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Association between Autopsy Status and the Reporting of Well-Defined Causes of Death in Fetal Death Certificates

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B.S., Marist College, 2016

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Abstract

Association between Autopsy Status and the Reporting of Well-Defined Causes of Death in Fetal Death Certificates

By Beckley Miller

The fetal autopsy is one of the most useful diagnostic tests for determining the cause of death among stillbirths; however, in 2014, only 11.7% of stillbirths received an autopsy in the United States. Additionally, only about two thirds of stillbirths were reported to have a well-defined cause of death (i.e. a cause of death that is known or provides insight into the underlying etiology of the stillbirth). This population-based cross-sectional study used fetal death certificates (FDCs) of stillbirths from Utah and Georgia between 2010 and 2014 to understand the underlying association between the receipt of a fetal autopsy and well-defined cause of death reporting. A descriptive analysis of 2,506 FDCs from Utah and 4,923 FDCs from Georgia investigated genetic and non-genetic maternal and fetal characteristics in connection with well-defined cause of death reporting and autopsy status. State-specific receiver operating characteristic (ROC) curves identified influential characteristics for predicting the cause of death status, with odds ratios (OR) and 95% confidence intervals (CI). Among Utah FDCs, stillbirths without an autopsy were less likely to report a well-defined cause of death if they were delivered early in gestation (OR = 0.64 CI: 0.47, 0.87) or had one or more unspecified birth defect (OR = 0.431 CI: 0.355, 0.522). Among FDCs from Georgia, stillbirths without an autopsy were less likely to report a well-defined cause of death if they were delivered early in gestation (OR = 0.639 CI: 0.469, 0.872) or had one or more unspecified defects (OR = 0.575 CI: 0.389, 0.849). ROC analysis determined the most influential characteristics for predicting cause of death status on their own were number of birth defects (Area under curve (AUC) = 0.57) and gestational age (AUC = 0.53) among Georgia FDCs and gestational age (AUC = 0.54) among Utah FDCs. The most consistently influential factors associated with reporting well-defined causes of death across states, autopsy statuses were gestational age, and the number of birth defects reported. Increasing the quality of the cause of death reporting in stillbirths, especially those occurring early in gestation may unearth underlying causes that could lead to measures to prevent future losses.

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BACKGROUND AND LITERATURE REVIEW

Stillbirth, defined as *in utero* fetal death after at least 20 weeks of gestation or birthweight of greater than 350 grams, continues to be a relatively commonplace occurrence in the United States (US); and affects nearly one in every 160 pregnancies that reach 20 weeks' gestation (1, 2). Despite improvements in antenatal care, and modern medical technology, the stillbirth rate in the US is higher than that of many other developed countries (2). From 1990 to 2006 in the US, the stillbirth rate has declined slowly at a rate of 1.4% per year and has remained relatively unchanged since then (2, 3). In contrast, the infant mortality rate has declined 11% since 2006 and is now relatively equal to the stillbirth rate (3). This suggests that efforts have focused on the survival after birth but there has been little impact on preventing stillbirths.

The lack of major improvements in stillbirth rate in the US suggests that these outcomes either are overlooked or are not prioritized as a serious public health concern. Despite having nearly the same incidence as infant mortality, the US continues to provide few resources for programs and research funding for identifying factors associated with stillbirth (4). Continuation of the current trajectory seriously ignores the magnitude of the stillbirth problem and may further exacerbate it.

The psychological and economic impact of stillbirths on families and communities are also of increasing relevance for prioritizing stillbirth research and intervention activities. An estimated 15% of spontaneous fetal deaths (pregnancy losses occurring at any period of gestation) are preventable in high-income countries, like the US, which would translate into approximately 90,000 families being directly impacted by preventable fetal deaths each year (5). Given that 17% of women report feeling some psychological distress three months after a

stillbirth, the impact stillbirths have on parental mental health is substantial (5). Bereaved parents were found to have had significantly higher rates of psychological disorders such as depression, general anxiety disorders, post-traumatic stress disorder, and suicidal ideation (6). The economic cost for anxiety disorders alone in the US in 1990 exceeded $46 billion (7). If US stillbirth rates are not reduced, the costs associated with stillbirths, as well as the associated psychological sequela, will only be further exacerbated. Since the effects of stillbirth are likely associated with significantly increased costs to healthcare services and society, the impact of stillbirth extends beyond the families who endure them (6). Investigation into the underlying causes of stillbirth is of importance to all individuals and thus a decline in the prevalence of stillbirths would positively affect society as a whole.

Etiology of Stillbirths

A number of genetic and environmental factors are associated with stillbirth. It is important to identify individuals who are at high-risk for each of these factors to assist in identifying and targeting the most effective and successful prevention methods and policies.

a) Genetic Risk Factors

Approximately 15 to 30% of stillborn fetuses are reported to have at least one dysmorphic feature or skeletal abnormality and up to 13% of stillbirths have karyotype-detected chromosomal anomalies (8, 9). The most common of the genetic/chromosomal abnormalities in stillbirths are Turner Syndrome (23%), Down Syndrome (23%) and Edward Syndrome (21%) (8). The rate of genetic abnormalities exceeds 20% among fetuses with anatomic abnormalities, compared to only 4.6% in normally formed fetuses (10). Consider, however, a karyotype may be more likely to be performed on a fetus with an overt anatomic abnormality, so the rate of genetic abnormalities in normally formed fetuses may be biased. Additionally, even the rate

among those with anatomic abnormalities is likely an underestimate due to the underutilization of karyotyping and the failure of growth of cultured cells from the obtained tissues (11).

Chromosomal abnormalities and congenital defects were found to be the cause of death in 10.2% of all fetal deaths (12). Further, the proportion of fetal deaths whose cause of death was attributable to birth defects differed by race, maternal age, and the plurality of the birth (12). Stillborn fetuses of non-Hispanic White mothers were reported to have a congenital defect or chromosomal abnormality listed as the cause of death more than twice as often as those born to non-Hispanic Black mothers (12). Fifteen percent of fetal deaths occurring to mothers older than 40 years of age were attributed to a congenital defect or chromosomal abnormality, whereas mothers younger than 40 had frequencies of less than 10% (12). Older mothers were found to be less likely to have fetal deaths due to placental complications, and were more likely to have fetuses with genetic abnormalities (12). Among non-singleton births, only about 5% of the fetal deaths were attributable to a congenital defect or chromosomal abnormality (12). This major decline in the number of defects is likely be due to the much larger number of fetal deaths due to maternal complications of pregnancy in non-singleton births. Genetic factors are influenced by the environmental/demographic factors as well. Thus, when studying the etiology of stillbirth, all underlying causes and their interactions must be considered together.

b) Non-Genetic Risk Factors

In the absence of genetic risk factors, other environmental factors have been associated with stillbirths. Non-Hispanic black male fetuses are known to be the most susceptible racial and ethnic group to stillbirth occurrence in the US (2, 13, 14). Racial comparisons showed that non-Hispanic black women have a stillbirth rate that is more than twice that of non-Hispanic White women (2, 3, 10, 14). The disparity was the greatest among singleton births with non-Hispanic

White women having a rate of 5.5 per 1,000 live births, while non-Hispanic Black mothers had a rate of 12.1 per 1,000 live births (14). Other races and ethnicities such as Hispanic, Asian and native American women each had stillbirth rates below 6 per 1,000 live births (2, 3, 10). Previous studies attributed the racial difference in stillbirth rate to lack of access to prenatal care; however, even among cohorts that had received prenatal care, the racial disparity persisted (2, 15). Much of the underlying rationale for the racial disparity still remains unexplained, although, Flenady *et al.* (2011) reported multiple studies that supported an independent association between African American race and stillbirth in the United States (13). Further research of risk factors, including the prevalence of maternal conditions such as diabetes or hypertension, between racial groups is necessary.

Stillbirth rates vary by maternal age, with mothers aged 35 years and older having an increased likelihood of stillbirth, even after controlling for medical conditions (3, 10). Additionally, teen mothers (less than 18 years old) had nearly the same stillbirth rate as mothers greater than 45 years old, which was twice the rate of mothers aged 25-29 years (10). Overall, the stillbirth rates were higher among teenagers and those over 35 years of age with the lowest rates occurring in women aged 25 to 34 years (3). Multiple studies have hypothesized that higher stillbirth rates among teenagers may be related to less favorable socioeconomic status and behavioral conditions, although biologic immaturity also plays a role (16, 17). A significant number of the stillbirths in women over 35 years of age were related to lethal chromosomal and congenital abnormalities, which is consistent with Hoyert *et al.* (2014) which reported the highest frequencies of congenital malformations were listed as the cause of stillbirth among women over 40 years of age (10, 12).

Maternal education and urbanicity can act as indicators of socioeconomic status (SES), which is associated with stillbirth. Even among differences in education systems, mothers in high

income countries who had received less than 10 years of education had a 70% increase in the odds of a stillbirth (13). Regarding urbanicity, a Canadian study that defined urbanicity based upon metropolitan influence from workforce commuting found a 40% increase in the risk of stillbirths in rural areas with weak metropolitan influence (18). However, other international studies conducted in high-income countries did not show any significant associations between urbanicity and stillbirth (13). Overall, SES, although defined differently among high income countries, has been found to be consistently interrelated with factors such as maternal education, employment, income, urbanicity and marital status (13). In an Australian study, low SES was found to be associated with a 20% increase in the odds of stillbirth and a Swedish study found that blue-collar workers had almost double the odds of stillbirth compared to white-collar workers (19, 20).

Rates of stillbirths in the US vary significantly by the gestational age of the fetus at delivery. In general, a much larger percentage of stillbirths occur early in the pregnancy, with half of all stillbirths occurring between 20 and 27 weeks' gestation (3). The highest rates of stillbirth were found at the earliest (less than 22 weeks) and latest (greater than 42 weeks) gestational ages, and the lowest rate was found between 29 and 33 weeks (3). The two distinct peaks suggest etiologic differences between the gestational age groups. Among stillbirths in the earliest gestational age category, maternal complications was the most frequently reported cause of death; however, as gestational age increased, maternal complications were less common (12). Congenital anomalies were reported as the cause of death more frequently in stillbirths with gestational ages greater than 40 weeks (12). Unearthing the etiology of stillbirth must account for differences by gestational age and target prevention measures accordingly.

Plurality of pregnancy remains one of the strongest risk factors for stillbirth, with a stillbirth rate among non-singleton births that was 4-6 times that of singleton births (3, 10, 13). Multiple

gestations accounts for only 3% of all births but approximately 10% of all reported stillbirths and the stillbirth rate for twins is 2.5 times that of singleton births (3, 14). Higher stillbirth rates among multiple gestations is likely due to an increased risk of common complications such as growth restrictions and fetal abnormalities (10). Maternal complications accounted for 40.4% of the fetal deaths among non-singleton births, and only 11.7% among singleton births (12).

Out of the risk factors influencing stillbirth, the most common preventable risk factor for stillbirth is maternal tobacco smoking (14). Smoking status is a serious public health concern and mothers who smoke have a 1.6 times greater odds of stillbirth than non-smokers (3). Continued tobacco use through the second and third trimesters increased the risk of stillbirth. Mothers who stopped smoking in the first trimester have rates of stillbirth equivalent to those who reported no tobacco use during pregnancy (14).

Stillbirth rates also vary by the sex of the fetus. The rate of stillbirth among male fetuses in the United States is 6% higher than that of females and among non-Hispanic Black males the rate is 12% higher than that of non-Hispanic Black females (3). Sex-specific risks of stillbirth also vary by gestational period, and recent studies have reported slightly elevated risks for male fetuses (3). Female stillbirths had congenital malformations noted as a cause of death slightly more frequently than males, but this difference was not significant and there were no sex-specific differences between the top five reported causes of death (12).

Stillbirth tracking

Stillbirth reporting in the US lacks a consistent, centralized method, leading to the exacerbation of many stillbirth-related problems without an adequate public health response. Each eligible pregnancy loss, determined from state-by-state gestational age and/or birthweight requirements, should receive a fetal death certificate (FDC) (i.e. the vital record used to report

stillbirth). Additionally, each state in the US has a different reporting protocol even for what is to be considered a stillbirth, which leads to incompatible data that is difficult to aggregate into a country-wide report (4). These reporting inconsistencies hinder the ability to provide large scale preventative public health policy (13). The cause of death is also reported differently on FDCs based upon the state and, while it is recommended to use *International Classification of Disease* (ICD)-10 codes for cause of death reporting, many states continue to use a free-text reporting field thus leading to difficulties in aggregating cause of death data (4, 14).

Well-Defined Cause of Death

Determination of a well-defined cause of death (i.e. a cause of death that provides sufficient clinical insight into the underlying etiology of the stillbirth) after the occurrence of a stillbirth is essential in providing clinicians, counselors, parents and public health officials the necessary data to combat stillbirth (5, 21). Causes of death were ill-defined (i.e. the cause of death is unknown or does not provide sufficient insight into the underlying etiology of the stillbirth) in 29.7% of stillbirths in the United States in 2014 (12). Failure to provide parents and medical professionals with information surrounding a stillbirth may hinder our ability to identify adequate interventions to prevent future losses (1, 10). Due to the lack of well-defined causes of death among stillbirths, much of the focus has been moved from the etiology of stillbirth to that of infant mortality since there is a greater amount of usable data for development of prevention strategies (3).

Currently, 37 US states report the cause of death using the ICD-10 coding scheme, allowing for comparisons of the causes of death across state lines and in comparison with other countries (12). Without complete uniformity among states for reporting the fetal cause of death, the identification of etiologies of stillbirth on a country-wide scale is hampered and

valuable data is left unanalyzed (3, 10). Inconsistencies among statewide comparisons for causes of death among stillbirths has led to more confusion about stillbirths, further hindering the investigations into stillbirths and their use in designing public health policies (4).

Reporting well-defined causes of death provides valuable insight into the causes and underlying risk factors of a stillbirth and improves the impact of preventive measures (12, 22). Often, multiple factors contribute to the stillbirth (e.g. maternal risk factors, genetic predispositions, demographic risk factors, etc.). However, providing a well-defined cause of death can elucidate some of the underlying conditions and allow clinicians to provide specialized care and counseling to prevent future stillbirths (12, 14). In low risk women with an ill-defined or unexplained cause of stillbirth, the risk of recurrence is up to 10.5 per 1,000 births (10). Increasing the proportion of stillbirths with well-defined causes of death would allow for the modification of risk factors and provision of benefits to extended family members, leading to a decrease in the risk of recurrence and overall risk of stillbirth (12, 22). Without valuable information presented in a well-defined cause of death, clinicians are restricted on their treatment, public health officials are unable to develop the most effective policies, and parents are unable to receive the best care (2).

Fetal Autopsy

For clinicians, parents, and researchers attempting to understand the etiology of stillbirth, the fetal autopsy remains the gold standard for identifying the cause of the fetal loss. The fetal autopsy is the most useful diagnostic test for determining the cause of stillbirth; however, in the United States in 2004, only 11.7% of fetal deaths reported performing an autopsy and 49.5% of fetal deaths did not report having any exam performed (10-12, 22). More alarmingly, Flenady *et al.* (2011), reported that stillbirth autopsy rates are continuing to decline

in the US (21). Underutilization of the fetal autopsy hinders the clinician's ability to report accurate causes of stillbirth and prevents parents from receiving adequate counseling or testing, when necessary. Valuable information that is received from fetal autopsies can be used by parents to plan for future pregnancies to decrease the risk of later stillbirth incidence, and allow public health officials to identify underlying causes of stillbirth (1, 8, 22, 23). Fetal autopsies can provide parents and communities with information to improve maternal quality of life, assist with seeking closure, and diagnose previously unknown causes of death (6, 14).

Major inhibiting factors associated with the reception of fetal autopsies are found among both clinicians and parents. Among clinicians, discomfort or reluctance to broach the subject of a fetal autopsy acts as the greatest non-parental barrier to the performance of a fetal autopsy (24). Among parents, the most prominent factors preventing the reception of consent for a fetal autopsy were cultural and/or religious beliefs (11, 21). Often, in these cases, parents will not fully understand the logistics and the value of the autopsy, leading to a reluctance to provide consent for the examination (11, 24). If patients' obstetricians who are responsible for obtaining parental consent are able to adequately educate parents on the potential benefits of the fetal autopsy, fetal autopsy rates are likely to rise (14, 22, 25).

Promotion of fetal autopsies is necessary and can be performed through increased clinician involvement and education, increased patient awareness of the autopsy and overall education on autopsy utility. Since the fetal autopsy requires consent from the next of kin before it can be performed, it is extremely important that clinical practitioners are able to thoroughly explain the details of the procedure (23). This places a large significance on the practitioner's familiarity and opinion towards the fetal autopsy so that the value of the procedure can be conveyed and the parents' concerns can be eased. One large survey based study on the views towards autopsies determined that patients were most interested in

information about the cause of death and risk of recurrence, whereas, providers ranked workload, negative publicity, and religion and cultural issues as the most important barriers to obtaining autopsy consent (26). Educating clinicians, who will not be performing the autopsy but will be obtaining consent, so that they are able to answer patient's questions is essential in promoting awareness and comfort in the procedure and providing the best possible care (25). Increased education on the value of the autopsy will also provide a willingness among clinicians to promote fetal autopsies and allow communities to feel more comfortable consenting to these procedures (9). Overall, increased awareness among patients and clinicians alike will assist in promoting the utility of the fetal autopsy and providing each patient the right to the highest level of care.

Increasing the rate of fetal autopsy usage among stillbirths would likely lead to more accurately diagnosed causes of death. The utility of the fetal autopsy is apparent when there is an ambiguous clinical diagnosis or when there is a fetal malformation (22). A change of diagnosis in the cause of death after a fetal autopsy was reported in 22% to 76% of stillbirths and provided additional information in up to 24.3% of stillbirths (22, 27). Increasing the rate of autopsy among stillbirths will lead to a more accurate and well-defined diagnosis of the cause of death and will provide more information for prevention of subsequent stillbirths (1).

Histological and placental pathology exams alone, or in conjunction with fetal autopsies, can provide useful information to diagnose the cause of death of stillbirth. In the US, 47.7% of stillbirths receive histological or placental exams, but only 8.9% of stillbirths receive both a fetal autopsy and a placental exam (12). Page *et al.* (2017) determined that the placental pathology exam was the most useful diagnostic test in determining the cause of stillbirth, except in cases where a suspected fetal anomaly was present (24). The placental pathology exam was approximately twice as useful as the fetal autopsy in cases of preterm and intrapartum stillbirths

(24). Conversely, the fetal autopsy was more than twice as useful as the placental pathology exam in cases of stillbirths with suspected fetal anomalies (24). Although histological and placental pathology exams and fetal autopsy will not always be necessary, utilizing the diagnostic capabilities of these assessments in the proper situations may assist in accurately elucidating the underlying causes of death in the majority stillbirths.

Current data for stillbirth etiology is inadequate, due to insufficient post-mortem investigation protocol and differences among cause of death reporting techniques (21). When the fetal autopsy is performed, a possible or probable cause of death is determined in more than 75% of cases, an increase in the fetal autopsy rate would provide be integral in increasing the number of well-defined causes of death and decreasing the number of ill-defined causes of death (14, 22, 23). Lack of uniform reporting measures for the cause of death among stillbirths creates difficulties in determining underlying risk factors associated with stillbirth across states (10). Uniform reporting measures are essential for translating the value of the fetal autopsy into stillbirth etiology data that can be extrapolated across states to better understand and the underlying etiology of stillbirth in the US (5, 21, 22).

Although stillbirth autopsy rates are low, it is understood that not all stillbirths require an autopsy as the cause of death may be determined prior to delivery, or due to characteristics that are visible upon delivery. This population-based study evaluated whether there was an association between having a fetal autopsy and having a well-defined cause of death reported on the FDC, and whether the association differed by select maternal and fetal characteristics. Further, we aimed to identify which factors, if any, were predictive of having a well-defined cause of death reported on the FDC. Findings from this analysis will attempt to elucidate the underlying factors associated with a well-defined cause of death and the association with fetal autopsy status.

METHODS

We conducted a population-based, cross-sectional study using the FDCs of stillbirths delivered in Georgia and Utah from 2010 to 2014. FDCs were obtained from the Georgia Department of Public Health (GDPH) and the Utah Department of Health's (UDOH) Office of Vital Records and Statistics and analyzed separately due to differences in reporting practices and demographics.

A stillbirth was defined as a fetal death occurring at 20 weeks' gestation or later, or a fetal weight greater than 350 grams in both Georgia and Utah (12). Eligible stillbirths were those with a fetal death certificate on file in Georgia or Utah between January 1, 2010 and December 31, 2014.

The cause of death was classified dichotomously as well-defined or ill-defined. Well-defined and ill-defined causes of death were determined through cause of death reporting using ICD-10 codes (available in Utah FDCs) and free text fields (available in Georgia FDCs). An ill-defined cause of death fails to provide sufficient information for a meaningful or explanatory cause of death. As per CDC guidelines, an ill-defined cause of death was present if one of the following ICD-10 codes was reported as the cause of death: P042 (Newborn affected by maternal tobacco use), P070 (Extremely low birth weight newborn), P071 (Other low birth weight newborn), P072 (extreme immaturity), P073 (prematurity), P095 (fetal death of unspecified cause), or R000-R99 (Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified) (28). All other ICD-10 codes were classified as well-defined causes of death. Georgia FDCs, which did not use ICD-10 codes to report cause of death, were classified as ill-defined if they contained any of the entries presented in Table 1 and well-defined otherwise. All FDCs without a reported cause of death were classified as missing.

Since there is a short window during which a FDC must be filed, there are some stillbirths with an autopsy status noted as “planned.” Autopsy status was determined according to a two-stage classification system. Those with a “planned autopsy” and “performed autopsy” were considered as having had an autopsy. All others were considered as not having had an autopsy.

The number of birth defects was determined using the total number of congenital anomalies reported in the FDC. FDCs with “Unknown Fetal Anomaly” or “Other Fetal Anomaly” were classified separately as “one or more unknown congenital anomalies” to differentiate these reports from those without any congenital anomalies listed. Maternal race and ethnicity was classified as “White” or “Black” reported only “White” or “Black” and did not have Hispanic ethnicity, “Hispanic” reported “Hispanic” as the primary race or the ethnicity. The “Multi-racial” category contained those with “White” or “Black” as the primary race accompanied by another race or ethnicity and the “Other” category contained all other racial combinations. Urbanicity of the county of delivery was determined by cross-referencing the Federal Information Processing Standards (FIPS) code for the county of delivery in each FDC with the National Center for Health Statistics Urbanicity data. A three-level categorization, using the Urban-Rural Classification Scheme for Counties, differentiated the “Large metropolitan” (collapsed from large central metro and large fringe metro), “Medium and Small Metropolitan” (collapsed from medium metro and small metro), and “Rural” (collapsed from micropolitan and non-core) counties (29). The final route and delivery method variable was formed using a three level classification differentiating Cesarean births, spontaneous vaginal births, and assisted vaginal births.

To ensure sufficient data, variables missing more than 10% of their values were excluded from analyses. The maternal education level, maternal WIC status, whether autopsy/histological results were used to determine cause of death, reception of prenatal care,

and maternal tobacco use during pregnancy variables were excluded from analyses in Georgia after failing to satisfy the aforementioned criteria for missing data.

Statistical Analysis

Descriptive analyses were conducted to examine the distribution of maternal and fetal characteristics by autopsy cause of death. The X^2 test was used to assess associations and the Fisher's exact test was used when cell values had less than five observations. Crude odds ratios and 95% confidence intervals for the association between maternal and fetal characteristics and well-defined cause of death status were obtained using logistic regression. Similar methods were used to determine whether there were associations between maternal and fetal characteristics and having one or more birth defect listed on the FDC.

Receiver operating characteristic (ROC) curves were used to identify the efficacy of various models for the correct prediction of the well-defined cause of death status. Area under the curve (AUC) values were used to provide quantitative representation of ROC model efficacies and allow for comparison between models. Models excluding each individual variable were generated to assess the contribution of variables based upon their exclusion from the full model. Models containing only the variable of interest were generated to identify the sole contribution of each variable in the full model. Separate analyses for the Utah group were performed, one using all potential variables and the other using only the variables that contained sufficient data in the Georgia. The model of Georgia stillbirths used the following as predictors for well-defined cause of death: Autopsy status, maternal age, maternal race/ethnicity, fetal sex, gestational age, final route and delivery method, plurality, number of birth defects, and urbanicity of the county of delivery. The Utah model used the predictors in the Georgia model as well as: maternal education level, WIC receipt, histologic/placental exam

results usage in determining cause of death, receipt of prenatal care, and maternal tobacco use. AUC values for different models were compared to infer the relative importance of variables in determining well-defined cause of death status. SAS software version 9.4 of the SAS System for Windows was used for data analyses.

The institutional review boards of Utah Department of Health, Georgia Department of Public Health and Emory University approved this study.

RESULTS

There were 7,429 total eligible stillbirth FDCs between 2010 and 2014, with 2,506 (33.7%) in Utah and 4,923 (66.3%) in Georgia. Stillbirths were ineligible if the FDC did not report a delivery date between January 1, 2010 and December 31, 2014, reported a gestational age of less than 20 weeks, or a fetal weight of less than 350 grams (Records excluded: Utah n=0; Georgia n=69,185) (Figure 1). Additionally, only FDCs with an autopsy status and cause of death reported were included.

Georgia Analyses by Autopsy Status

Among those that did not receive or plan to receive an autopsy in Georgia (n=4,320), the well-defined cause of death status differed significantly by maternal race/ethnicity ($p < 0.01$), the gestational age at stillbirth ($p = 0.04$), number of birth defects ($p < 0.01$) and the urbanicity of the county of delivery ($p < 0.01$) (Table 2a). Among these stillbirths that did not receive an autopsy, well-defined causes of death were more likely to be reported among non-Hispanic Black mothers (OR = 1.44; 95% CI: 1.18, 1.75), stillbirths delivered in medium/small metropolitan counties (OR = 1.73; 95% CI: 1.45, 2.07), and stillbirths delivered in rural counties (OR = 1.82; 95% CI: 1.43, 2.31). Additionally, well-defined causes of death were less likely to be reported among stillbirths that occurred earlier in gestation (OR = 0.84; 95% CI: 0.71, 0.99) and stillbirths that had at least one unspecified birth defect (OR = 0.43; 95% CI: 0.36, 0.52).

Among Georgia stillbirths that received or planned to receive and autopsy (n= 603), the well-defined cause of death status did not differ significantly by any of the observed characteristics (Table 2a). However, within this group, well-defined causes of death were more likely to be reported among stillbirths among non-Hispanic Black mothers (OR = 1.84; 95% CI: 1.05, 3.21). Conversely, within this group, well-defined causes of death were less likely to be

reported among stillbirths that had reported one or more unspecified birth defects (OR = 0.61; 95% CI: 0.38, 0.98).

Utah Analyses by Autopsy Status

Among those that did not receive or plan to receive an autopsy in Utah (n=1,835), the well-defined cause of death status differed significantly by the gestational age of the stillbirth ($p = 0.01$), number of birth defects ($p < 0.01$), and the plurality ($p = 0.03$) (Table 2b). Within this group, well-defined causes of death were more likely to be reported among stillbirths with one (OR = 2.45; 95% CI: 1.48, 4.04) and two (OR = 3.82; 95% CI: 1.55, 9.39) specified birth defects, stillbirths from multiple birth pluralities (OR = 1.80; 95% CI: 0.97, 3.33), and stillbirths that used the histological placental results to determine the cause of death (OR = 1.61; 95% CI: 1.03, 2.52). Well-defined causes of death were less likely to be reported among stillbirths that occurred earlier in gestation (OR = 0.64; 95% CI: 0.47, 0.87) and were diagnosed with one or more unspecified birth defects (OR = 0.58; 95% CI: 0.39, 0.85).

Of those in Utah that received or planned to receive an autopsy (n=671), the well-defined cause of death status was significantly associated with the gestational age of the stillbirth ($p = 0.01$), the number of birth defects ($p < 0.01$), and whether the autopsy or histological placental results were used to determine the cause of death ($p = 0.03$) (Table 2b). Among the group of Utah stillbirths that received or planned to receive an autopsy, well-defined causes of death were more likely to be reported when stillbirths were diagnosed with one (OR = 2.55; 95% CI: 1.76, 3.68), two (OR = 2.19; 95% CI: 1.10, 4.38), or three (OR = 4.34; 95% CI: 1.01, 18.73) specified birth defects and used the autopsy or histological placental results to determine the cause of death (OR = 1.61; 95% CI: 1.03, 2.52). However, well-defined deaths were less likely

to be reported when stillbirths occurred earlier in gestation (OR = 0.76; 95% CI: 0.63, 0.93) or reported one or more unspecified birth defects (OR = 0.41; 95% CI: 0.31, 0.55).

Georgia Analyses by Number of Birth Defects

Of those in Georgia that did not report a birth defect (n=3,092), there were significant differences in the well-defined cause of death status by the gestational age of the stillbirth ($p = 0.01$), maternal race and ethnicity ($p = 0.01$), route of delivery ($p = 0.03$), sex ($p < 0.01$) and the urbanicity of the county of delivery ($p < 0.01$) (Table 3a). Among Georgia stillbirths with no reported birth defects, well-defined causes of death were more likely to be reported among non-Hispanic Black mothers (OR = 1.40; 95% CI: 1.22, 2.66), stillbirths delivered via cesarean section (OR = 1.61; 95% CI: 1.30, 2.00), and stillbirths delivered in medium/small metropolitan (OR = 2.25; 95% CI: 1.86, 2.74) or rural counties (OR = 1.94; 95% CI: 1.49, 2.53). In contrast, well-defined causes of death were less likely to be reported among stillbirths delivered through assisted vaginal methods (OR = 0.18; 95% CI: 0.04, 0.74).

Among Georgia stillbirths that reported one or more birth defects (n=1,803), the well-defined cause of death status varied significantly by race and ethnicity ($p=0.01$), sex ($p<0.01$), gestational age ($p=0.04$), and the route of delivery ($p<0.01$) (Table 3a). Within this group, well-defined causes of death were more likely to be reported among non-Hispanic Black mothers (OR = 1.80; 95% CI: 1.22, 2.66) and stillbirths delivered vis cesarean section (OR = 1.28; 95% CI: 0.87, 1.89). Well-defined causes of death were less likely to be reported among female stillbirths (OR = 0.72; 95% CI: 0.52, 0.99), stillbirths that occurred early in gestation (OR = 0.80; 95% CI: 0.58, 1.09), and stillbirths delivered through assisted vaginal methods (OR = 0.73; 95% CI: 0.22, 2.41).

Utah Analyses by Number of Birth Defects

The distributions of the well-defined cause of death status for stillbirths from Utah that did not report a birth defect on the FDC (n=1,644) differed significantly by maternal education (p=0.01), gestational age (p<0.01), autopsy status (p<0.01), the receipt of prenatal care (p=0.01), and maternal smoking status during pregnancy (p=0.03) (Table 3b). Among Utah stillbirths with no reported birth defects, those with a mother that reported using tobacco during pregnancy were more likely to have a well-defined cause of death reported (OR = 1.49; 95% CI: 1.04, 2.13). Additionally, well-defined causes of death were less likely to be reported among mothers with Associate's (OR = 0.65; 95% CI: 0.45, 0.96) or Bachelor's (OR = 0.68; 95% CI: 0.50, 0.93) degrees, stillbirths that occurred earlier in gestation (OR = 0.68; 95% CI: 0.56, 0.84), and stillbirths that had received or planned to receive an autopsy (OR = 0.60; 95% CI: 0.47, 0.76).

The final group examined was 862 stillbirths from Utah that had one or more birth defects reported on their FDCs. Among this group, the distribution of the well-defined cause of death status differed significantly by the routes of delivery of the stillbirths (p=0.04), plurality of birth (p<0.01), autopsy status (p=0.04), receipt of prenatal care (p=0.04), and the urbanicity of the county of the delivery hospital (p=0.01) (Table 3b). Among Utah stillbirths with at least one reported birth defect, well-defined causes of death were more likely to be reported among multiple birth pluralities (OR = 2.31; 95% CI: 1.27, 4.20), mothers that received prenatal care (OR = 2.30; 95% CI: 1.04, 5.12), and stillbirths delivered in medium/small metropolitan counties (OR = 1.55; 95% CI: 1.14, 2.09). Additionally, well-defined causes of death were less likely to be reported among stillbirths that received or planned to receive an autopsy (OR = 0.73; 95% CI: 0.55, 0.99).

ROC Curve Analysis

In Utah, the characteristics with the greatest sole impact on the prediction of a well-defined cause of death were the autopsy status (AUC = 0.55) and the gestational age (AUC = 0.55) (Table 4). Gestational age and the number of birth defects also had the greatest predictive impact after their individual exclusions from the full model (AUC = 0.61 and AUC = 0.59, respectively). In comparison, in Georgia, the characteristics with the greatest sole predictive value were the number of birth defects (AUC = 0.57) and the urbanicity of the county of delivery (AUC = 0.57). The number of birth defects and the urbanicity of the county of delivery had the greatest impact upon the prediction of a well-defined cause of death after their exclusions (Respectively, AUC = 0.60, AUC =0.61). The removal of autopsy status and maternal race and ethnicity from the full model had no impacts upon the predictive ability (AUC = 0.63 for full model and model without autopsy status) of the model.

DISCUSSION

Using population-based data from two states in the US, our study determined that overall, the number of birth defects, urbanicity, gestational age and autopsy status were important factors for reporting a well-defined cause of stillbirth. Georgia and Utah, although culturally and demographically unique, presented similarities in the significant association between those with one or more birth defects and a well-defined cause of death. Ultimately, the number of birth defects proved to be a crucial component to the predictive models of each group. Additionally, the significance of gestational age differences illustrates the underlying difficulties present in reporting the cause of death for an extremely preterm fetus. Lastly, the importance of autopsy status in the Utah group poses further questions into the relationship of cause of death reporting on FDCs and the performance of autopsies.

Georgia Analyses by Autopsy Status

Among Georgia stillbirths both receiving and not receiving fetal autopsies, FDCs that reported one or more unknown or unspecified birth defects were less likely to have a well-defined cause of death compared to those with no birth defects reported. Fetuses with unknown or unspecified fetal anomalies have ill-defined causes of death despite the assistance of a fetal autopsy, suggesting that these cases may be complicated and require additional workup. Georgia stillbirths without an autopsy that were delivered in medium/small metropolitan areas or rural areas were significantly more likely to report a well-defined cause of death. Conversely, there were no significant differences in well-defined cause of death reporting by urbanicity among Georgian stillbirths that received an autopsy. This suggests that in Georgia when autopsies are not performed on stillbirths, well-defined cause of death reporting is more impacted by the urbanicity of the county of delivery. Comparing these associations with the

associations from Utah stillbirths can provide insight into the factors that influence cause of death reporting between two demographically, and culturally unique states.

Utah Group by Autopsy Status

In Utah, regardless of autopsy status, stillbirths that occurred early in gestation were less likely to receive a well-defined cause of death compared to those that occurred later in gestation. This could be due to the use of ICD-10 codes classifying stillbirths of "extreme immaturity" or "extremely low birth weight" that would be associated with stillbirths of low gestational age but were assigned as ill-defined causes of death since they offer little to no information with regards to the actual mechanism behind the fetal demise. Utah stillbirths with at least one specified birth defect were more than two times as likely to reporting a well-defined cause of death compared with stillbirths that did not report any birth defect. However, due to the specified birth defects being considered well-defined causes of death, there may be a dependency between the well-defined cause of death status and the presence of one or more specified birth defects. Therefore, the association between the presence of a specified birth defect and a well-defined cause of death should be interpreted with caution.

Georgia Analyses by Number of Birth Defects

Georgia stillbirths were observed to have significant differences the well-defined cause of death status across races and ethnicities along with significant differences across urbanicities for those without a reported birth defect. Racial differences by cause of death reporting could be due to the hospitals' reporting procedures close to areas with larger concentrations of certain racial or ethnic groups. Since Georgia stillbirths that had birth defects had a greater likelihood of reporting a well-defined cause of death in medium/small metropolitan or rural counties, stillbirths from these counties may have a higher percentage of defects that are more

easily diagnosed. In addition, since non-Hispanic black women have the highest rate of stillbirth among all races and ethnic groups, there may be an underlying factor acting as an intermediate in the association with well-defined cause of death reporting.

Utah Analyses by Number of Birth Defects

Utah stillbirths that received or planned an autopsy were, surprisingly, less likely to have a well-defined cause of death than those stillbirths that did not have an autopsy. This association is consistent across stillbirth groups both with and without birth defects. Since it is unlikely that the receipt of a fetal autopsy is decreasing the likelihood of reporting a well-defined cause of death, it is possible that there is another factor that might explain this finding. If a FDC is not corrected or updated following an autopsy, then the autopsy status may have no impact upon the reported cause of death status. Moreover, since stillbirths with more ambiguous causes of death would be more likely to receive an autopsy, then stillbirths that had received an autopsy may retain an initial, ill-defined cause of death status.

ROC Curve Analysis

Results from the receiver operating characteristic (ROC) curve models quantified the predictive value of the underlying characteristics for Georgia and Utah to identify the most relatively impactful characteristics for predicting a well-defined cause of death. Given that the birth defect variable likely has some dependency with the well-defined cause of death outcome, its impact in classification was expected. However, the impact of the urbanicity suggests that there should be the focus of further investigation into associations between urbanicity and the reporting of well-defined causes of death. Differences in the AUC values after the removal of the urbanicity variable supports the assertion that urbanicity has an impact on determining well-defined causes of death of stillbirths in Georgia. Regarding the Utah model, the initial hypothesis

that autopsy status had an association with well-defined cause of death was affirmed its impact on the predictive capability. Accompanying the gestational age variable's aforementioned impact on the likelihood of reporting a well-defined cause of death, the ROC curve results suggest that, in Utah, gestational age may play a role in predicting whether a well-defined cause of death was reported. Additional establishment of the importance of gestational age in predicting the presence of a well-defined cause of death after removing it from the model further supports the assertion that the variable has an association with well-defined stillbirth cause of death reporting in Utah.

Although the relative predictive impact illustrates the importance of the predictors such as gestational age, number of birth defects, urbanicity, and autopsy status in Georgia and Utah, it should be noted that no single predictor provided an AUC value greater than 0.6. A ROC predictor with an AUC of 0.5 has no impact a prediction ability equivalent to that of random chance. In Georgia and Utah, the autopsy status predictor had AUC values of 0.51 and 0.55, respectively, so their predictive capabilities were only slightly better than random chance. The most impactful predictor overall was urbanicity in Georgia (AUC = 0.57) but it still did not provide an exceptional impact. The models illustrate the relative importance of certain characteristics, however, they will require much more investigation to be used as effective predictive models for classifying cause of death status.

Comparison to other studies

Although well-defined cause of death remains a relatively unstudied outcome in association with autopsy status, the distribution of maternal and fetal characteristics in relation with autopsy status and the factors influencing cause of death reporting in stillbirths is an area gaining focus. The Stillbirth Collaborative Research Network Writing Group's (SCRN) prospective

case-control study from five U.S. states between 2006 and 2008 and Hoyert *et al.'s* 2014 report from the FDCs of 35 U.S. states each corroborate the importance of gestational age upon the etiology of stillbirths (2, 12). SCRN observed that the prevalence of fetal genetic/structural defects increased significantly for antepartum compared to intrapartum gestational age categories (10.9%, 95% CI: 5.3% – 16.5%, p = 0.007), suggesting an association between birth defects and gestational age (2). Hoyert *et al.* (2014) also reported the number of congenital malformations listed on FDCs differs between gestational age categories (12). Since our study observed associations between both the presence of birth defects and gestational age, and the reporting of a well-defined cause of death, this may suggest that further dependencies are present between fetal characteristics that may influence the cause of death status together. Further, Page *et al.*'s (2017) secondary analysis of the aforementioned SCRN study reports that fetal autopsy is most useful at earlier gestation ages, which would provide reasoning behind our study's decreased likelihood of reporting a well-defined cause of death among stillbirths without an autopsy in the younger gestational age category (24). If the autopsy is not taken advantage of during the time bearing the greatest utility, there may be an increased likelihood in the presence of ambiguity in the classification of the stillbirth etiology resulting in an ill-defined cause of death.

The use and utility of the results of placental histological exams in determining the cause of death in stillbirths has been widely studied. Three studies quantified the utility of a placental histological exam in tandem with a fetal autopsy as being able to determine a cause of death in 74% of cases and 61% if only the placental exam was performed (12, 22, 24). Furthermore, the SCRN study previously mentioned identified the placental histological exam as having the highest proportion of identifying abnormalities that would contribute to determining and probable or possible cause of death compared to other fetal exams (2). These studies

provide support to our findings in which stillbirths receiving an autopsy with placental histological exam results used to determine the cause of death had increased odds of reporting a well-defined cause of death. Although, none of the prior studies identified the quality of the cause of death as the outcome, this study attempts to mend that gap and provide quantifiable results to support not only the increased ability to report causes of death using these tools but also to support the improved quality of the causes of death reported. In identifying potential solutions to data quality problems for cause of death reporting, the implementation of placental histological exams along with fetal autopsies can better understand the etiology of stillbirth.

There is difficulty in directly contrasting this study with similar published studies because the quality of the cause of death outcome as it is related to autopsy or other maternal characteristics is not an association that has been widely studied. Current literature may assess the association between maternal or fetal risk characteristics and causes of death; however, a well-defined cause of death is largely understudied. The Hoyert *et al.* (2014) report begins to focus on the reported causes of death and this study looks to build upon that to explicitly define a well-defined cause of death and provide foundational models to predict the presence of a well-defined cause of death.

Strengths and Limitations

The main strength of this study was the focus on the underlying factors associated with reporting a well or ill-defined cause of death for a stillbirth across states with different reporting procedures. Hoyert *et al.* (2014) identified major causes of death over 37 states with consistent reporting techniques; however, this study was able to provide statewide comparisons between regions with inconsistent reporting protocol (12). While several studies identify complications with stillbirth reporting and its extrapolation to multiple states or multiple countries, there has

been little published on the quality of cause of death reporting and its underlying characteristics (3, 4, 12, 21, 22, 30). Given that this study observed two unique groups of FDCs (Utah and Georgia) with cultural, demographic and socioeconomic differences, the results from the two groups concerning stillbirth cause of death reporting and autopsy status could be extrapolated to an extremely diverse series of regions. This methodology increased the generalizability of the study and allowed us to identify the factors that surpassed demographic or cultural influence. With the presented data, this study was able to explore some of the underlying characteristics behind cause of death data quality and identify new components to better understand stillbirth. The ROC curve methodology allowed characteristics to be quantified for their predictive impact to scale the importance of certain factors, thus working to prioritize certain characteristics for continued research. Using ROC curves identified specific characteristics with the greatest impact for the most effective characterization and set the foundation for future well-defined cause of death classification models to be developed. The data presented establishes a relationship between fetal autopsy status and well-defined cause of death reporting to introduce a new variable into the current conversation on fetal autopsies and their efficacy.

Due to inconsistencies in the reporting procedures between Utah and Georgia's FDCs, a major limitation on this study was the inability to provide between-state comparisons using the full breadth of potential maternal and fetal characteristics. Additionally, because only two states were explored, it was difficult to provide results that could be extrapolated past the state-level. Future investigations into a majority of U.S. states would provide relevance and generalizability for countrywide policy implications. Due to the limitation of receiving only the county of delivery, the urbanicity category was determined based upon the reported county and analyses with greater granularity in terms of location or hospital were unable to be performed. The amount of missing or unreported data, especially on Georgia FDCs, for the maternal and fetal

characteristics prevented the most comprehensive models from being developed for ROC curves and limited the characteristics that could be analyzed.

Public Health Implications

Stillbirth reporting in the US is inadequate and not prioritized or standardized. Not all states even have agreed upon a comprehensive criterion for the definition of a stillbirth and so the reporting of stillbirths is different throughout the country. There is a necessity for a universal stillbirth definition and cause of death reporting methods as supported by the various factors this study found to influence the reporting of a well-defined cause of death. If the quality of a FDC is contingent upon the location that the FDC was reported, the data provided to public health policy makers and advocates will be biased. Improving reporting methods for the cause of death of stillbirths will allow epidemiologists; physicians and public health officials to provide the most efficient and effective care and better understand the true etiology of stillbirths in the US. The current trend in the US is gradually decreasing stillbirth by approximately 1% per year, however, with better reporting methods and a better understanding of the populations most affected by stillbirths this could begin to decrease at a rate closer to that of infant death. Decreasing stillbirth incidence at a greater rate will greatly decrease the direct and indirect impacts of stillbirth on the healthcare industry and reduce the economic burden as well. In 2017, a study in the United Kingdom determined the annual health and social care costs exceeded $19.5 million (31). Developing reporting techniques to understand the underlying stillbirth population and create public health interventions targeted at the groups with the great risk will not only be beneficial on an individual level but also on a societal level as well. Since this study was able to identify underlying associations between stillbirths occurring early in gestation and ill-defined causes of death reported among those that did not receive an autopsy, cause of death reporting for preterm stillbirths could be targeted for investigation. Increasing the quality

of the cause of death reporting in stillbirths occurring early in gestation may unearth underlying causes that could lead to measures that would prevent future losses. Public health officials require accurate data to provide effective prevention strategies. By increasing the quality of cause of death reporting on stillbirth FDCs, public health officials will be able to provide more effective and efficient prevention strategies at individual, communal and societal levels.

Future Direction

Future opportunities with the results obtained from this study will aim to gain more data over multiple other states to provide more generalizable results for countrywide extrapolation of the results. Extending the scope of the collected data to a larger number of states will adjust for cultural, demographic and socioeconomic differences between states and reporting practices. Additional data would allow additional characteristics to be studied to receive a more nuanced representation of the underlying stillbirth population with a reported cause of death in the United States. This could, in turn, improve the ability of the model to accurately predict if the cause of death would be well-defined. Given the time and data, more rigorous analyses using machine learning capabilities, such as Classification and Regression Tree (CaRT) models, could be integrated to support the ROC curve results and establish insight into the underlying components of cause of death reporting in stillbirths.

In conclusion, the findings of this study regarding the utility of the placental and/or histological exam in tandem with the fetal autopsy and that association with providing a well-defined cause of death, taken in context with the results of the previous studies, suggests that performing a fetal autopsy and using the results from a placental and/or histological exam may increase the odds that a well-defined cause of death is reported. The association between gestational age and reporting a well-defined cause of death also suggests that stillbirths with

lower gestational ages may be susceptible to declining cause of death reporting quality and should be diagnosed with greater care and consideration. Additionally, urbanicity in association with cause of death reporting should be identified, as the results from Georgia in this study suggest that large metropolitan areas have decreased odds of reporting a well-defined cause of death.

REFERENCES

1. Leduc, L., et al., *Stillbirth and Bereavement: Guidelines for Stillbirth Investigation.* Journal of Obstetrics and Gynaecology Canada, 2006. **28**(6): p. 540-545.
2. SCRN, *Causes of Death Among Stillbirths.* Jama, 2011. **306**(22): p. 2459-68.
3. MacDorman, M.F. and E.C. Gregory, *Fetal and Perinatal Mortality: United States, 2013.* Natl Vital Stat Rep, 2015. **64**(8): p. 1-24.
4. Lawn, J.E., et al., *Stillbirths: Where? When? Why? How to make the data count?* The Lancet, 2011. **377**(9775): p. 1448-1463.
5. Hogue, C.J., *Invited Commentary: Preventable Pregnancy Loss Is a Public Health Problem.* Am J Epidemiol, 2016. **183**(8): p. 709-12.
6. Burden, C., et al., *From grief, guilt pain and stigma to hope and pride - a systematic review and meta-analysis of mixed-method research of the psychosocial impact of stillbirth.* BMC Pregnancy Childbirth, 2016. **16**: p. 9.
7. DuPont, R.L., et al., *Economic costs of anxiety disorders.* Anxiety, 1996. **2**(4): p. 167-72.
8. Heller, D.S. and O.M. Faye-Petersen, *Pathology of the stillborn infant for the general pathologist: part 1.* Adv Anat Pathol, 2015. **22**(1): p. 1-28.
9. Taylor, G.P., et al., *Small Patients, Complex Challenging Cases: A Reappraisal of the Professional Efforts in Perinatal Autopsies.* Archives of Pathology & Laboratory Medicine, 2014. **138**(7): p. 865-868.
10. ACOG, *ACOG Practice Bulletin No. 102: management of stillbirth.* Obstet Gynecol, 2009. **113**(3): p. 748-61.
11. Silver, R.M. and C.C. Heuser, *Stillbirth workup and delivery management.* Clin Obstet Gynecol, 2010. **53**(3): p. 681-90.

12. Hoyert, D.L. and E.C. Gregory, *Cause of Fetal Death: Data From the Fetal Death Report, 2014.* Natl Vital Stat Rep, 2016. **65**(7): p. 1-25.

13. Flenady, V., et al., *Major risk factors for stillbirth in high-income countries: a systematic review and meta-analysis.* The Lancet, 2011. **377**(9774): p. 1331-1340.

14. Silver, R.M., et al., *Work-up of stillbirth: a review of the evidence.* Am J Obstet Gynecol, 2007. **196**(5): p. 433-44.

15. Vintzileos, A.M., et al., *Prenatal care and black-white fetal death disparity in the United States: heterogeneity by high-risk conditions.* Obstet Gynecol, 2002. **99**(3): p. 483-9.

16. Gibbs, C.M., et al., *The impact of early age at first childbirth on maternal and infant health.* Paediatr Perinat Epidemiol, 2012. **26 Suppl 1**: p. 259-84.

17. Balayla, J., et al., *Effect of maternal age on the risk of stillbirth: a population-based cohort study on 37 million births in the United States.* Am J Perinatol, 2011. **28**(8): p. 643-50.

18. Luo, Z.C. and R. Wilkins, *Degree of rural isolation and birth outcomes.* Paediatr Perinat Epidemiol, 2008. **22**(4): p. 341-9.

19. Mohsin, M., A.E. Bauman, and B. Jalaludin, *The influence of antenatal and maternal factors on stillbirths and neonatal deaths in New South Wales, Australia.* J Biosoc Sci, 2006. **38**(5): p. 643-57.

20. Stephansson, O., et al., *The influence of socioeconomic status on stillbirth risk in Sweden.* Int J Epidemiol, 2001. **30**(6): p. 1296-301.

21. Flenady, V., et al., *Stillbirths: the way forward in high-income countries.* The Lancet, 2011. **377**(9778): p. 1703-1717.

22. Corabian, P., et al., *Guidelines for Investigating Stillbirths: An Update of a Systematic Review.* Journal of Obstetrics and Gynaecology Canada, 2007. **29**(7): p. 560-567.

23. Ernst, L.M., *A pathologists perspective on the perinatal autopsy.* Semin Perinatol, 2015. **39**(1): p. 55-63.

24. Page, J.M., et al., *Diagnostic Tests for Evaluation of Stillbirth: Results From the Stillbirth Collaborative Research Network.* Obstet Gynecol, 2017. **129**(4): p. 699-706.

25. RCOG, *Fetal and perinatal pathology.* Royal College of Obstetricians and Gynaecologists, 2011.

26. Heazell, A.E., et al., *A difficult conversation? The views and experiences of parents and professionals on the consent process for perinatal postmortem after stillbirth.* Bjog, 2012. **119**(8): p. 987-97.

27. Désilets, V., et al., *Fetal and Perinatal Autopsy in Prenatally Diagnosed Fetal Abnormalities With Normal Karyotype.* Journal of Obstetrics and Gynaecology Canada, 2011. **33**(10): p. 1047-1057.

28. Statistics, N.C.f.H., *ICD-10-Mortality Fetal Manual - 2014: General Concepts For Coding Fetal Death*, N.C.f.H. Statistics, Editor. 2014.

29. Ingram, D.D. and S.J. Franco, *2013 NCHS Urban-Rural Classification Scheme for Counties.* Vital Health Stat 2, 2014(166): p. 1-73.

30. Lee, E., et al., *Implications for Improving Fetal Death Vital Statistics: Connecting Reporters' Self-Identified Practices and Barriers to Third Trimester Fetal Death Data Quality in New York City.* Matern Child Health J, 2016. **20**(2): p. 337-46.

31. Campbell, H.E., et al., *Healthcare and wider societal implications of stillbirth: a population-based cost-of-illness study.* Bjog, 2018. **125**(2): p. 108-117.

TABLES

Table 1. Ill-Defined Causes of Death for Free-Text Entries[a]

Cause not found	Immediate cause unknown
Cause unknown	Intrauterine death
Cause undetermined	No specific etiology identified
Could not be determined	No specific known causes
Deadborn fetus NOS	Non-specific causes
Etiology never determined	Not known
Etiology not defined	Obscure etiology
Etiology uncertain	Stillborn
Etiology unexplained	Undetermined
Etiology unknown	Uncertain
Etiology undetermined	Unclear
Etiology unspecified	Unexplained cause
Fetal Death	Unknown
Fetal Demise	? Cause
Final event undetermined	? Etiology
Immediate cause not determined	

[a]Ill-defined cause of death criteria determined from CDC's ICD-10-Mortality Fetal Manual (28)

Table 2a. Characteristics of Georgia Stillbirths without a Reported Autopsy by Well-Defined Cause of Death Based on the 2010 - 2014 Fetal Death Certificate (FDC) Data

		Received or Planned to Receive Fetal Autopsy[a] (n=603)			
	Overall (n=4923)	Well-Defined Cause of Death (n=103)	Ill-Defined Cause of Death[b] (n=500)	Crude Odds Ratio	P-Value[c]
Characteristics	n (%)[t]	n (%)	n (%)	OR (95% CI)[d]	
Maternal Demographics					
Maternal age, years					
20-39*	4298(87.3)	91(88.3)	441(88.2)	1.0	
<20	373(7.6)	8(7.8)	34(6.8)	1.14 (0.51, 2.54)	0.921
40+	163(3.3)	3(2.9)	16(3.2)	0.91 (0.26, 3.18)	
Missing	89(1.8)	1(1.0)	9(1.8)		
Maternal race/ethnicity					
White*	1366(27.7)	18(17.5)	130(26.0)	1.0	
Black	2581(52.4)	72(69.9)	283(56.6)	1.84 (1.05, 3.21)**	
Hispanic	720(14.6)	10(9.7)	62(12.4)	1.17 (0.51, 2.67)	0.073
Multi-racial	161(3.3)	3(2.9)	12(2.4)	1.81 (0.46, 7.02)	
Other	95(1.9)	0(0)	13(2.6)	N/A	
Missing	0(0)	0(0)	0(0)		
Fetal Characteristics					
Sex of stillbirth					
Male*	2400(48.8)	62(60.2)	266(53.2)	1.0	
Female	2095(42.6)	39(37.9)	218(43.6)	0.77 (0.50, 1.19)	0.237
Missing	428(8.7)	2(1.9)	16(3.2)		
Gestational age, weeks					
20-27	2509(51.0)	44(42.7)	206(41.2)	0.94 (0.61, 1.45)	
28+*	2240(45.5)	58(56.3)	289(57.8)	1.0	0.777
Missing	174(3.5)	1(1.0)	5(1.0)		
Final Route and Delivery Method					
Vaginal/Spontaneous *	3656(74.3)	80(77.7)	382(76.4)	1.0	
Vaginal/Assisted	84(1.7)	0(0)	6(1.2)	N/A	0.607
Cesarean	799(16.2)	23(22.3)	93(18.6)	1.181 (0.71, 1.98)	
Missing	384(7.8)	0(0)	19(3.8)		
Multiple Births					
No, Singleton*	4467(90.7)	98(95.1)	466(93.2)	1.0	
Yes, Multiple Births	425(8.6)	5(4.9)	34(6.8)	0.70 (0.27, 1.83)	0.465
Missing	31(0.6)	0(0)	0(0)		

Continued

Table 2a. Continued

		Received or Planned to Receive Fetal Autopsy[a] (n=603)			
	Overall (n=4923)	**Well-Defined Cause of Death (n=103)**	**Ill-Defined Cause of Death[b] (n=500)**	**Crude Odds Ratio**	**P-Value[c]**
Characteristics	**n (%)[t]**	**n (%)**	**n (%)**	**OR (95% CI)[d]**	
Number of Birth Defects					
0*	3092(62.8)	74(71.8)	307(61.4)	1.0	
1	53(1.1)	0(0)	4(0.8)	N/A	
2	4(0.1)	0(0)	1(0.2)	N/A	
3	0(0)	0(0)	0(0)	N/A	
4	0(0)	0(0)	0(0)	N/A	0.142
5	0(0)	0(0)	0(0)	N/A	
6	0(0)	0(0)	0(0)	N/A	
One or more unknown congenital anomalies	1746(35.5)	27(26.2)	184(36.8)	0.61 (0.38, 0.98)**	
Missing	28(0.6)	2(1.9)	4(0.8)		
Maternal Risk Factors					
Urbanicity of county of delivery					
Large Metropolitan*	2792(56.7)	65(63.1)	349(69.8)	1.0	
Medium/Small Metropolitan	1560(31.7)	28(27.2)	114(22.8)	1.32 (0.81, 2.16)	0.399
Rural	570(11.6)	10(9.7)	37(7.4)	1.45 (0.69, 3.06)	
Missing	1(0)	0(0)	0(0)		

Continued

Table 2a. Continued

		No Planned or Performed Fetal Autopsy (n=4320)			
	Overall (n=4923)	**Well-Defined Cause of Death (n=708)**	**Ill-Defined Cause of Death[b] (n=3612)**	**Crude Odds Ratio**	**P-Value[c]**
Characteristics	**n (%)[t]**	**n (%)**	**n (%)**	**OR (95% CI)[d]**	
Maternal Demographics					
Maternal age, years					
20-39*	4298(87.3)	616(87.0)	3150(87.2)	1.0	
<20	373(7.6)	63(8.9)	268(7.4)	1.20 (0.90, 1.60)	0.371
40+	163(3.3)	21(3.0)	123(3.4)	0.87 (0.55, 1.40)	
Missing	89(1.8)	8(1.1)	71(2.0)		
Maternal race/ethnicity					
White*	1366(27.7)	166(23.4)	1052(29.1)	1.0	
Black	2581(52.4)	412(58.2)	1814(50.2)	1.44 (1.18, 1.75)**	
Hispanic	720(14.6)	98(13.8)	550(15.2)	1.13 (0.86, 1.48)	0.001**
Multi-racial	161(3.3)	26(3.7)	120(3.3)	1.37 (0.87, 2.16)	
Other	95(1.9)	6(0.8)	76(2.1)	0.50 (0.22, 1.17)	
Missing	0(0)	0(0)	0(0)		
Fetal Characteristics					
Sex of stillbirth					
Male*	2400(48.8)	387(54.7)	1685(46.7)	1.0	
Female	2095(42.6)	303(42.8)	1535(42.5)	0.86 (0.73, 1.01)	0.073
Missing	428(8.7)	18(2.5)	392(10.9)		
Gestational age, weeks					
20-27	2509(51.0)	402(56.8)	1857(51.4)	0.84 (0.71, 0.99)**	
28+*	2240(45.5)	292(41.2)	1601(44.3)	1.0	0.042**
Missing	174(3.5)	14(2.0)	154(4.3)		
Final Route and Delivery Method					
Vaginal/Spontaneous *	3656(74.3)	529(74.7)	2665(73.8)	1.0	
Vaginal/Assisted	84(1.7)	5(0.7)	73(2.0)	0.35 (0.14, 0.86)**	<0.001**
Cesarean	799(16.2)	165(23.3)	518(14.3)	1.61 (1.32, 1.96)**	
Missing	384(7.8)	9(1.3)	356(9.9)		
Multiple Births					
No, Singleton*	4467(90.7)	646(91.2)	3257(90.2)	1.0	
Yes, Multiple Births	425(8.6)	61(8.6)	325(9.0)	0.95 (0.71, 1.26)	0.706
Missing	31(0.6)	1(0.1)	30(0.8)		

Continued

Table 2a. Continued

		No Planned or Performed Fetal Autopsy (n=4320)			
	Overall (n=4923)	**Well-Defined Cause of Death (n=708)**	**Ill-Defined Cause of Death[b] (n=3612)**	**Crude Odds Ratio**	**P-Value[c]**
Characteristics	**n (%)[t]**	**n (%)**	**n (%)**	**OR (95% CI)[d]**	
Number of Birth Defects					
0*	3092(62.8)	548(77.4)	2163(59.9)	1.0	
1	53(1.1)	7(1.0)	42(1.2)	0.66 (0.29, 1.47)	
2	4(0.1)	1(0.1)	2(0.1)	1.97 (0.18, 21.81)	
3	0(0)	0(0)	0(0)	N/A	
4	0(0)	0(0)	0(0)	N/A	<0.001**
5	0(0)	0(0)	0(0)	N/A	
6	0(0)	0(0)	0(0)	N/A	
One or more unknown congenital anomalies	1746(35.5)	151(21.3)	1384(38.3)	0.43 (0.36, 0.52)**	
Missing	28(0.6)	1(0.1)	21(0.6)		
Maternal Risk Factors					
Urbanicity of county of delivery					
Large Metropolitan*	2792(56.7)	307(43.4)	2071(57.3)	1.0	
Medium/Small Metropolitan	1560(31.7)	290(41.0)	1128(31.2)	1.73 (1.45, 2.07)**	<0.001**
Rural	570(11.6)	111(15.7)	412(11.4)	1.82 (1.43, 2.31)**	
Missing	1(0)	0(0)	1(0)		

[a]Autopsy was reported to be performed or was planned to be performed on the FDC

[b]Ill-defined cause of death determined from Table 4 criteria

[c]P value generated from Chi-Square test or Fisher's Exact Test when one or more cell values are less than 5

[d]Crude Unadjusted Odds Ratio (OR) and 95% Confidence Interval (95% CI)

[t]Number and percentage of FDCs in each category

*Reference group

**Result significant at 95% confidence level

Table 2b. Characteristics of Utah Stillbirths without a Reported Autopsy by Well-Defined Cause of Death, FDC Data, 2010 - 2014

		Received or Planned to Receive Fetal Autopsy[a] (n=671)			
	Overall (n=2506)	Well-Defined Cause of Death (n=399)	Ill-Defined Cause of Death[a] (n=272)	Crude Odds Ratio	P-Value[c]
Characteristics	n (%)[t]	n (%)	n (%)	OR (95% CI)[d]	
Maternal Demographics					
Maternal age, years					
20-39*	2218(88.5)	350(87.7)	243(89.3)	1.0	
<20	189(7.5)	33(8.3)	18(6.6)	0.97 (0.67, 1.41)	0.702
40+	75(3.0)	13(3.3)	10(3.7)	1.36 (0.72, 2.57)	
Missing	24(1.0)	3(0.8)	1(0.4)		
Maternal race/ethnicity					
White*	1610(64.2)	255(63.9)	170(62.5)	1.0	
Black	34(1.4)	8(2.0)	8(2.9)	1.47 (0.48, 4.50)	
Hispanic	425(17.0)	73(18.3)	47(17.3)	0.83 (0.63, 1.08)	0.309
Multi-racial	21(0.8)	5(1.3)	0(0)	1.26 (0.40, 3.94)	
Other	416(16.6)	58(14.5)	47(17.3)	0.80 (0.62, 1.05)	
Missing	0(0)	0(0)	0(0)		
Maternal education level					
Less than High School	297(11.9)	57(14.3)	35(12.9)	0.86 (0.60, 1.22)	
High School*	580(23.1)	76(19.0)	61(22.4)	1.0	
Some College	619(24.7)	95(23.8)	58(21.3)	1.12 (0.84, 1.50)	
Associates	242(9.7)	34(8.5)	26(9.6)	0.71 (0.50, 1.02)	0.752
Bachelor's	468(18.7)	76(19.0)	60(22.1)	0.86 (0.63, 1.16)	
Graduate Degree	101(4.0)	23(5.8)	13(4.8)	1.11 (0.62, 1.98)	
Missing	199(7.9)	38(9.5)	19(7.0)		
Received WIC					
No*	2169(86.6)	335(84.0)	233(85.7)	1.0	
Yes	337(13.4)	64(16.0)	39(14.3)	0.99 (0.74, 1.33)	0.548
Missing	0(0)	0(0)	0(0)		
Fetal Characteristics					
Sex of stillbirth					
Male*	1279(51.0)	213(53.4)	148(54.4)	1.0	
Female	1182(47.2)	174(43.6)	121(44.5)	0.87 (0.71, 1.06)	0.996
Missing	45(1.8)	12(3.0)	3(1.1)		

Continued

Table 2b. Continued

			Received or Planned to Receive Fetal Autopsy[a] (n=671)			
	Overall (n=2506)		**Well-Defined Cause of Death (n=399)**	**Ill-Defined Cause of Death[a] (n=272)**	**Crude Odds Ratio**	**P-Value[c]**
Characteristics	**n (%)[t]**		**n (%)**	**n (%)**	**OR (95% CI)[d]**	
Gestational age, weeks						
20-27	1342(53.6)		219(54.9)	119(43.8)	0.76 (0.63, 0.93)**	0.005**
28+*	1164(46.4)		180(45.1)	153(56.3)	1.0	
Missing	0(0)		0(0)	0(0)		
Final Route and Delivery Method						
Vaginal/Spontaneous *	2162(86.3)		336(84.2)	233(85.7)	1.0	0.585
Vaginal/Assisted	44(1.8)		10(2.5)	9(3.3)	0.50 (0.23, 1.10)	
Cesarean	300(12.0)		53(13.3)	30(11.0)	1.32 (0.96, 1.82)	
Missing	0(0)		0(0)	0(0)		
Multiple Births						
No, Singleton*	2286(91.2)		361(90.5)	256(94.1)	1.0	0.061
Yes, Multiple Births	219(8.7)		38(9.5)	15(5.5)	1.52 (1.04, 2.20)**	
Missing	1(0)		0(0)	1(0.4)		
Histological/Placental Results used to determine cause of death						
No*	2184(87.2)		283(70.9)	184(67.6)	1.0	0.365
Yes	321(12.8)		116(29.1)	88(32.4)	1.61 (1.03, 2.52)**	
Missing	1(0)		0(0)	0(0)		
Number of Birth Defects						
0*	1644(65.6)		211(52.9)	161(59.2)	1.0	<0.001**
1	344(13.7)		77(19.3)	24(8.8)	2.55 (1.76, 3.68)**	
2	94(3.8)		30(7.5)	6(2.2)	2.19 (1.10, 4.38)**	
3	37(1.5)		16(4.0)	0(0)	4.34 (1.01, 18.73)**	
4	9(0.4)		2(0.5)	0(0)	2.74 (0.33, 22.85)	
5	6(0.2)		1(0.3)	0(0)	N/A	
6	2(0.1)		1(0.3)	0(0)	N/A	
One or more unknown congenital anomalies	370(14.8)		61(15.3)	81(29.8)	0.41 (0.31, 0.55)**	
Missing	0(0)		0(0)	0(0)		
Maternal Risk Factors						
Received prenatal care						
No*	92(3.7)		13(3.3)	8(2.9)	1.0	0.726
Yes	2310(92.2)		349(87.5)	252(92.6)	1.13 (0.68, 1.86)	
Missing	104(4.2)		37(9.3)	12(4.4)		
Maternal tobacco use during pregnancy						
No*	2278(90.9)		357(89.5)	251(92.3)	1.0	0.221
Yes	228(9.1)		42(10.5)	21(7.7)	1.18 (0.83, 1.68)	
Missing	0(0)		0(0)	0(0)		
Urbanicity of county of delivery						
Large Metropolitan*	1174(46.8)		262(65.7)	189(69.5)	1.0	0.468
Medium/Small Metropolitan	1172(46.8)		116(29.1)	73(26.8)	1.08 (0.88, 1.33)	
Rural	160(6.4)		21(5.3)	10(3.7)	1.01 (0.67, 1.51)	
Missing	0(0)		0(0)	0(0)		

Continued

Table 2b. Continued

		No Planned or Performed Fetal Autopsy (n=1835)			
	Overall (n=2506)	**Well-Defined Cause of Death (n=1266)**	**Ill-Defined Cause of Death[a] (n=569)**	**Crude Odds Ratio**	**P-Value[c]**
Characteristics	**n (%)[t]**	**n (%)**	**n (%)**	**OR (95% CI)[d]**	
Maternal Demographics					
Maternal age, years					
20-39*	2218(88.5)	1118(88.3)	507(89.9)	1.0	
<20	189(7.5)	94(7.4)	44(7.7)	1.27 (0.70, 2.31)	0.622
40+	75(3.0)	39(3.1)	13(2.3)	0.90 (0.39, 2.09)	
Missing	24(1.0)	15(1.2)	5(0)		
Maternal race/ethnicity					
White*	1610(64.2)	834(65.9)	351(61.7)	1.0	
Black	34(1.4)	14(1.1)	4(0.7)	0.67 (0.25, 1.81)	
Hispanic	425(17.0)	202(16)	103(18.1)	1.04 (0.68, 1.57)	0.330
Multi-racial	21(0.8)	12(0.9)	4(0.7)	N/A	
Other	416(16.6)	204(16.1)	107(18.8)	0.82 (0.54, 1.27)	
Missing	0(0)	0(0)	0(0)		
Maternal education level					
Less than High School	297(11.9)	137(10.8)	68(12)	1.31 (0.76, 2.24)	
High School*	580(23.1)	311(24.6)	132(23.2)	1.0	
Some College	619(24.7)	338(26.7)	128(22.5)	1.32 (0.82, 2.10)	
Associates	242(9.7)	114(9)	68(12)	1.05 (0.57, 1.94)	0.159
Bachelor's	468(18.7)	222(17.5)	110(19.3)	1.02 (0.63, 1.64)	
Graduate Degree	101(4.0)	47(3.7)	18(3.2)	1.42 (0.67, 3.03)	
Missing	199(7.9)	97(7.7)	45(7.9)		
Received WIC					
No*	2169(86.6)	1105(87.3)	496(87.2)	1.0	
Yes	337(13.4)	161(12.7)	73(12.8)	1.14 (0.74, 1.76)	0.947
Missing	0(0)	0(0)	0(0)		
Fetal Characteristics					
Sex of stillbirth					
Male*	1279(51.0)	648(51.2)	270(47.5)	1.0	
Female	1182(47.2)	600(47.4)	287(50.4)	1.00 (0.73, 1.37)	0.176
Missing	45(1.8)	18(1.4)	12(2.1)		

Continued

Table 2b. Continued

			No Planned or Performed Fetal Autopsy (n=1835)			
	Overall (n=2506)		Well-Defined Cause of Death (n=1266)	Ill-Defined Cause of Death[a] (n=569)	Crude Odds Ratio	P-Value[c]
Characteristics	**n (%)[t]**		**n (%)**	**n (%)**	**OR (95% CI)[d]**	
Gestational age, weeks						
20-27	1342(53.6)		719(56.8)	285(50.1)	0.64 (0.47, 0.87)**	0.008**
28+*	1164(46.4)		547(43.2)	284(49.9)	1.0	
Missing	0(0)		0(0)	0(0)		
Final Route and Delivery Method						
Vaginal/Spontaneous *	2162(86.3)		1092(86.3)	501(88.1)	1.0	0.044**
Vaginal/Assisted	44(1.8)		13(1.0)	12(2.1)	0.77 (0.31, 1.93)	
Cesarean	300(12.0)		161(12.7)	56(9.8)	1.23 (0.76, 1.98)	
Missing	0(0)		0(0)	0(0)		
Multiple Births						
No, Singleton*	2286(91.2)		1139(90)	530(93.1)	1.0	0.028**
Yes, Multiple Births	219(8.7)		127(10)	39(6.9)	1.80 (0.97, 3.33)	
Missing	1(0)		0(0)	0(0)		
Histological/Placental Results used to determine cause of death						
No*	2184(87.2)		1175(92.8)	542(95.3)	1.0	0.034**
Yes	321(12.8)		91(7.2)	26(4.6)	0.86 (0.61, 1.20)	
Missing	1(0)		0(0)	1(0.2)		
Number of Birth Defects						
0*	1644(65.6)		873(69)	399(70.1)	1.0	<0.001**
1	344(13.7)		206(16.3)	37(6.5)	2.45 (1.48, 4.04)**	
2	94(3.8)		48(3.8)	10(1.8)	3.82 (1.55, 9.39)**	
3	37(1.5)		19(1.5)	2(0.4)	N/A	
4	9(0.4)		6(0.5)	1(0.2)	N/A	
5	6(0.2)		5(0.4)	0(0)	N/A	
6	2(0.1)		1(0.1)	0(0)	N/A	
One or more unknown congenital anomalies	370(14.8)		108(8.5)	120(21.1)	0.58 (0.39, 0.85)**	
Missing	0(0)		0(0)	0(0)		
Maternal Risk Factors						
Received prenatal care						
No*	92(3.7)		47(3.7)	24(4.2)	1.0	0.642
Yes	2310(92.2)		1176(92.9)	533(93.7)	0.85 (0.35, 2.09)	
Missing	104(4.2)		43(3.4)	12(2.1)		
Maternal tobacco use during pregnancy						
No*	2278(90.9)		1147(90.6)	523(91.9)	1.0	0.362
Yes	228(9.1)		119(9.4)	46(8.1)	1.41 (0.81, 2.43)	
Missing	0(0)		0(0)	0(0)		
Urbanicity of county of delivery						
Large Metropolitan*	1174(46.8)		492(38.9)	231(40.6)	1.0	0.731
Medium/Small Metropolitan	1172(46.8)		686(54.2)	297(52.2)	1.15 (0.81, 1.62)	
Rural	160(6.4)		88(7)	41(7.2)	1.52 (0.70, 3.29)	
Missing	0(0)		0(0)	0(0)		

[a]Autopsy was reported to be performed or was planned to be performed on the FDC
[b]Ill-defined cause of death determined from Table 4 criteria
[c]P value generated from Chi-Square test or Fisher's Exact Test when one or more cell values are less than 5
[d]Crude Unadjusted Odds Ratio (OR) and 95% Confidence Interval (95% CI)
[t]Number and percentage of FDCs in each category
*Reference group
**Result significant at 95% confidence level

Table 3a. Characteristics of Georgia Stillbirths With and Without Reported Birth Defects by Well-Defined Cause of Death, FDC Data, 2010 - 2014

		One or More Birth Defects[a] (n=1803)			
	Overall (n=4923)	Well-Defined Cause of Death (n=186)	Ill-Defined Cause of Death[b] (n=1617)	Crude Odds Ratio	P-Value[c]
Characteristics	n (%)[t]	n (%)	n (%)	OR (95% CI)[d]	
Maternal Demographics					
Maternal age, years					
20-39*	4298(87.3)	164(88.2)	1414(82.4)	1.0	
<20	373(7.6)	15(8.1)	127(7.4)	1.02 (0.58, 1.78)	0.951
40+	163(3.3)	5(2.7)	53(3.1)	0.81 (0.32, 2.06)	
Missing	89(1.8)	2(1.1)	23(1.3)		
Maternal race/ethnicity					
White*	1366(27.7)	36(19.4)	463(27)	1.0	
Black	2581(52.4)	118(63.4)	842(49.1)	1.80 (1.22, 2.66)**	
Hispanic	720(14.6)	19(10.2)	206(12)	1.19 (0.66, 2.12)	0.006**
Multi-racial	161(3.3)	11(5.9)	58(3.4)	2.44 (1.18, 5.05)**	
Other	95(1.9)	2(1.1)	48(2.8)	0.54 (0.13, 2.30)	
Missing	0(0)	0(0)	0(0)		
Fetal Characteristics					
Sex of stillbirth					
Male*	2400(48.8)	110(59.1)	764(44.5)	1.0	
Female	2095(42.6)	69(37.1)	665(38.8)	0.72 (0.52, 0.99)**	0.001**
Missing	428(8.7)	7(3.8)	188(11)		
Gestational age, weeks					
20-27	2509(51.0)	110(59.1)	842(49.1)	0.80 (0.58, 1.09)	
28+*	2240(45.5)	75(40.3)	721(42)	1.0	0.038**
Missing	174(3.5)	1(0.5)	54(3.1)		
Final Route and Delivery Method					
Vaginal/Spontaneous *	3656(74.3)	143(76.9)	1075(62.6)	1.0	
Vaginal/Assisted	84(1.7)	3(1.6)	31(1.8)	0.73 (0.22, 2.41)	<0.001**
Cesarean	799(16.2)	37(19.9)	217(12.6)	1.28 (0.87, 1.89)	
Missing	384(7.8)	3(1.6)	294(17.1)		
Multiple Births					
No, Singleton*	4467(90.7)	163(87.6)	1444(84.1)	1.0	
Yes, Multiple Births	425(8.6)	23(12.4)	154(9)	1.32 (0.83, 2.11)	0.165
Missing	31(0.6)	0(0)	19(1.1)		
Maternal Risk Factors					
Urbanicity of county of delivery					
Large Metropolitan*	2792(56.7)	105(56.5)	880(51.3)	1.0	
Medium/Small Metropolitan	1560(31.7)	58(31.2)	577(33.6)	0.84 (0.60, 1.18)	0.352
Rural	570(11.6)	23(12.4)	160(9.3)	1.21 (0.74, 1.95)	
Missing	1(0)	0(0)	0(0)		
Autopsy Status					
No - No Autopsy*	4320(87.8)	159(85.5)	1428(83.2)	1.0	
Yes - Autopsy Planned/Performed	603(12.2)	27(14.5)	189(11)	1.28 (0.83, 1.98)	0.261
Missing	0	0(0)	0(0)		

Continued

Table 3a. Continued

			No Birth Defects (n=3092)			
	Overall (n=4923)		**Well-Defined Cause of Death (n=622)**	**Ill-Defined Cause of Death[b] (n=2470)**	**Crude Odds Ratio**	**P-Value[c]**
Characteristics	**n (%)[t]**		**n (%)**	**n (%)**	**OR (95% CI)[d]**	
Maternal Demographics						
Maternal age, years						
20-39*	4298(87.3)		541(87)	2156(87.3)	1.0	
<20	373(7.6)		56(9)	175(7.1)	1.28 (0.93, 1.75)	0.125
40+	163(3.3)		18(2.9)	85(3.4)	0.84 (0.50, 1.42)	
Missing	89(1.8)		7(1.1)	54(2.2)		
Maternal race/ethnicity						
White*	1366(27.7)		147(23.6)	708(28.7)	1.0	
Black	2581(52.4)		364(58.5)	1249(50.6)	1.40 (1.14, 1.74)**	
Hispanic	720(14.6)		89(14.3)	399(16.2)	1.07 (0.80, 1.44)	0.004**
Multi-racial	161(3.3)		18(2.9)	73(3)	1.19 (0.69, 2.05)	
Other	95(1.9)		4(0.6)	41(1.7)	0.47 (0.17, 1.33)	
Missing	0(0)		0(0)	0(0)		
Fetal Characteristics						
Sex of stillbirth						
Male*	2400(48.8)		339(54.5)	1178(47.7)	1.0	
Female	2095(42.6)		270(43.4)	1076(43.6)	0.87 (0.73, 1.04)	<0.001**
Missing	428(8.7)		13(2.1)	216(8.7)		
Gestational age, weeks						
20-27	2509(51.0)		336(54)	1210(49)	0.85 (0.71, 1.01)	
28+*	2240(45.5)		272(43.7)	1155(46.8)	1.0	0.013**
Missing	174(3.5)		14(2.3)	105(4.3)		
Final Route and Delivery Method						
Vaginal/Spontaneous *	3656(74.3)		465(74.8)	1955(79.1)	1.0	
Vaginal/Assisted	84(1.7)		2(0.3)	47(1.9)	0.18 (0.04, 0.74)**	<0.001**
Cesarean	799(16.2)		149(24)	389(15.7)	1.61 (1.30, 2.00)**	
Missing	384(7.8)		6(1)	79(3.2)		
Multiple Births						
No, Singleton*	4467(90.7)		578(92.9)	2255(91.3)	1.0	
Yes, Multiple Births	425(8.6)		43(6.9)	204(8.3)	0.82 (0.59, 1.16)	0.315
Missing	31(0.6)		1(0.2)	11(0.4)		
Maternal Risk Factors						
Urbanicity of county of delivery						
Large Metropolitan*	2792(56.7)		265(42.6)	1520(61.5)	1.0	
Medium/Small Metropolitan	1560(31.7)		260(41.8)	662(26.8)	2.25 (1.86, 2.74)**	<0.001**
Rural	570(11.6)		97(15.6)	287(11.6)	1.94 (1.49, 2.53)**	
Missing	1(0)		0(0)	1(0)		
Autopsy Status						
No - No Autopsy*	4320(87.8)		548(88.1)	2163(87.6)	1.0	
Yes - Autopsy Planned/Performed	603(12.2)		74(11.9)	307(12.4)	0.95 (0.73, 1.25)	0.718
Missing	0		0(0)	0(0)		

[a]One or more birth defects were identified on the FDC (birth defects could be specified or unspecified)
[b]Ill-defined cause of death determined from Table 4 criteria
[c]P value generated from Chi-Square test or Fisher's Exact Test when one or more cell values are less than 5
[d]Crude Unadjusted Odds Ratio (OR) and 95% Confidence Interval (95% CI)
[t]Number and percentage of FDCs in each category
*Reference group
**Result significant at 95% confidence level

Table 3b. Characteristics of Utah Stillbirths With and Without Reported Birth Defects by Well-Defined Cause of Death, FDC Data, 2010 - 2014

		One or More Birth Defects[a] (n=862)			
	Overall (n=2506)	**Well-Defined Cause of Death (n=581)**	**Ill-Defined Cause of Death[b] (n=281)**	**Crude Odds Ratio**	**P-Value[c]**
Characteristics	**n (%)[t]**	**n (%)**	**n (%)**	**OR (95% CI)[d]**	
Maternal Demographics					
Maternal age, years					
20-39*	2218(88.5)	498(85.7)	248(88.3)	1.0	
<20	189(7.5)	45(7.7)	23(8.2)	0.97 (0.58, 1.65)	0.290
40+	75(3.0)	30(5.2)	8(2.8)	1.87 (0.84, 4.13)	
Missing	24(1.0)	8(1.4)	2(0.7)		
Maternal race/ethnicity					
White*	1610(64.2)	392(67.5)	175(62.3)	1.0	
Black	34(1.4)	6(1)	5(1.8)	0.54 (0.16, 1.78)	
Hispanic	425(17.0)	106(18.2)	57(20.3)	0.83 (0.58, 1.20)	0.522
Multi-racial	21(0.8)	3(0.5)	1(0.4)	1.34 (0.14, 12.96)	
Other	416(16.6)	74(12.7)	43(15.3)	0.77 (0.51, 1.17)	
Missing	0(0)	0(0)	0(0)		
Maternal education level					
Less than High School	297(11.9)	64(11)	48(17.1)	0.71 (0.44, 1.14)	
High School*	580(23.1)	131(22.5)	70(24.9)	1.0	
Some College	619(24.7)	139(23.9)	55(19.6)	1.35 (0.88, 2.07)	
Associates	242(9.7)	57(9.8)	27(9.6)	1.13 (0.66, 1.94)	0.080
Bachelor's	468(18.7)	119(20.5)	44(15.7)	1.45 (0.92, 2.27)	
Graduate Degree	101(4.0)	25(4.3)	11(3.9)	1.21 (0.56, 2.61)	
Missing	199(7.9)	46(7.9)	26(9.3)		
Received WIC					
No*	2169(86.6)	498(85.7)	242(86.1)	1.0	
Yes	337(13.4)	83(14.3)	39(13.9)	1.03 (0.69, 1.56)	0.872
Missing	0(0)	0(0)	0(0)		
Fetal Characteristics					
Sex of stillbirth					
Male*	1279(51.0)	288(49.6)	148(52.7)	1.0	
Female	1182(47.2)	270(46.5)	126(44.8)	1.10 (0.82, 1.47)	0.515
Missing	45(1.8)	0(0)	0(0)		
Gestational age, weeks					
20-27	1342(53.6)	337(58)	147(52.3)	0.79 (0.60, 1.06)	
28+*	1164(46.4)	244(42)	134(47.7)	1.0	0.115
Missing	0(0)	0(0)	0(0)		
Final Route and Delivery Method					
Vaginal/Spontaneous *	2162(86.3)	505(86.9)	249(88.6)	1.0	
Vaginal/Assisted	44(1.8)	7(1.2)	9(3.2)	0.38 (0.14, 1.04)	0.038**
Cesarean	300(12.0)	69(11.9)	23(8.2)	1.48 (0.90, 2.43)	
Missing	0(0)	0(0)	0(0)		

Continued

Table 3b. Continued

		One or More Birth Defects[a] (n=862)			
	Overall (n=2506)	**Well-Defined Cause of Death (n=581)**	**Ill-Defined Cause of Death[b] (n=281)**	**Crude Odds Ratio**	**P-Value[c]**
Characteristics	**n (%)[t]**	**n (%)**	**n (%)**	**OR (95% CI)[d]**	
Multiple Births					
No, Singleton*	2286(91.2)	518(89.2)	266(94.7)	1.0	
Yes, Multiple Births	219(8.7)	63(10.8)	14(5)	2.31 (1.27, 4.20)**	0.005**
Missing	1(0)	0(0)	1(0.4)		
Histological/Placental Results used to determine cause of death					
No*	2184(87.2)	498(85.7)	233(82.9)	1.0	
Yes	321(12.8)	83(14.3)	48(17.1)	0.81 (0.55, 1.19)	0.284
Missing	1(0)	0(0)	0(0)		
Autopsy Status					
No - No Autopsy*	1835(73.2)	393(67.6)	170(60.5)	1.0	
Yes - Autopsy Planned/Performed	671(16.8)	188(32.4)	111(39.5)	0.73 (0.55, 0.99)**	0.039**
Missing	0	0(0)	0(0)		
Maternal Risk Factors					
Received prenatal care					
No*	92(3.7)	12(2.1)	13(4.6)	1.0	
Yes	2310(92.2)	544(93.6)	256(91.1)	2.30 (1.04, 5.12)**	0.036**
Missing	104(4.2)	25(4.3)	12(4.3)		
Maternal tobacco use during pregnancy					
No*	2278(90.9)	542(93.3)	258(91.8)	1.0	
Yes	228(9.1)	39(6.7)	23(8.2)	0.81 (0.47, 1.38)	0.433
Missing	0(0)	0(0)	0(0)		
Urbanicity of county of delivery					
Large Metropolitan*	1174(46.8)	277(47.7)	159(56.6)	1.0	
Medium/Small Metropolitan	1172(46.8)	267(46)	99(35.2)	1.55 (1.14, 2.09)**	0.011**
Rural	160(6.4)	37(6.4)	23(8.2)	0.92 (0.53, 1.61)	
Missing	0(0)	0(0)	0(0)		

Continued

Table 3b. Continued

		No Birth Defects (n=1644)			
	Overall (n=2506)	**Well-Defined Cause of Death (n=1084)**	**Ill-Defined Cause of Death[b] (n=560)**	**Crude Odds Ratio**	**P-Value[c]**
Characteristics	**n (%)[t]**	**n (%)**	**n (%)**	**OR (95% CI)[d]**	
Maternal Demographics					
Maternal age, years					
20-39*	2218(88.5)	970(89.5)	502(89.6)	1.0	
<20	189(7.5)	82(7.6)	39(7)	1.09 (0.73, 1.62)	0.787
40+	75(3.0)	22(2)	15(2.7)	0.76 (0.39, 1.48)	
Missing	24(1.0)	10(0.9)	4(0.7)		
Maternal race/ethnicity					
White*	1610(64.2)	697(64.3)	346(61.8)	1.0	
Black	34(1.4)	16(1.5)	7(1.3)	1.14 (0.46, 2.78)	
Hispanic	425(17.0)	169(15.6)	93(16.6)	0.90 (0.68, 1.20)	0.247
Multi-racial	21(0.8)	14(1.3)	3(0.5)	2.32 (0.66, 8.16)	
Other	416(16.6)	188(17.3)	111(19.8)	0.84 (0.64, 1.10)	
Missing	0(0)	0(0)	0(0)		
Maternal education level					
Less than High School	297(11.9)	130(12)	55(9.8)	1.14 (0.78, 1.66)	
High School*	580(23.1)	256(23.6)	123(22)	1.0	
Some College	619(24.7)	294(27.1)	131(23.4)	1.08 (0.80, 1.45)	
Associates	242(9.7)	91(8.4)	67(12)	0.65 (0.45, 0.96)**	0.008**
Bachelor's	468(18.7)	179(16.5)	126(22.5)	0.68 (0.50, 0.93)**	
Graduate Degree	101(4.0)	45(4.2)	20(3.6)	1.08 (0.61, 1.91)	
Missing	199(7.9)	89(8.2)	38(6.8)		
Received WIC					
No*	2169(86.6)	942(86.9)	487(87)	1.0	
Yes	337(13.4)	142(13.1)	73(13)	1.01 (0.74, 1.36)	0.971
Missing	0(0)	0(0)	0(0)		
Fetal Characteristics					
Sex of stillbirth					
Male*	1279(51.0)	573(52.9)	270(48.2)	1.0	
Female	1182(47.2)	504(46.5)	282(50.4)	0.84 (0.69, 1.03)	0.075
Missing	45(1.8)	7(0.6)	8(1.4)		
Gestational age, weeks					
20-27	1342(53.6)	601(55.4)	257(45.9)	0.68 (0.56, 0.84)**	
28+*	1164(46.4)	483(44.6)	303(54.1)	1.0	0.001**
Missing	0(0)	0(0)	0(0)		
Final Route and Delivery Method					
Vaginal/Spontaneous *	2162(86.3)	923(85.1)	485(86.6)	1.0	
Vaginal/Assisted	44(1.8)	16(1.5)	12(2.1)	0.70 (0.33, 1.49)	0.305
Cesarean	300(12.0)	145(13.4)	63(11.3)	1.21 (0.88, 1.66)	
Missing	0(0)	0(0)	0(0)		

Continued

Table 3b. Continued

		No Birth Defects (n=1644)			
	Overall (n=2506)	**Well-Defined Cause of Death (n=1084)**	**Ill-Defined Cause of Death[b] (n=560)**	**Crude Odds Ratio**	**P-Value[c]**
Characteristics	**n (%)[t]**	**n (%)**	**n (%)**	**OR (95% CI)[d]**	
Multiple Births					
No, Singleton*	2286(91.2)	982(90.6)	520(92.9)	1.0	
Yes, Multiple Births	219(8.7)	102(9.4)	40(7.1)	1.35 (0.92, 1.98)	0.121
Missing	1(0)	0(0)	0(0)		
Histological/Placental Results used to determine cause of death					
No*	2184(87.2)	960(88.6)	493(88)	1.0	
Yes	321(12.8)	124(11.4)	66(11.8)	0.97 (0.70, 1.33)	0.371
Missing	1(0)	0(0)	1(0.2)		
Autopsy Status					
No - No Autopsy*	1835(73.2)	873(80.5)	399(71.3)	1.0	
Yes - Autopsy Planned/Performed	671(16.8)	211(19.5)	161(28.8)	0.60 (0.47, 0.76)**	<0.001**
Missing	0	0(0)	0(0)		
Maternal Risk Factors					
Received prenatal care					
No*	92(3.7)	48(4.4)	19(3.4)	1.0	
Yes	2310(92.2)	981(90.5)	529(94.5)	0.73 (0.43, 1.26)	0.009**
Missing	104(4.2)	55(5.1)	12(2.1)		
Maternal tobacco use during pregnancy					
No*	2278(90.9)	962(88.7)	516(92.1)	1.0	
Yes	228(9.1)	122(11.3)	44(7.9)	1.49 (1.04, 2.13)**	0.030**
Missing	0(0)	0(0)	0(0)		
Urbanicity of county of delivery					
Large Metropolitan*	1174(46.8)	477(44)	261(46.6)	1.0	
Medium/Small Metropolitan	1172(46.8)	535(49.4)	271(48.4)	1.08 (0.88, 1.33)	0.322
Rural	160(6.4)	72(6.6)	28(5)	1.41 (0.89, 2.23)	
Missing	0(0)	0(0)	0(0)		

[a]One or more birth defects were identified on the FDC (birth defects could be specified or unspecified)

[b]Ill-defined cause of death determined from Table 4 criteria

[c]P value generated from Chi-Square test or Fisher's Exact Test when one or more cell values are less than 5

[d]Crude Unadjusted Odds Ratio (OR) and 95% Confidence Interval (95% CI)

[t]Number and percentage of FDCs in each category

*Reference group

**Result significant at 95% confidence level

Table 4. Model Comparisons using Area Under the Curve Values of Receiver Operating Characteristic Curves to Predict Well-Defined Cause of Death for Utah and Georgia Stillbirths, FDC Data, 2010 - 2014

	Utah Stillbirths (n=2506)		Georgia Stillbirths[a] (n=4923)
Model	**All Variables**	**Georgia Comparison[a]**	
Full Model	0.6293	0.6231	0.6306
Variable Excluded from Full Model[b]			
Autopsy Status	0.6200	0.6147	0.6306
Maternal age, years	0.6286	0.6217	0.6306
Maternal race/ethnicity	0.6278	0.6203	0.6297
Maternal education level	0.6262		
Received WIC	0.6292		
Sex of stillbirth	0.6286	0.6196	0.6313
Gestational age, weeks	0.6141	0.605	0.6194
Final Route and Delivery Method	0.6279	0.6209	0.6221
Multiple Births	0.6273	0.6241	0.6311
Autopsy/Histological Placental Results used to determine cause of death	0.6274		
Number of Birth Defects	0.5917	0.5836	0.6031
Received prenatal care	0.6291		
Maternal tobacco use during pregnancy	0.6285		
Urbanicity of county of delivery	0.6281	0.6213	0.6116
Effect of Variable Alone[c]			
Autopsy Status	0.5482	0.5425	0.505
Maternal Age	0.5046	0.503	0.5054
Maternal Race	0.5191	0.5229	0.5205
Maternal education level	0.5128		
Received WIC	0.5014		
Sex of stillbirth	0.505	0.5107	0.5189
Gestational age, weeks	0.5446	0.5436	0.5323
Final Route and Delivery Method	0.5041	0.5107	0.528
Multiple Births	0.5171	0.5177	0.5038
Autopsy/Histological Placental Results used to determine cause of death	0.5085		
Number of Birth Defects	0.5118	0.5177	0.5655
Received prenatal care	0.5005		
Maternal tobacco use during pregnancy	0.5082		
Urbanicity of county of delivery	0.5265	0.5214	0.5672

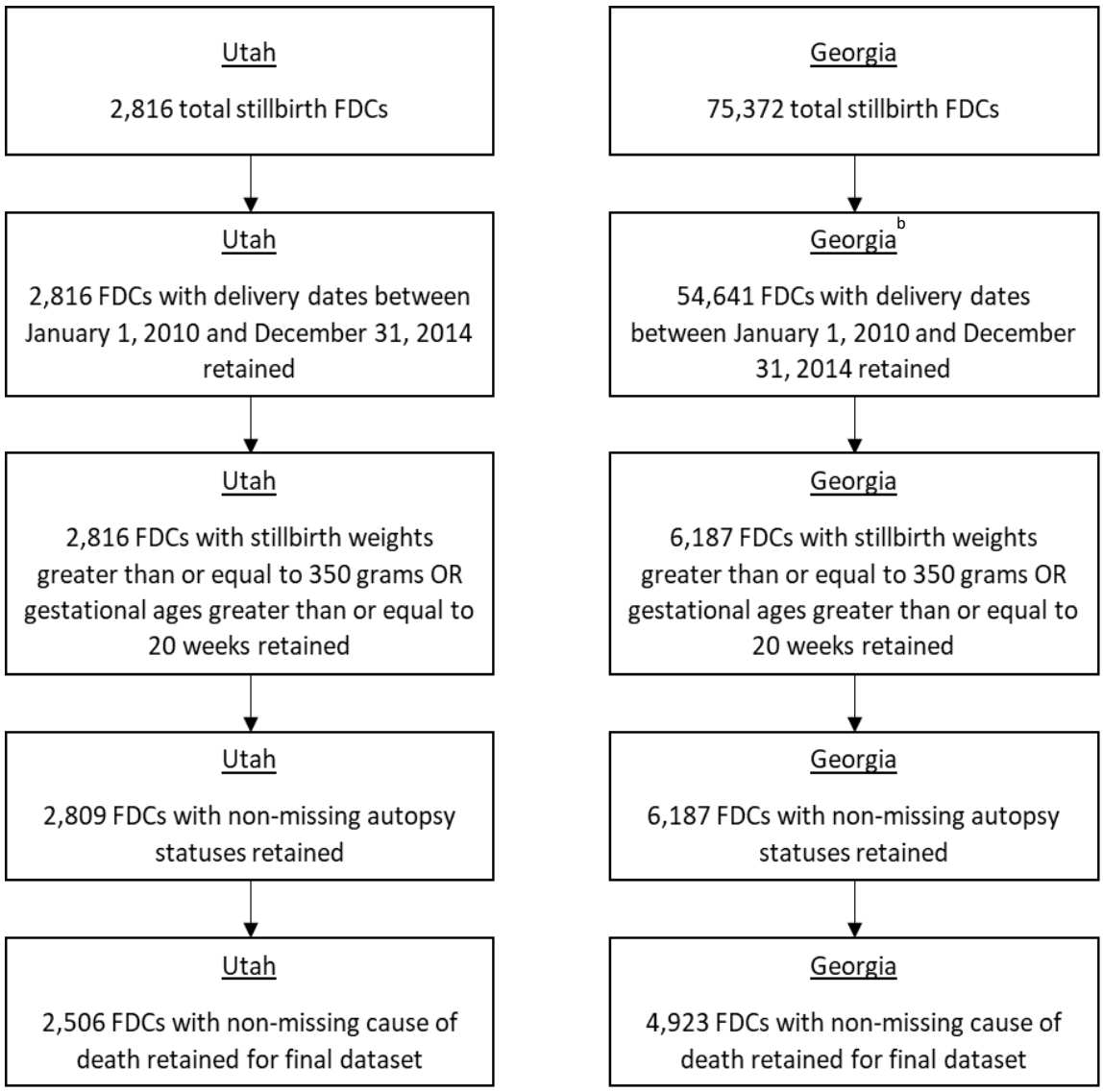
[a]These models only include variables with sufficient data to be included in the Georgia cohort analyses

[b]Model analyzed is full model excluding only the indicated variable

[c]Model analyzed contains only indicated variable

FIGURES

Figure 1. Selection of Fetal Death Certificates to Assess Study Eligibility[a], Georgia and Utah



[a]Study eligibility for stillbirth FDCs included delivery dates between January 1, 2010 and December 31, 2014, fetal weight of 350 grams or more or a gestational age of at least 20 weeks, non-missing autopsy status, and non-missing cause of death

[b]Note: Georgia requires reporting of all fetal deaths, regardless of the period of gestation. Many of these records were due to early losses, where its very common to have the birthweight and/or gestational age missing.