be attributed to severe bleeding after childbirth, infections after childbirth, high blood pressure during pregnancy, delivery complications, and unsafe abortion.[1] The known factors associated with neonatal deaths include infections (sepsis/pneumonia, tetanus, and diarrhea), pre-term birth, and birth asphyxia.[19] The major causes of stillbirth include: childbirth complications, post-term pregnancies, maternal infections in pregnancy (malaria, syphilis and HIV), maternal disorders (hypertension, preeclampsia, obesity, and diabetes), fetal growth restriction, and congenital abnormalities.[7; 8]

HDP Research in the Developed World

Hypertension and preeclampsia have been studied extensively in the past few decades. They are known to be substantial causes of maternal mortality, accounting for

15-20% of deaths in the developed world.[20] Studies in the United States and other high-income countries have found that preeclampsia not only causes maternal mortality, neonatal mortality, and stillbirths, but is also associated with preterm birth, low birth weight, intrauterine growth restriction, and hypoxia for the infant.[20] It is believed that the prevalence and severity of these adverse outcomes depend heavily on gestational age, severity of disease, quality of medical care received, and other pre-existing medical conditions. Known factors that place a mother at an increased risk of HDP include prior history of HDP in previous pregnancies, high BMI, chronic kidney disease, autoimmune disease, diabetes, and chronic hypertension.[21]

Treatment for HDP varies based on severity of condition and the country of residence.[21] In the United States, for women with mild gestational hypertension it is recommended that women monitor blood pressure regularly, get sufficient amounts of rest and exercise, consume a low sodium diet, and consider taking oral antihypertensive medication.[21] Mothers with preeclampsia are advised to monitor blood pressure multiple times a day, have routine blood tests, and may be admitted into the hospital for observation, tests, and potentially induced labor. If a mother's condition progresses to eclampsia, care requires hospitalization and often induced labor.[21] Such intensive medical care can be challenging, and is often unavailable, in lower income countries such as Haiti.

The underlying causes of preeclampsia and eclampsia are poorly understood.[21; 22] Aspirin has been shown to have a protective effect for at-risk women and is currently recommended.[21] The main reason for the gestational age at delivery association with HDP is that the only known effective treatment for preeclampsia and eclampsia is delivery.[21; 22] Thus, if the condition arises in earlier gestation, treatment will result in

preterm birth, which is associated with complications and increased risk of neonatal death.[21; 22]

Despite the plethora of research regarding HDP in high-income countries over the last decade, little improvement has been made in predicting or preventing preeclampsia.[20; 23] Even with advances in medical prenatal care, the prevalence of preeclampsia has been relatively stable.[23] More studies are needed globally, and especially in resource scarce settings, for researchers and health professionals to attempt to understand the determinants of HDP and to seek ways to lessen the global burden of these disorders.

Health System in Haiti

For decades, Haiti has been known as an underdeveloped country that is lacking adequate health services and resources.[24] Advancements in health infrastructure in the early 21st century were severely damaged following the earthquake in 2010, widening the health disparity between the Haitian population and the developed world.[25] Haiti has a population of over 10 million people, with over 80% living below the federal poverty line.[26] The average age in Haiti is 21 years old and the life expectancy at birth is 62 years.[27]

Haiti is a relatively small country that is divided into 10 Departments. There are over 700 primary health care facilities in Haiti, most of which are concentrated around the capital, Port-au-Prince.[27] There are also 10 Departmental hospitals and 4 university hospitals for secondary and tertiary care. Haiti's health infrastructure is highly fragmented as there is no national coordination between facilities and national treatment standards are nonexistent.[27] Most hospitals are for-profit and even most free primary

health facilities charge patients for medications. Currently, there is no national standardization for cost of medicine or medical consultations, which restricts many from seeking medical care. There are several non-governmental organizations (NGO) who have small antenatal clinics offering services (including low-risk deliveries in some clinics) in certain areas of the country.[28] These NGO are all privately supported and there is currently no governmental coordination or regulations in place for NGO.

In 2008, a free obstetric care project, Soins Obstetricaux Gratuits (SOG), was initiated in Haiti. This project promoted prenatal care and hospital deliveries for pregnant mothers, with the result that 80-85% of Haitian mothers received at least one prenatal visit.[27] Even though this program showed favorable results in increasing prenatal utilization, it was abandoned in 2014. Despite the high rates of antenatal care, institutional deliveries remained less common. It is estimated that less than 40% of women in Haiti deliver in a medical facility.[26; 29; 30] One study estimates that less than 10% of women in rural Haiti deliver in a medical facility.[28] A large majority of women are giving birth at home with the assistance from lay midwives ("matrons"), who are not skilled medical professionals.[31] Barriers that have been identified for why Haitian women do not seek medical care include distance to health facility, lack of affordable services, concerns of no provider available, lack of transportation or having to take public transportation, and not wanting to go alone.[30; 31] The concern of lack of providers is justified, as there are only 0.25 maternal health physicians per 1,000 people. Specialized nurses and midwives are even more common at 0.11 per 1,000 people.[31] The health system in Haiti limits mothers' ability to receive adequate health care services and their

ability to deliver under the supervision of trained medical staff, leading to higher rates of adverse outcomes for themselves and their babies.[28]

Health Complications Faced by Haitian Women

Haiti has a poor country health profile with many adverse health outcomes. The leading causes of death include stroke, lower respiratory infections, HIV/AIDS, heart disease, diarrheal disease, and diabetes.[32] Preterm birth complications and birth asphyxia and trauma make up over 5% of all deaths in Haiti.[32] Haitian women are at a high risk of certain comorbidities that not only affect their daily life, but can also lead to further complications during pregnancy. These comorbidities include obesity, high blood glucose, anemia, and chronic high blood pressure. Of women who are 20 years of age and older, 8.4% of them are considered obese.[32] Almost 10% of Haitian women suffer from high blood glucose.[32] Women, especially while pregnant, are at exceptionally higher risk of anemia, which is defined as having a hemoglobin less than 110 g/L.[31] In fact, it is estimated that 63% of all pregnant women in Haiti are anemic.[31] This medical conditional drastically increases their risk of preterm delivery, low birth weight babies, stillbirths, and newborn deaths.[31]

The WHO has identified hypertension to be the greatest adult risk factor among females in Haiti. In 2008, it was estimated that over 28% of women over the age of 25 suffered from chronic high blood pressure.[32] There have been few studies conducted over the past two decades examining this issue in Haiti. Jiao et al. conducted a study that examined medical charts at two Haitian clinics: one urban and one rural. Researchers found an overall prevalence of hypertension to be 34.4%.[33] The study found a slightly higher prevalence among women and also among those living in rural Haiti. While this

study highlights the major health problem, it was unable to provide evidence on what caused these elevated rates of hypertension.[33] Another study that compared urban and rural patients in Haiti found 33% of rural patients were diagnosed with hypertension, while 13% of urban patients had the same diagnosis.[34] One final study conducted a cross-sectional survey in Port-au-Prince and found hypertension in 48.7% of men and 46.5% in women.[35] Research conducted outside of Haiti, also shows that being born in Haiti predisposes a woman to HDP, as even emigrants are at higher risk when compared to other residents of the areas where the Haitians now live.[36; 37] The etiology behind this association has yet to be determined. While each of these studies has limitations to the validity of the data, the consistency of high prevalence rates demonstrates that hypertension is a serious public health issue among Haitians and further research is needed in this area.

Hypertensive Disorders in Pregnancy Research in Haiti

Haiti, as in most LMIC, faces major challenges in addressing medical issues affecting maternal and child mortality. These challenges include delays in triage, transport, and treatment, health care worker shortage, and lack of medical resources and training for professionals.[24; 38] These issues along with lack of donor funding and interest have lead to very little research on HDP in Haiti.

To our knowledge, there have only been three studies that have aimed to examine the issue of preeclampsia and eclampsia in Haiti. The first published study in Haiti in 2004 used hospital and laboratory data from one hospital, Hôpital Albert Schweitzer (HAS), to examine maternal deaths due to preeclampsia and eclampsia.[39] This study

analyzed 2,295 pregnancies from 1999-2001 from HAS and found the prevalence of preeclampsia and eclampsia to be 18%. Of the 423 deliveries that were affected by preeclampsia and eclampsia, 19 maternal deaths were reported. Investigators concluded that intrauterine fetal distress, eclampsia, and oliguria were predictors of maternal mortality. This study only focused on maternal mortality and did not look into any other adverse maternal or neonatal outcomes.[39]

Another study published a decade later (2014), also from HAS, aimed at defining the prevalence and clinical characteristics of eclampsia and preeclampsia from 2011-2012.[40] Researchers in this study obtained medical records from 1,743 pregnancies and found that 290 (16.6%) women were diagnosed with preeclampsia and eclampsia, resulting in 48 stillbirths and 5 maternal deaths. Researchers also compared women with antepartum eclampsia to women with antepartum preeclampsia and found that those with eclampsia were younger, more likely to be nulliparous, and had less prenatal care compared to those who presented with preeclampsia. They concluded that eclampsia was associated with placental abruption and maternal deaths.[40] One major limitation of this study was lack of medical data on women with no hypertensive disorders; thus they were unable to have a control group to compare complications and other associations.

Finally, a third study published in 2014 studied preeclampsia and eclampsia among women delivering at Maison de Naissance, a birthing center in the South District of Haiti. Researchers in this study aimed to determine the prevalence of pregnancy related hypertensive disorders among women seeking prenatal care at the facility and the extent to which maternal weight and age were associated.[41] They obtained medical records and examined 689 pregnant women who presented at this one facility between April 2010 and

October 2012. Researchers found an incidence of preeclampsia and eclampsia to be 7% and concluded that older maternal age and higher maternal weight were significantly associated with hypertensive disorders in pregnancy. This study gave a much smaller prevalence of preeclampsia, which may be due to difference in the population seeking prenatal care as opposed to a population of women delivering in-hospital (since many low-risk pregnancies are delivered at home).[41] That is, in areas with very low percentage of hospital births, it is likely that hospital-based data overstate the incidence/prevalence of major complications since women without complications may avoid delivering in hospital; thus, a lower incidence among women seeking prenatal care would be expected.[41] Differences in the incidence of preeclampsia between these three studies display the need for further research to get an accurate and nationwide representation of the true incidence of HDP.

Challenges in Health Statistics in Haiti

Health statistics in Haiti are extremely limited and there are many barriers that keep researchers from obtaining accurate and representative data. Haiti is known to have one of the highest maternal mortality ratios in the world at an estimated 359 per 100,000 live births.[17] This number varies by organization or study and has a huge range of uncertainty as the confidence interval on the ratio ranges from 236 to 601 deaths per 100,000 live births.[17] This example of uncertainty in Haiti's MMR, along with the statistics on hypertension and preeclampsia in Haiti presented earlier, exemplifies the need for improved, population-based health statistics in Haiti.

Improving health statistics in Haiti is hindered by the large percentage of the population giving birth outside of medical facilities. Due to this fact and due to the absence of community-based surveillance, many complications and maternal deaths go unreported.[28; 30; 31; 40] On the other hand, hospital-based reports may be an overrepresentation of HDP and maternal mortality as those who present at the hospital are more likely to have higher-risk pregnancies.[41] Finally, data reporting and management in Haiti is mediocre at best for many reasons. Medical clinics in Haiti have a shortage of staff and lack financial resources including lack of computers and irregular Internet or electricity availability.[42; 43] Other factors include a lack of training, a lack of recognition of the importance of data quality, or simply a lack of capacity to maintain records for an extended amount of time.[42; 43]

Conclusion

In summary, it is evident that HDP is a concern for both mothers and newborns in Haiti. Researchers have been attempting to study the associations of this complex issue, with limited success. Despite the fact that the global burden of disease and mortality due to HDP is highly concentrated in LMIC, most of the research has focused only in high-income countries. Barriers for researchers to study low and middle income countries include a lack of health infrastructure, poor medical records systems, lack of access, and lack of funding.[5; 42; 43; 44] The limited research in these impoverished areas, including Haiti, combined with a large population that could benefit from scientific advancements demonstrates the need of further studies and thus is the driving force for this study.

Chapter II: Manuscript

The Associations of Hypertensive Disorders in Pregnancy with Maternal and Neonatal Outcomes in Haiti

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Abstract

Objective: The objective of this study was to determine reported prevalence of hypertensive disorders in pregnancy (HDP) and maternal and neonatal outcomes associated with these disorders among women delivering at selected hospitals across Haiti.

Methods: A retrospective review of 8,822 singleton deliveries between January 2012 and December 2014 was conducted at four hospitals in separate Departments throughout Haiti. Researchers examined the proportion of women with reported HDP (hypertension, preeclampsia, eclampsia) in 4 hospitals and the association between women with HDP and three neonatal outcomes: low birth weight (<2500 grams), preterm birth (<37 weeks' gestation), and stillbirths; and two maternal outcomes: placental abruption and maternal death (prior to hospital discharge) in Hôpital Albert Schweitzer (HAS). Odds ratios for associations between HDP and perinatal outcomes were assessed using logistic regression, adjusting for potential confounders.

Results: Of the 8,822 singleton births included in the study, 510 (5.8%) had a reported HDP (including 285 (55.9%) were preeclamptic, 119 (23.3%) eclamptic, and 106 (20.8%) hypertensive diagnoses). Prevalence of HDP among each hospital was: HAS (13.5%), HIC (3.2%), Fort Liberté (4.3%), and HSC (3.0%). Among women at HAS with HDP, the adjusted odds of having a low birth weight baby was four times that of women without HDP (aOR 4.17, 95% CI 3.19-5.45), more than three times that for stillbirths (aOR 3.51, 95% CI 2.43-5.06), and five times as likely to result in maternal death (aOR 5.13, 95% CI 1.53-17.25). Among the 3 types of HDP, eclampsia was associated with the greatest odds of adverse events with five times the odds of having a low birth weight baby (aOR 5.00, 95% CI 2.84), six times the odds for stillbirths (aOR 6.34, 95% CI 3.40-11.82), and more than twelve times as likely to result in maternal death (aOR 12.70, 95% CI 2.33-69.31).

Conclusions: HDP was associated with higher rates of adverse maternal and neonatal outcomes in one hospital with possibly better reporting of maternal complications than other hospitals in Haiti. This finding is comparable to studies of HDP conducted in high-income countries.

Introduction

Haiti is known to have one of the highest maternal mortality ratios (MMR) in the world at an estimated 359 per 100,000 live births.[17] The stillbirth rate is also high with an annual estimated rate of 15.5 stillbirths per 1,000 live births, resulting in 4,300 deaths per year.[8] Hypertensive disorders in pregnancy (HDP) are one of the leading causes of maternal mortality and stillbirths.[1] The World Health Organization (WHO) has identified hypertension to be the greatest adult risk factor among Haitian women, yet the etiology behind this association is currently unknown.[32; 33; 34; 35] Few studies have attempted to study hypertensive disorders among pregnant women in Haiti; thus the true impact HDP has on mothers and babies is largely unknown.

In 2012, the Centers for Disease Control and Prevention (CDC) partnered with the Ministère de la Santé Publique et de la Population (MSPP) to set up an Enhanced Routine Pregnancy Outcome Surveillance System (ePOSS) in Haiti. The goal of this system is to improve collection and analysis of routine epidemiologic indicators used to measure pregnancy outcomes at the facility and community levels in selected regions of Haiti.[45] Initially this system was set up within three departments, Artibonite, Nord, and Nord Est, which serve 11 communes collectively. The facilities that were targeted in these communes were upper-level healthcare facilities and/or comprehensive emergency obstetric care facilities (EmOC).

As of 2014, the ePOSS system has been introduced and implemented in 19 target facilities and in 6 of Haiti's Departments: Artibonite, Nord, Nord Est., Sud, Sud Est., and Nippes. Four hospitals, each representing a different department, were included in this study. Hôpital Albert Schweitzer (HAS) represents the Artibonite Department, while

Hôpital de Fort Liberté is in Nord Est. Hôpital Sacré Coeur de Milot (HSC) and Hôpital Immaculée Conception des Cayes (HIC) are in Nord and Sud, respectively. No data were available for hospitals in Sud Est. and Nippes for the current study.

Prior studies in Haiti have found a prevalence of HDP among their samples to be 7-18%.[39; 40; 41] One of these studies by Raghuraman et al. examined associations between HDP and adverse maternal and fetal outcomes in HAS hospital records from January 2011- December 2012.[40] Investigators found the prevalence of preeclampsia and eclampsia to be 16.6% and an association between preeclampsia and eclampsia with maternal death and placental abruption.[40] The study was limited to data from one hospital in Haiti and was unable to compare preeclamptic and eclamptic women with normotensive women due to a lack of data on women who were normotensive.[40]

This study will expand upon the research by Raghuraman et al. by using more recent data from four hospitals in Haiti, including HAS, and exploring differences in adverse maternal and neonatal outcomes between hypertensive and normotensive women delivering at HAS. The research aims of this study are to determine: (1) the prevalence of hypertensive disorders in pregnant women with singleton births delivering at 4 Departmental hospitals in Haiti; and (2) the extent to which certain maternal and neonatal outcomes are associated with these disorders. Answers to these questions will add to the limited research on HDP in low resource areas by studying linkages of maternal and newborn outcomes. This study will also allow researchers to identify areas for further improvement at the hospital level and provide data that can aid in evidence-based intervention strategies.

Methods

Data

Secondary analyses were based on data received from the ePOSS system in Haiti. For this study, data from four hospitals (HAS, Fort Liberté, HSC, and HIC) were selected based on the following criteria, 1) being the largest referral hospitals in their distinct Departments, and 2) having the most complete records known by the research team, who participate in ePOSS. HAS and Fort Liberté had complete data from 2013 and 2014. For HSC, only 2012 data were available at the time of the analysis. For HIC, data from 2014 (its first year in ePOSS) were included.

These four hospitals are located in different Departments throughout Haiti (Fig. 1). HAS is located in Verrettes commune in Artibonite. Fort Liberté is located in the Fort Liberté commune in Nord Est.; HSC is in the Milot commune in Nord; and HIC is in the Port-de-paix commune in Sud (Fig. 1).

Data were collected at the hospital level and combined into a single registry. All hospitals recorded data into multiple reporting systems (maternity registry, major and minor operating theatre, emergency unit registry, and abortion registry). ePOSS was able to combine these multiple registries for all hospitals except for HIC. Due to reporting issues, HIC still had 2 separate registries: one maternal registry and one operating theater (OT) registry. Women in the OT registry were those who required surgery, while the maternity registry captured vaginal births or low-risk cesarean sections. Both registries were used for the HDP prevalence calculation, but due to lack of data on outcomes of interest (infant status, maternal status, and birth weight) in the OT registry, only the maternal registry was used in further analyses.

The primary outcomes of interest in ePOSS are the results of conception including maternal deaths, stillbirths, neonatal deaths, birth complications, birth defects, and live births.[45] Maternal and neonatal deaths were defined by status at discharge. An offspring's status at birth was recorded as live birth, macerated stillbirth, fresh stillbirth, or undetermined stillbirth. Maternal, neonatal, and birth complications were recorded in three columns. Up to three complications were recorded for each birth.[45]

Data Management and IRB

Prior to the start of the study, the protocol was submitted to and approved by the Emory University Institutional Review Board (IRB) using the expedited procedure.

Sample

A retrospective review was conducted of 9,069 women entered into ePOSS (Fig. 2). Women who had multiple birth pregnancies (n=237) or who had an abortion (n=10) were excluded from this study. 8,822 women were included in the prevalence estimates, but due to a lack of further data collected at HIC's OT Registry, 864 women had to be omitted from further analyses. The final cohort size was 7,958 women (Fig. 2).

Exposure Variable

The exposure of interest was HDP, defined as a diagnosis of one the following complications during pregnancy: hypertension (systolic blood pressure level of ≥ 140 mmHg with no other symptoms), preeclampsia, and/or eclampsia. Preeclampsia was characterized as a systolic blood pressure level of ≥ 140 mmHg with proteinuria (≥ 300

mg/24 hour). Eclampsia was defined as a systolic blood pressure level of ≥ 160 mmHg, proteinuria, and seizures.

Outcome Variables

The variables included in this study were maternal and neonatal outcomes that are thought to be associated with HDP based on current research in high-income countries.[20; 21] The main neonatal outcomes of interest were low birth weight (<2500 grams), preterm birth (<37 weeks' gestation), and stillbirths. The two maternal outcomes of interest were placental abruption and maternal death (prior to hospital discharge). Other variables included in the analyses were maternal age, parity (dichotomized as nulliparous vs. parous), mode of delivery (vaginal vs. Caesarian section), and gestational age in weeks.

Data Analysis

Comparative analyses, including prevalence, between women with HDP and those without were conducted between the hospitals. Continuous data were summarized using mean and standard deviation and categorical data were presented as frequencies and percentages. Comparisons were assessed using T-tests for continuous variables, chi-square tests for categorical variables, and Fisher's exact tests for categorical variables with small values.

Logistic regression was used to calculate adjusted odds ratios with 95% confidence intervals using HAS data exclusively (2,080 pregnancies). The outcomes analyzed were low birth weight, stillbirth, and maternal death. There were not enough

cases of placental abruption to analyze further. Odds ratios were adjusted for the following potential confounders: maternal age, parity, and year of delivery.

Statistical analyses were performed using SAS 9.4 (Cary, NC).

Results

HDP Prevalence

Among the 8,822 women with singleton births included in the study, 510 (5.8%) had a HDP. Prevalence of HDP among each hospital was as follows: HAS (13.5%), HIC (3.2%), Fort Liberté (4.3%) and HSC (3.0%). Among the 510 women with HDP, 285 (55.9%) were preeclamptic, 119 (23.3%) were eclamptic, and 106 (20.8%) were hypertensive (Table 1).

Study population characteristics and obstetric and perinatal outcomes

Of the 8,822 women included in the study, clinical characteristics were available for 7,958 (90.2%) women. These women had a mean maternal age at delivery of 27.7 years (SD=6.7). 4,194 (52.7%) women had already had a prior delivery, and 6,263 (78.7%) had a vaginal delivery. The full cohort had a mean gestational age at delivery of 38.2 weeks (SD=4.3). There were 738 (9.3%) preterm deliveries and 1,240 (15.6%) low birth weight babies. There were 392 (4.9%) stillbirths, 26 (0.3%) maternal deaths, and 38 (0.5%) women who had a placental abruption (Table 2).

Characteristics among HDP vs. No HDP associated with outcome variables

Table 2 also shows characteristics and outcomes by hospital and by HDP status. In all hospitals except Fort Liberté, women with HDP were significantly more likely to have a low birth weight baby ($p<0.05$). Women at HAS and HIC with HDP had significantly higher numbers of preterm deliveries and stillbirths. Maternal death was significantly linked to HDP women at HAS ($p=0.002$), but due to death being a rare outcome, no other hospitals found a significant relationship. Results from HIC revealed that maternal deaths were poorly reported and appear to be differentially missing; women with reported HDP appear to me missing maternal status more than women without HDP. Placenta abruption was significantly more likely among women with HDP in comparison to those without HDP in all hospitals except Fort Liberté ($p<0.05$).

Characteristics among stillbirths vs. live births at HAS

There were 156 (7.5%) stillbirths and 1,917 (92.2%) live births at HAS; mortality data were not available for 7 (0.3%) births (Table 3). Women with stillbirths were slightly older, more likely to be parous, and more likely to have a vaginal birth. A stillbirth was significantly associated with an earlier gestational age, higher rates of preterm birth, and lower birth weight babies. A live birth was significantly associated with a normotensive mother, while stillbirths were more common among mothers with preeclampsia or eclampsia. A stillbirth was also significantly associated with maternal death and placenta abruptions. All significant thresholds were set at a p-value<0.05.

Among women with HDP, there were 52 (18.6%) stillbirths and 227 (81.1%) live births; mortality information was not available for 1 woman. There was no significant

difference in maternal age by infant outcome. Women with stillbirths were more likely than women with live births to be parous and have a vaginal delivery. A stillbirth was significantly related to having a shorter gestational age at delivery, a preterm birth, and to be of low birth weight. Women with stillbirths were more likely than women with live births to have eclampsia, less likely to have only hypertension, and equally likely to have preeclampsia. More maternal deaths and placental abruptions were seen among the women having stillbirths (Table 3).

Characteristics among maternal deaths vs. survivors at HAS

As seen in Table 4, there were 11 maternal deaths (0.5% of women with singleton deliveries) at HAS; maternal status was not available for 9 women. Women who died were slightly older than those who survived (30.9 years vs. 27.7 years), were more likely to be parous, and to have had a caesarean section. The women who died had a slightly shorter gestational age (36.1 weeks vs. 38.3) and were more likely to deliver a low birth weight baby. Women who died were more likely to suffer from preeclampsia and eclampsia and women who survived were more likely to be normotensive. Those with a maternal death were also significantly more likely to deliver a stillborn baby.

Five of the 11 maternal deaths occurred among mothers with HDP and 274 mothers (97.9%) who survived pregnancy; maternal status was not available for 1 mother. Women who died were older, more likely to be parous, and more likely to have a Caesarean section delivery. All other adverse outcomes were not significantly different between the two groups (Table 4).

Association between HDP and adverse outcomes

Among women at HAS who had HDP, the adjusted odds of having a low birth weight baby was four times that for women without HDP (aOR 4.17, 95% CI 3.19-5.45), more than three times for stillbirths (aOR 3.51, 95% CI 2.43-5.06), and five times for maternal death (aOR 5.13, 95% CI 1.53-17.25). Among the 3 types of HDP, eclampsia was associated with the greatest odds of adverse events with five times the odds of having a low birth weight baby (aOR 5.00, 95% CI 2.84), six times for stillbirths (aOR 6.34, 95% CI 3.40-11.82), and more than twelve times for maternal death (aOR 12.70, 95% CI 2.33-69.31). Crude odds ratios were similar to the adjusted odds ratios (Table 5).

Discussion

Maternal mortality and stillbirths are global issues, particularly in low and middle-income countries (LMIC). Worldwide, over 300,000 women die annually due to complications during pregnancy.[1] Alarmingly, 99% of these maternal deaths occur in these LMIC.[1; 3; 5] Additionally, stillbirths are abnormally high in the underdeveloped world. Of the 2.6 millions third trimester stillbirths that occur throughout the world every year, 98% of them occur in LMIC.[7; 8]

WHO has identified hypertension to be the greatest adult risk factor among females in Haiti. In 2008, it was estimated that over 28% of Haitian women over the age of 25 suffered from high blood pressure.[32] Hypertensive disorders in pregnancy (HDP) are one of the leading causes of maternal morality and stillbirths.[1] Haiti, as in most LMIC, faces three major challenges in addressing medical issues affecting maternal and child mortality. These challenges include delays in triage, transport, and treatment,

health care worker shortage, and lack of medical resources and training for professionals.[24; 38] These issues along with lack of donor funding and interest have led to very little research on HDP in Haiti.

This study is one of the few that attempts to study the impact of HDP among Haitians and link adverse pregnancy outcomes to these disorders. The results indicate that women with HDP are more likely to be older when they deliver, have a prior birth history, and have a Caesarean section delivery compared to normotensive mothers. Women with HDP in this sample were more likely to have pregnancies that resulted in low birth weight babies, stillbirths, and maternal death. Women with eclampsia were at greatest risk for these adverse maternal and neonatal outcomes.

The few prior studies in Haiti have estimated prevalence of HDP among their samples to be between 7-18%.[39; 40; 41] This study found an overall HDP prevalence to be 5.8%, with individual hospitals' prevalence ranging from 3.0% to 13.5%. However, these statistics are not directly comparable due to variations in the definitions of HDP among the studies.

Haiti's MMR is estimated to be 359 deaths per 100,000 live births.[17] Although this study classified maternal mortality based on deaths occurring prior to discharge, a similar MMR of 327 deaths per 100,000 live births was found. The research team expects more maternal deaths would be captured if these mothers were followed for 42 days post delivery. The estimated stillbirth rate for Haiti is 15.5 stillbirths per 1,000 live births.[8] The current study found a much higher stillbirth rate of 49.3 stillbirths per 1,000 live births. It is likely that this hospital-based sample overestimated the incidence/ prevalence of major complications (HDP, maternal death, stillbirth) since women without

complications may be less likely to deliver at a facility. Conversely, there are many women with complications who never reach facilities, which may lead to an underreporting of HDP and adverse outcomes.

One of the few studies that aimed to study HDP in Haiti was by Raghuraman et al. This study is comparable to the current study, as they were both conducted at HAS. The previous study used data from 2011-2012, while the current study used data from 2013-2014. Researchers in the prior study obtained medical records from 1,743 pregnancies, and found that 16.6% (290) of women were diagnosed with preeclampsia and eclampsia, resulting in 48 stillbirths and 5 maternal deaths. The current study used records from 2,080 pregnancies and found the prevalence of HDP at HAS to be 13.5% (280) with 156 stillbirths and 11 maternal deaths. Raghuraman et al. looked at women who were diagnosed with antepartum preeclampsia, antepartum eclampsia, postpartum preeclampsia, and postpartum eclampsia, while the present study analyzed diagnoses of pregnancy induced hypertension, preeclampsia, and eclampsia. Chart review and systematic data entry were used to assess maternal complications for both studies, and the resulting estimates of HDP prevalence are similar. Both studies found that there was no difference in maternal age among women with HDP and who had a stillbirth compared to women who had a live birth. Both studies also found that stillbirth was significantly associated with shorter gestational age at delivery. More maternal deaths and placental abruptions were seen among the women with HDP and who had stillbirths in both studies. Thus, it is not clear why the numbers of fetal and maternal losses would be greater for deliveries for 2013-2014 than for deliveries for 2011-2012.

One key difference between this study and the Raghuraman et al. study is the ability to compare women with HDP to women without HDP in this study. The Raghuraman study lacked medical data on women with no hypertensive disorders; thus they were unable to have a control group to compare complications and other associations.[40]

The current study also examined HDP in three additional hospitals in other areas of Haiti, thereby allowing comparisons among different samples and obtaining a broader perspective on hospital-based prevalence estimates. Prevalence of HDP varied among the four hospitals, and was much higher at HAS compared to the others. This could be due to HAS having a known electronic medical records system that has been implemented for many years; thus they may have more extensive records and better record keeping. The lack of consistency between the four hospitals may not be differences among samples, but rather differences in surveillance and record keeping. All hospitals, except Fort Liberté, found an association between HDP and higher rates of low birth weight babies and stillbirths. The relative small number of women with HDP at HIC, Fort Liberté, and HSC may have masked some of the associations that were seen at HAS.

The limitations to this study include the retrospective nature of this hospital-based study. These findings are not generalizable to the Haitian population due to the large number of women who do not give birth inside a hospital or medical facility. Data were collected from existing surveillance records that had incomplete records and missing data. Gestational age was not collected in the surveillance system until July 2013, which affected records from HAS, HIC, and HSC. HIC outcomes were not recorded for women

presenting at the OT, which may have caused associations to be missed due to the large number of women who require surgery normally have more high-risk pregnancies and complications. HIC is also missing data for August 2013 as they were closed while remodeling the maternity ward. Maternal deaths at HIC were poorly reported and appear to be differentially missing; women with reported HDP appear to me missing maternal status more than women without HDP. Data from Fort Liberté may not be representative of the population in that commune and District as this hospital does not have a surgery ward. Women who present at Fort Liberté with a high-risk pregnancy requiring surgery are referred out to other health facilities. A further limitation to this study is the inconsistency of years of data used for the various hospitals. Researchers expect that more years of implementing the surveillance system may be associated with more complete and accurate data reporting.

A further limitation of this study is the lack of specific blood pressure readings. Researchers were unable to confirm the readings, thus there is a potential for misclassification of HDP. HDP and placental abruption complications are captured in the surveillance as three complication variables. Not having a specific recording section for each of these separately leads to a potential underreporting of these data. Maternal Body Mass Index (BMI), which has been shown to be associated with higher rates of HDP in Haiti, was also not recorded in this system.[41]

In conclusion, the results of this study highlight the importance of HDP as a major cause of adverse maternal and neonatal outcomes among this population in Haiti, which is comparable to studies conducted in high-income countries. Specifically, women with eclampsia, the most severe form of HDP, had the worst health outcomes. Due to this fact

and the high burden of HDP-related mortality, triaging women at risk for pregnancy induced hypertension needs to emphasized as a priority.

This study adds to the limited work studying HDP in LMIC's and in Haiti specifically. Additional studies are needed to further examine the etiology of why Haitian women are abnormally affected by hypertension, especially during pregnancy. Further studies on other risk factors of HDP among Haitians, such as BMI or diet, need to also be conducted.

Given the large number of women delivering outside of hospitals due in part to the 3 delays mentioned above, there could be many other maternal deaths and stillbirths that are occurring and almost certainly women with HDP that are not being managed. The lack of consistency between the four hospitals in this study exemplify not only the flaws in surveillance in Haiti, but also further drives home the fact that the true burden of HDP in this country remains unknown. Not only should improved surveillance be made a priority, but also future studies should attempt to collect data on women who do not give birth at a facility, as they represent a large, unrepresented portion of the maternal population in Haiti.

Table 1. Prevalence of hypertensive disorders in pregnancy in 4 hospitals by 6 month intervals

		Jan-June 2012	July-Dec 2012	Jan-June 2013	July-Dec 2013	Jan-June 2014	July-Dec 2014	Overall Hospital Total
		Number of HDP Cases (Hospital Specific Prevalence)	Number of HDP Cases (Hospital Specific Prevalence)	Number of HDP Cases (Hospital Specific Prevalence)	Number of HDP Cases (Hospital Specific Prevalence)	Number of HDP Cases (Hospital Specific Prevalence)	Number of HDP Cases (Hospital Specific Prevalence)	Total Number of HDP Cases (Total Hospital Specific Prevalence)
HAS (n=2,080)	Hypertension			1 (0.2)	16 (2.8)	10 (2.0)	7 (1.3)	34 (1.6)
	Preeclampsia			0 (0.0)	78 (13.8)	54 (11.1)	52 (9.7)	184 (8.8)
	Eclampsia			0 (0.0)	34 (6.0)	10 (2.0)	18 (3.3)	62 (3.0)
	Total HDP in HAS	---	---	1 (0.2)	128 (22.6)	74 (15.1)	77 (14.3)	**280 (13.5)**
HIC (n=4,072)	Hypertension					0 (0.0)	11 (0.5)	11 (0.3)
	Preeclampsia					15 (0.8)	65 (2.9)	80 (2.0)
	Eclampsia					12 (0.7)	27 (1.2)	39 (1.0)
	Total HDP in HIC	---	---	---	---	27 (1.5)	103 (4.6)	**130 (3.2)**
Fort Liberté (n=1,569)	Hypertension			4 (1.0)	14 (2.8)	33 (11.6)	8 (2.1)	59 (3.8)
	Preeclampsia			0 (0.0)	0 (0.0)	0 (0.0)	5 (1.3)	5 (0.3)
	Eclampsia			2 (0.5)	0 (0.0)	1 (0.4)	0 (0.0)	3 (0.2)
	Total HDP in Fort Liberté	---	---	6 (1.5)	14 (2.8)	34 (11.9)	13 (3.4)	**67 (4.3)**
HSC (n=1,101)	Hypertension	0 (0.0)	2 (0.3)					2 (0.2)
	Preeclampsia	10 (1.9)	6 (1.0)					16 (1.4)
	Eclampsia	9 (1.7)	6 (1.0)					15 (1.4)
	Total HDP in HSC	19 (3.7)	14 (2.4)	---	---	---	---	**33 (3.0)**
Total (n=8,822)	Hypertension							106 (1.2)
	Preeclampsia							285 (3.2)
	Eclampsia							119 (1.3)
	Total HDP							**510 (5.8)**

Data shown as number of HDP cases (Prevalence by hospital and time period).

Empty cells represent time periods where data were not available.

Table 2. Comparison of HDP vs. No HDP and obstetric characteristics of women at 4 hospitals in Haiti

	Full Cohort (n=7,958)	HAS No HDP (n=1,800)	HAS HDP (n=280)	p[a]	HIC No HDP (n=3,148)*	HIC HDP (n=60)*	p[b]	Fort Liberté No HDP (n=1,502)	Fort Liberté HDP (n=67)	p[c]	HSC No HDP (n=1,068)	HSC HDP (n=33)	p[d]
Maternal age (years)[e]	27.7 ± 6.7	27.6 ± 6.8	28.4 ± 8.0	0.08	27.7 ± 6.5	28.4 ± 8.0	0.46	26.8 ± 6.4	28.8 ± 6.8	**0.01**	29.1 ± 6.4	26.8 ± 7.4	**0.05**
Parity				**0.02**			0.61			0.58			0.44
Nulliparous	3,483 (43.8)	836 (46.4)	109 (38.9)		1,332 (42.3)	23 (38.3)		617 (41.1)	30 (44.8)		523 (49.0)	13 (39.4)	
Parous	4,194 (52.7)	962 (53.4)	171 (61.1)		1,556 (49.4)	31 (51.7)		874 (58.2)	37 (55.2)		545 (51.0)	18 (54.5)	
Missing	281 (3.5)	2 (0.1)	0 (0.0)		260 (8.3)	6 (10.0)		11 (0.7)	0 (0.0)		0 (0.0)	2 (6.1)	
Mode of Delivery				**0.04**			**0.02**			0.16			**<0.0001**
Vaginal	6,263 (78.7)	1,259 (69.9)	179 (63.9)		2,496 (79.3)	38 (63.3)		1,421 (94.6)	61 (91.0)		808 (75.7)	1 (3.0)	
Caesarean section	1,310 (16.5)	541 (30.1)	101 (36.1)		290 (9.2)	10 (16.7)		76 (5.1)	6 (9.0)		254 (23.8)	32 (97.0)	
Missing	385 (4.8)	0 (0.0)	0 (0.0)		362 (11.5)	12 (20.0)		5 (0.3)	0 (0.0)		6 (0.6)	0 (0.0)	
Low Birthweight (<2500 g)				**<0.0001**			**0.0004**			0.80			**0.0006**
Yes	1,240 (15.6)	394 (21.9)	149 (53.2)		343 (10.9)	14 (23.3)		135 (9.0)	7 (10.5)		186 (17.4)	12 (36.4)	
No	5,667 (71.2)	1,327 (73.7)	121 (43.2)		2,409 (76.5)	33 (55.0)		900 (59.9)	42 (62.7)		823 (77.1)	12 (36.4)	
Missing	1,051 (13.2)	79 (4.4)	10 (3.6)		396 (12.6)	13 (21.7)		467 (31.1)	18 (26.9)		59 (5.5)	9 (27.3)	
Gestational age (weeks)[f]	38.2 ± 4.3	38.6 ± 3.5	36.3 ± 4.4	**<0.0001**	38.6 ± 4.7	37.2 ± 4.2	**0.047**	37.0 ± 3.7	37.2 ± 2.3	0.65	---	---	---
Preterm delivery (<37 weeks)				**<0.0001**			**<0.0001**			0.30			---
Yes	738 (9.3)	179 (9.9)	78 (27.9)		241 (7.7)	13 (21.7)		211 (14.0)	16 (23.9)		---	---	
No	3,880 (48.8)	991 (55.1)	135 (48.2)		2,163 (68.7)	30 (50.0)		532 (35.4)	29 (43.3)		---	---	
Missing	3,340 (42.0)	630 (35.0)[g]	67 (23.9)[g]		744 (23.6)	17 (28.3)		759 (50.5)	22 (32.8)		1,068 (100.0)[g]	33 (100.0)[g]	
Stillbirth				**<0.0001**			**0.01**			0.15			0.08
Yes	392 (4.9)	104 (5.8)	52 (18.6)		124 (3.9)	6 (10.0)		46 (3.1)	0 (0.0)		56 (5.2)	4 (12.1)	
No	7,168 (90.1)	1,690 (93.9)	227 (81.1)		2,652 (84.2)	40 (66.7)		1,454 (96.8)	67 (100.0)		1,010 (94.6)	28 (84.9)	
Missing	398 (5.0)	6 (0.3)	1 (0.4)		372 (11.8)	14 (23.3)		2 (0.1)	0 (0.0)		2 (0.2)	1 (3.0)	
Maternal death				**0.002**			0.98			0.55			0.68
Yes	26 (0.3)	6 (0.3)	5 (1.8)		1 (0.03)	0 (0.0)		8 (0.5)	0 (0.0)		6 (0.5)	0 (0.0)	
No	6,043 (75.9)	1,786 (99.2)	274 (97.9)		1,370 (43.5)	1 (1.7)		1,455 (96.9)	66 (98.5)		1,061 (99.3)	30 (90.9)	
Missing	1,889 (23.7)	8 (0.4)	1 (0.4)		1,777 (56.4)	59 (98.3)		39 (2.6)	1 (1.5)		1 (0.1)	3 (9.1)	
Placenta abruption				**0.04**			**<0.0001**			0.83			**<0.0001**
Yes	38 (0.5)	11 (0.6)	5 (1.8)		7 (0.2)	2 (3.3)		1 (0.1)	0 (0.0)		8 (0.7)	4 (12.1)	
No	7,920 (99.5)	1,789 (99.4)	275 (98.2)		3,141 (99.8)	58 (96.7)		1,501 (99.9)	67 (100.0)		1,060 (99.3)	29 (87.9)	
Missing	0 (0.0)	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	

Data are shown as mean ± SD or n (%).

* HIC data from Maternal Registry Only

[a]Compares No HDP and HDP for women at HAS

[b]Compares No HDP and HDP for women at HIC

[c]Compares No HDP and HDP for women at Fort Liberte

[d]Compares No HDP and HDP for women at Milot

[e]411 mothers missing maternal age (5.2%)

[f]3,340 mothers missing gestational age (42.0%)

[g]Gestational age was not collected until July 2013, thus it is missing if prior

Table 3. Clinical presentation of women with and without stillbirth at HAS, by entire cohort and by HDP mothers only

	Entire HAS Cohort (n=2,080)				HDP women only (n=280)[b]		
	Live birth (n=1,917)	**Stillbirth (n=156)**	**p**	**Unknown (n=7)**	**Live birth (n=227)**	**Stillbirth (n=52)**	**p**
Maternal age (years)[c]	27.6 ± 6.9	28.9 ± 7.8	0.08	31.6 ± 7.0	28.1 ± 7.9	29.5 ± 8.3	0.27
Parity			**0.001***				**0.047***
Nulliparous	892 (46.5)	52 (33.3)		1 (14.3)	95 (41.9)	14 (26.9)	
Parous	1,023 (53.4)	104 (66.7)		6 (85.7)	132 (58.2)	38 (73.1)	
Missing	2 (0.1)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	
Mode of Delivery			**0.006***				**0.0005***
Vaginal	1309 (68.3)	123 (78.8)		6 (85.7)	134 (59.0)	44 (84.6)	
Caesarean section	608 (31.7)	33 (21.2)		1 (14.3)	93 (41.0)	8 (15.4)	
Missing	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	
Low Birthweight (<2500 g)			**<0.0001***				**<0.0001***
Yes	435 (22.7)	108 (69.2)		0 (0.0)	107 (47.1)	42 (80.8)	
No	1,404 (73.2)	43 (27.6)		1 (14.3)	114 (50.2)	7 (13.5)	
Missing	78 (4.07)	5 (3.2)		6 (85.7)	6 (2.6)	3 (5.8)	
Gestational age (weeks)[a]	38.7 ± 3.1	32.9 ± 6.4	**<0.0001**	35.0 ± 5.7	37.0 ± 3.9	32.4 ± 5.3	**<0.0001**
Preterm delivery (<37 weeks)			**<0.0001***				**0.05***
Yes	192 (10.0)	64 (41.0)		1 (14.3)	58 (25.6)	20 (38.5)	
No	1,088 (56.8)	37 (23.7)		1 (14.3)	126 (55.5)	9 (17.3)	
Missing[a]	637 (33.2)	55 (35.3)		5 (71.4)	43 (18.9)	23 (44.2)	
Diagnosis							
Normotensive	1,690 (88.2)	104 (66.7)	**<0.0001***	6 (85.7)	--	--	--
Hypertension	32 (1.7)	2 (1.3)	0.74	0 (0.0)	32 (14.1)	2 (3.9)	**0.04***
Preeclampsia	150 (7.8)	34 (21.8)	**<0.0001***	0 (0.0)	150 (66.1)	34 (65.4)	0.92*
Eclampsia	45 (2.3)	16 (10.3)	**<0.0001**	1 (14.3)	45 (19.8)	16 (30.77)	0.09
Maternal death			**0.007**				0.23
Yes	7 (0.4)	4 (2.6)		0 (0.0)	3 (1.3)	2 (3.85)	
No	1,902 (99.2)	151 (96.8)		7 (100.0)	224 (98.7)	49 (94.2)	
Missing	8 (0.4)	1 (0.6)		0 (0.0)	0 (0.0)	1 (1.9)	
Placenta abruption			**<0.0001***				**0.01**
Yes	7 (0.4)	9 (5.8)		0 (0.0)	1 (0.4)	4 (7.7)	
No	1,910 (99.6)	147 (94.2)		7 (100.0)	226 (99.6)	48 (92.3)	
Missing	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	

Data are shown as mean ± SD or n (%).

Statistically significant P-values are shown in bold.

*P-value calculated using chi-square, all other P-values calculated by Fisher's exact test.

[a]Gestational age was not collected until July 2013, thus it is missing if prior

[b]Missing 1 observation for Stillbirth status

Table 4. Clinical presentation of women by maternal death status at HAS, by entire cohort and by HDP mothers only

	Entire HAS Cohort (n=2,080)				HDP women only (n=280)[b]		
	No maternal death (n=2,060)	**Maternal death (n=11)**	**p**	**Unknown (n=9)**	**No maternal death (n=274)**	**Maternal death (n=5)**	**p**
Maternal age (years)[c]	27.7 ± 7.0	30.9 ± 8.4	0.13	28.3 ± 8.6	28.3 ± 7.9	36.0 ± 7.0	**0.03**
Parity			0.07*				0.08
Nulliparous	940 (45.6)	2 (18.1)		3 (33.3)	109 (39.8)	0 (0.0)	
Parous	1,118 (54.3)	9 (81.8)		6 (66.7)	165 (60.2)	5 (100.0)	
Missing	2 (0.001)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	
Mode of Delivery			**0.001**				**0.01**
Vaginal	1,430 (69.4)	2 (18.1)		6 (66.7)	178 (65.0)	0 (0.0)	
Caesarean section	630 (30.6)	9 (81.8)		3 (33.3)	96 (35.0)	5 (100.0)	
Missing	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	
Low Birthweight (<2500 g)			**0.01**				0.26
Yes	535 (26.0)	7 (63.6)		1 (11.1)	145 (52.9)	4 (80.0)	
No	1,437 (69.8)	4 (36.4)		7 (77.8)	120 (43.8)	1 (20.0)	
Missing	88 (4.3)	0 (0.0)		1 (11.1)	9 (3.3)	0 (0.0)	
Gestational age (weeks)[a]	38.3 ± 3.8	36.1 ± 5.0	0.11	39.7 ± 1.3	36.4 ± 4.3	34.6 ± 5.8	0.37
Preterm delivery (<37 weeks)			0.17				0.60
Yes	254 (12.3)	3 (27.3)		0 (0.0)	76 (27.7)	2 (40.0)	
No	1114 (54.1)	5 (45.5)		7 (77.8)	132 (48.2)	3 (60.0)	
Missing[a]	692 (33.6)	3 (27.3)		2 (22.2)	66 (24.1)	0 (0.0)	
Diagnosis							
Normotensive	1,786 (86.7)	6 (54.5)	0.01	8 (88.9)	--	--	--
Hypertension	34 (1.7)	0 (0.0)	1.00	0 (0.0)	34 (12.4)	0 (0.0)	1.00
Preeclampsia	181 (8.8)	3 (27.3)	0.07	0 (0.0)	181 (66.1)	3 (60.0)	0.78
Eclampsia	59 (2.9)	2 (18.2)	**0.04**	1 (11.1)	59 (21.5)	2 (40.0)	0.30
Stillbirth			**0.01**				0.23
Yes	151 (7.3)	4 (36.4)		1 (11.1)	49 (17.9)	2 (40.0)	
No	1,902 (92.3)	7 (63.6)		8 (88.9)	224 (81.8)	3 (60.0)	
Missing	7 (0.3)	0 (0.0)		0 (0.0)	1 (0.4)	0 (0.0)	
Placenta abruption			0.08				0.09
Yes	15 (0.7)	1 (9.1)		0 (0.0)	4 (1.5)	1 (20.0)	
No	2,045 (99.3)	10 (90.9)		9 (100.0)	270 (98.5)	4 (80.0)	
Missing	0 (0.0)	0 (0.0)		0 (0.0)	0 (0.0)	0 (0.0)	

Data are shown as mean ± SD or n (%).

Statistically significant P-values are shown in bold.

*P-value calculated using chi-square, all other P-values calculated by Fisher's exact test.

[a]Gestational age was not collected until July 2013, thus it is missing if prior

[b]Missing 1 observation for Maternal death status

Table 5. Logistic regression on the association between HDP and outcomes for women at HAS

	NT vs. All HDP			
Outcomes	**OR**	**95% CI**	**aOR***	**95% Ci**
Low Birthweight (<2500 g)	4.15	**3.18-5.41**	4.17	**3.19-5.45**
Stillbirth	3.72	**2.60-5.34**	3.51	**2.43-5.06**
Maternal death	5.43	**1.65-17.92**	5.13	**1.53-17.25**

	NT vs. HTN			
Outcomes	**OR**	**95% CI**	**aOR***	**95% Ci**
Low Birthweight (<2500 g)	1.47	0.69-3.10	1.49	0.70-3.18
Stillbirth	1.02	0.24-4.30	0.87	0.20-3.75
Maternal death	3.98	0.03-34.83	4.14	0.03-35.76

	NT vs. PEC			
Outcomes	**OR**	**95% CI**	**aOR***	**95% Ci**
Low Birthweight (<2500 g)	4.64	**3.39-6.35**	4.79	**3.48-6.59**
Stillbirth	3.68	**2.42-5.62**	3.34	**2.17-5.14**
Maternal death	4.93	**1.22-19.89**	5.21	**1.26-21.56**

	NT vs. ECC			
Outcomes	**OR**	**95% CI**	**aOR***	**95% Ci**
Low Birthweight (<2500 g)	5.29	**3.03-9.25**	5.00	**2.84-8.79**
Stillbirth	5.78	**3.16-10.57**	6.34	**3.40-11.82**
Maternal death	10.09	**2.00-51.05**	12.70	**2.33-69.31**

NT, normotensive women; HDP, Hypertensive disorder in pregnancy; HTN, Hypertension; PEC, Preeclampsia; ECC, Eclampsia; OR, odds ratio; aRR, adjusted odds ratio

Statistically significant CI's are shown in bold.

*Adjusted for maternal age, parity, year of delivery

Figure 1. Geographic Distribution of Targeted Hospitals

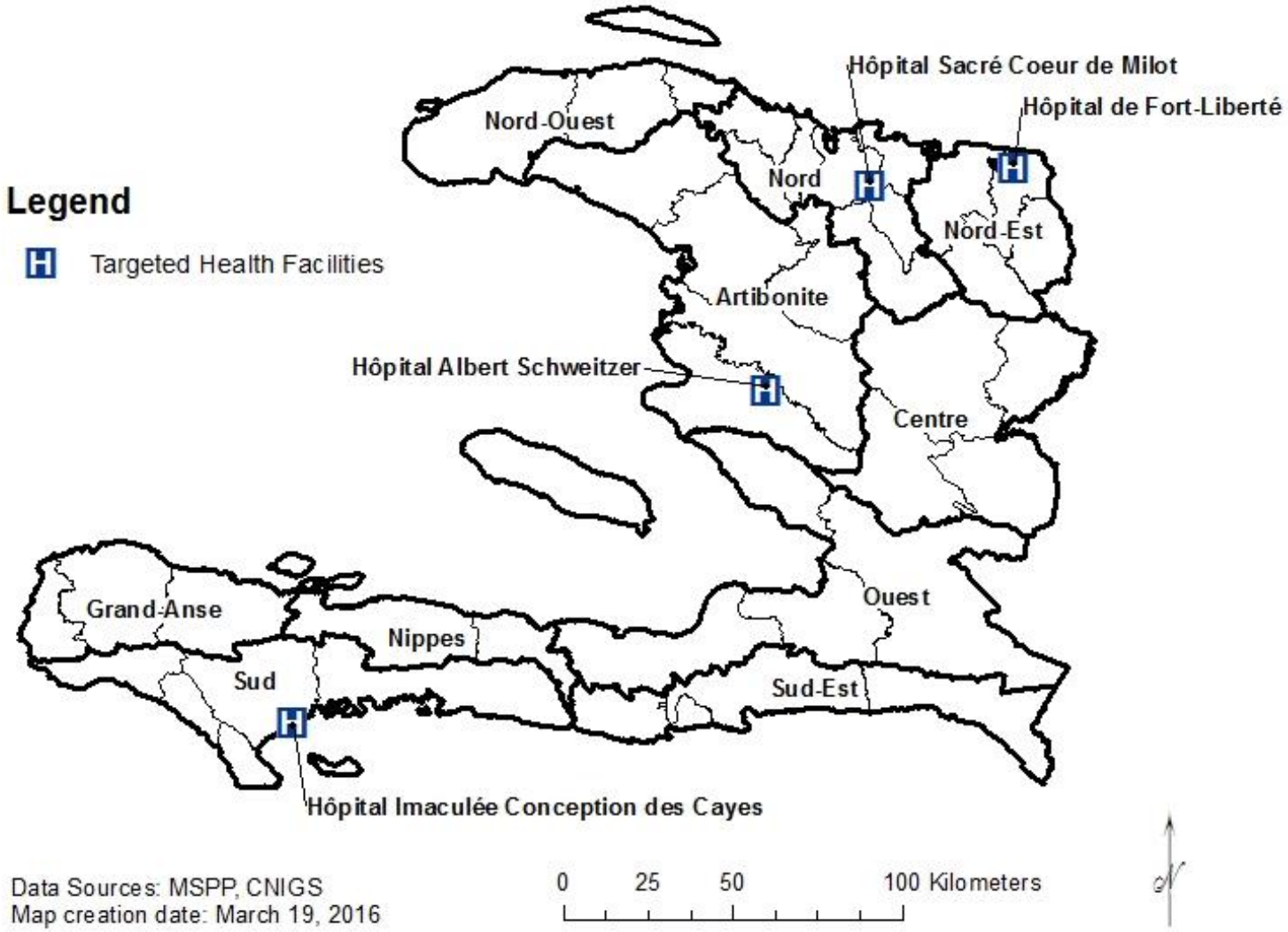
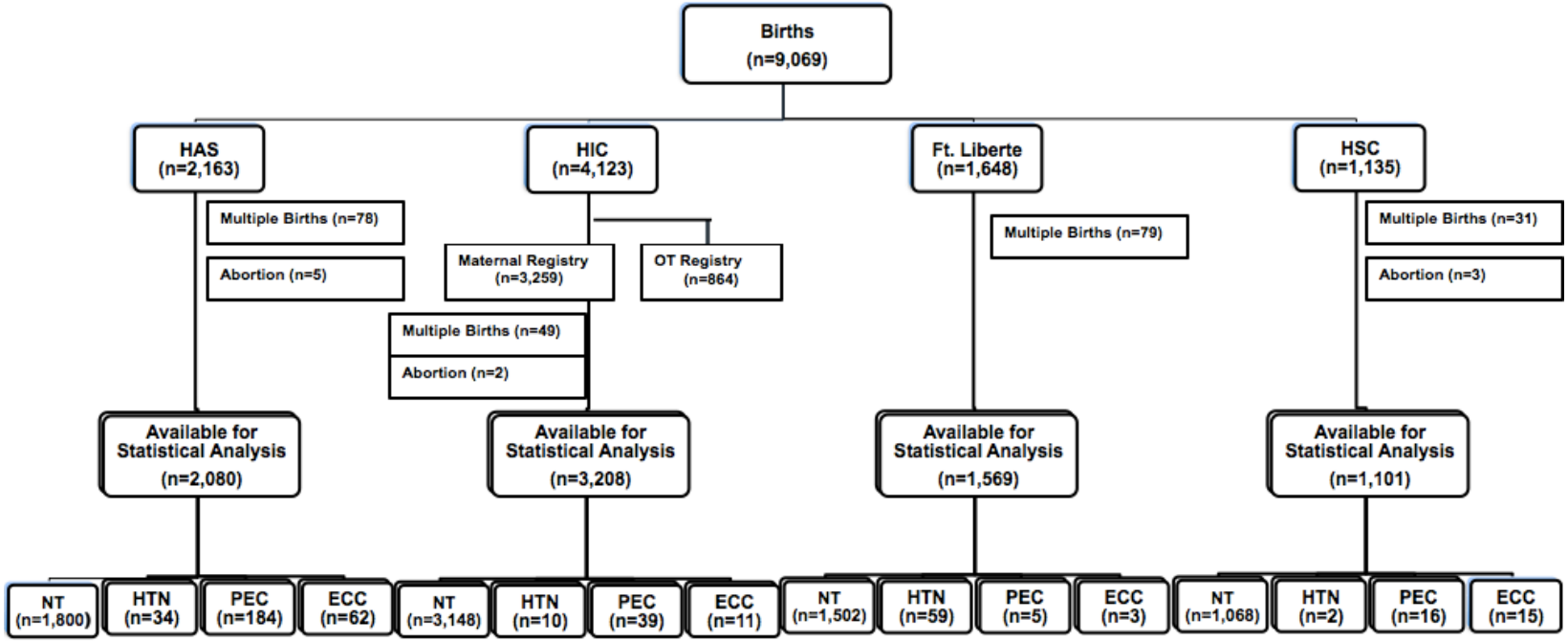


Figure 2: Cohort chart



NT= Normotensive Pregnancies
HTN = Hypertension
PEC = Preeclampsia
ECC = Eclampsia

Hypertensive disorders during pregnancy		
Pregnancy Induced Hypertension -Systolic blood pressure ≥ 140 mmHg -Without proteinuria -No other symptoms	**Preeclampsia** -Systolic blood pressure ≥ 140 mmHg -Proteinuria (≥ 300 mg/24 hours)	**Eclampsia** -Systolic blood pressure ≥ 160 mmHg -Proteinuria (≥ 300 mg/24 hours) -Seizures

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Chapter III: Public Health Implications

The results of this study highlight the importance of HDP as a major cause of adverse maternal and neonatal outcomes among this population in Haiti, which is comparable to studies conducted in high-income countries. Specifically, women with eclampsia, the most severe form of HDP, had the worst health outcomes. These women were at increased odds of having a low birth weight baby, delivering a stillbirth, and were more likely to die due to complications of pregnancy.

This study adds to the limited work studying HDP in LMIC's and in Haiti specifically. Results from this study display several implications for public health. Due to the frequency of adverse outcomes among women with HDP and the high burden of HDP-related mortality, triaging women at risk for pregnancy induced hypertension needs to be emphasized as a priority. Early detection and consistent monitoring of women at-risk for hypertension during pregnancy can help prevent progressing preeclampsia or eclampsia and lesson the odds of serious adverse outcomes.

Research has shown that majority of Haitian women are delivering at home or under the care of unqualified health professionals. Due to the high number of maternal deaths among women with HDP in this sample of women delivering at these four hospitals, the research team would speculate that mothers delivering outside of a medical facility would be at even higher odds of dying from a complication of HDP or other pregnancy complication. Haitian women need to be educated on the signs of hypertension, preeclampsia, and eclampsia and on the increased risks associated with lack of prenatal care, poor disease management, and unsafe delivery practices.

The lack of consistency between the four hospitals in this study exemplify not only the flaws in surveillance in Haiti, but also further drives home the fact that the true burden of HDP in this country remains unknown. Improved surveillance in maternity wards, operating theaters, and medical facilities can help better capture maternal and neonatal outcomes and complications, allowing medical professional to recognize trends among Haitian women. These discoveries can allow researchers to tailor future studies and plan potential interventions that can improve the quality of lives of Nicaraguan mothers and babies.

Results from this study can be used to motivate future research. Additional studies are needed to further examine the etiology of why Haitian women are abnormally affected by hypertension, especially during pregnancy. Other risk factors of HDP among Haitians, such as BMI or diet, need to also be studied to discover any unknown associations with HDP.

Additionally, knowledge could be gained by conducting research at the community level. Due to the majority of mothers delivering outside of a medical facility, this large sample of the population remains unrepresented in statistics and in the literature. Qualitative and quantitative research on these mothers can allow researchers to obtain more representative analysis of HDP among Haitians.

Appendix

SAS Code

```
options nofmterr;

libname c 'H:\Thesis';

*Milot 2012;
data one;
set c.milot2012_2014;
if naissance3=0 then triplet=1;
else triplet=0;

if naissance2=0 and naissance3 in (88,99) then twin=1;
else if naissance2=1 and naissance3 in (88,99) then twin=1;
else if naissance2=2 and naissance3 in (88,99) then twin=1;
else if naissance2=3 and naissance3 in (88,99) then twin=1;
else twin=0;

if naissance1 in (0,1,2,3,99) and twin=0 and triplet=0 then
singleton=1;
else singleton=0;

if complic1_cleaned='PES' or complic1_cleaned='ECC' or
complic1_cleaned='HTA' or complic1_cleaned='HTA + G' or
complic2_cleaned='PES' or complic2_cleaned='ECC' or
complic2_cleaned='HTA' or complic2_cleaned='HTA + G' or
complic3_cleaned='PES' or complic3_cleaned='ECC' or
complic3_cleaned='HTA' or complic3_cleaned='HTA + G' then exposed=1;
else exposed=0;
run;

data finalMilot;
set one;
if singleton=0 then delete;
if annee=2013 then delete;
if annee=2014 then delete;
if complic1_cleaned='AP' or complic2_cleaned='AP' or
complic3_cleaned='AP' then PA=1;
else PA=0;
drop mois datevih datesyph codeM codeP;
if month = "Aout" then month2=8;
else if month="Avril" then month2=4;
else if month in ("DÈcembre", "Decembre") then month2=12;
else if month = "Fevrier" then month2=2;
else if month="Janvier" then month2=1;
else if month in ("Juillet", "juillet") then month2=7;
else if month="Juin" then month2=6;
else if month="Mai" then month2=5;
else if month in ("Novembre", "NOVEMBRE") then month2=11;
else if month in ("OCTOBRE", "Octobre") then month2=10;
else if month="Septembre" then month2=9;
else if month="Mars" then month2=3;
else month2=month;
drop month;
```

```
rename month2=month;

complic2r=put(complic2, 7.);
drop complic2;
rename complic2r=complic2;
complic3r=put(complic3, 7.);
drop complic3;
rename complic3r=complic3;
run;


proc freq data=finalMilot;
tables exposed*mois;
run;

proc freq data=finalMilot;
tables exposed*annee*mois;
run;

********HAS*;

proc contents varnum data=c.has2012_2014;
run;

data two;
set c.has2012_2014;
if naissance3=0 then triplet=1;
else triplet=0;

if naissance2=0 and naissance3 in (88,99) then twin=1;
else if naissance2=1 and naissance3 in (88,99) then twin=1;
else if naissance2=2 and naissance3 in (88,99) then twin=1;
else if naissance2=3 and naissance3 in (88,99) then twin=1;
else twin=0;

if naissance1 in (0,1,2,3,99) and twin=0 and triplet=0 then
singleton=1;
else singleton=0;

if complic1_cleaned='PES' or complic1_cleaned='ECC' or
complic1_cleaned='HTA' or complic1_cleaned='HTA + G' or
complic2_cleaned='PES' or complic2_cleaned='ECC' or
complic2_cleaned='HTA' or complic2_cleaned='HTA + G' or
complic3_cleaned='PES' or complic3_cleaned='ECC' or
complic3_cleaned='HTA' or complic3_cleaned='HTA + G' then exposed=1;
else exposed=0;

if complic1_cleaned='AP' or complic2_cleaned='AP' or
complic3_cleaned='AP' then PA=1;
else PA=0;
run;

data finalHAS;
set two;
if singleton=0 then delete;
if annee=2012 then delete;
drop mois datevih datesyph codeM codeP;
```

```
run;

proc freq data=finalHAS;
tables exposed*annee*mois;
run;

*********All Ft Liberte 2012-2014*;
proc contents varnum data=c.fortlib2012_2014;
run;

data three;
set c.fortlib2012_2014;
if naissance3=0 then triplet=1;
else triplet=0;

if naissance2=0 and naissance3 in (88,99) then twin=1;
else if naissance2=1 and naissance3 in (88,99) then twin=1;
else if naissance2=2 and naissance3 in (88,99) then twin=1;
else if naissance2=3 and naissance3 in (88,99) then twin=1;
else twin=0;

if naissance1 in (0,1,2,3,99) and twin=0 and triplet=0 then
singleton=1;
else singleton=0;

if complic1_cleaned='PES' or complic1_cleaned='ECC' or
complic1_cleaned='HTA' or complic1_cleaned='HTA + G' or
complic2_cleaned='PES' or complic2_cleaned='ECC' or
complic2_cleaned='HTA' or complic2_cleaned='HTA + G' or
complic3_cleaned='PES' or complic3_cleaned='ECC' or
complic3_cleaned='HTA' or complic3_cleaned='HTA + G' then exposed=1;
else exposed=0;

if complic1_cleaned='AP' or complic2_cleaned='AP' or
complic3_cleaned='AP' then PA=1;
else PA=0;
run;

data finalFL;
set three;
if singleton=0 then delete;
if annee=2012 then delete;
if month in ("AOUT", "Aout") then month2=8;
else if month="AVRIL" then month2=4;
else if month="DECEMBRE" then month2=12;
else if month="JANVIER" then month2=1;
else if month="JUIN" then month2=6;
else if month="MAI" then month2=5;
else if month in ("Novembre", "NOVEMBRE") then month2=11;
else if month in ("OCTOBRE", "Octobre") then month2=10;
else month2=month;
drop month;
rename month2=month;
drop mois datevih datesyph codeM codeP;
run;
```

```
proc freq data=finalFL;
tables exposed*annee*mois;
run;

proc freq data=finalFL;
tables exposed  lbw gesage APGAR1 APGAR5 MODE NAISSANCE1 MERE PA;
run;

*********HIC;
proc contents varnum data=c.sud_merged6;
run;

proc freq data=c.sud_merged6;
tables institution;
run;

data four;
set c.sud_merged6;
if institution ne 'HIC' then delete;
run;

data five ;
set four;
if naissance3=0 then triplet=1;
else triplet=0;

if naissance2=0 and naissance3 in (88,99) then twin=1;
else if naissance2=1 and naissance3 in (88,99) then twin=1;
else if naissance2=2 and naissance3 in (88,99) then twin=1;
else if naissance2=3 and naissance3 in (88,99) then twin=1;
else twin=0;

if naissance1 in (0,1,2,3,99) and twin=0 and triplet=0 then
singleton=1;
else singleton=0;

if complic1_cleaned='PES' or complic1_cleaned='ECC' or
complic1_cleaned='HTA' or complic1_cleaned='HTA + G' or
complic2_cleaned='PES' or complic2_cleaned='ECC' or
complic2_cleaned='HTA' or complic2_cleaned='HTA + G' or
complic3_cleaned='PES' or complic3_cleaned='ECC' or
complic3_cleaned='HTA' or complic3_cleaned='HTA + G' then exposed=1;
else exposed=0;

if complic1_cleaned='AP' or complic2_cleaned='AP' or
complic3_cleaned='AP' then PA=1;
else PA=0;
run;

data finalHIC;
set five;
if singleton=0 then delete;
gesage2=input(gesage, 2.);
drop gesage;
rename gesage2=gesage;
drop mois datevih datesyph codeM codeP;
run;
```

```
proc freq data=finalHIC;
tables exposed*month;
run;

proc freq data=finalHIC;
tables exposed  lbw gesage APGAR1 APGAR5 MODE NAISSANCE1 MERE PA;
run;

*Data exploration for more complications;
proc print data=finalHIC;
where mois_n='Janvier' and age=19; *1_17_14;
run;

proc print data=finalHIC (obs=10);
where exposed=1;
run;

**Combining Datasets*****;
data final;
set finalMilot finalHAS finalFL finalHIC;
run;

proc contents data=final;
run;

data final2;
set final;
if age=99 then age=.;
if para=40 then para=.;
if para=99 then para=.;
if para>0 then paracat=1;
if para=0 then paracat=0;
if para=. then paracat=.;
if gesage=88 then gesage=.;
if gesage=99 then gesage=.;
if gesage=8989 then gesage=.;
if mode=99 then mode=.;
if mode=5 then mode=1;
if gesage=. then PT=.;
if gesage<37 and gesage ne . then PT=1;
if gesage>=37 then PT=0;
if mode=4 then delete;        *Delete abortions;
if mode=3 then mode=1;
if mere=99 then mere=.;
if naissance1=1 then stillbirth=1;
if naissance1=2 then stillbirth=1;
if naissance1=3 then stillbirth=1;
if naissance1=0 then stillbirth=0;
if naissance1=99 then stillbirth=.;
if mode=1 then modef=0;       *Vag;
if mode=2 then modef=1;       *CS;
if mode=. then modef=.;
if LBW=99 then LBW=.;
run;
```

```
proc freq data=final2;
tables mode LBW/missing;
run;

proc freq data=final2;
tables age para modef/missing;
run;

proc freq data=final2;
tables mode*institution*exposed;
where mode=4;
run;

*HAS;
data two;
set c.has2012_2014;
if naissance3=0 then triplet=1;
else triplet=0;

if naissance2=0 and naissance3 in (88,99) then twin=1;
else if naissance2=1 and naissance3 in (88,99) then twin=1;
else if naissance2=2 and naissance3 in (88,99) then twin=1;
else if naissance2=3 and naissance3 in (88,99) then twin=1;
else twin=0;

if naissance1 in (0,1,2,3,99) and twin=0 and triplet=0 then
singleton=1;
else singleton=0;

if complic1_cleaned='PES' or complic1_cleaned='ECC' or
complic1_cleaned='HTA' or complic1_cleaned='HTA + G' or
complic2_cleaned='PES' or complic2_cleaned='ECC' or
complic2_cleaned='HTA' or complic2_cleaned='HTA + G' or
complic3_cleaned='PES' or complic3_cleaned='ECC' or
complic3_cleaned='HTA' or complic3_cleaned='HTA + G' then exposed=1;
else exposed=0;

if complic1_cleaned='AP' or complic2_cleaned='AP' or
complic3_cleaned='AP' then PA=1;
else PA=0;
run;

data HASf;
set two;
if singleton=0 then delete;
if annee=2012 then delete;
if complic1_cleaned='PES' then complicf='PES';
if complic1_cleaned='ECC' then complicf='ECC';
if complic1_cleaned='HTA'  then complicf='HTA';
if complic1_cleaned ='HTA + G' then complicf='HTA';
if complic2_cleaned='PES' then complicf='PES';
if complic2_cleaned='ECC' then complicf='ECC';
if complic2_cleaned='HTA + G' then complicf='HTA';
if complic2_cleaned='HTA' and complic1_cleaned NE 'PES' then
complicf='HTA';
if complic3_cleaned='ECC' then complicf='ECC';
if complic3_cleaned='PES' then complicf='PES';
```

```
run;

proc freq data=HASf;
tables complicf*mois*annee/missing;
run;

*HIC;
data four;
set c.sud_merged6;
if institution ne 'HIC' then delete;
run;

data five ;
set four;
if naissance3=0 then triplet=1;
else triplet=0;

if naissance2=0 and naissance3 in (88,99) then twin=1;
else if naissance2=1 and naissance3 in (88,99) then twin=1;
else if naissance2=2 and naissance3 in (88,99) then twin=1;
else if naissance2=3 and naissance3 in (88,99) then twin=1;
else twin=0;

if naissance1 in (0,1,2,3,99) and twin=0 and triplet=0 then
singleton=1;
else singleton=0;

if complic1_cleaned='PES' or complic1_cleaned='ECC' or
complic1_cleaned='HTA' or complic1_cleaned='HTA + G' or
complic2_cleaned='PES' or complic2_cleaned='ECC' or
complic2_cleaned='HTA' or complic2_cleaned='HTA + G' or
complic3_cleaned='PES' or complic3_cleaned='ECC' or
complic3_cleaned='HTA' or complic3_cleaned='HTA + G' then exposed=1;
else exposed=0;

if complic1_cleaned='AP' or complic2_cleaned='AP' or
complic3_cleaned='AP' then PA=1;
else PA=0;
run;

data HICf;
set five;
if singleton=0 then delete;
gesage2=input(gesage, 2.);
drop gesage;
rename gesage2=gesage;
if complic1_cleaned='PES' then complicf='PES';
if complic1_cleaned='ECC' then complicf='ECC';
if complic1_cleaned='HTA'  then complicf='HTA';
if complic2_cleaned='PES' then complicf='PES';
if complic2_cleaned='HTA' and complic1_cleaned NE 'PES' then
complicf='HTA';
if complic3_cleaned='PES' then complicf='PES';
run;
```

```
proc freq data=HICf;
tables complicf/missing;
run;

proc freq data=HICf;
tables complicf*month/missing;
run;

*Fort Liberte;
data three;
set c.fortlib2012_2014;
if naissance3=0 then triplet=1;
else triplet=0;

if naissance2=0 and naissance3 in (88,99) then twin=1;
else if naissance2=1 and naissance3 in (88,99) then twin=1;
else if naissance2=2 and naissance3 in (88,99) then twin=1;
else if naissance2=3 and naissance3 in (88,99) then twin=1;
else twin=0;

if naissance1 in (0,1,2,3,99) and twin=0 and triplet=0 then
singleton=1;
else singleton=0;

if complic1_cleaned='PES' or complic1_cleaned='ECC' or
complic1_cleaned='HTA' or complic1_cleaned='HTA + G' or
complic2_cleaned='PES' or complic2_cleaned='ECC' or
complic2_cleaned='HTA' or complic2_cleaned='HTA + G' or
complic3_cleaned='PES' or complic3_cleaned='ECC' or
complic3_cleaned='HTA' or complic3_cleaned='HTA + G' then exposed=1;
else exposed=0;

if complic1_cleaned='AP' or complic2_cleaned='AP' or
complic3_cleaned='AP' then PA=1;
else PA=0;
run;

data FLf;
set three;
if singleton=0 then delete;
if annee=2012 then delete;
if month in ("AOUT", "Aout") then month2=8;
else if month="AVRIL" then month2=4;
else if month="DECEMBRE" then month2=12;
else if month="JANVIER" then month2=1;
else if month="JUIN" then month2=6;
else if month="MAI" then month2=5;
else if month in ("Novembre", "NOVEMBRE") then month2=11;
else if month in ("OCTOBRE", "Octobre") then month2=10;
else month2=month;
drop month;
rename month2=month;
if complic1_cleaned='PES' then complicf='PES';
if complic1_cleaned='ECC' then complicf='ECC';
if complic1_cleaned='HTA'  then complicf='HTA';
if complic2_cleaned='ECC' then complicf='ECC';
if complic2_cleaned='HTA' then complicf='HTA';
```

```
if complic2_cleaned='PES' then complicf='PES';
run;

proc freq data=FLf;
tables complicf/missing;
run;

proc freq data=FLf;
tables complicf*mois*annee/missing;
run;

*Milot;
data one;
set c.milot2012_2014;
if naissance3=0 then triplet=1;
else triplet=0;

if naissance2=0 and naissance3 in (88,99) then twin=1;
else if naissance2=1 and naissance3 in (88,99) then twin=1;
else if naissance2=2 and naissance3 in (88,99) then twin=1;
else if naissance2=3 and naissance3 in (88,99) then twin=1;
else twin=0;

if naissance1 in (0,1,2,3,99) and twin=0 and triplet=0 then
singleton=1;
else singleton=0;

if complic1_cleaned='PES' or complic1_cleaned='ECC' or
complic1_cleaned='HTA' or complic1_cleaned='HTA + G' or
complic2_cleaned='PES' or complic2_cleaned='ECC' or
complic2_cleaned='HTA' or complic2_cleaned='HTA + G' or
complic3_cleaned='PES' or complic3_cleaned='ECC' or
complic3_cleaned='HTA' or complic3_cleaned='HTA + G' then exposed=1;
else exposed=0;
run;

data Milotf;
set one;
if singleton=0 then delete;
if annee=2013 then delete;
if annee=2014 then delete;
if complic1_cleaned='AP' or complic2_cleaned='AP' or
complic3_cleaned='AP' then PA=1;
else PA=0;
if month = "Aout" then month2=8;
else if month="Avril" then month2=4;
else if month in ("DÈcembre", "Decembre") then month2=12;
else if month = "Fevrier" then month2=2;
else if month="Janvier" then month2=1;
else if month in ("Juillet", "juillet") then month2=7;
else if month="Juin" then month2=6;
else if month="Mai" then month2=5;
else if month in ("Novembre", "NOVEMBRE") then month2=11;
else if month in ("OCTOBRE", "Octobre") then month2=10;
else if month="Septembre" then month2=9;
else if month="Mars" then month2=3;
else month2=month;
```

```
drop month;
rename month2=month;

complic2r=put(complic2, 7.);
drop complic2;
rename complic2r=complic2;
complic3r=put(complic3, 7.);
drop complic3;
rename complic3r=complic3;
if complic1_cleaned='PES' then complicf='PES';
if complic1_cleaned='ECC' then complicf='ECC';
if complic1_cleaned='HTA'  then complicf='HTA';
if complic2_cleaned='HTA'  then complicf='HTA';
if complic2_cleaned='PES' then complicf='PES';
run;

proc freq data=Milotf;
tables exposed;
run;

proc freq data=Milotf;
tables complicf*mois/missing;
run;

*Base code for filling out Prevelance table;
proc freq data=Milotf;
tables complic1_cleaned;
where complic1_cleaned='PES' or complic1_cleaned='ECC' or
complic1_cleaned='HTA' or complic1_cleaned ='HTA + G' ;
run;

proc freq data=Milotf;
tables complic2_cleaned;
where complic2_cleaned='PES' or complic2_cleaned='ECC' or
complic2_cleaned='HTA' or complic2_cleaned='HTA + G';
run;

proc freq data=Milotf;
tables complic3_cleaned;
where complic3_cleaned='PES' or complic3_cleaned='ECC' or
complic3_cleaned='HTA' or complic3_cleaned='HTA + G';
run;

proc print data=Milotf;
where complic2_cleaned='PES';
run;

*Table 2;

proc means data=final2;
var age gesage;
run;

proc freq data=final2;
tables paracat Mode lbw PT naissance1 mere PA/ missing;
run;
```

```
*HAS;
data HAS2;
set final2;
if institution ne 'HAS' then delete;
run;

proc sort data=HAS2;
by exposed;
run;

proc means data=HAS2;
var age gesage;
by exposed;
run;

proc freq data=HAS2;
tables paracat*exposed modef*exposed lbw*exposed PT*exposed
stillbirth*exposed mere*exposed PA*exposed / missing;
run;

proc ttest data=HAS2;
class exposed;
var age gesage;
run;

proc freq data=HAS2;
tables paracat*exposed modef*exposed lbw*exposed PT*exposed
stillbirth*exposed mere*exposed PA*exposed /chisq;
run;

*HIC;
data HIC2;
set final2;
if institution ne 'HIC' then delete;
run;

proc sort data=HIC2;
by exposed;
run;

proc means data=HIC2;
var age gesage;
by exposed;
run;

proc freq data=HIC2;
tables paracat*exposed modef*exposed lbw*exposed PT*exposed
stillbirth*exposed mere*exposed PA*exposed / missing;
run;

proc ttest data=HIC2;
class exposed;
var age gesage;
run;

proc freq data=HIC2;
tables paracat*exposed modef*exposed lbw*exposed PT*exposed
```

```
stillbirth*exposed mere*exposed PA*exposed /chisq;
run;

*FL;
data FL2;
set final2;
if institution ne 'HOPITAL F' then delete;
run;

proc sort data=FL2;
by exposed;
run;

proc means data=FL2;
var age gesage;
by exposed;
run;

proc freq data=FL2;
tables paracat*exposed modef*exposed lbw*exposed PT*exposed
stillbirth*exposed mere*exposed PA*exposed / missing;
run;

proc ttest data=FL2;
class exposed;
var age gesage;
run;

proc freq data=FL2;
tables paracat*exposed modef*exposed lbw*exposed PT*exposed
stillbirth*exposed mere*exposed PA*exposed /chisq;
run;

*Milot;
data Milot2;
set final2;
if institution ne 'HSC MILOT' then delete;
run;

proc sort data=Milot2;
by exposed;
run;

proc means data=Milot2;
var age gesage;
by exposed;
run;

proc freq data=Milot2;
tables paracat*exposed modef*exposed lbw*exposed PT*exposed
stillbirth*exposed mere*exposed PA*exposed / missing;
run;

proc ttest data=Milot2;
class exposed;
var age gesage;
run;
```

```
proc freq data=Milot2;
tables paracat*exposed modef*exposed lbw*exposed PT*exposed
stillbirth*exposed mere*exposed PA*exposed /chisq;
run;

*Table 3- HAS Stillbirth;
data HAS3;
set final2;
if institution ne 'HAS' then delete;
if complic1_cleaned='PES' then complicf='PES';
if complic1_cleaned='ECC' then complicf='ECC';
if complic1_cleaned='HTA'  then complicf='HTA';
if complic1_cleaned ='HTA + G' then complicf='HTA';
if complic2_cleaned='PES' then complicf='PES';
if complic2_cleaned='ECC' then complicf='ECC';
if complic2_cleaned='HTA + G' then complicf='HTA';
if complic2_cleaned='HTA' and complic1_cleaned NE 'PES' then
complicf='HTA';
if complic3_cleaned='ECC' then complicf='ECC';
if complic3_cleaned='PES' then complicf='PES';
if complicf='PES' then PES=1;
else PES=0;
if complicf='HTA' then HTA=1;
else HTA=0;
if complicf='ECC' then ECC=1;
else ECC=0;
if complicf NE 'HTA' and complicf NE 'PES' and complicf NE 'ECC' then
NT=1;
else NT=0;
run;

proc sort data=HAS3;
by stillbirth;
run;

proc means data=HAS3;
var age gesage;
by stillbirth;
run;

proc freq data=HAS3;
tables paracat*stillbirth modef*stillbirth lbw*stillbirth PT*stillbirth
complicf*stillbirth mere*stillbirth PA*stillbirth / missing;
run;

proc ttest data=HAS3;
class exposed;
var age gesage;
run;

proc freq data=HAS3;
tables paracat*stillbirth modef*stillbirth lbw*stillbirth PT*stillbirth
complicf*stillbirth mere*stillbirth PA*stillbirth /chisq;
run;
```

```
proc freq data=HAS3;
tables NT*stillbirth HTA*stillbirth PES*stillbirth
ECC*stillbirth/chisq;
run;

*Table 4- HAS Maternal Death;
data HAS4;
set final2;
if institution ne 'HAS' then delete;
if complic1_cleaned='PES' then complicf='PES';
if complic1_cleaned='ECC' then complicf='ECC';
if complic1_cleaned='HTA'  then complicf='HTA';
if complic1_cleaned ='HTA + G' then complicf='HTA';
if complic2_cleaned='PES' then complicf='PES';
if complic2_cleaned='ECC' then complicf='ECC';
if complic2_cleaned='HTA + G' then complicf='HTA';
if complic2_cleaned='HTA' and complic1_cleaned NE 'PES' then
complicf='HTA';
if complic3_cleaned='ECC' then complicf='ECC';
if complic3_cleaned='PES' then complicf='PES';
if complicf='PES' then PES=1;
else PES=0;
if complicf='HTA' then HTA=1;
else HTA=0;
if complicf='ECC' then ECC=1;
else ECC=0;
if complicf NE 'HTA' and complicf NE 'PES' and complicf NE 'ECC' then
NT=1;
else NT=0;
run;

proc sort data=HAS4;
by mere;
run;

proc means data=HAS4;
var age gesage;
by mere;
run;

proc freq data=HAS4;
tables paracat*mere modef*mere lbw*mere PT*mere complicf*mere
stillbirth*mere PA*mere / missing;
run;

proc ttest data=HAS4;
class mere;
var age gesage;
run;

proc freq data=HAS4;
tables paracat*mere modef*mere lbw*mere PT*mere NT*mere HTA*mere
PES*mere ECC*mere stillbirth*mere PA*mere /chisq;
run;
```

```
*Logistics- HAS table;
proc freq data=HAS4;
tables stillbirth mere exposed age para annee NT HTA PES ECC/missing;
run;

data HAS5;
set HAS4;
if annee='2013' then year=0;
if annee='2014' then year=1;
if NT=1 then HTAf=0;
if HTA=1 then HTAf=1;
if NT=1 then PESf=0;
if PES=1 then PESf=1;
if NT=1 then ECCf=0;
if ECC=1 then ECCf=1;
run;

proc freq data=HAS5;
tables NT HTAf PESf ECCf exposed/ missing;
run;

proc logistic data=HAS5 descending;
model stillbirth=exposed;
title 'Stillbirth vs NT Unadjusted';
run;

proc logistic data=HAS5 descending;
model stillbirth=exposed age para year;
title 'Stillbirth vs NT adjusted';
run;

proc logistic data=HAS5 descending;
model mere=exposed;
title 'Maternal Death vs NT Unadjusted';
run;

proc logistic data=HAS5 descending;
model mere=exposed age para year;
title 'Maternal Death vs NT adjusted';
run;

proc logistic data=HAS5 descending;
model stillbirth=HTAf;
title 'Stillbirth vs HTA Unadjusted';
run;

proc logistic data=HAS5 descending;
model stillbirth=HTAf age para year;
title 'Stillbirth vs HTA adjusted';
run;

proc logistic data=HAS5 descending;       *Error;
model mere=HTAf;
title 'Maternal Death vs HTA Unadjusted';
run;
```

```
proc logistic data=HAS5 descending;       *Error Fixed using Firth's
Penalized Likelihood Method;
model mere=HTAf / firth clodds=PL;
title 'Maternal Death vs HTA Unadjusted';
run;

proc logistic data=HAS5 descending;       *ERROR;
model mere=HTAf age para year;
title 'Maternal Death vs HTA adjusted';
run;

proc logistic data=HAS5 descending;       *ERROR fixed using the
Firth's Penalized Likelihood Method;
model mere=HTAf age para year / firth clodds=PL;
title 'Maternal Death vs HTA adjusted';
run;

proc logistic data=HAS5 descending;
model stillbirth=PESf;
title 'Stillbirth vs PES Unadjusted';
run;

proc freq data=HAS5;
tables PESf/missing;
run;

proc logistic data=HAS5 descending;
model stillbirth=PESf age para year;
title 'Stillbirth vs PES adjusted';
run;

proc logistic data=HAS5 descending;
model mere=PESf;
title 'Maternal death vs PES Unadjusted';
run;

proc logistic data=HAS5 descending;
model mere=PESf age para year;
title 'Maternal death vs PES adjusted';
run;

proc logistic data=HAS5 descending;
model stillbirth=ECCf;
title 'Stillbirth vs ECC Unadjusted';
run;

proc logistic data=HAS5 descending;
model stillbirth=ECCf age para year;
title 'Stillbirth vs ECC adjusted';
run;

proc logistic data=HAS5 descending;
model mere=ECCf;
title 'Maternal death vs ECC Unadjusted';
run;

proc logistic data=HAS5 descending;
```

```
model mere=ECCf age para year;
title 'Maternal death vs ECC adjusted';
run;

*Code for Log 2 table;

proc freq data=HAS5;
tables lbw PT/missing;
run;

proc logistic data=HAS5 descending;
model PT=exposed;
title 'Preterm vs NT Unadjusted';
run;

proc logistic data=HAS5 descending;
model PT=exposed age para year;
title 'Preterm vs NT adjusted';
run;

proc logistic data=HAS5 descending;
model lbw=exposed;
title 'Low birthweight vs NT Unadjusted';
run;

proc logistic data=HAS5 descending;
model lbw=exposed age para year;
title 'Low birthweight vs NT adjusted';
run;

proc logistic data=HAS5 descending;
model PT=HTAf;
title 'Preterm vs HTA Unadjusted';
run;

proc logistic data=HAS5 descending;
model PT=HTAf age para year;
title 'Preterm vs HTA adjusted';
run;

proc logistic data=HAS5 descending;
model lbw=HTAf;
title 'Low birthweight vs HTA Unadjusted';
run;

proc logistic data=HAS5 descending;       *ERROR;
model lbw=HTAf age para year;
title 'Low Birthweight vs HTA adjusted';
run;

proc logistic data=HAS5 descending;
model PT=PESf;
title 'Preterm vs PES Unadjusted';
run;
```

```
proc logistic data=HAS5 descending;
model PT=PESf age para year;
title 'Preterm vs PES adjusted';
run;

proc logistic data=HAS5 descending;
model lbw=PESf;
title 'Low Birthweight vs PES Unadjusted';
run;

proc logistic data=HAS5 descending;
model lbw=PESf age para year;
title 'Low birthweight vs PES adjusted';
run;

proc logistic data=HAS5 descending;
model PT=ECCf;
title 'Preterm vs ECC Unadjusted';
run;

proc logistic data=HAS5 descending;
model PT=ECCf age para year;
title 'Preterm vs ECC adjusted';
run;

proc logistic data=HAS5 descending;
model lbw=ECCf;
title 'Low Birthweight vs ECC Unadjusted';
run;

proc logistic data=HAS5 descending;
model lbw=ECCf age para year;
title 'Low birthweight vs ECC adjusted';
run;

*NEW Additional Tables...for Publication...maybe for thesis;
*Table 3- HAS Stillbirth for HDP only;
data HAS3;
set final2;
if institution ne 'HAS' then delete;
if complic1_cleaned='PES' then complicf='PES';
if complic1_cleaned='ECC' then complicf='ECC';
if complic1_cleaned='HTA'  then complicf='HTA';
if complic1_cleaned ='HTA + G' then complicf='HTA';
if complic2_cleaned='PES' then complicf='PES';
if complic2_cleaned='ECC' then complicf='ECC';
if complic2_cleaned='HTA + G' then complicf='HTA';
if complic2_cleaned='HTA' and complic1_cleaned NE 'PES' then
complicf='HTA';
if complic3_cleaned='ECC' then complicf='ECC';
if complic3_cleaned='PES' then complicf='PES';
if complicf='PES' then PES=1;
else PES=0;
if complicf='HTA' then HTA=1;
else HTA=0;
if complicf='ECC' then ECC=1;
else ECC=0;
```

```
if complicf NE 'HTA' and complicf NE 'PES' and complicf NE 'ECC' then
NT=1;
else NT=0;
run;

data HAS3_HDPonly;
set HAS3;
if exposed=0 then delete;
run;

proc sort data=HAS3_HDPonly;
by stillbirth;
run;

proc means data=HAS3_HDPonly;
var age gesage;
by stillbirth;
run;

proc freq data=HAS3_HDPonly;
tables paracat*stillbirth modef*stillbirth lbw*stillbirth PT*stillbirth
complicf*stillbirth mere*stillbirth PA*stillbirth / missing;
run;

proc ttest data=HAS3_HDPonly;
class stillbirth;
var age gesage;
run;

proc freq data=HAS3_HDPonly;
tables paracat*stillbirth modef*stillbirth lbw*stillbirth PT*stillbirth
complicf*stillbirth mere*stillbirth PA*stillbirth /chisq;
run;

proc freq data=HAS3_HDPonly;
tables NT*stillbirth HTA*stillbirth PES*stillbirth
ECC*stillbirth/chisq;
run;

*Table 4- HAS Maternal Death for HDP only ;
data HAS4;
set final2;
if institution ne 'HAS' then delete;
if complic1_cleaned='PES' then complicf='PES';
if complic1_cleaned='ECC' then complicf='ECC';
if complic1_cleaned='HTA'  then complicf='HTA';
if complic1_cleaned ='HTA + G' then complicf='HTA';
if complic2_cleaned='PES' then complicf='PES';
if complic2_cleaned='ECC' then complicf='ECC';
if complic2_cleaned='HTA + G' then complicf='HTA';
if complic2_cleaned='HTA' and complic1_cleaned NE 'PES' then
complicf='HTA';
if complic3_cleaned='ECC' then complicf='ECC';
if complic3_cleaned='PES' then complicf='PES';
if complicf='PES' then PES=1;
else PES=0;
if complicf='HTA' then HTA=1;
```

```
else HTA=0;
if complicf='ECC' then ECC=1;
else ECC=0;
if complicf NE 'HTA' and complicf NE 'PES' and complicf NE 'ECC' then
NT=1;
else NT=0;
run;

data HAS4_HDPonly;
set HAS4;
if exposed=0 then delete;
run;

proc sort data=HAS4_HDPonly;
by mere;
run;

proc means data=HAS4_HDPonly;
var age gesage;
by mere;
run;

proc freq data=HAS4_HDPonly;
tables paracat*mere modef*mere lbw*mere PT*mere complicf*mere
stillbirth*mere PA*mere / missing;
run;

proc ttest data=HAS4_HDPonly;
class mere;
var age gesage;
run;

proc freq data=HAS4_HDPonly;
tables paracat*mere modef*mere lbw*mere PT*mere NT*mere HTA*mere
PES*mere ECC*mere stillbirth*mere PA*mere /chisq;
run;
```