THE RECORDING OF CEREBRAL PALSY RISK FACTORS IN BIRTH CERTIFICATES, HOSPITAL DISCHARGE ABSTRACTS, AND MATERNAL INTERVIEWS: A RELIABILITY STUDY

By

Laura Christine Mark

A THESIS

Submitted to
Michigan State University
in partial fulfillment of the requirements
for the degree of

Epidemiology—Master of Science

2016

ABSTRACT

THE RECORDING OF CEREBRAL PALSY RISK FACTORS IN BIRTH CERTIFICATES, HOSPITAL DISCHARGE ABSTRACTS, AND MATERNAL INTERVIEWS: A RELIABILITY STUDY

By

Laura Christine Mark

PURPOSE: To determine the reliability of the recording of cerebral palsy (CP) risk factors in birth certificates, hospital discharge abstracts, and maternal interviews. METHODS: Responses to a maternal interview previously given in the Origins, Wellness, and Life-History (OWL) in Cerebral Palsy case-control study were used to compare with responses recorded in birth certificates and hospital discharge abstracts in regards to CP risk factors. The PROC FREQ command in SAS version 9.4 was used to calculate the kappa statistic for agreement among the three data sources. RESULTS: The level of agreement differed greatly by variable. Agreement was especially high between birth certificates and discharge abstracts for the method of delivery variables, with a kappa value of at least 0.98 for each method. Agreement between these two data sources was also perfect for maternal smoking. Agreement was highest between maternal interviews and discharge abstracts for assisted ventilation and neonatal seizures, with kappa values reflecting substantial and moderate agreement, respectively. CONCLUSION: This reliability study demonstrates that more care should be taken by medical staff when recording events occurring before and during labor and delivery. Better recording of abnormal perinatal events would benefit future research in understanding CP.

ACKNOWLEDGEMENTS

First and foremost, I would like to acknowledge and express incredible gratitude for the guidance of my advisor, Dr. Nigel Paneth, who has helped me every step of the way since I began this program. My experience the past two years would have been entirely different had I not had the great fortune of having him as a professor and then an advisor. I would to thank Dr. Qing Lu and Mr. Glenn Copeland for joining my committee and offering help in any way possible. I would also like to thank Madeleine Lenski for coming to my rescue countless times with gathering the data, planning my approach, and providing a laugh when I needed one. I also greatly appreciate the understanding and encouragement from my bosses at the Institute for Health Policy. Thank you for offering advice and allowing me to take time off when needed.

I would like to thank my mom and my brother for supporting me through the past two years. I am also incredibly grateful for my friends, who have encouraged me and reassured me I could do this, even when things were difficult.

Finally, I would like to thank my wonderful friends from my cohort, Lauren, Sam, and Danielle. You three have been my biggest stress relievers and greatest support system. I cannot imagine having gone through this program without having you all along with me. I'm lucky to know you.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

KEY TO SYMBOLS

ADDM – Autism and Developmental Disabilities Monitoring

BC – Birth certificate

CNM – Certified nurse midwife

CP – Cerebral palsy

ICD-9-CM – International Classification of Diseases, Ninth Revision, Clinical Modification

GMFCS – Gross Motor Function Classification System

K – Kappa statistic

OWL – Origins, Wellness, and Life History

PROM – Premature rupture of membrane

VBAC – Vaginal birth after previous C-section

CHAPTER 1:

BACKGROUND AND OBJECTIVES

1.1 Background

Definition

Cerebral palsy (CP), the most common motor disability in childhood, is defined as "a group of permanent disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain".[1] In 2008, the Autism and Developmental Disabilities Monitoring (ADDM) Network estimated that cerebral palsy affected one in 323 school-aged children.[2] The presence of CP can be determined by many different signs and symptoms, which differ with each type of the disorder and vary greatly from case to case. The variations can range from mild cases in which the individual may have slight difficulty walking to more severe cases in which the individual may need a wheelchair or other special equipment to move. The breadth of the impacts of CP makes it a disorder of great public health importance and research should continually be done to improve the lives of those affected.

Types of cerebral palsy

The differences in CP types are reflected in a classification system that reflects the areas of the brain most affected, producing different forms of disorders of movement. The most common type of CP is spastic cerebral palsy, which affects the majority of those with the disease. Those suffering from the spasticity exhibit increased muscle tone, which causes stiff muscles and difficult movement. Spastic CP can further be categorized by which muscle groups are affected. In spastic diplegia, muscle stiffness

occurs mainly in the legs and to a much lesser degree in the arms, if at all. Children with this type of CP may exhibit scissoring, which is the term used when the legs pull inward toward one another due to tight hip and leg muscles. In spastic hemiplegia, the person experiences tightness on only one side of his body, with an arm typically being more affected than a leg. The third subtype of spastic CP is spastic quadriplegia, which is the most severe. It is characterized by muscle stiffness in all four limbs, the trunk of the body, and the face. It is common for the individual to be incapable of walking and to have comorbidities such as epilepsy, cognitive impairment, or problems with vision, hearing, or speech.[1-3]

A second, less common general type of the disorder is dyskinetic CP, which describes CP that causes the individual to have bodily movements that are outside of their control. This type of CP is subcategorized by the type of dyskinetic movement the disorder causes. These subcategories include chorea, athetosis, and dystonia. However, chorea and athetosis are commonly grouped together and referred to as choreoathetosis. Choreoathetosis is characterized by movements that are slow and writhing, worsening when movement is attempted. Unless the individual is completely relaxed, unwanted movements will persist and often will be exacerbated by emotional stress. The constant writhing of muscles make everyday activities, such as writing or eating, very difficult or impossible. Further, those impacted by choreoathetosis often experience variation between hypotonia and hypertonia throughout the day, causing the muscles to alternate between being floppy and tense. Sudden and unpredictable movements caused by the disorder can cause the affected person to look clumsy. The unintentional motions, sometimes dramatic and violent, can worsen with stress.[3] Dystonia is characterized by

twisting and repetitive movements that are involuntary and can result in abnormal postures. Intentional motion is often a trigger for the unintentional muscle contractions, which can be painful. Dystonia can exist in only one area of the body, called focal dystonia, or may affect the whole body, called generalized dystonia. Dyskinesia and spasticity commonly co-occur, often making it difficult for doctors to classify a patient who has both types of CP.[3]

The third general type of CP is ataxic, which is the least common form. The symptoms presented with this form of CP include severe incoordination, causing disorganized and jerky movements. When individuals with ataxic CP attempt to walk, balance is easily lost and gait becomes unsteady. Because of this, they will often adapt a wider gait to compensate for the instability. Affected individuals also have difficulty performing tasks with repetitive motions, such as clapping. While these three general types of CP are the most common, it is also possible for the individual to suffer from mixed CP, in which symptoms are exhibited from more than one form of the disease.[3]

Disease recognition

Because most of the symptoms associated with CP can often disappear during infancy even if they were once impressive, proper diagnoses are often not made until the child is around two years of age. However, there are signs present in infants that can suggest CP. For example, in infants younger than six months, signs include the baby feeling stiff or floppy or scissoring of the legs when held, inability to hold his head up, and overextension of the back and neck. When the baby is older than six months, signs include not rolling over, inability to bring hands together or to mouth, and keeping one hand in a fist while reaching for objects with the other. When the baby is older than ten

months of age, signs include lopsided crawling, easier use of one side of the body than the other, and scooting on the child's rear end or bouncing on knees as opposed to crawling on all fours.[4] Doctors search for these developmental delays during wellness visits and if abnormalities are suspected, neuroimaging techniques are often used to determine other possible causes.[5] If no other causes are found and the child is diagnosed with CP, the severity is assessed so proper therapies can be administered. To determine the severity of the impact of CP on gross motor function, the Gross Motor Function Classification System (GMFCS) is widely used among clinicians for children age six through 12. This scale has five levels to describe the movement abilities of the affected child. Level one describes a more able-bodied child and the levels increase with increasing disease severity. Table 1 below describes this scale.[5]

Table 1: Description of the Gross Motor Function Classification System for children with cerebral palsy

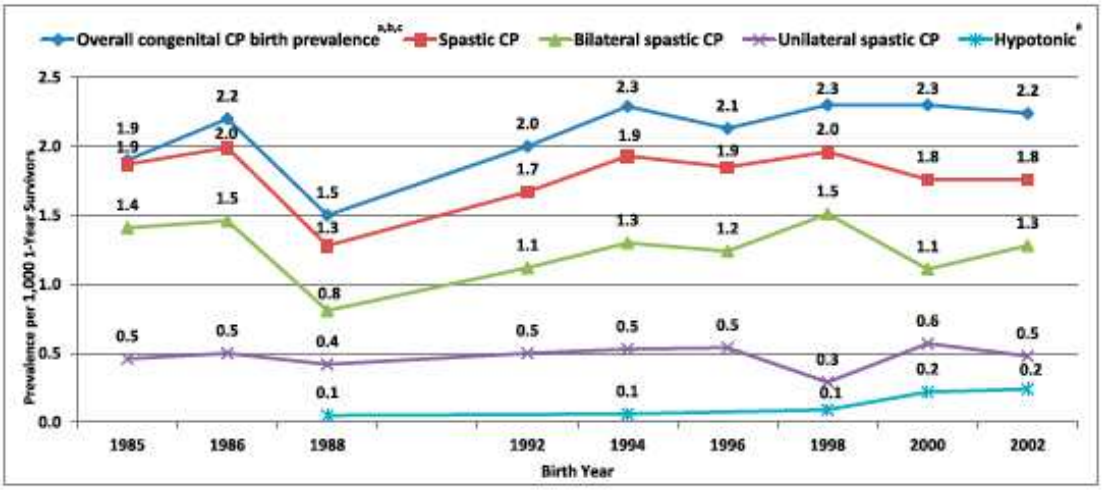
GMFCS	Description
Level I	Children can walk independently and can perform motor skills such as running and jumping, but speed, balance, and coordination are limited
Level II	Children can walk in most settings without assistance, but may require assistance over long distances or uneven terrain. Motor skills such as running and jumping are minimally achievable
Level III	Children walk with a handheld mobility device in most settings and require wheeled mobility over long distances
Level IV	Children require physical assistance or powered mobility in most settings. They may be able to walk for short distances using a walker or physical assistance but powered mobility is usually required
Level V	Children have severely limited self-mobility and a wheelchair is required in all settings. Children have limited ability to maintain head and postures, as well as limb movements

The classification of disease severity is useful to determine appropriate therapies and treatments to improve the quality of life of the patient.

Prevalence

The prevalence of CP has remained relatively steady over the past few decades. This is shown in figure 1 below, which depicts the prevalence of spastic CP from 1985 to 2002 in metropolitan Atlanta, Georgia.

Figure 1: Trends in prevalence of spastic CP per 1000 1-year survivors from birth years 1985 to 2002



As shown in the figure, the prevalence of spastic CP was 1.9 per 1000 1-year survivors in 1985 and decreased to its lowest rate at 1.5 per 1000 in 1988. Since then, rates increased somewhat steadily and reached a prevalence of 2.2 per 1000 1-year survivors in 2002. These data represent an average annual increase of 1.2%.[6] It is important to note that these findings are specific to metropolitan Atlanta, Georgia. While the figure above represents the average change in prevalence data across all races and ethnicities, not all groups experienced the same change. For example, rates in Hispanic children decreased from 2.1 to 1.3 per 1000 1-year survivors from 1994 to 2002. Further, prevalence of CP

among non-Hispanic black children was about 80% higher than the prevalence in non-Hispanic white children. Additionally, over this time frame the rates of survival of infants born at lower birth weights and gestational ages have increased because of improved technology and implementation of measures for decreased mortality. There have been reports of this increased survival leading to an increase in CP cases[7]; however, a recent study by Durkin et al. was the first to have evidence of a decline in CP at the population level.[8] The paper provides CP prevalence data for four surveillance points in the United States for 2006, 2008, and 2010. The overall prevalence of CP was found to significantly decrease from 3.5 per 1000 in 2006 to 2.9 per 1000 in 2010. There was also a decline in the number of cases in babies born at a low birth weight or a very low birth weight, though these findings were not significant.[8] The recent findings of a decrease in CP rates, which is the first notable occurrence of a decrease in decades, reflect a need for further research on this condition.

Causes and risk factors

While CP impacts populations on a global scale, there are factors that exist that will increase the risk of developing the disease. A major risk factor for developing the congenital form of the disease, which accounts for 85-90% of CP cases, is the baby being born at a low birth weight.[5] Infants have an increasing risk of developing CP as birth weight decreases. For example, the prevalence of CP in children born weighing 2500 grams or greater is 1.5 cases per 1000 neonatal survivors, while the prevalence in children born weighing less than 1000 grams is 90 cases per 1000 neonatal survivors.[9] Much of the effect low birth weight has on CP prevalence can ultimately be attributed to the baby being born preterm. Preterm birth is defined as an infant being born before the

37th week of gestation, but risk dramatically increases when infants are birthed before the 32nd week. Preterm birth accounts for around half of all CP cases.[9] Multiple births will also increase the risk of CP, with greater risk associated with higher order pregnancies. Much of this increased risk can likely be attributed to the premature births and low birth weights that result from multiple pregnancies. However, the risk for CP is especially great if one of the multiples dies in utero.[10] Infections during pregnancy may also increase the risk of CP in the child. Infections can raise cytokine levels in the blood, which cause an inflammatory response in both mother and child. This inflammatory response can lead to brain damage in the baby, resulting in CP. Further, multiple birth complications can increase the risk of CP. These complications include breech presentation, abruption of the placenta, uterine rupture, or difficulty with the umbilical cord.[11]

Many CP cases are the result of factors that were present in utero or during the labor and delivery process. However, it is possible for CP to be acquired up to six months after birth.[7] Acquired CP can be caused by an infection of the brain, such as meningitis. It can also be caused by injuries that affect blood flow to the developing brain, causing permanent neurodevelopmental issues. Both congenital and acquired CP have many risk factors associated with their presence.

Birth certificates

Collecting vital statistics has been in human practice for centuries. Ancient populations would conduct censuses to gather information on potential military power and taxation purposes, and as early as the 16th century, churches recorded birth records. Early colonists in America maintained the practice of keeping records of christenings and

other church-related events, which eventually evolved into recording births. By 1639, Massachusetts was the first colony to transfer the responsibility of recording births to the government. The systematic use of vital data for public health intervention began in 1836 in England and Wales and by 1875, it was officially the responsibility of those present at birth to register the event.[12] When these birth records were used more often for public health purposes, a movement was formed to improve the methods of data collection in the mid 1800s. This led to Massachusetts being the first state to instill a law requiring birth registration. The first official standardized birth certificate (BC) for the United States was developed in 1900 and by 1915, 10 states and Washington D.C. were using the birth certificates. By 1933, all of the states adopted the use of the standardized forms and Hawaii and Alaska followed suit when they became states in 1959. The birth certificate finally became a legal document during World War II when it became necessary for employment.[12, 13] However, each state has its own revision of the birth certificate, so forms are not identical across the country.

The U.S. standardized birth certificate has undergone 12 revisions since its initial creation. The original form had a strictly open ended format and collected information on 33 items. After over a century of changes, the most recent revision from 2003 has over 60 items, many of which can be answered by checkboxes. A tabulation of the major changes in the birth certificate through each revision is shown in table 2 below.[12, 13] However, because each state has its own version of the birth certificate, there are variations. For example, some jurisdictions were not originally permitted to ask about marital status and many states included detailed information on smoking well before the 2003 version.

Table 2: Important changes in the birth certificates through the 2003 revision

Revision	Major changes
Early 1900s	Information includes birthdate., birthplace, whether it was a multiple birth, mother's age and race, legitimacy, father's name and age, previous live births
1949	Added birth weight and length of pregnancy
1968	Prenatal care questions, date of last menstrual period, parental education, congenital malformations, pregnancy complications added
1979	Question on legitimacy was changed to asking mother's marital status, Apgar scores added, spontaneous or induced terminations of pregnancy added
1989	Estimated gestational age, maternal medical risk factors, whether parents were of Hispanic origin, smoking and alcohol use, methods of delivery, complications, and obstetrical procedures added. Checklists added for the first time
2003	Information added on maternal smoking by trimester, before/after pregnancy weight and height, infertility and use of fertility treatments, WIC status, breastfeeding at discharge, and maternal morbidities during labor and delivery

While the information recorded on birth certificates has become more comprehensive over the last century, the reliability of this information varies greatly. A major factor for what causes variation in the reliability of birth certificate data is who is responsible for completing the form. A study by Bradford et al. examined the differences in the accuracy of data recording based on the staff member that completed the forms. The highest accuracy occurred when the data was collected by the certified nurse-midwife (CNM). The CNM had consistently more accurate reports than did medical doctors when recording medical conditions in the mother, pregnancy complications, and events occurring both during and after labor.[14] While accuracy of information may be compromised by the staff member that fills out the certificates, there are other factors that contribute to a lack of accuracy of collected data. To understand the value of variables

recorded in birth certificates, reliability and validity studies can be conducted, which will also help show how data collection can be improved.

Research focus

Since the first standardized U.S. birth certificate was developed, birth records have increasingly been used to track disease trends and adverse birth outcomes.[15] Birth certificates provide pertinent information on events that occurred during pregnancy and labor that may contribute to disease status. Other medical records, such as hospital discharge abstracts, are often used for the same purpose. Because of the breadth of information on these records, as well as the ease of their ascertainment, many studies focusing on CP incidence and associated risk factors rely on medical records data. However, the reliability of information on these documents can vary greatly. The inaccurate reporting of events occurring during birth hinders the progress of CP research. Many past studies have been conducted to gain a better understanding of the reliability and validity of vital records data. These various methodologies and results yielded from these studies will be discussed. The purpose of this thesis is to examine the agreement in data reporting among birth certificates, hospital discharge abstracts, and a maternal interview within a specific case-control population used to study CP.

A study by Zollinger et al. conducted a study in 2006 that analyzed the reliability of birth certificate data compared to medical records in the state of Indiana. Their analysis included measurements of agreement for 115 birth certificate variables in 1200 total hospital births. Variables were taken from multiple portions of the birth certificates including demographic information, prenatal care and pregnancy information, risk factors, complications of pregnancy, concurrent illnesses, methods of delivery, obstetric

procedures, delivery and labor complications, birth outcomes, and congenital anomalies and abnormal conditions of the newborn. After responses on the birth certificates were compared to information provided in mothers' medical records, the Kappa statistic for agreement was calculated for discrete variables and the Pearson's product-moment correlation coefficient was calculated for continuous variables. The demographics variables that had high agreement between the birth certificates and medical records were maternal race, age, education, and marital status; however, there was extremely low agreement for race in those with reported Hispanic origin. The variables race and ethnic origin were distinct from one another. In data associated with prenatal care and risk factors, there was a problem with missing data. Information on pregnancy history was often missing, but had high agreement between the two data sources when it was available. Data regarding behavioral risk factors in the mothers had relatively high variation. For example, there was moderate agreement in questions about tobacco use but much lower reliability in questions about alcohol or other substance use during pregnancy. There was poor agreement in variables reporting complications during pregnancy and concurrent illnesses in the mother. Several specific events during pregnancy, such as eclampsia, Rh sensitization, and uterine bleeding, had no agreement, largely due to absence of information in one of the sources. There was also very poor reliability in the recording of obstetric procedures, as well as events of unsuccessful vaginal birth after caesarian and the prolapse of the umbilical cord. Agreement for method of delivery, however, was moderate to good.[16] Findings from this study suggest that there is higher reliability in the recording of standard information than there is in the recording of abnormal events. Therefore, abnormal events are likely to have the lowest

agreement between data sources. While this study was comprehensive in the variables it assessed, it only focused on birth certificates. The study could be improved by analyzing the data recording in both birth certificates and hospital discharge abstracts.

A study by Lydon-Rochelle et al. focused on the recording of data regarding existing medical conditions in the mother, as well as pregnancy complications. The investigators assessed accuracy of data from birth certificates and hospital discharge abstracts, using medical records as the gold standard. True positive fractions were calculated by finding the proportion of women that had a specific medical condition or pregnancy complication in the medical records as well as the birth certificates, discharge abstracts, or both. False positive fractions were calculated by finding the proportion of women that did not have a specific medical condition or pregnancy complication in the medical records, but the conditions were marked as present in the birth certificates or discharge abstracts. This study found that there were lower prevalences of maternal medical conditions in birth certificates and discharge abstracts compared to medical records, showing a failure to record information. Further, birth certificate data, when not combined with data on discharge abstracts, had low true positive fractions for most maternal medical conditions, including chronic and gestational diabetes, chronic and gestational hypertension, lung disease, and eclampsia. Variables included in the analysis for pregnancy complications, including placenta previa, also had very low accuracy in recording in the birth certificates. Combining information from birth certificates and hospital abstracts was helpful in increasing the true positive fractions to at least 70% for many variables; however, this demonstrates that even when data sources are combined, the accuracy of data reporting in hospitals is very low. The investigators also noted a

substantial issue with missing data in both sources. This study provided further evidence that data collection within hospitals, especially in birth certificates and discharge abstracts, lacks accuracy. When birth certificates or hospital discharge abstracts alone are used for research purposes, pregnancy complications and maternal medical conditions will likely be largely underreported.[17]

As mentioned from previous studies, there is notable variation in the reliability of data collected on birth certificates. Demographic information tends to have higher reliability than risk factor information, as suggested by Zollinger et al.[16] Reichman and Schwartz-Soicher conducted a study to better understand which risk factors and birth outcomes have the greatest and least accuracy, and how the recording of this information varies by characteristics of the mother. Further, this study is one of few that assess how problematic data reporting in birth certificates varies by outcome. Overall, the investigators found that while risk factors, obstetric procedures, and complications of labor were largely underreported in general, they were especially underreported in ethnic minorities. Similarly, rates of underreporting were more positively associated with women who lacked English-speaking proficiency. The investigators also found there was higher sensitivity in the recording of previous preterm or small-for-gestational-age data was higher in births that had adverse outcomes compared to normal births. There also tended to be higher sensitivities in births that required an infant transfer. Additionally, while the reporting of gestational diabetes and gestational hypertension has shown to be unreliable in previous studies, Reichman and Schwartz-Soicher found that sensitivities for these variables increased in births that were low birth weight, preterm, and very preterm. This study demonstrated that while there are general trends of underreporting

risk factors, obstetric procedures, and pregnancy complications on birth certificates, this can be impacted by specific events during labor and conditions of the newborn, such as the requirement of an infant transfer or a premature birth.[18]

In recent decades, there have been two major revisions to the U.S. standard birth certificate. In most reliability and validity studies, the 1989 version is used; however, in more recent studies, the 2003 version is analyzed. The more recent version has been criticized because its creation did not include input from perinatal epidemiologists with clinical experience, but rather health organization representatives, clinicians, and public health researchers.[19] The newest revision had a gradual national uptake, but all jurisdictions put it to use by January 2015. In a study by Dietz et al., the 2003 revision of the United States birth certificate was assessed by comparing information with medical records of an existing study population of women in Vermont and New York City. The purpose was to find strengths and limitations of using the recently revised birth certificate, as there were few existing validation studies using this form. The study included the analysis of pregnancy complications, as well as variables unique to the 2003 revision, including insurance, gestational diabetes, previous caesarian delivery, augmented labor, and induced labor. Insurance status at time of delivery was found to have high validity, as did previous birth outcomes and delivery methods. However, variables with lower validity included presence of gestational diabetes and complications during labor, such as the premature rupture of membranes.[20] This study provided further evidence that events with lower prevalence, like induced labor, tend to be poorly recorded on birth certificates.

A study recently conducted by Li et al. had a similar research focus to this thesis. The research group used a case-control study population from the Origins, Wellness, and Life History (OWL) study, which aims to learn more about children with CP.[21] Information from birth certificates from this population was compared to data on hospital discharge abstracts and maternal interviews to assess the accuracy of recording of neonatal seizures, which can result in deleterious neurological events in the newborn, including mortality, intellectual disabilities, epilepsy, and CP.[22] From these sources, there were 38 total neonatal seizures reported in at least one source. Discharge abstracts reported 17 of these seizures, maternal interviews reported 20, and just one was reported in birth certificates. The findings of this study show the low sensitivity of the recording of neonatal seizures on birth certificates.[21] This can be troublesome for studies that use vital statistics for research data collection. This study was successful in finding the inaccuracy of reporting for neonatal seizures, but further investigation should be conducted to understand the effectiveness of the reporting of other variables in this study population.

1.2 Objective

Review of the literature provides consistent evidence of the lack of accuracy that exists in birth data collection. Generally, basic family information, as well as demographic information, was well reported. However, abnormal events that occur during labor and delivery have shown to yield a much lower reliability. This is problematic because many risk factors for CP are events that do not occur often during normal pregnancies, as outlined above. To understand the reliability of data collection for CP risk factors recorded on birth certificates, the responses from the birth certificates

will be compared to information on hospital discharge abstracts as well as a maternal interview given to mothers of children with CP.

CHAPTER 2:

RESEARCH DESIGN AND METHODS

2.1 Overview

Maternal Interview data collected from the Origins, Wellness, and Life-history in Cerebral Palsy case-control study will be compared with data recorded on birth certificates and hospital discharge abstracts. Agreement of variable responses among the three sources will be assessed. Variables analyzed include maternal smoking during pregnancy, maternal fever during labor, presence of meconium staining of the amniotic fluid, meconium aspiration in the newborn, abnormally slow or fast labor, fetal presentation, method of delivery, premature rupture of membranes, requirement of newborn assisted ventilation for any length of time, and newborn seizures.

2.2 Design

This reliability study will compare responses to several variables among birth certificates, maternal interviews, and hospital discharge abstracts.

2.3 Participants

The New Paradigms of Cerebral Palsy: a Comprehensive Case-Control Study (R01-N5-055101), referred to as CP-OWL, was conducted to expand knowledge on antenatal and intrapartum risk factors for CP. Participants of the OWL study were children ages 2-16 who were born between 1993 and 2010. CP cases were recruited from specialty clinics (CP clinics, rehabilitation hospitals, child neurologic practices, high risk newborn follow up programs) in Michigan that served children with cerebral palsy. Controls were recruited from general pediatric practices in Michigan who were referral sources for the specialty clinics. To be classified as cases, children had to have a clinical

diagnosis of CP, excluding CP acquired postnatally. Further, the diagnosis of CP could not be part of a major malformation syndrome, nor part of a genetic syndrome. When cases were born at 32 weeks of gestation or earlier, they were usually recruited from newborn follow-up programs. Controls were enrolled from primary care practices and had to be free of major brain disorders. Cases and controls were matched on birth year, gender, and gestational age. Gestational age was separated into categories of less than 28 weeks, 29-32 weeks, 33-36 weeks, and 37 weeks or more. This study includes all subjects with available birth certificates, maternal interviews, and discharge abstracts. This totaled 596 subjects with birth certificates, 64 of which were the 2003 revision and 532 were the 1989 revision; 492 maternal interviews; 506 child discharge abstracts, and 465 maternal discharge abstracts.[21]

2.4 Data Sources

Birth certificates

The National Center for Health Statistics, alongside state vital statistics offices, revises birth certificates every 10-15 years. The versions follow federal suggestions, but each state is allowed to have their own form, resulting in many different birth certificates across the country. Further, there is a gradual uptake of each version by hospitals, so at the time the original case-control study was conducted, both the 1989 and 2003 versions were in circulation.[15] Birth certificate data from the 1989 and 2003 revisions were provided by the Michigan Department of Community Health. The data was already coded and available for use. Table 2 below shows the entries of the variables studied in both the 1989 and 2003 revisions of the Michigan birth certificate.

Table 3: Variable entries in the 1989 and 2003 revisions of the Michigan birth certificate

Variable	1989 Birth Certificate Revision	2003 Birth Certificate Revision
Smoking	Tobacco use during pregnancy	Did mother smoke before or during pregnancy? Did the mother quit smoking?
Fever	Febrile during labor and delivery (> 100º F)	Clinical chorioamnionitis diagnosed during labor or maternal temperature ≥ 100.4º F
Meconium staining	Meconium, moderate/heavy	Moderate/heavy meconium staining of the amniotic fluid
Meconium aspiration	Meconium aspiration syndrome	N/A
Abnormally fast labor	Precipitate labor (< 3 hours)	Precipitous labor (< 3 hours)
Abnormally slow labor	Prolonged labor (> 20 hours)	Prolonged labor (≥ 20 hours)
Fetal presentation	Breech/Malpresentation	Cephalic, breech, other
Method of delivery	Vaginal, vaginal birth after previous C-section, repeat C-section, forceps, vacuum	Vaginal/spontaneous, vaginal/forceps, vaginal/vacuum, Cesarean
Premature rupture of membrane (PROM)	Premature rupture of membrane (> 12 hours)	Premature rupture of the membranes (≥ 12 hours)
Assisted ventilation	Assisted ventilation < 30 minutes, assisted ventilation ≥ 30 minutes	Assisted ventilation required immediately following delivery, assisted ventilation required for more than six hours
Seizure	Seizures	Seizure or serious neurologic dysfunction

Maternal interviews

The data assessed from maternal interviews had been collected previously in the case-control study and is used in this secondary data analysis. Maternal interviews were conducted over the telephone by trained research assistants. During the interview, mothers of children ages two to fifteen years of age, both with and without CP, answered

questions on pregnancy, family history, and health. Table 3 below describes the relevant variables used in this study.[23]

Table 4: Variables attained from questions in the maternal interview

Variable	Maternal interview question
Smoking	After you found out you were pregnant, did you smoke cigarettes or use tobacco?
Fever	While you were in the hospital for labor and delivery, did a doctor or other health care provider tell you you had a fever/measured temperature over 101º F?
Meconium staining	While you were in the hospital for labor and delivery, did a doctor or other health care provider tell you you had stained amniotic fluid (meconium/baby bowel movement in utero)?
Abnormally fast labor	While you were in the hospital for labor and delivery, did a doctor or other health care provider tell you you had unusually fast (precipitous) delivery ($\leq$ 3 hours)
Abnormally slow labor	While you were in the hospital for labor and delivery, did a doctor or other health care provider tell you you had an usually long delivery ($\geq$ 12 hours from start of regular/painful contractions)
PROM	While you were in the hospital for labor and delivery, did a doctor or other health care provider tell you your water broke/membranes ruptured more than 24 hours prior to delivery?
Assisted ventilation	Did your child need artificial ventilation?
Seizure	Do you recall if your child experienced any seizures or convulsions within the first 24 hours of life?

Discharge abstracts

Hospital discharge abstracts were supplied by the Michigan Department of Community Health. The hospital discharge summaries were prepared by trained medical coders, using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes. The abstracts feature one primary diagnosis or primary procedure code and up to 30 secondary diagnosis and procedure codes that reflect details of the mothers' and children's hospital stays. Table 4 shows which abstracts were used

for each variable, as well as the ICD-9-CM codes used to define diagnoses and procedures.

Table 5: Variables and ICD-9-CM codes from discharge abstracts

Variable	Abstract used	ICD-9-CM code	Code meaning
Smoking	Maternal	N/A	N/A
Fever	Child	760.2	Maternal infections affecting fetus or newborn
		762.8	Other specified abnormalities of chorion and amnion affecting fetus or newborn
		659.2	Maternal pyrexia during labor, unspecified
Meconium staining of amniotic fluid	Child	N/A	N/A
Meconium aspiration	Child	770.11	Meconium aspiration without respiratory symptoms
		770.12	Meconium aspiration with respiratory symptoms
Fetal presentation	Maternal	763.0	Breech delivery and extraction affecting newborn
		761.7	Malpresentation before labor affecting fetus or newborn
		763.1	Other malpresentation, malposition, and disproportion during labor and delivery affecting fetus or newborn
Method of delivery	Maternal	N/A	N/A
PROM	Child	761.1	Premature rupture of membranes affecting fetus or newborn
Assisted ventilation	Child	96.70	Continuous invasive mechanical ventilation of unspecified duration
		96.71	Continuous invasive mechanical ventilation for less than 96 consecutive hours
		96.72	Continuous invasive mechanical ventilation for more than 96 consecutive

Table 5 (cont'd.)

			hours
Seizure	Child	779.0	Convulsions in newborn
		780.3	Convulsions

A note of "N/A" in table 4 above represents variables that did not use ICD-9-CM codes because there were existing variables for them in the abstracts.

2.5 Variable Definitions and Comparisons

Smoking

The maternal smoking variable was available for comparison among all three data sources. In both revisions of the birth certificates, data were collected on tobacco use during pregnancy. The maternal interviewer asked women if they smoked after they learned that they were pregnant, either from a doctor or otherwise. In the provided dataset for hospital discharge abstracts, there was a variable for maternal smoking.

Maternal fever

The fever variable aimed to determine whether the mother had a fever during labor and delivery, and was available for comparison among all three data sources. The 1989 and 2003 revisions of the birth certificates differed slightly in their definitions of fever. As shown in table 2 above, the 1989 revision referenced whether the mother was febrile, with a temperature of at least 100^{o} F. This is located in the "Complications of Labor and/or Delivery" portion of the birth certificate. The 2003 revision referenced whether the mother had a diagnosis of clinical chorioamnionitis or a fever of greater than or equal to 100.4^{o} F. This is located in the "Characteristics of Labor and Delivery" portion. The maternal interview asked women to recall if they had a fever of 101^{o} F during labor and delivery. To compare these responses with data from hospital discharge abstracts, codes 760.2 and 659.2 were used. These ICD-9-CM codes correspond to

maternal infections affecting the fetus or newborn and unspecified maternal pyrexia during labor. The code 762.8, which is used for abnormalities of the chorion and amnion, was also used to represent maternal fever because the 2003 birth certificate joins maternal fever and chorioamnionitis in the same checkbox. Further, if the mother has chorioamnionitis, a fever will likely accompany the infection.[24]

Meconium staining

Meconium staining, referring to staining of the amniotic fluid due to a fetus' bowel movement in utero,[25] was compared between birth certificates and maternal interview, but not discharge abstracts, as the codes were not present in the dataset. In the 1989 birth certificate, moderate to heavy meconium staining is located in the "Complications of Labor and/or Delivery" portion and in the 2003 revision, it is located in the "Characteristics of Labor and Delivery" portion. In the maternal interview, mothers were asked to recall whether a health professional told them there was meconium staining in the amniotic fluid.

Meconium aspiration

The variable for meconium aspiration, which describes the event of a fetus expelling meconium in utero and then breathing it in, was available for comparison in the 1989 revision of the birth certificate and the hospital discharge abstracts.[26] The 2003 birth certificate revision does not collect information on meconium aspiration and mothers were not asked about this in the maternal interview. Meconium aspiration is referenced in the "Abnormal Conditions of the Newborn" portion of the birth certificate and ICD-9-CM codes 770.11 and 770.12 were used in the maternal discharge abstracts.

These codes correspond to meconium aspiration in the newborn without and with respiratory symptoms, respectively.

Abnormally fast labor

Occurrences of abnormally fast labor were compared between birth certificates and maternal interviews, as information on this was not available in the discharge abstracts. In both revisions of the birth certificate, this was referred to as precipitate labor, or labor lasting less than three hours. It is located in the "Complications of Labor and/or Delivery" and the "Onset of Labor" categories of the 1989 and 2003 revisions, respectively. There is a slight deviation in the definition of precipitate labor in the maternal interview. Mothers were asked if their labor was less than or equal to three hours.

Abnormally slow labor

Similarly to abnormally fast labor, occurrences of abnormally slow labor were compared between birth certificates and maternal interviews, as a code was not available for discharge abstracts. Both revisions of the birth certificate referred to abnormally slow labor as prolonged labor. The 1989 revision defines prolonged labor as labor lasting more than 20 hours, and the 2003 revision defines it as labor lasting 20 hours or more. This variable is located in the "Complications of Labor and /or Delivery" and "Onset of Labor" categories of the 1989 and 2003 revisions, respectively. The definition of abnormally slow labor in the maternal interview differs from that in the birth certificate, as mothers were asked if their labor lasted for at least twelve hours.

Fetal presentation

To suggest a potentially difficult delivery, this study was interested in events of breech or malpresentation in the newborn, as opposed to a cephalic presentation. This was available for comparison between the birth certificates and the maternal discharge abstracts. The 1989 revision of the birth certificate had a checkbox for breech or malpresentation combined, and the 2003 revision had checkboxes for breech presentation, cephalic presentation, or other. A marked checkbox for "other" in the 2003 revision was considered malpresentation. The ICD-9-CM codes used for the discharge abstracts were 763.0, 763.1, and 761.7. These codes represent malpresentations and malpositions that affect the newborn before and during labor and delivery.

Method of delivery

The method of delivery was compared between the birth certificates and the discharge abstracts. The 1989 revision of the birth certificate had six options for the method of delivery, including vaginal, vaginal birth after previous C-section (VBAC), primary C-section, repeat C-section, forceps, and vacuum. For this study, vaginal and VBAC were categorized together as vaginal births and the primary and repeat C-sections were categorized together as C-sections. The 2003 revision of the birth certificate had four options for method of delivery, including vaginal/spontaneous, vaginal/forceps, vaginal/vacuum, and cesarean. For this study, these responses were classified as vaginal, forceps, vacuum, or C-section. In both revisions of the birth certificate, this information is found in the "Method of Delivery" category of the forms. In the maternal discharge abstracts, method of delivery was determined by appropriate existing coded variables.

PROM

The premature rupture of membranes was compared among all three data sources. The 1989 revision of the birth certificate defined PROM as a rupturing of the membrane more than 12 hours before the onset of labor and is located in the "Complications of Labor and/or Delivery" category of the form. The 2003 revision defines PROM as the membranes rupturing at least 12 hours before the onset of labor, and it collects this information in the "Onset of Labor" category. The definition of PROM differed in the maternal interview. Mothers were asked to recall if a health professional told them their membrane ruptured 24 hours before delivery. The ICD-9-CM code used in the hospital abstracts was 761.1, which was coded in the child abstract if the event of PROM affected the newborn.

Assisted ventilation

Data on whether the newborn required assisted ventilation after birth was compared among all three sources. The 1989 revision of the birth certificate classifies this information in two variables under the "Abnormal Conditions of the Newborn" category. The two variables are the requirement of assisted ventilation for less than 30 minutes or for greater than or equal to 30 minutes. The 2003 revision also collects this information in the "Abnormal Conditions of the Newborn" category, but references whether the newborn required ventilation immediately after delivery or for more than six hours. For this study, any of these options were accepted. In the maternal interview, mothers were asked if their child required assisted ventilation, regardless of the time frame. The procedure codes used in the hospital discharge abstracts were 96.70, 96.71, and 96.72. These codes applied when mechanical ventilation was required for an

unspecified period of time, for less than 96 hours, and for more than 96 hours, respectively.

Seizure

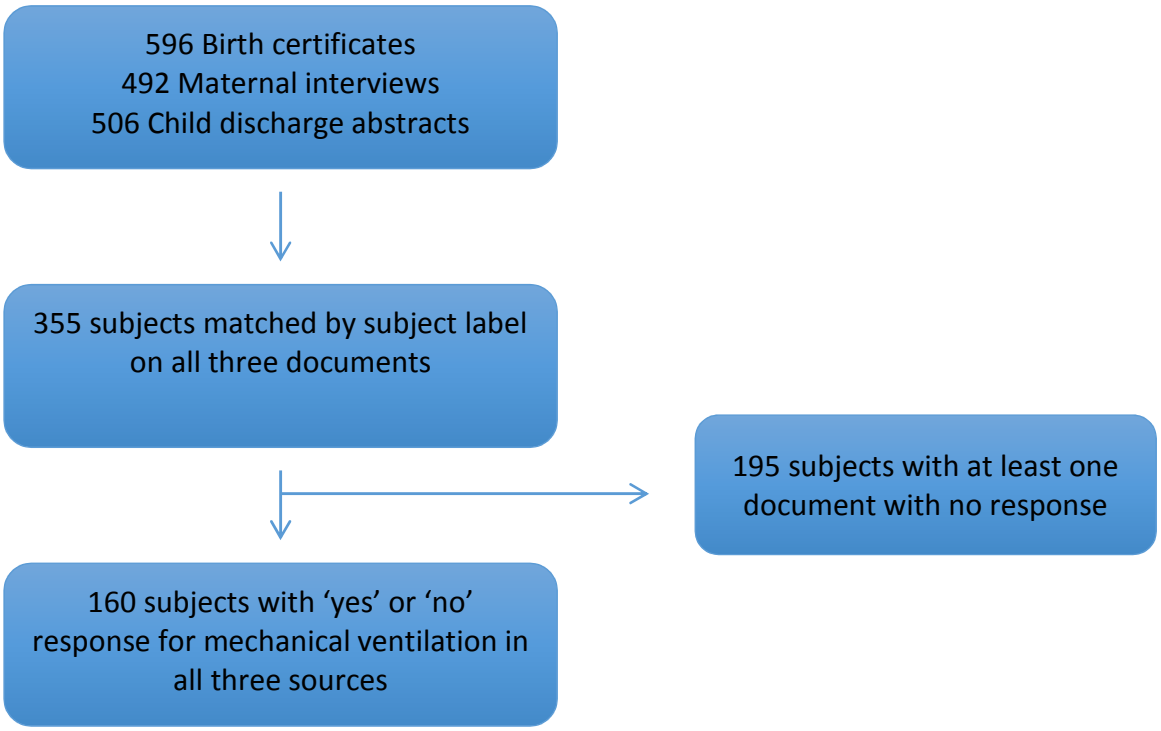
Recording of the occurrence of a seizure in the newborn was compared among the three data sources. In the 1989 revision of the birth certificate, the variable for seizure was classified under "Abnormal Conditions of the Newborn." In the 2003 revision, it was defined as the occurrence of a seizure or other neurologic dysfunction, which was also categorized under "Abnormal Conditions of the Newborn." In the maternal interview, mothers were asked to recall any seizures or convulsions in their baby in the first 24 hours of life. In the child's hospital discharge abstracts codes 779.0 and 780.3 were used, which referenced convulsions in the newborn and seizures or convulsions, respectively. The recording of neonatal seizures has previously been analyzed by Li et al.[21]

2.6 Procedure and Statistical Analysis

The relevant data from the OWL study had been collected previously and were accessible through a SharePoint drive, which is a secure team collaboration website. The necessary variables were extracted from each dataset and coded into a yes/no format. These responses from each data source were matched by an encrypted subject identification variable in SAS version 9.4. Response comparisons were only made among subjects that had all three corresponding data sources available. An example of the process used to find the comparison group for each variable is shown below in figure 2, using the mechanical ventilation variable. The process begins with the raw data available in the birth certificates, maternal interviews, and discharge abstracts. The

process ends with subjects that have all three data sources available with no missing responses for the variable in question.

Figure 2: Flowchart of the comparison group selection process



Any responses of "don't know" or refusals to answer the question in the maternal interviews were removed from the comparisons for the affected variable. The agree option of the PROC FREQ procedure was used to calculate the kappa statistic (k). The kappa statistic provides a rating of agreement between two sources, taking into account how much agreement would occur by chance alone.[27] The kappa scale ranges from -1 to 1, where a value of 0 represents the agreement that is expected due to chance. Negative values represent agreement less than what is expected by chance, and large negative values represent general disagreement between the two sources, or raters. The

interpretation of positive kappa values is shown in table 6.[28] Kappa values of 1.00 represent perfect agreement. This interpretation tabulated below is just one of several commonly used interpretations of the kappa value.

Table 6: Interpretation of kappa values

Kappa value	Interpretation of agreement
< 0	Less than chance agreement
0.01-0.20	Slight agreement
0.21-0.40	Fair agreement
0.41-0.60	Moderate agreement
0.61-0.80	Substantial agreement
0.81-0.99	Almost perfect agreement

CHAPTER 3:

RESULTS

3.1 Characteristics of Study Population

A total of 596 unique birth certificates were used in this study. These birth certificates were used to gather descriptive statistics of the study population, which is described in table 7. In the population used, 56.7% of the children born were male. The majority of the children were reported as being white (87.7%), while 10.3% were black. There was an exact even division of children born preterm and children born at term, with preterm being defined as fewer than 37 weeks gestation. Among the mothers, 16.6% reported not finishing high school, 22.2% reported receiving a high school diploma or GED, and 36% reported completing either four years of college or a professional degree. The majority of mothers reported having private insurance (79.5%), while 20.5% reported using Medicaid. According to responses in the maternal interviews, 55.5% of the children were cases and the remaining were controls. There is not an even division of cases and controls, which suggests either birth certificates or hospital discharge abstracts were not successfully retrieved for some controls.

Table 7: Descriptive statistics of study population

Variable	Category	Frequency	Percent (%)
Child gender	Male	338	56.7
	Female	258	43.3
Child race	White	518	87.7
	Black	61	10.3
	Other	12	2.0
Gestation	Preterm	298	50.0
	Term	298	50.0

Table 7 (cont'd.)

Maternal Education	Less than high school	98	16.6
	High school/GED	131	22.2
	Some college	149	25.3
	Four years of college	106	18.0
	Professional degree/5+ years college	105	17.8
Insurance	Private	458	76.9
	Medicaid	118	19.8
	Self	20	3.4
Case status	Case	273	55.5
	Control	219	44.5

3.2 Agreement Results

Smoking

The results for agreement between birth certificates and maternal interview for the maternal smoking variable are shown in table 8. There were 18 "yes" responses from the birth certificates and only three from the maternal interviews. Of those three responses, one was in agreement with the birth certificate. The kappa statistic for agreement in these two sources was 0.072, which suggests slight agreement.[28] There was much higher agreement between birth certificates and maternal discharge abstracts for this variable, with a perfect kappa value of 1.00. This is shown in table 9. The agreement between maternal interviews and discharge abstracts was the same as the maternal interview and birth certificate comparison, with the kappa value of 0.072. The two sources agreed on only one maternal "yes" response of the three given in the available interviews.

Table 8: Agreement in maternal smoking recording between birth certificate and maternal interview

k = 0.072 (P = 0.0643)	Smoking in maternal interview		Total
Smoking in BC	No	Yes	
No	186	2	188
Yes	17	1	18
Total	203	3	206

Table 9: Agreement in maternal smoking recording between birth certificates and maternal discharge abstracts

k = 1.00 (P < 0.0001)	Smoking in maternal discharge abstracts		Total
Smoking in BC	No	Yes	
No	188	0	188
Yes	0	18	18
Total	188	18	206

Table 10: Agreement in maternal smoking recording between maternal interviews and discharge abstracts

k = 0.072 (P = 0.0643)	Smoking in maternal discharge abstracts		Total
Smoking in maternal interview	No	Yes	
No	186	17	203
Yes	2	1	3
Total	188	18	206

Method of delivery

The agreement in the recording of vaginal births between birth certificates and maternal discharge abstracts is shown in table 11. Vaginal births included occurrences of VBAC. The kappa statistic was calculated to be 0.99, which correlates to almost perfect agreement between the two sources. There was only one occurrence of vaginal birth that was not agreed upon between the two sources, out of a total of 206 births. Table 12 shows the agreement between these sources in the recording of births by C-section. The kappa value for this comparison also correlated to almost perfect agreement (k = 0.98).

The agreements in the recordings of vaginal births using forceps and vacuum are shown in tables 13 and 14, respectively. The recording of the use of forceps showed perfect agreement between maternal interviews and discharge abstracts (k = 1.00), as well as for the use of vacuum.

Table 11: Agreement in vaginal birth recording between birth certificates and discharge abstracts

k = 0.99 (P < 0.0001)	Vaginal birth in discharge abstracts		Total
Vaginal birth in BC	No	Yes	
No	94	1	95
Yes	0	111	111
Total	94	112	206

Table 12: Agreement in C-section recording between birth certificates and discharge abstracts

k = 0.98 (P < 0.0001)	C-section in discharge abstracts		Total
C-section in BC	No	Yes	
No	111	1	112
Yes	1	93	94
Total	112	94	206

Table 13: Agreement in recording use of forceps between birth certificates and discharge abstracts

k = 1.00 (P < 0.0001)	Forceps in discharge abstracts		Total
Forceps in BC	No	Yes	
No	202	0	202
Yes	0	4	4
Total	202	4	206

Table 14: Agreement in recording use of vacuum between birth certificates and discharge abstracts

k = 1.00 (P < 0.0001)	Vacuum in discharge abstracts		Total
Vacuum in BC	No	Yes	
No	199	0	199
Yes	0	7	7
Total	199	7	206

Assisted ventilation

The results for agreement between birth certificates and maternal interviews for the requirement of assisted ventilation are shown in table 15. Maternal responses of "don't know" or a refusal to answer were excluded from the results. The agreement for this variable was slight, with a kappa value of 0.096. The agreement was higher between the birth certificates and discharge abstracts, but was still only slight (k = 0.13). The agreement was highest between maternal interviews and discharge abstracts. The kappa value of 0.63 correlates to substantial agreement between the sources. Because the maternal interview did not specify a time limit for the ventilation, mothers reported more occurrences than were recorded in the birth certificates, which did specify a time limit.

Table 15: Agreement in assisted ventilation recording between birth certificates and maternal interviews

k = 0.096 (P = 0.0252)	Ventilation in maternal interview		Total
Ventilation in BC	No	Yes	
No	37	83	120
Yes	6	34	40
Total	43	117	160

Table 16: Agreement in assisted ventilation recording between birth certificates and child discharge abstracts

k = 0.13 (P = 0.0148)	Ventilation in child discharge abstracts		Total
Ventilation in BC	No	Yes	
No	50	70	120
Yes	9	31	40
Total	59	101	160

Table 17: Agreement in assisted ventilation recording between maternal interview and child discharge abstracts

k = 0.63 (P < 0.0001)	Ventilation in child discharge abstracts		Total
Ventilation in maternal interview	No	Yes	
No	38	5	43
Yes	21	96	117
Total	59	101	160

The child discharge abstract was considered the gold standard for recording the use of mechanical ventilation. In total, these discharge abstracts recorded 101 uses of mechanical ventilation and, of these, 92 (91%) uses were in babies born preterm and 73 (72%) were later diagnosed with CP.

Fever

The results for agreement between birth certificates and maternal interviews for the event of a maternal fever during labor and delivery are shown in table 18. Maternal responses of "yes, but uncertain" were classified under "yes," and responses of "don't know" or a refusal to answer were excluded from the results. The agreement for this data is only slight, with a kappa value of 0.13. There were over twice as many maternal recollections of a fever during labor and delivery than what was recorded in the birth certificates, and the two sources only agreed on two of them.

Table 18: Agreement in maternal fever recording between birth certificates and maternal interviews

k = 0.13 (P = 0.0069)	Fever in maternal interview		Total
Fever in BC	No	Yes	
No	306	16	322
Yes	6	2	8
Total	312	18	330

Agreement statistics for the recording of maternal fever between birth certificates and child discharge abstracts could not be generated because of a lack of reporting in the

abstracts. Similarly, agreement statistics between maternal interview and child discharge abstracts could not be generated because of the lack of reporting in the abstracts.

Meconium staining

The agreement statistics for the agreement between birth certificates and maternal interviews for meconium staining is shown in table 19. Maternal responses of "yes, but uncertain" were classified as "yes" and responses of "don't know" or refusals to answer were excluded from the analysis. The kappa value for this comparison was 0.34, which represents fair agreement.

Table 19: Agreement in recording of meconium staining between birth certificates and maternal interview

k = 0.34 (P < 0.0001)	Meconium staining in maternal interview		Total
Meconium staining in BC	No	Yes	
No	304	6	310
Yes	11	5	16
Total	315	11	326

Agreement statistics could not be generated for the comparison of birth certificates and discharge abstracts, as well as maternal interviews and discharge abstracts. None of the available abstracts had any coded instances of meconium staining. Of the 16 reported events of meconium staining in the birth certificates, 11 (69%) were in children later diagnosed with CP.

Meconium aspiration

No agreement statistics could be generated for comparisons with the maternal interviews, as mothers were not asked about meconium aspiration syndrome in the newborn. The 2003 revision of the birth certificate was excluded from this analysis because only the 1989 revision had a variable for meconium aspiration. Because there

were no events of meconium aspiration reported in the discharge abstracts, agreement statistics could not be generated. In total, the birth certificates reported 4 events of meconium aspiration syndrome in the newborn. All four of these events occurred in children with CP.

PROM

The agreement statistics calculated for responses in the birth certificates and maternal interviews for PROM are shown in table 20. Any responses of "don't know" or refusals to answer in the maternal interview were excluded from the results and responses of "yes, but uncertain" were categorized under "yes." Agreement between these two data sources was fair, with a kappa value of 0.30. Birth certificates and maternal interviews had the highest rate of agreement. Table 21 shows the agreement between birth certificates and discharge abstracts, which is a negative value. The kappa value of -0.017 suggests that the two data sources disagree and any agreement seen is less than what would occur by chance alone. The agreement between maternal interviews and discharge abstracts was slight (k = 0.13).

Table 20: Agreement in PROM recording between birth certificates and maternal interviews

k = 0.30 (P < 0.0001)	PROM in maternal interview		Total
PROM in BC	No	Yes	
No	265	25	290
Yes	23	15	38
Total	288	40	328

Table 21: Agreement in PROM recording between birth certificates and child discharge abstracts

k = -0.017 (P = 0.2644)	PROM in child discharge abstracts		Total
PROM in BC	No	Yes	
No	287	3	290
Yes	38	0	38
Total	325	3	328

Table 22: Agreement in PROM recording between maternal interviews and child discharge abstracts

k = 0.13 (P < 0.0001)	PROM in child discharge abstracts		Total
PROM in maternal interview	No	Yes	
No	288	0	288
Yes	37	3	40
Total	325	3	328

Abnormally fast labor

The agreement results for the event of an abnormally fast labor as recorded in the birth certificate compared to maternal interview are shown in table 23. Maternal responses in the interview of "don't know" or refusals to answer were excluded from the results and responses of "yes, but uncertain" were categorized under "yes." The agreement between these two data sources yielded a kappa value of 0.035, which corresponds to slight agreement.

Table 23: Agreement in precipitate labor recording between birth certificates and maternal interviews

k = 0.035 (P = 0.0877)	Precipitate labor in maternal interview		Total
Precipitate labor in BC	No	Yes	
No	233	91	324
Yes	4	4	8
Total	237	95	332

Abnormally slow labor

The agreement results for the event of an abnormally slow labor as recorded in the birth certificate compared to maternal interview are shown in table 24. Maternal responses of "don't know" or refusals to answer in the interview were excluded from the results and responses of "yes, but uncertain" were categorized under "yes." The kappa value for agreement between these two data sources was 0.040, corresponding to slight agreement.

Table 24: Agreement in prolonged labor recording between birth certificates and maternal interviews

k = 0.040 (P = 0.0224)	Prolonged labor in maternal interview		Total
Prolonged labor in BC	No	Yes	
No	266	66	332
Yes	1	2	3
Total	267	68	335

Fetal presentation

The agreement for the recording of a breech or malpresentation of the baby between birth certificates and maternal discharge abstracts is shown in table 25. Similar to the findings for PROM in birth certificates and discharge abstracts, this kappa value was negative (k = -0.0095). Of the 30 recorded events in the birth certificates of breech or malpresentation in the fetus, 28 were reported to be born by C-section.

Table 25: Agreement in breech/malpresentation recording between birth certificates and discharge abstracts

k = -0.0095 (P = 0.3395)	Breech/malpresentation in discharge abstracts		Total
Breech/malpresentation in BC	No	Yes	
No	175	1	176
Yes	30	0	30
Total	205	1	206

Seizure

The agreement for the recording of neonatal seizures in birth certificates and maternal interview are shown in table 26. Maternal responses of "don't know" or a refusal to answer the question were excluded from the results. The kappa value for this comparison was 0.095, which correlates to slight agreement. The agreement between birth certificates and discharge abstracts was not much different, with a kappa value of 0.12. This also is categorized as slight agreement in table 27. Agreement was higher between maternal interviews and discharge abstracts, as shown in table 28. These two data sources had moderate agreement (k = 0.57).

Table 26: Agreement in seizure recording between birth certificates and maternal interviews

k = 0.095 (P < 0.0001)	Seizure in maternal interview		Total
Seizure in BC	No	Yes	
No	307	18	325
Yes	0	1	1
Total	307	19	326

Table 27: Agreement in seizure recording between birth certificates and child discharge abstracts

k = 0.12 (P < 0.0001)	Seizure in child discharge abstracts		Total
Seizure in BC	No	Yes	
No	311	14	325
Yes	0	1	1
Total	311	15	326

Table 28: Agreement in seizure recording between maternal interview and child discharge abstracts

k = 0.57 (P < 0.0001)	Seizure in child discharge abstracts		Total
Seizure in maternal interview	No	Yes	
No	302	5	307
Yes	9	10	19
Total	311	15	326

Assuming maternal recall as the gold standard in seizure recording, these responses were used to find how many infants with seizures in the first 24 hours of life were eventually diagnosed with CP. Of the 19 reported seizures, 18 (95%) occurred in eventual CP cases.

CHAPTER 4:

DISCUSSION

4.1 Summary of Findings

After comparison among the birth certificates, maternal interviews, and hospital discharge abstracts, the level of agreement varied greatly by variable. Agreement was especially high between birth certificates and discharge abstracts for the method of delivery variables, with perfect agreement or almost perfect agreement for each method. Agreement between these two data sources was also perfect for maternal smoking. Agreement was highest between maternal interviews and discharge abstracts for assisted ventilation and neonatal seizures, with kappa values representing substantial and moderate agreement, respectively. Negative kappa values were generated for the comparison of responses between birth certificates and discharge abstracts for breech or malpresentation, as well as PROM, representing general disagreement. Sufficient data was not available for maternal fever, meconium staining, meconium aspiration, and neonatal seizures in at least one comparison. A particularly interesting finding was that in the only five instances of meconium aspiration recorded in the birth certificates, four could be matched with maternal interview responses about CP status, and all were CP cases.

4.2 Interpretation

The findings for method of delivery and neonatal seizures reflect what has been found previously in the literature. Method of delivery is consistently found to have reliable recording in birth certificates. In a reliability study by Zollinger et al., method of delivery variables were found to have a group average kappa value of 0.763 when birth

certificates were compared with medical records, which was classified as moderate agreement.[16] Birth certificates were also found by Dietz et al. to have excellent positive predictive value and sensitivity (> 90%) for method of delivery variables when compared to medical records.[20] Further, Buescher et al. found a 91.9% agreement of method of delivery variables when comparing data from the 1989 revision of the birth certificate to corresponding medical records.[29] In this study, birth certificates were compared with discharge abstracts and all method of delivery variables had kappa values of 0.98 or greater.

Agreement between birth certificates and discharge abstracts in the reporting of maternal smoking was perfect, with a kappa value of 1.00. The two sources agreed on all of the 206 subjects that were compared. In a validation study by Roohan et al., tobacco use during pregnancy was found to have a high sensitivity in birth certificates (89%) when compared with recording in medical records.[30] While medical records and discharge abstracts are not the same documents and medical records are considered to be the gold standard for accurate data recording, these findings suggest that tobacco use is generally well recorded. However, the agreement between the recording of smoking in the maternal interview compared with both birth certificates and discharge abstracts was only slight. The maternal interviews revealed only three women who admitted to smoking after they learned they were pregnant, while the birth certificates found 15 more. The p-value associated with agreement calculations involving the maternal interview are not statistically significant, which suggests that there is insufficient evidence to say the agreements are beyond what would be found by chance alone.[28] This is in stark contrast to findings by Howland et al. in a recent study that compared recording of maternal

smoking in birth certificate, maternal worksheets, and hospital medical records. The investigators of this study found a nearly perfect agreement between birth certificates and maternal worksheets ($k = 0.92$).[31] The maternal worksheets also revealed 12 more smokers during pregnancy than were recorded in the birth certificates. Because of the high agreement in the hospital documents, this data suggests that there may be an underreporting of tobacco use during pregnancy in the maternal interview, which may be due to the stigma attached or because the interview took place many years after delivery. A similar underreporting of smoking during pregnancy in a maternal interview was found by Kharrazi et al. The investigators compared maternal responses to a series of questions about smoking during pregnancy with results from blood cotinine tests. Results showed a significant underreporting of smoking, as shown by presence of cotinine, a biomarker for cigarette smoking, in blood samples.[32] Another possibility is an overreporting in the birth certificates and discharge abstracts that would occur if the medical professional completing the forms looked at the patient's medical records for smoking history and did not confirm that she stopped using tobacco during pregnancy.

The recording of assisted ventilation had the highest agreement between maternal interviews and discharge abstracts, although the kappa value reflected only moderate agreement ($k = 0.63$). The agreement between birth certificates and both maternal interviews and discharge abstracts was very low. It is possible that this is due to a combination of underreporting in the birth certificates and overreporting in the maternal interview. Birth certificates have been shown to be unreliable in recording complications during labor and delivery, as well as certain obstetric procedures, so it is possible that there is unreliability in reporting the use of assisted ventilation.[33] Maternal recall has

been reported to have poor reliability for adverse events occurring after labor,[34] especially when the child has an illness. Mothers may overreport adverse events at birth to provide a rationale for why her child became sick.[35] Assisted ventilation is a procedure that would need to be coded for in hospital discharge abstracts for insurance billing purposes, recording in these documents is expected to be reliable. Because of this, the gold standard for assisted ventilation was considered to be the discharge abstracts. Of the 101 instances of mechanical ventilation recorded in the discharge abstracts, 92 (91%) were associated with infants born preterm. Additionally, 73 (72%) of the infants that needed mechanical ventilation were eventually diagnosed with CP.

The agreement for the recording of maternal fever during labor and delivery could only be calculated for the birth certificate and maternal interview comparison. These two sources had slight agreement, reflected by the kappa value of 0.13. There were 18 positive responses in the maternal interviews for this variable and eight in the birth certificates, revealing that more mothers report having a fever than what is documented by the medical staff. This is supported by previous the findings of previous studies that report only slight to moderate agreement of maternal risk factors between birth certificates and medical records.[16, 36] Agreement for comparisons involving the hospital discharge abstracts could not be assessed because of the lack of recording in this source. The codes used for the abstracts were for maternal infections affecting the fetus or newborn, abnormalities of the chorion and amnion, and unspecified maternal pyrexia during labor. Because the diagnosis codes are only to be used when an infection or fever definitively impacted the infant, uses of them are not common. Because maternal interviews reported 10 more instances of fever during labor and delivery than did the

birth certificates and because of past research that shows maternal recall is more reliable than birth certificates for this variable, the interviews were considered the gold standard for this comparison.[24, 34] Of the 18 cases of maternal fever reported, 14 (78%) of them were in children later diagnosed with CP. This is supported by previous findings that a maternal fever is a risk factor for CP.[37, 38]

The agreement for recording of meconium staining of the amniotic fluid was completed only for the birth certificate and maternal interview comparison. The kappa value reflected a fair agreement between the two sources (k = 0.34), with birth certificates reporting slightly more events than maternal recall. In a maternal recall study by Liu et al., the recall reliability of meconium staining was particularly low.[34] Reasoning behind this could be that while meconium stained amniotic fluid is associated with difficult labors and low Apgar scores, the outcomes are typically good so mothers may not recollect the event happening at all.[34] Because of this, the birth certificate was considered to be the gold standard in this comparison. Of the recorded events of meconium stained amniotic fluid from the birth certificate, 15 (79%) were CP cases. Meconium staining was not recorded in the available abstracts so no agreement statistics could be generated.

Because no meconium aspiration syndrome was recorded in the hospital discharge abstracts and the maternal interview did not ask mothers about it, the 1989 revision of the birth certificate was the only source for this variable. There were four cases of meconium aspiration out of the 532 available birth certificates, yielding a rate of 0.75%. This is greater than the recorded incidence of 0.043%[39]; however, given this particular study population, this is to be expected. When these subjects were compared with maternal interview responses, all four were reported to develop CP. Meconium aspiration

syndrome is associated with difficult labors resulting in fetal distress, intubation of the infant, and low Apgar scores,[39] which are all also associated with CP.[1, 11, 37]

The PROM variable had the highest agreement between birth certificates and maternal interviews. The kappa value calculated was 0.30, which is only fair agreement between the two sources. The agreement between maternal interviews and discharge abstracts even less impressive, with a kappa of 0.13. The birth certificates and discharge abstracts yielded a negative kappa value, reflecting a general disagreement between the two sources that is greater than what would be seen by chance alone ($k = -0.017$). The discharge abstracts provided only three instances of PROM, while the birth certificate provided 38 in the documents that could be matched by subject identification numbers. The two sources did not agree on any of these positive responses. The p-value associated with the calculated kappa value suggests that the findings are not statistically significant ($p = 0.2644$). In a study by Lydon-Rochelle et al. that investigated reporting in birth certificates and discharge data compared with medical records as the gold standard, PROM data was not reliably recorded in the former two sources.[17] It was more likely to be recorded in the birth certificate than the discharge data and had a higher reliability in women that had a three day stay or longer in the hospital. The OWL study population showed much lower recording in the discharge abstracts than did the study by Lydon-Rochelle et al. The lack of recording in the discharge abstracts is likely largely due to PROM not resulting in a final diagnosis in the baby and subsequently not being recorded. The low agreement in the three sources can be further explained by similar findings by Dobie et al., which reported low recording of maternal complications in the birth certificates.[33] Further, the variable definitions of PROM between birth certificates and

maternal interviews differed. The birth certificates defined PROM as the membranes rupturing at least 12 hours before the onset of labor, while the maternal interviews defined it as membranes rupturing 24 hours before delivery. The difference in variable definitions could result in disagreeing responses for the same event.

Because there was no ICD-9-CM code for abnormally fast labor or abnormally slow labor in the available discharge abstracts, the only comparisons available were between birth certificates and maternal interviews. The kappa value represented only slight agreement between the two sources for precipitate labor ($k = 0.035$); however, this calculation was not statistically significant. Maternal recall reported many more events of precipitate labor than did birth certificates, with 95 and 8 events, respectively. Prolonged labor saw a similar pattern with 68 reports of abnormally slow labor in the maternal interview and only three in the birth certificates. The calculated kappa value for prolonged labor was not much different from precipitate labor, which suggests that maternal recall and recording by health professionals regarding length of labor does not differ between either extreme. However, the agreement in responses for prolonged labor was impacted by some degree by the differences in variable definitions. The birth certificates defined prolonged labor as labor lasting 20 hours or more, while the maternal interview asked mothers if labor lasted at least 12 hours. This would result in more positive responses to prolonged labor in the maternal interview than in the birth certificates.

The agreement findings for breech or malpresentation in the birth certificates and discharge abstracts were similar to the findings for PROM, as the birth certificates and discharge abstracts yielded a negative kappa value ($k = -0.0095$). The negative kappa

value represents disagreement between the data sources. The p-value associated with the kappa calculation was 0.3395, which reflects a lack of statistical significance.[28] Regardless, there was only one recorded breech or malpresentation in the discharge abstracts and a reported 30 in the birth certificates. This can be explained by the events of malpresentation reported by the birth certificates not producing a definitive diagnosis in the newborn, so there was no reason to record the event in the discharge abstract.

The recording of seizures in the newborn showed moderate agreement between sources. When the recording of neonatal seizures was compared between maternal interviews and discharge abstracts by Li et al., agreement was moderate with a kappa value of 0.55.[21] This study used the same maternal interview and vital records datasets as in the study by Li et al. and yielded a kappa value of 0.57, using slightly different inclusion criteria. Li et al. included all child hospital discharge abstracts in the neonatal period, which extends to 28 days after birth, and found 17 reported seizures in the discharge abstracts, 20 in the maternal interviews, and one in the birth certificates. This study, which only used discharge abstracts from the infants' original discharges from the hospital after birth, found 15 reported seizures in the discharge abstracts, 19 in the maternal interviews, and one in the birth certificates.

4.3 Limitations of the Study

There are several limitations to this study that should be considered. A major limitation is that the true gold standard of data reliability, the medical record, was not available for comparison. The majority of birth certificate reliability studies use the medical record to calculate agreement statistics, as well as positive predictive values and sensitivities; however, because only maternal interviews and discharge abstracts were

available, a gold standard had to be estimated for each variable using results from previous studies.

Another limitation is that the reliability of maternal recall is questionable for multiple variables. For the majority of variables on the birth certificate, maternal recall is excellent. There is significantly lower reliability for variables such as medical problems during pregnancy that did not require medication and certain events during delivery, including meconium staining.[34] It is also possible that the maternal interviews were affected by recall bias. Because roughly half of the study population consisted of children with CP, the mothers of these children may remember events during pregnancy and labor differently in an attempt to rationalize why her child developed the disability. On the other hand, it is possible that mothers of affected children have better recollection of adverse events during pregnancy and labor than mothers of children that were controls.

This study was also likely impacted by different definitions of certain variables between birth certificates and maternal interviews. The prolonged labor variable, for example, had a considerably different definition between the two sources, with the birth certificate referencing labor lasting at least 20 hours and the interview referencing labor lasting at least 12 hours. Some variables differed between the two revisions of the birth certificate. The 1989 revision of the birth certificate referenced assisted ventilation for either less than 30 minutes or 30 minutes or more. The 2003 revision referenced assisted ventilation immediately after birth or for more than six hours. Other variables, such as PROM, fever, abnormal length of labor differed between the two revisions, but to a lesser extent than assisted ventilation.

Another large limitation is that many of the variables investigated in this study were not referenced often in the discharge abstracts, which resulted in low agreements or even negative kappa values. This does not mean there was an error in data recording, but rather if the event, such as PROM, occurred, it did not result in an immediate diagnosis in the newborn.

4.4 Conclusions

Because data recorded on birth certificates are so frequently used for research purposes, it is crucial for the information to be as reliable as possible. Results from this study generally suggest that the recording of events during labor and delivery need improvement. Agreement between birth certificates and discharge abstracts was perfect or almost perfect for recording of smoking and method of delivery, which is reflective of the findings of previous studies.[18, 20] There is evidence of underreporting of assisted ventilation, abnormally fast or slow labor, seizure in the newborn, and maternal fever in the birth certificates. The discharge abstracts were the most reliable source for the recording of assisted ventilation and neonatal seizures because the procedure and diagnostic codes were required. Abnormal length of labor and maternal fever seem to be the most reliably recorded in the maternal interviews. Conclusions could not be drawn about the quality of birth certificate recording for meconium staining, meconium aspiration, PROM, or fetal presentation due to the lack of reporting in the other data sources. While birth certificates had more reports of meconium staining than maternal interviews, there were no reports in the discharge abstracts for additional investigation. Past studies have suggested that both maternal recall and birth certificate recording of this variable are unreliable.[33, 34, 36] Mothers were not asked about meconium aspiration in the

interviews and there was no reporting of these events in the available discharge abstracts. Further, the PROM variable had different definitions between the birth certificates and maternal interviews, which likely contributed to the lack of agreement. These variables did not have high recording in the discharge abstracts because to be reported, the events need to result in a diagnosis in the newborn.

To enhance the results of this study, medical records should be obtained and used for additional comparison. Because these documents are the gold standard in data collection,[16] comparing birth certificates and maternal interview responses with medical records would provide more informative results. Additionally, quality of data collection in the birth certificate has been shown to differ depending on who is completing the forms.[14] A beneficial next step would be to gather information on who filled out the birth certificates for the children in this study. The ultimate goal is to better data collection and, subsequently, better the research that uses that data. By determining the shortcomings of data recording in these documents, steps can be taken to make improvements and increase reliability. The increased accuracy of birth certificate data will greatly benefit the future research of cerebral palsy and its associated risk factors.

REFERENCES

REFERENCES

1) Rosenbaum, Peter, et al. "A report: the definition and classification of cerebral palsy April 2006." *Dev Med Child Neurol Suppl* 109.suppl 109 (2007): 8-14.

2) Christensen, Deborah, et al. "Prevalence of cerebral palsy, co-occurring autism spectrum disorders, and motor functioning–Autism and Developmental Disabilities Monitoring Network, USA, 2008." *Developmental Medicine & Child Neurology* 56.1 (2014): 59-65.

3) Sanger, Terence D., et al. "Classification and definition of disorders causing hypertonia in childhood." *Pediatrics* 111.1 (2003): e89-e97.

4) O'Shea, T. Michael. "Diagnosis, treatment, and prevention of cerebral palsy in near-term/term infants." *Clinical obstetrics and gynecology* 51.4 (2008): 816.

5) Palisano, Robert, et al. "Development and reliability of a system to classify gross motor function in children with cerebral palsy." *Developmental Medicine & Child Neurology* 39.4 (1997): 214-223.

6) Braun, Kim Van Naarden, et al. "Birth Prevalence of Cerebral Palsy: A Population-Based Study." *Pediatrics* (2016): peds-2015.

7) Paneth, Nigel. "Establishing the diagnosis of cerebral palsy." *Clinical obstetrics and gynecology* 51.4 (2008): 742-748.

8) Durkin, Maureen S., et al. "Prevalence of Cerebral Palsy among 8-Year-Old Children in 2010 and Preliminary Evidence of Trends in Its Relationship to Low Birthweight." *Paediatric and perinatal epidemiology* (2016).

9) Colver, A. F., et al. "Increasing rates of cerebral palsy across the severity spectrum in north-east England 1964–1993." *Archives of Disease in Childhood-Fetal and Neonatal Edition* 83.1 (2000): F7-F12.

10) Pharoah, P. O. D., and Y. Adi. "Consequences of in-utero death in a twin pregnancy." *The Lancet* 355.9215 (2000): 1597-1602.

11) Reddihough, Dinah S., and Kevin J. Collins. "The Epidemiology and Causes of Cerebral Palsy." Australian Journal of Physiotherapy 49.1 (2003): 7-12. Web.

12) Brumberg, H. L., D. Dozor, and S. G. Golombek. "History of the birth certificate: from inception to the future of electronic data." *Journal of Perinatology* 32.6 (2012): 407-411.

13) Brown, Earle G. "Value of the Vital Statistics Data on Birth and Death Certificates in County Health Work*." *American Journal of Public Health and the Nations Health* 28.12 (1938): 1398-1402.

14) Bradford, Heather M., et al. "Accuracy of birth certificate and hospital discharge data: a certified nurse-midwife and physician comparison." *Maternal and child health journal* 11.6 (2007): 540-548.

15) Taffel, Selma M., Stephanie J. Ventura, and George A. Gay. "Revised US certificate of birth—new opportunities for research on birth outcome." *Birth* 16.4 (1989): 188-193.

16) Zollinger, Terrell W., Michael J. Przybylski, and Roland E. Gamache. "Reliability of Indiana birth certificate data compared to medical records." *Annals of epidemiology* 16.1 (2006): 1-10.

17) Lydon-Rochelle, Mona T., et al. "The reporting of pre-existing maternal medical conditions and complications of pregnancy on birth certificates and in hospital discharge data." *American journal of obstetrics and gynecology* 193.1 (2005): 125-134.

18) Reichman, Nancy E., and Ofira Schwartz-Soicher. "Accuracy of birth certificate data by risk factors and outcomes: analysis of data from New Jersey." *American Journal of Obstetrics and Gynecology* 197.1 (2007): 32-e1.

19) Kirby, Russell S., and Hamisu M. Salihu. "Back to the future? A critical commentary on the 2003 US national standard certificate of live birth." *Birth* 33.3 (2006): 238-244.

20) Dietz, Patricia, et al. "Validation of selected items on the 2003 US standard certificate of live birth: New York City and Vermont." *Public Health Reports* 130.1 (2015).

21) Li, Qing, et al. "Recording of Neonatal Seizures in Birth Certificates, Maternal Interviews, and Hospital Discharge Abstracts in a Cerebral Palsy Case-Control Study in Michigan." *Journal of child neurology* (2015): 0883073815620678.

22) Pisani, Francesco, and Carlotta Spagnoli. "Neonatal Seizures: A Review of Outcomes and Outcome Predictors." *Neuropediatrics* (2015).

23) *CPON-The Cerebral Palsy Outreach Network*. Michigan State University, n.d. Web. 2 Aug. 2016.

24) Romero, Roberto, et al. "Clinical chorioamnionitis at term IV: the maternal plasma cytokine profile." *Journal of perinatal medicine* 44.1 (2016): 77-98.

25) Pariente, Gali, et al. "Meconium-stained amniotic fluid–risk factors and immediate perinatal outcomes among SGA infants." *The Journal of Maternal-Fetal & Neonatal Medicine* 28.9 (2015): 1064-1067.

26) Haakonsen Lindenskov, P. H., et al. "Meconium aspiration syndrome: possible pathophysiological mechanisms and future potential therapies." *Neonatology* 107.3 (2015): 225-230.

27) McHugh, Mary L. "Interrater reliability: the kappa statistic." *Biochemia medica* 22.3 (2012): 276-282.

28) Viera, Anthony J., and Joanne M. Garrett. "Understanding interobserver agreement: the kappa statistic." *Fam Med* 37.5 (2005): 360-363.

29) Buescher, Paul A., et al. "The Quality Of The New Birth Certificate Data: A Validation Study In North Carolina." *American Journal Of Public Health* 83.8 (1993): 1163. *Environment Complete*. Web. 17 Apr. 2016.

30) Roohan, Patrick J., et al. "Validation of birth certificate data in New York State." *Journal of community health* 28.5 (2003): 335-346.

31) Howland, Renata E., et al. "Reliability of Reported Maternal Smoking: Comparing the Birth Certificate to Maternal Worksheets and Prenatal and Hospital Medical Records, New York City and Vermont, 2009." *Maternal and child health journal* 19.9 (2015): 1916-1924.

32) Kharrazi, Martin, et al. "Evaluation of four maternal smoking questions." *Public Health Reports* 114.1 (1999): 60.

33) Dobie, Sharon A., et al. "How well do birth certificates describe the pregnancies they report? The Washington State experience with low-risk pregnancies." *Maternal and child health journal* 2.3 (1998): 145-154.

34) Liu, Jianghong et al. "Medical Record Validation of Maternal Recall of Pregnancy and Birth Events From a Twin Cohort." *Twin research and human genetics : the official journal of the International Society for Twin Studies* 16.4 (2013): 845–860. *PMC*. Web. 17 Apr. 2016.

35) Walshe, Muriel, et al. "Long-term maternal recall of obstetric complications in schizophrenia research." *Psychiatry research* 187.3 (2011): 335-340.

36) DiGiuseppe, David L., et al. "Reliability of birth certificate data: a multi-hospital comparison to medical records information." *Maternal and child health journal* 6.3 (2002): 169-179.

37) Streja, Elani, et al. "Congenital cerebral palsy and prenatal exposure to self-reported maternal infections, fever, or smoking." *American journal of obstetrics and gynecology* 209.4 (2013): 332-e1.

38) Neufeld, Michael D., et al. "Maternal infection and risk of cerebral palsy in term and preterm infants." *Journal of perinatology* 25.2 (2005): 108-113.

39) Dargaville, Peter A., and Beverley Copnell. "The epidemiology of meconium aspiration syndrome: incidence, risk factors, therapies, and outcome." *Pediatrics* 117.5 (2006): 1712-1721.