NOTE TO USERS

Fetal Deaths in the United States, 1997 vs 1991

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Abstract

Objective: To examine the temporal change in fetal death risk in the U.S. from 1991 to 1997 and to assess the extent to which changes in registration practices and labor induction have contributed to that change. **Setting:** United States. **Design:** Cohort study. **Participants:** All singleton pregnancies 20-43 weeks of gestation in 1991 and 1997. **Main Outcome Measure:** Fetal death risk (fetal deaths per 10,000 fetuses at risk at each completed gestational week).

Results: From 1991 to 1997, the overall fetal death rate fell from 77.7 to 67.8 per 10,000 total births. However, fetal deaths at 20-22 weeks as a proportion of total births increased from 14.5 to 16.9 per 10,000. In a Cox regression analysis, the crude period effect (1997 vs 1991) at 40-43 weeks was 0.87 (95% CI 0.80-0.94) and remained virtually unchanged (HR 0.88, 95% CI 0.81-0.96) after adjustment for maternal sociodemographic, medical, and life-style risk factors. In ecologic (Poisson regression) analysis based on states as the unit of analysis, the crude period effect in non-Hispanic Whites (RR 0.79, 95% CI 0.74-0.84) disappeared (RR 0.98, 95% CI 0.82-1.16) after adjusting for induction of labor. No such effect of induction was observed in Blacks.

Conclusions: Increased registration is probably responsible for an increase in fetal death risk at 20-22 weeks of gestation, whereas the increasing trend toward routine labor induction at and after term appears to have reduced the risk of fetal death, at least among Whites.

Résumé

Objectif: Examiner la tendance temporelle du risque de la mort foetale aux Etats-Unis durant la période entre 1991 et 1997; évaluer l'influence apportée par les changements dans l'enregistrement pratique et l'induction de travail pour cette tendance. **Fond:** Les Etats-Unis. **Conception:** L'analyse de la cohorte. **Participants:** Toutes les grossesses singletonnes des 20-43 semaines de gestation en 1991 et 1997. **Mesure Principale des Résultats:** Le risque de mort foetale (les décès foetales par 10,000 foetus en risque à chaque semaine de gestation réalisée).

Résultats: De 1991 à 1997, le taux global de mortalité foetal est tombé de 77.7 à 67.8 par 10,000 naissances totales. Cependant, les décès foetales aux 20-22 semaines considérés comme une proportion de naissances totales ont augmenté de 14.5 à 16.9 par 10,000. Dans une analyse par la régression de Cox, l'effet brut de période (1997 vs 1991) aux 40-43 semaines était 0.87 (95% CI 0.80-0.94) et restait pratiquement inchangé (HR 0.88, 95% CI 0.81-0.96) après l'ajustement pour des facteurs sociodémographique maternels, médicaux, et de risque du style de vie. Dans l'analyse écologique (la régression de Poisson) basée sur chaque état comme unité d'analyse, l'effet brut de période dans les blancs non Hispanique (RR 0.79, 95% CI 0.74- 0.84) a disparu (RR 0.98, 95% CI 0.82-1.16) après l'ajustement pour l'induction du travail. Aucun tel effet d'induction n'est observé dans les noirs.

Conclusions: L'enregistrement accru est probablement responsable pour l'augmentation de risque de la mort foetale aux 20-22 semaines de gestation, tandis que la tendance accrue pour l'induction de travail de routine pendant et après cette période semble avoir réduit le risque de la mort foetale, au moins parmi les blancs.

Glossary

Fetal death (FD) - the World Health Organization (WHO) definition (1950):
Death prior to the complete expulsion or extraction from its mother of a product of conception, irrespective of the duration of pregnancy; the death is indicated by the fact that after such separation, the fetus does not breathe or show any other evidence of life such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles. In practice, a birth weight (>=500 g) and/or gestational age (>=20 weeks) criterion is used for fetal death reporting in most developed countries including the United States.

Stillbirth - an alternative term for fetal death >=20 completed weeks of gestation. Since 1950, the term fetal death has been used in preference to other terms (spontaneous abortion, miscarriage etc.) to reflect the adoption of WHO's recommended definition.

Early fetal death - refers to fetal death occurring between >=20 and <28 completed weeks of gestation.

Late fetal death - refers to fetal death occurring >=28 completed weeks of gestation.

Fetal mortality rate (FMR) =

$$\frac{\text{No. of fetal deaths >=20 completed weeks' gestation}}{\text{No. of total births >=20 completed weeks' gestation}}$$

Early neonatal death - refers to death of an infant <7 days of age.

Late neonatal death - refers to death of an infant between 7 days and 28 days of age.

Neonatal death - refers to death of an infant <28 days (4 weeks) of age. The neonatal mortality rate is calculated as the number of neonatal deaths per 1000 live births in a given year.

Perinatal mortality rate (PMR) - refers to the number of fetal deaths (>=20 completed weeks' gestation) and neonatal deaths (<7 days of age) per 1,000 total births (>=20 completed weeks of gestation).

Ultrasound - visualization of the fetus and placenta by means of sound waves.

Electronic fetal monitoring (EFM) - monitoring with external devices applied to the maternal abdomen, or with internal devices with an electrode attached to the fetal scalp and a catheter through the cervix into the uterus, to detect and record fetal heart tones and uterine contractions.

Induction of labor - the initiation of uterine contractions before the spontaneous onset of labor by medical and/or surgical means for the purpose of delivery. Traditionally, oxytocin and amniotomy are most frequently used. Since 1990s, prostaglandin E2 (PGE2) has become widely applied.

Stimulation of labor - augmentation of previously established labor by use of oxytocin.

Amniocentesis - surgical transabdominal perforation of the uterus to obtain amniotic fluid to be used in the detection of genetic disorders, amniotic infections, fetal abnormalities, and fetal lung maturity.

Contraction stress test (CST) – the first technique introduced in antepartum (before labor) fetal surveillance to assess fetal well-being. With the use of a standard Doppler ultrasound transducer and tocodynamometer, a baseline tracing of fetal heart rate is obtained for 10-20 minutes.

Non-stress test (NST) – the most widely used and primary technique in antepartum fetal surveillance. Patient electronic fetal monitoring is similar to those in the CST; however, the NST is less invasive, simple to perform and interpret.

Biophysical profile (BPP) – the antepartum fetal surveillance test is consisted of ultrasound monitoring of fetal body movements, fetal tone, fetal breathing, assessment of amniotic fluid volume and fetal heart rate reactivity by electronic fetal monitoring. Each parameter is given a score of 2 when normal or score of 0 when abnormal for a total of 10 possible points.

Low birth weight (LBW) - refers to a birth weight of <2,500 g (5 lb, 8 oz).

Gestational age (GA) - refers to the interval between the onset of the last menstrual period and the date of delivery.

Intrauterine Growth Restriction (IUGR) - refers to impaired fetal growth in utero. In practice, small for gestational age (SGA) is used as a measure of IUGR based on a criterion of either $<10^{th}$ percentile or <2 standard deviations (SD) below the mean birth weight for gestational age.

Preterm, term and postterm - Births occurring before 37 completed weeks of gestation are considered to be "preterm" or "premature". At 37-41 weeks gestation, births are considered to be "term", and at 42 completed weeks and over, "postterm". These distinctions are according to the ICD-9 definitions.

Abbreviation

FD=Fetal death

BW=Birth weight

GA=Gestational age

FDR=Fetal death risk

FMR=Fetal mortality rate

PMR=Perinatal mortality rate

LMP=Last menstrual period

IUGR=Intrauterine growth restriction

EFM=Electric fetal monitoring

PPV=Positive predictive value

CI=Confidence Interval

NCHS=National Center for Health Statistics

PIH=Pregnancy-induced hypertension

Statement of Originality

For many years, the fetal mortality trends in the United States had not been properly measured and interpreted. According to my knowledge, this is the first study using an appropriate definition to estimate the fetal death risk and its changes over time in this country. The role of registration artifacts and the impact of increased use of induction of labor on the temporal changes were investigated. The protective effect of induction of labor on fetal death which has not been observed in previous randomized controlled studies was presented in our study. These results are of important implications for clinical practice and public health surveillance.

Some methodologic features of this study are also noteworthy. The ecologic Poisson regression was used to avert the issue of confounding by indication which is believed an intractable problem in observational study. Cox proportional hazards model was used in analyzing the determinants of fetal death. This regression model is inherently compatible with the concept of fetal death hazard that we used in this study. The combined use of these two modeling approaches is valuable to enhance the robustness of our findings.

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Chapter 1. INTRODUCTION

1.1 General Background

Since the 1980s, the fall in fetal mortality has been much slower than the fall in neonatal mortality, and for the first time in history, fetal death (FD) has become the leading contributor to perinatal mortality in the United States (National Vital Statistical Report, Vol 48, 1999). In 1989, for example, FDs represented 54.8 percent of perinatal deaths (Gaudino et al., 1994). Historically, however, attention has been primarily directed toward the well-being of newborns and older infants, not the *in utero* survival of fetuses. One important reason for the lack of research is concern about the poor data quality of the FD files in the U.S. (Kleinman JC, 1986; Gaudino et al, 1997; Kirby RS, 1997) and in particular, the completeness of data on FDs for the analysis of fetal mortality trends and their determinants.

In addition, studies on FD have long been jeopardized by a number of methodologic issues. It has been recognized that registration of FDs near the borderline of viability has varied substantially over time and across nations/regions. The United States and Canada use >=20 weeks GA and/or birth weight (BW) >=500 g cut-offs (as in most developed countries) for the reporting of fetal deaths and live births. As shown, the variations are due to two registration artifacts in practices: increasing registration of FDs <500 g BW and/or classification of deaths as early neonatal vs fetal deaths (Joseph et al, 1999; Kramer et al, 2000). The National Center for Health Statistics (NCHS) reported that from 1989 to 1997 in the United States, a constant fall was observed in overall fetal mortality rate (6.4 to 5.8 per 1,000 total births; 9% decline) and more strikingly in late fetal mortality rate (4.0 to 3.2; 20% decline) (National Vital Statistics Report, Vol 48, 1999). However, these statistics may have concealed important registration artifacts, especially close to the 20-week GA or 500 g BW cut-offs in FD reporting. The impact of an increasing registration of early FDs on the fetal mortality trend may have been counterbalanced by a shift in classification of deaths near the borderline of viability from FDs to early neonatal deaths. After 28 weeks of gestation, the reporting of FDs appears to be complete (Harter et al, 1986; Kleinman JC, 1986; Goldhabar MK, 1989; Martin and Hoyert, 2002).

Another key methodologic issue in FD studies is how to define fetal death risk (FDR). By definition, risk is the probability of disease or death occurring in a specified period of time. Incidence proportion (or cumulative incidence) is the proportion of a closed population at risk of becoming diseased or of dying within a given period of time. Although risk is usually applied to individuals and incidence proportion to populations, the latter is often called 'risk' or more accurately 'average risk' in epidemiologic research (Rothman and Greenland, 1998). According to this definition, in calculating the risk for FD, the numerator is the number of FDs occurring at a specified GA, while the denominator should be the total number of fetuses at risk of dying *in utero* (for singletons, equivalent to all ongoing pregnancies) at the beginning of that specific GA. This definition of GA-specific fetal death risk (first proposed by Yudkin et al in 1987), however, has been ignored for many years. Conventionally, the GA- or BW-specific fetal mortality rate (FMR) has been frequently used and misinterpreted as a measure of fetal death risk. FMR is the number of FDs per 1,000 total births (live births + stillbirths) (see Glossary for definition). Although this quantity is appropriate for the measurement of overall fetal death risk (>=20 completed weeks in gestation), when applied to various GA- or BW-specific categories, a major problem arises; the denominator includes the number of total births (live births + stillbirths) occurring at a given GA, but not the number of ongoing (undelivered) pregnancies at risk for FD at that GA. As a consequence, the conventional approach largely overestimates the fetal death risk preterm, whereas it underestimates the risk at term and postterm. Unfortunately, most previous studies including the studies of U.S. fetal mortality trends (Goldenberg et al, 1987; Hsieh et al, 1997) have applied the conventional approach. In this thesis, GA-specific fetal death risk is used (hereafter, also referred to as the 'fetal death hazard').

Another important issue concerns about how to appropriately measure the study outcome in evaluating the effectiveness of obstetric interventions (induction of labor in particular). Most often, the perinatal mortality rate (FDs >=20 completed weeks' gestation + neonatal deaths <7 days of age) (PMR) is used. However, as demonstrated in a recent report, combining FDs and neonatal deaths is a misleading concept, given the differences in their indices of risk and etiologic determinants (Kramer et al, 2002). As noted above, the risk for

FD needs to be measured by GA using a proper denominator of all fetuses at risk at the beginning of that GA. In contrast, the risk for neonatal death is usually reported as a fraction of total live births (therefore, the two quantities have completely different denominators). In addition, obstetric interventions such as induction of labor would not necessarily be expected to reduce neonatal mortality. In fact, it is possible that labor induction results in earlier delivery of distressed fetuses who would have otherwise died *in utero* but are born alive and die as newborns (i.e., early neonatal deaths). As a consequence, induction may prevent FDs but result in no overall reduction in perinatal deaths.

Clinical studies (i.e., randomized controlled trials) have frequently reported no beneficial effect of certain obstetric procedures, e.g., continuous electronic fetal monitoring (EFM) or induction or stimulation of labor, particularly among uncomplicated low-risk pregnancies. The rapid increase in use of these procedures is therefore disturbing and has incurred intense criticism (Albers LL, 1994; Thacker et al, 1997; Rooks JP, 1999). Induction of labor, for example, was used in 18% of births in 1997, twice the 1989 level of 9% (National Vital Stat Rep, Vol. 47, No. 27, 1999). During the same time period, the late fetal mortality rate, as noted above, experienced a remarkable 20% decline from 4.0 to 3.2 per 1,000 total births (even though not an appropriate measure) (National Vital Statistics Report, Vol 48, 1999). Whether elective use of labor induction (in postterm pregnancies) has reduced FDs remains inconclusive, however, even after the largest multi-centre randomized controlled trial (Hannah et al, 1993). Owing to insufficient statistical power, an experimental approach may not be able to detect a true beneficial effect of induction on FD risk. Large population-based observational studies may be the only choice for events that are extremely rare (Black N, 1996).

Nevertheless, challenges from the observational approach are formidable including the inability to completely control for confounding, especially confounding by indication (Salas et al, 1999). The latter refers to a medical condition (e.g., diabetes) that is an indication for the intervention and is also a risk factor for FD. The difficulties are added when vital statistics data are used. The data structure is cross-sectional by nature; data on exposures and covariates are not collected prospectively; and finally, the quality of data is sub-optimal

(e.g., high missing rate for obstetric procedures). These difficulties may not be intractable. The key is to find appropriate strategies when tackling these problems. For example, the issue of confounding by indication, to some extent, can be alleviated if ecologic analysis is properly implemented (Greenland et al, 1989; 1994; Wen et al, 1999), and data quality can be assured if data have been adequately checked and processed (i.e., deleting records with implausible GA for BW).

U.S. vital statistics data are collected under the guidelines developed by the National Center for Health Statistics (NCHS). The 1989 revision of the U.S. standard reports of live birth and fetal death added new items for data collection on maternal life-style risk factors (cigarette smoking and alcohol consumption) and obstetric procedures (EFM, induction of labor, stimulation of labor, and use of ultrasound). Unfortunately, such data are absent from the Statistics Canada live birth and stillbirth databases. For this reason, this thesis project is based on U.S. data.

Using the live birth and fetal death files for 1991 and 1997 (the latter year being the most recent with available data when the project was begun), the focus of this thesis is to estimate the temporal changes in FDR (using the correct definition), and to assess the extent to which these changes can be attributed to changes in registration practices and the increased use of induction of labor over the same time period. Whites are separated from Blacks for analyses because of the well-known disparity in fetal mortality between the two racial groups (Gaudino et al, 1994) and their marked differences in socioeconomic status and access to and quality of perinatal health care (Brett et al, 1994; Tossounian et al, 1997). Specifically, the following objectives are addressed:

1.2 Objectives

(1) To estimate changes in fetal death hazard from 20 to 43 weeks of gestation between 1991 and 1997 in the United States.

(2) To assess the extent to which changes in registration practices have impacted on the change in early fetal hazard. Specifically, two major potential artifacts will be explored: **a)** increasing registration of early fetal deaths, and **b)** classification of deaths as early neonatal vs fetal deaths, especially at 20-22 weeks.

(3) To identify and quantify determinants of the change in fetal death hazard. Specifically, to examine whether the fall in late FDs has been associated with increasing use of induction of labor.

1.3 Outline

Chapter 1 provides a brief outlook on the study of FD, including the proper definition of FDR, registration artifacts, and data quality of FD files.

Chapter 2 presents a detailed literature review on the U.S. Standard Certificate of Live Birth and Report of Fetal Death, including variations in state law and policy in registration, the validity of U.S. vital statistics, the etiology of FD, fetal mortality trends, as well as the evaluation on obstetric procedures including induction of labor and management of postterm pregnancies. Finally, a brief summary is provided about the methodologic limitations and insufficiencies of previous studies.

Chapter 3 elaborates the study methodology such as the definition of fetal death hazard and the indices for registration artifacts and their computational formulae as well as the data quality assurance of the present study, including Alexander's approach in detecting improbable GA records. It also explains the limited inclusion of 39 states and D.C. with complete data on covariates of key importance, e.g., induction of labor, maternal cigarette smoking, and medical conditions for analytic study of determinants underlying the trends for FDs. Finally, the rationale and methods are presented for multivariate analyses with the Cox proportional hazards and Poisson regression model.

Chapter 4 summarizes the results of the study. It begins with a comparison of the distributions of maternal sociodemographic characteristics, obstetric procedures, medical

and life-style risk factors between live births and fetal deaths, in Whites and Blacks separately. A contrast of the fetal death hazard is made between 1991 and 1997, and between Whites and Blacks. Finally, the results of the Cox proportional model and Poisson regression analyses are presented.

Chapter 5 discusses the results of the study, i.e., interpretation, validity issues, and study limitations, and briefly summarizes the findings and their implications.

Chapter 2. LITERATURE REVIEW

This literature review was conducted primarily by searching the MEDLINE and Cochrane database abstracts via Internet using key words. Official documents (e.g., the U.S. Standard Certificates) and reports (e.g., Vital and Health Statistics) were downloaded from U.S. government websites. A secondary source was the references cited in the primary publications. Special topics on FD were sought. A number of articles, manuscripts (unpublished papers and theses), and other materials were obtained from my supervisor, Dr. Michael S. Kramer. In this Chapter, the literature review is divided into separate sections on registration practices, data quality of U.S. vital statistics, fetal mortality trends, labor induction, and management of postterm pregnancy as well as a critique of previous studies.

2.1 U.S. Fetal Death Registration

In the United States, FD registration is based on state law, and reports are filed and maintained at the state vital statistics offices. NCHS is responsible for the development and periodic revision of the U.S. Standard Certificate of Live Birth and Standard Report of Fetal Death (see Appendix A and B). In 1930, the first standard fetal death certificate was issued in the United States; the 1989 revision of the Standard Certificates and Reports added new items to obtain information on "obstetric procedures," "method of delivery," and "abnormal conditions of the newborn" (Freedman et al, 1988; Tolson et al, 1991). Although individual states developed their own forms (under state regulations) to meet the state's own needs for data collection, the U.S. Standard Certificates and Reports are recommended to serve as the model for registration of vital events.

Registration regulations, however, continue to vary in many states. The 1977 NCHS revision of the "Model State Vital Statistics Act and Regulations" recommended reporting of all spontaneous losses occurring at >=20 weeks in gestation or weighing >=350 g (NCHS, 1978). Most states have adopted very similar requirements (as of 1994, 10 states exactly followed the NCHS recommendation; 25 states adopted a requirement for reporting fetal deaths >=20 weeks of gestation; 3 states required reporting of decease of a fetus weighing >=500 g, whereas 6 states (including the District of Columbia) used different GA

(16 weeks or 20 weeks) or BW (400 g or 350 g) requirements or a combination of both GA and BW) (Vital Statistics of the United States: Mortality, Technical Appendix, 1994). Meanwhile, a number of states have modified their regulations to accommodate their own needs (Vital Statistics of the United States, 1988, Vol II. Mortality, part A: Technical Appendix, 1991); as of 1994, 7 states (including New York City) required reporting all spontaneous losses regardless of gestational duration (Vital Statistics of the United States: Mortality, Technical Appendix, 1994).

Differences in the legal requirements for registration have been found to be associated with the disparities among these states concerning the completeness of FD reports. The NCHS report shows that, in 1980, six states reporting FDs for *all* GAs had a fetal mortality rate (>=20 weeks) among whites 33% above the U.S. rate (Vital Statistics of the United States, Vol. II, Mortality, Part A, 1985). Yet the neonatal mortality rate in these states was only 3% above the national average. Thus, it seems that underreporting of fetal losses between 20 and 27 weeks was substantial among those states setting legal requirements at >=20 weeks GA or BW >=350 g (instead of all GAs) for reporting. In addition, parts of the United States were reported to have an increased trend of reporting of deliveries <500 g as live births, rather than as fetal deaths (Goldenberg RL, 1989).

Registration practices may have also varied according to racial group (Whites and Blacks). Using data for 1987-1988, Kramer et al (2001) reported a striking 3-fold disparity in the occurrence of births <750 g (live births + stillbirths), and a substantially different ratio of fetal to early neonatal deaths in this BW category between U.S. Blacks and U.S. Whites. These disparities are probably due to differences between the two racial groups in the registration of live births and stillbirths and/or their classification as stillbirths vs live births near the borderline of viability (close to 20 weeks GA).

In 1979, Shapiro et al demonstrated a more complete registration of late FDs (>=28 weeks) relative to early FDs (20-27 weeks) in the U.S. and emphasized the need to separate them in studies using national vital statistics data (Shapiro et al, 1979). In fact, one-third of FDs with known gestation of 20 weeks or more have a gestation between 20 and 27 weeks (Vital

Statistics of the United States, Vol. II, Mortality, Part A, 1985). Therefore, such a separation would have a major impact on reported rates. In fact, underreporting of early FDs is most likely to occur at gestational ages close to the 20-week GA or 500 g BW cut-offs and, moreover, is nonrandom (Harter et al, 1986; Greb et al, 1987); for example, if the fetus is macerated, malformed, or very small, its chances of being reported are diminished. This selective underreporting not only results in an underestimate of the overall fetal death rate, but also creates a nonrepresentative sample for studying all FDs. In addition, as demonstrated by Harter et al (1986) and others (Susser et al, 1985; Mellin et al, 1962), greater ascertainment of FDs between 20 and 28 weeks occurs among states with reporting requirements based on GA less than 20 weeks. After 28 weeks, however, reporting of FDs appears to be fairly complete (Harter et al, 1986; Kleinman JC, 1986; Goldhaber MK, 1989).

Unfortunately, no clear evidence is available about the inconsistency and incompleteness (over time and across states) in the registration of FDs over the last decade in the United States. The number and proportion of early FDs at 20-27 weeks GA (relative to fetal and infant deaths combined) increased from 1985 to 1991: an approximate 2,500 increase in number and 3.9 increase in percentage (from 15.7 to 19.6) (Vital and Health Statistics, Series 20, No. 26, 1995). With the constant decline in late FDs (at >=28 weeks GA) and early neonatal deaths (<7 days), such an increase in early FDs is highly likely a consequence of registration artifact, unless we assume that a sharp increase in incidence of early FD occurred in the United States. It is unlikely, however, that extrinsic risk factors (e.g., environmental pesticide exposure or cigarette smoking) could account for such an increase, because, no evidence suggests a sharp increase in such exposures among the pregnant women. Moreover, the hazardous effect, if it existed, would not necessarily be limited to early GAs.

In fact, an increasing registration of early FDs <500 g BW has been documented in the state of Alabama from 1974 to 1984 (Goldenberg et al, 1989) and 1974 to 1994 (Phelan et al, 1998) (not studied in whole U.S. before) and in Canada, 1985-95 (Joseph et al, 1999). NCHS reported that the overall fetal mortality rate (>=20 completed weeks GA) declined

from 6.4 to 5.8 per 1,000 total births (a 9 percent decline) from 1989 to 1997 in the United States (National Vital Statistics Report, Vol 48, 1999). However, that report did not take into account possible registration artifacts in early FDs. Therefore, the magnitude of fall may have been underestimated. It also remains unknown whether the early fetal mortality rate differs by state or region in the United States, and whether the disparities, if any, parallel the differences in state or region registration regulations for the reporting of FDs at the borderline of viability. In fact, Kramer et al have reported a substantial variation with regard to the registration of births <750 g among and within 5 developed nations (including the United States), which was strongly suspected to be an artifact of different countries' use of different GA and/or BW cut-offs for the reporting of fetal deaths and live births (Kramer et al, 2001).

2.2 Validity of U.S. Vital Statistics Data

Completeness and validity are two important indices in gauging the quality of vital statistics data. Theoretically, there are two basic requirements for reporting vital events. First, each birth event (live birth or stillbirth) should be registered if it meets the relevant reporting criterion, i.e., >=20 weeks (completeness of registration). Second, information on specific items (e.g., life-style risk factors, obstetric procedures) needs to be provided (completeness of data or item completeness) and valid.

As noted above, the completeness of registration is particularly an issue near the borderline of viability, whereas the reporting of FDs at >=28 weeks GA is relatively complete. However, even where registration is complete, if a large amount of information is missing or is invalid on maternal medical and life-style risk factors, obstetric procedures or complications of labor/delivery, the usefulness of the data would be very limited. Validity studies of the U.S. vital statistics data have been carried out to specifically address the data quality of the following items: GA, BW, medical risk factors, obstetric procedures, and congenital anomalies. These studies primarily focused on the data quality of live births and, moreover, were based on data from individual states. Perhaps this is because live birth data have been frequently used in monitoring state infant mortality trends, implementing state

maternal and child health programs, and investigating potential determinants of infant deaths.

The quality of U.S. fetal death data has rarely been evaluated. The small number of FD studies is at least partially due to the high missing rates (incompleteness of data) and/or error rates (poor validity) in the FD files (Gaudino et al, 1994; 1997; Alexander GR, 1997). The high missing and error rates on one key variable, GA, are of particular concern in mortality study (Platt et al, 2002). In the U.S. vital records, GA is computed (by NCHS) in completed weeks by subtracting the date of the onset of the last menstrual period (LMP) from the date of birth. When the date of LMP is incomplete, i.e., missing day when there is a valid month and year, GA is imputed with the value of the preceding record with a complete LMP date and the same computed month of gestation and the same 500 g BW interval. The clinical estimate of GA is used when information on the date of LMP is missing, invalid, or inconsistent with BW. The clinical estimate of GA is usually based on clinician's pediatric assessment of the physical or neurological development of the newborn, early ultrasound dating (if available), or combinations of the measures (Alexander et al, 1996; 1997). These NCHS procedures have sharply reduced the high missing rate on GA due particularly to incomplete date of LMP (i.e., missing day when there is a valid month and year).

The LMP-based GA has been a conventional data source for the estimate of GA. For 95% of births, the GA values in U.S. vital statistics are based on the woman's LMP (NCHS, instruction manual, 1991). Previous large population-based studies have clearly preferred LMP-based GA to the clinical estimate of GA (Alexander et al, 1989; 1995). However, a marked overestimate of postterm pregnancies by LMP-based GA has been observed (i.e., only one-eighth of the infants classified as postterm based on LMP are actually postterm). Of course, errors can occur throughout the whole GA range from 20 to 43 weeks. Most errors appear due to women's recall, variations in the preovulatory interval, unrecognized abortions, or sporadic bleeding during pregnancy (Kramer et al, 1988; Alexander et al, 1995).

These errors in GA can be investigated by examining the compatibility of the recorded GA with the recorded BW. It is believed that data on BW from the birth registration are more valid than data on GA (Alexander et al, 1996). Unfortunately, studies on the validity of GA are still scanty. The only study using U.S. vital statistics data examined 2,226 singleton FD records with GA >=20 weeks (or with no GA but BW >=479 g) for 1989 and 1990 from the state of Georgia. Of which, 817 with values for GA are either improbable or missing. The improbable values of GA for BW represent more than 60 percent of the problem records (Gaudino et al, 1997). This study used BW values plus and minus 2 standard deviations (97.7^{th} vs 2.3^{th} percentile) from the means as the upper and lower bounds, respectively. The improbable GA values are those with BW values out of the referent range for a given GA. Unfortunately, this study did not show whether the GA values in late FDs are of better quality (lower error and/or missing rate) than those in early FDs.

Using the U.S. vital statistics data for an epidemiologic study, one may first have to identify and exclude records with implausible BW-GA data. In 1996, Alexander et al developed techniques for this purpose as part of their effort to establish a United States national reference for fetal growth (using the 1991 U.S. live birth data). Briefly, BW and GA inclusion criteria (a group of cut-points) were created based on clinical (neonatology) consultation (see Appendix C). GA distributions were examined for births grouped into 125g BW intervals. Out-of-range values were trimmed as implausible. The implausible GA-BW records appeared in the whole GA range, but most errors occurred among FDs <28 weeks in gestation (Alexander et al, 1996). Alexander's approach has been adopted in this thesis project (see Chapter 3).

Apart from GA, the quality of other data items is also an important concern, as is the completeness in the reporting of these items (Kirby RS, 1997; 2001). First, data may be missing simply because the relevant data item has not been included on the state registration form. The 1989 revision of the U.S. Standard Certificates and Reports created new items for data collection on obstetric procedures (e.g., induction of labor) and maternal life-style risk factors (e.g., cigarette smoking) (Freedman et al, 1988; Tolson et al, 1991). Unfortunately, a number of states failed to incorporate the new items into their data

collection forms in the following years. As a consequence, for example, data on maternal cigarette smoking are completely absent from these states. Second, data may be missing because a specific item on the files remained 'not stated' (perhaps due to absence of related information or simply due to omission by the practicing physician who is responsible for filling out the forms). This second scenario is relevant only to a small proportion of total records in the state (which is often referred to as incompleteness of data in a validity study).

Validity studies of the revised 1989 birth certificates have been carried out in several individual states in the U.S. (Piper et al., 1993; Parrish et al., 1993; Buescher et al., 1993; Watkins et al., 1996). Most studies used hospital medical records as the "gold standard" for comparison under the assumption that information on the hospital medical records is complete and valid. The completeness and validity of data on a specific item are usually measured by sensitivity and positive predictive value (PPV), respectively (e.g., against the corresponding hospital medical records). Sensitivity indicates how completely an item is reported on the birth certificate; PPV determines how often a documented item is correctly identified. Previous studies consistently demonstrate that overall, data on women's sociodemographic characteristics are well reported on U.S. birth certificates (i.e., both sensitivity and PPV were 80% or better). This comprises such variables as maternal age, race, educational attainment, and marital status. In addition, BW, GA (based on LMP or clinical estimate), and the Apgar score also have good completeness and validity when compared to the hospital medical records.

Obstetric procedures, including induction of labor, however, have been shown to have poor to fair completeness of data. In general, the overall PPVs values for obstetric procedures are high (>80%), indicating that these procedures, if reported, are accurate, while the sensitivities are relatively low (<70%), indicating underreporting on these items. For example, one study reported (using the 1991 birth certificate data of Maryland) that the sensitivity of induction of labor was about 63%, while the PPV was 81% (Master's dissertation: Validity study of Maryland birth certificate data, 1996). This study also showed that the sensitivity was 86% for EFM but was low for ultrasound (37%) and stimulation of labor (41%). The Maryland study used hospital medical records as the 'gold

standard.' A similar report (using the 1989 birth certificate data in Washington state) showed that the sensitivity for induction of labor was only about 56%, while the PPV was 88% (Parrish et al, 1993). A study (using a random sample of infants with BW >=1,500 g) of the validity of 1989 Tennessee birth certificate data reported sensitivities of 61% for induction of labor, 81% for EFM, and 25% for stimulation of labor (Piper et al, 1993).

Underreporting of maternal medical risk factors, complications of labor/delivery, and congenital anomalies of the newborn is of concern as well (Buescher et al, 1993; Piper et al, 1993; Watkins et al, 1996). However, the reporting of maternal medical conditions such as diabetes, chronic hypertension, and pregnancy-induced hypertension (PIH) is relatively complete when compared to the reporting on most medical risk factors (e.g., anemia, cardiac diseases, acute or chronic lung diseases, and renal diseases). Moreover, data on these items, if reported, are valid compared to the hospital medical records (Piper et al, 1993; Master's dissertation, 1996). Maternal life-style items such as tobacco use during pregnancy are moderately well reported (about 70% sensitivity), while completeness of data on alcohol consumption is poor (sensitivity <40%) (Buescher et al, 1993).

In general, except for maternal sociodemographic characteristics and some basic items such as BW, GA, and gender of the newborns, it is likely that most checkbox data on the birth certificates are underreported, even though the rate of underreporting varies among different data items. However, the completeness and validity of GA (compared to the hospital medical records) may still be questionable. Errors may have been missed without further assessment of improbable GA-BW values. In general, studies using vital statistics data need to be careful both in data selection (e.g., based on states with better data completeness) and data error checks (e.g., detecting records with improbable GA for BW).

Nevertheless, the validation studies have their own limitations (Kirby, 2001). The most obvious is that hospital medical records or data from other research projects are relied on as the 'gold standard.' But medical records have not been subjected to analysis of completeness and validity (Reichman and Hade, 2001). A better 'gold standard' would be one that incorporates information from several other sources (Piper et al, 1993). Another

limitation is that validation studies have been unable to identify which portions of the vital statistics data are of better quality and can be used for research purposes. In fact, the latest NCHS data files (2000) show that the percent of records with missing values is much higher for fetal deaths than for live births. Moreover, the problem of high missing rates for FDs is attenuated somewhat with increased GA. For example, for FDs at 20-27 weeks, the missing rate for the 'month prenatal care began' was 17%, while it was 10.6% for FDs at >=28 weeks and only 2.8% for all live births regardless of GA (Martin and Hoyert, 2002). Similar patterns were observed for maternal characteristics (e.g., education), life-style risk factors (e.g., cigarette smoking), and obstetric procedures (e.g., induction of labor). It seems that at >=28 weeks, FDs are fairly completely registered and the data contained therein are of high quality, compared to those at 20-27 weeks. How to properly handle these data quality issues remains a major challenge in studies based on the U.S. vital statistics.

2.3 Fetal Death

2.3.1 Etiology

A large number of factors have been associated with FD. These include: maternal age, race, education, marital status, parity, prepregnancy weight, weight gain during pregnancy, maternal medical conditions (hypertension, diabetes, infections, renal disease, Rh isoimmunization), plurality, prenatal care, intrapartum obstetric care, fetal sex, IUGR, chromosomal abnormality, cigarette smoking, alcohol consumption, drug use, environmental toxins (Petitti DB, 1987). However, if divided by the timing of death, antepartum FDs (before the onset of labor) have been found to be etiologically different from intrapartum FDs (during labor) (Kiely et al, 1984; 1986; Gaudino et al, 1994). Unfortunately, the majority of previous studies have not separated antepartum FDs from intrapartum FDs (perhaps due to lack of data on the timing of FD).

2.3.1.1 Antepartum fetal death

In the United States, as in most developed countries, the majority of FDs occur during the antepartum period (Alessandri et al, 1992). It is estimated that more than 85% of total FDs occur before labor (Kramer et al, 2002). For antepartum FDs, the increased risk has been

associated with low socioeconomic status, maternal medical conditions, cigarette smoking, and adverse obstetric history. In 1993, Little and Weinberg conducted their analysis of the risk factors for antepartum vs intrapartum FD using data of the 1980 National Natality Survey and the National Fetal Mortality Survey of the United States. It was found that advanced maternal age (>=35 years), Black race, education <12 years and cigarette smoking during pregnancy were associated with antepartum FDs but not with intrapartum FDs, while nulliparity and high body mass index were associated both with antepartum and intrapartum FDs (Little et al, 1993). The differential impact of advanced maternal age (>=35 years) on FD (i.e., stronger impact on antepartum FD than on intrapartum FD) has also been reported using 1976-1978 birth data in New York City (Kiely et al, 1986).

Studies have further investigated risk factors for unexplained antepartum FDs by excluding those deaths with known causes. These causes include: severe maternal diseases (e.g., diabetes or hypertensions), fetal abnormalities (e.g., IUGR or lethal congenital anomalies), or placental complications (e.g., abruptio placenta, placenta previa) (Alessandri et al, 1992; Huang et al, 2000). Low socioeconomic status, nulliparity, fewer prenatal visits (<4 times), and high prepregnancy weight (>68 kg) were associated with unexplained antepartum FDs in the study reported by Huang et al; however, no statistically significant increase in risk was observed among mothers who smoked during pregnancy (Huang et al, 2000). Perhaps, this is because IUGR was adjusted for in the study's multivariate regression analyses (severe IUGR excluded), which as discussed below, is likely an intermediate step on the causal pathway between cigarette smoking and FD.

Advanced maternal age (>=35 years), cigarette smoking, and nulliparity have been frequently and consistently associated with FD (Meyer et al, 1976, 1977; Kiely et al, 1986; Kleinman et al, 1988; Cnattingius et al, 1988; Raymond et al, 1994; Fretts, et al, 1995, 1997; Ogunyemi et al, 1998; Tuthill et al, 1999; Nybo et al, 2001) (note: these studies have not separated antepartum FDs from intrapartum FDs). Using Swedish birth data from 1983 to 1985, Cnattingius et al found a strong effect of cigarette smoking on late fetal and early neonatal death (Cnattingius et al, 1988). Using the same dataset but from 1983 to 1992, an

effect modification between maternal age and cigarette smoking was reported for IUGR but not for late FD (Cnattingius et al, 1997).

In 1994, Raymond et al reported, for the first time, an increasing trend in the effect of advanced maternal age (>=35 years) on FD in contrast with a decreasing trend in the effect of cigarette smoking, when GA advanced from 28 to 45 weeks (using Swedish birth data from 1983 to 1989). Nulliparity showed impacts on FD preterm and postterm but not at term (Raymond et al, 1994). Unfortunately, similar reports on the variation of the effect across GA are lacking. Most previous studies investigated FDs as a whole (although a few separated antepartum from intrapartum deaths), but not stratified by GA. Consequently, possible etiologic differences (or effect modification) according to the duration of pregnancy have been ignored.

In the same study, Raymond et al reported that the effect of maternal cigarette smoking was eliminated when women with placental abruption, placenta previa, or IUGR were excluded from the analysis. However, the effect of advanced maternal age (>=35 years) and nulliparity persisted even when the study excluded maternal/fetal complications (known to be associated with older maternal age), such as hypertension, diabetes, placental abruption, placenta previa, and IUGR (Raymond et al, 1994). A recent study using the Latin American and Caribbean Perinatal Information System database (1985-1997) also found that the effect of cigarette smoking was completely diminished when adjusted for placental abruption, placenta previa, and IUGR (Conde-Agudelo et al, 2000).

Advanced maternal age (>=35 years) and cigarette smoking during pregnancy have been repeatedly associated with an increased risk for IUGR and placental complications (i.e., placental abruption, placenta previa) (Meyer et al, 1977; Kleinman et al, 1988, Williams et al, 1991, Raymond et al 1993, 1994, Kramer et al, 1997, Cnattingius et al, 1998). Complex causal pathways have been suggested from these risk factors to maternal placental/fetal complications, and to FD (although the effect of older maternal age cannot be completely accounted for, as noted above, by placental/fetal complications). Therefore, to evaluate the impact of older maternal age and cigarette smoking (as well as other risk factors such as

hypertension, diabetes) on FD, one should not adjust for placental/fetal complications, as they are possibly on the causal pathway between the risk factors and FD.

Certain maternal medical conditions have been reported as important risk factors for antepartum FD. These include chronic and pregnancy-induced hypertensions, diabetes, obesity, systematic lupus erythematosus, chronic renal disease, and thyroid disorders (Simpson et al, 2002). A marked increase in risk of FD among pregnancies complicated with hypertension is believed to be the result of placental abruption, severe pre-eclampsia, or eclampsia (Sibai et al, 1984; Abdella et al, 1984; Mabie et al, 1986; Ananth et al, 1995; Yadav et al, 1997; Martin et al, 1999). Diabetes mellitus (pre-gestational or gestational) is another important risk factor for antepartum FD. Type 2 diabetes is reported to have a much stronger impact on intrauterine FD than type 1 diabetes (Cundy et al, 2000). Although the underlying mechanism for FD occurring among diabetic pregnancies remains unclear, the majority of these deaths are reported to occur in the third trimester with complications of macrosomia, polyhydramnios, IUGR, and pre-eclampsia and, moreover, are associated with poor glycemic control (ACOG, Diabetes in pregnancy, Technical Bulletin, 1994). As a result of improvements in medical and obstetric care, FDs due to hypertensions and diabetes have been dramatically reduced in recent decades (Maternal-Fetal Medicine: Principles and Practices, 4th edition, 1999).

Maternal obesity has recently been identified as a risk factor for FD (Cnattingius et al, 1998; Huang et al, 2000; Stephansson et al, 2001). Further studies are needed, e.g., on the underlying mechanisms and prevention strategies, given the high current prevalence (20% to 40%) and the increasing trend in obesity among women of childbearing age in North America (NCHS, 2000) and other industrialized countries. Maternal intrauterine infections have been associated with both FD and preterm labor (Copper et al, 1994). In fact, chorioamnionitis has been associated with FD preterm (Moyo et al, 1996; Folgosa et al, 1997; Tolockiene et al, 2001). However, knowledge about the impact of many other infections still remains scanty.

2.3.1.2 Intrapartum fetal death

Studies on risk factors for intrapartum FD are few, compared with studies on antepartum FD. This is perhaps because intrapartum FD has become extremely uncommon in developed countries (Kramer et al, 2002), while developing countries still have a high incidence of these deaths (Conde-Agudelo et al, 2000). The low rate of intrapartum death in developed countries is possibly attributable to improvements in obstetric care (e.g., intrapartum fetal surveillance) (Erkkola, et al, 1984; Kiely et al, 1985; Georgsdottir et al, 1989).

Unlike the risk factors for antepartum FD, most risk factors for intrapartum FD are related to labor and delivery: preterm labor, intrapartum asphyxia, polyhydramnios, and placental abruption (Kiely et al, 1985; 1986; Albers et al, 1991; Alessandri et al, 1992; Sheiner et al, 2000). Kiely et al (1985) have reported a clear association between less available obstetric technology (as measured by level of hospital) and an increased risk of intrapartum FD - an association that did not occur in late antepartum FD (Kiely et al, 1985). One study confirmed this finding (Albers and Savitz, 1991), while another did not (Alessandri et al, 1992). Nonetheless, the latter study (with a matched case-control design) may have been limited by its small sample size (cases=77).

As mentioned above, intrapartum FD has not been associated with maternal sociodemographic factors, i.e., older maternal age (>=35 years), educational attainment (<12 years), cigarette smoking, or adverse obstetric history (Alessandri et al, 1992; Little and Weinberg, 1993). High parity (>4) has been shown to have a strong association with intrapartum FD but not with antepartum FD (Kiely et al, 1986). Maternal prepregnancy weight is associated with both types of FD; yet the effect was greater for intrapartum FD than for antepartum FD in one reported study (Little and Weinberg, 1993).

2.3.2 Temporal Trends

In 1992, a hospital-based study of the changing patterns of cause-specific FD over the past three decades was carried out in Montreal (Fretts et al, 1992). By taking advantage of a large hospital database with systematically recorded information on maternal, fetal,

placental and obstetric risk factors, the study identified a significant decline in unexplained antepartum FDs and a decline in IUGR-associated FDs. While FD due to abruptio placentae or intrauterine infection remained virtually unchanged, FD due to intrapartum asphyxia or Rh isoimmunization nearly disappeared. The Montreal study found that the risk of FD for women with hypertension, diabetes, or history of stillbirth decreased from the 1960s to 1980s. A more recently published Swedish study analyzed the late FD rate between 1984 and 1991 and observed little reduction, despite many improvements in antenatal care during the study period. The small drop was attributed to changes in maternal age and parity (Ahlenius and Thomassen, 1999).

To date, the only attempt at a U.S.-wide study of fetal mortality trends is based on data for 1979-1990 (Hsieh H et al, 1997), which attributed most of the reduction in the crude fetal mortality rate to improvements in BW-specific fetal mortality rates, rather than to a favorable change in BW distribution, particularly among Blacks. The study reported that over time, heavier fetuses (>=2,500 g) had a more rapid decline in fetal mortality rate. Goldenberg et al. (1987) reported similar findings in Alabama using data for 1974-83. From a clinical or etiologic perspective, however, the implications of such conclusions are not very clear. For example, why was the decline larger in fetuses with BW >=2,500g (the majority of which should have been delivered at term or postterm)? What is the relation between this fall and improvements in obstetric care? Why, during the same period, was no similar decline seen among lighter (preterm or premature) fetuses? Moreover, the study used BW-specific FMR, which is a flawed-concept (see Section 2.5.1).

2.4 Obstetric Practice

Recent decades have witnessed significant improvements in antenatal and intrapartum obstetric care. A marked increase in obstetric procedures, e.g., induction of labor, has been documented in the United States (see Section 2.4.4). However, it remains uncertain whether the increase has impacted on FD. This section systematically reviews studies on certain components of antenatal care (ultrasound), intrapartum care (EFM, induction and stimulation of labor), and management of postterm pregnancy. Many other clinical care

procedures cannot be examined, since U.S. vital statistics has no data collection on them, such as CST, NST or BPP (see Glossary for definitions).

2.4.1 Antenatal care

The effectiveness of antenatal care in reducing FDs in high-risk populations is widely acknowledged (Foster et al, 1992). Such care includes early detection and better management of maternal pre-pregnancy or pregnancy-induced medical disorders such as hypertension, diabetes, Rh-isoimmunization, and IUGR. Yet, the effectiveness of antenatal care in reducing fetal mortality among women at low risk is unclear (Grant et al, 1989; Khan-Neelofur D, 1998).

In antenatal surveillance (e.g., antenatal diagnostic testing), the clinical value of ultrasound use in the evaluation and management of women at high-risk for FD pregnancies is generally accepted (Maternal-Fetal Medicine, 4th edition, 1999). Routine ultrasound screening is effective in detecting congenital anomalies, multiple-gestation pregnancies, IUGR, placental abnormalities, and errors in estimation of gestational age. However, the value of routine ultrasound application to low-risk pregnancy is still controversial (Maternal-Fetal Medicine, 4th edition, 1999).

To date, the largest randomized controlled trial of routine ultrasound screening to be reported, the Routine Antenatal Diagnostic Ultrasound Study (RADUS) involving 15,151 pregnant women at low-risk for perinatal problems in 6 U.S. states showed no benefit. Women in the ultrasound-screening group underwent one sonographic examination at 15 to 22 weeks of gestation and one at 31 to 35 weeks; women in the control group underwent ultrasonography only for medical indications (Ewigman et al, 1993). However, the Helsinki trial, the only trial with the specific intent of routine ultrasound screening for congenital malformations, reported a remarkable decrease in perinatal mortality (Saari-Kemppained et al, 1990). The benefit was entirely attributable to women who received ultrasound and then aborted fetuses with detected lethal congenital anomalies. Accordingly, many proponents of routine scanning in pregnancy have criticized the low rate of detection of congenital anomalies in the RADUS study (DeVore GR, 1994).

The potential benefit of ultrasound may also come from early detection of IUGR. Although no truly effective therapeutic treatment is available for IUGR, early planned delivery may be of value. However, evidence from randomized controlled trials does not support this hypothesis (Larson et al, 1992; Secher et al, 1987). Meta-analyses of randomized trials suggests that routine ultrasound scanning as compared to selective ultrasound does not improve substantive pregnancy outcomes (including stillbirth) (Bucher et al, 1993; Neilson JP, 1998).

2.4.2 Intrapartum care

In intrapartum obstetric care, electronic fetal monitoring (EFM) has become routine since its introduction in the 1960s. Monitoring fetal heart rate electronically is believed to be a superior method for screening for fetal asphyxia as compared with intermittent auscultation. Early detection of fetal distress should lead to earlier interventions (e.g., cesarean section) and therefore result in reduction of perinatal death and/or fetal brain injury (e.g., cerebral palsy). Such benefits were first suggested in observational studies (Erkkola et al, 1984; Mueller-Heubach et al, 1980) but have not been demonstrated in subsequent randomized controlled trials (continuous EFM vs intermittent auscultation).

The first randomized trial of EFM was published in 1979 (Haverkamp et al, 1979). That trial did not find any reduction in perinatal mortality or low Apgar scores but did report a marked increase in cesarean deliveries among women randomized to EFM. By 1994, a total of 12 randomized controlled trials involving more than 55,000 pregnancies had reported similar findings: markedly increased rates of cesarean delivery (especially among low-risk pregnancies), but no substantial reduction in perinatal mortality or low Apgar scores (Thacker et al, 1995; 2003 (Cochrane Review); Rooks JP, 1999). In 1995, Vintzileos et al reported a meta-analysis of 9 randomized trials published in peer-reviewed journals (Vintzileos, 1995). A total of 18,561 pregnancies were included in the analysis (9,398 in the EFM group and 9,163 in the intermittent auscultation group). The analysis revealed that EFM was associated with decreased perinatal mortality due to fetal hypoxia but increased rates of surgical interventions (e.g., cesarean delivery, forceps or vacuum use).

Another important component of intrapartum obstetric care is stimulation/augmentation of labor (use of oxytocin to increase the strength and frequency of labor contractions). As with EFM, stimulation of labor has been listed as one of the obstetric practices that clearly have trade-offs between beneficial and adverse effects and that are frequently used inappropriately (Care in Normal Birth: A Practical Guide; WHO, 1996). The 1995 Guide to Effective Care in Pregnancy and Childbirth categorized early use of oxytocin as a form of care with unknown effectiveness (Enkin et al, 1995).

'Active management of labor' as defined by some investigators includes strict criteria for the diagnosis of labor, early rupture of membranes, and prompt intervention with high-dose oxytocin in the event of inefficient uterine contractions (Frigoletto et al, 1995). Using stringent criteria, studies at the National Maternal Hospital in Dublin with a very high rate of stimulation (40%) reported a low cesarean section rate of 6% (O'Driscoll et al, 1984; Boylan et al, 1989). In contrast, among low-risk pregnancies (defined as full-term, singleton, vertex presentation, spontaneous onset of labor, and uncomplicated pregnancies in the absence of severe maternal complications such as diabetes), a randomized trial in 1934 nulliparous women found no reduction in the incidence of cesarean section among the stimulation group (Frigoletto et al, 1995).

Stimulation is an important treatment for dystocia (weak and prolonged labor). However, it is unknown whether a decrease, if any, in the incidence of dystocia (a possible consequence of an increased use of stimulation) would help reduce fetal mortality. It is noteworthy, however, that stimulation of labor can cause obstetric complications such as fetal distress, adverse birth experiences (e.g., severe pain), and subsequent interventions (e.g., epidural analgesia and cesarean section) (Owen et al, 1992, Rooks JP, 1999).

In summary, the effectiveness of routine ultrasound screening and electronic fetal monitoring as the main techniques for fetal surveillance in low-risk pregnancies remains controversial, as does the use of oxytocin for labor augmentation (except that early ultrasound screening may reduce congenital anomaly-related FD). The rapid spread of these clinical practices (see Section 2.4.4) has been widely criticized because of the absence of

demonstrable benefits on perinatal outcomes. EFM and stimulation of labor in particular can lead to a 'cascade of medical interventions' with known side effects (Albers and Savitz, 1994; Thacker et al, 1997; Rooks JP, 1999). In fact, several professional organizations, including the American College of Obstetricians and Gynecologists, have endorsed the use of intermittent auscultation as equivalent to continuous EFM for the care of low-risk pregnant women (American Academy of Pediatrics and ACOG, 1988; 1989).

2.4.3 Management of postterm pregnancy

Prolonged pregnancy poses an increased risk to fetal survival. In the absence of severe maternal/fetal disorders or complications such as heart disease, diabetes, hypertension, congenital anomalies, placenta previa, and premature rupture of membrane, postterm perinatal deaths (fetal death + neonatal deaths) remain two- to threefold as high as perinatal deaths at term (Lucas et al, 1965). In fact, pathologic studies have revealed an increased incidence of placental histologic abnormalities such as placental infarcts, calcification, intervillous thrombosis, perivillous fibrin deposits, arterial thrombosis, and arterial endarteritis in postterm pregnancies (Vorherr H, 1975; Thliveris and Baskett, 1978). This has usually been attributed to 'placental insufficiency.' It is hypothesized that the postterm fetus may outgrow the ability of its placenta to provide sufficient nutrients and adequate oxygenation for continued fetal growth and therefore is at increased risk for adverse perinatal outcomes resulting from either malnutrition or asphyxia (Cunningham et al, 1997). The presence of IUGR in prolonged pregnancies is perhaps a direct consequence of 'placental insufficiency.' In fact, the increased perinatal mortality among these pregnancies can be independently attributed to IUGR (Campbell et al, 1997; Divon et al, 1998; Ingemarsson et al, 1997).

Despite many years of research, there are still considerable controversies over the optimal obstetric management of prolonged pregnancy (labor induction or expectant management). In fact, a dramatically increased risk of FD at >= 41 weeks GA is clear (Yudkin et al, 1987; Hilder et al, 1998). Current obstetric practice recommends induction of labor in the presence of 'a favorable cervix' between 41 and 42 weeks' gestation (Maternal-Fetal Medicine, 4th edition, 1999). Yet there is lack of agreement on the type of management

when the cervix is unfavorable. In this case, induction of labor is one option; another option is serial fetal monitoring (expectant management), including monitoring fetal heart rate patterns and ultrasonographic assessment of amniotic fluid volume. Delivery is suggested when evidence of fetal distress is obtained.

Randomized controlled trials of induction of labor vs expectant management have yielded inconclusive results (Cardozo et al, 1986; Dyson et al, 1987; Hannah et al, 1992; NICHD, 1994; Almstrom et al, 1995). These studies show no beneficial effect of induction of labor on perinatal morbidity or mortality. However, induction of labor may be expected to impact on FDs but may not necessarily impact on neonatal death. Indeed, it is possible that labor induction results in earlier delivery of distressed fetuses who would have otherwise died *in utero* but are born alive and die as newborns. Nevertheless, unless statistical power is adequate, it is unlikely that the potential protective effect on such an infrequent outcome as antepartum FD can be detected. Another important concern is whether induction of labor affects the rate of cesarean section (e.g., due to fetal distress, dystocia, or prolonged labor). While some studies report a lower cesarean section rate in the induction group (Dyson et al, 1987, Hannah et al, 1992), others report a lower rate in the fetal monitoring group (Katz et al, 1983; Cardozo et al 1986; Almstrom et al, 1995). Cardozo et al (1986) suggested that the lower cesarean section rate in their study was perhaps due to the use of prostaglandin E_2 (PGE_2), whereas most previous studies used a combination of amniotomy and oxytocin for labor induction. PGE_2 is known to be effective in reducing the risk of failed induction (Pearce et al, 1979). When the cervix is unripe, using oxytocin alone to provoke contraction is likely to increase the risk of cesarean section. It is now clear that PGE_2 is the best choice for labor induction, as it stimulates both cervical ripening and uterine contraction (Maternal-Fetal Medicine, 4th edition, 1999).

The largest randomized controlled trial on management of prolonged pregnancy studied 3,407 women with uncomplicated singleton pregnancies (i.e., absence of severe maternal diseases such as diabetes mellitus or complications of labor/delivery such as placenta previa, PROM, or malpresentation) of 41 or more weeks of gestation (Hannah et al, 1992). This trial compared a policy of routine induction of labor at 41 weeks' gestation or later

with a policy of expectant management. In the induction group, labor was induced with PGE_2, while in the expectant group labor was induced (or cesarean section was performed) only when there was evidence of compromised fetal status. Two cases of FDs were observed in the expectant group (n=1,706) and none in the induction group (n=1,701) and no neonatal deaths occurred in either group. The study concluded that there was no significant benefit of routine induction with regard to perinatal mortality and morbidity, except that the cesarean section rate was marginally lower in the induction group (21.2 vs 24.5%). In addition, the same study group subsequently reported that routine induction was more cost-effective than serial antenatal fetal monitoring (Goeree et al, 1995). A later but smaller randomized controlled trial (n=440) conducted by the National Institute of Child Health and Human Development also reported no advantage to elective induction of labor at 41 weeks GA relative to serial fetal monitoring (NICHD, 1994).

Due to limited sample size, a single randomized controlled trial clearly is unlikely to detect a meaningful reduction in FDs. In fact, the cumulative evidence shows that a policy of routine induction at 41 weeks or above might reduce the incidence of FDs compared with fetal serial monitoring (expectant management) (Crowley P, 1992; 1992; Keirse MJNC, 1993). Five out of 11 trials found in the literature have reported 1 or 2 cases of perinatal deaths in the expectant group but no such deaths in the induction group (Henry GR, 1969; Cardozo et al, 1986; Dyson et al, 1987; Bergsjo et al, 1989; Hannah et al, 1992). One small trial found 1 death in the induction group (n=78) but none in the expectant group (n=78) (Katz et al, 1983). Of the remaining 5 trials, no death was observed in either group (Suikkari et al, 1983; Augensen et al, 1987; Witter and Weitz, 1987; Martine et al, 1989; Medearis, 1990). Overall, for the above 11 trials, 1 death was observed in the induction groups (n=2,905) vs 7 in the expectant groups (n=2,822). A meta-analysis of the 11 trials also reported a beneficial effect of induction on perinatal death at >=41 weeks GA and no significant increase in cesarean section rate (Grant et al, 1994).

Large population-based observational studies are indispensable alternatives for the investigation of such infrequent events as FD. Unfortunately, observational studies of induction of labor and postterm pregnancies remain scanty. One population-based study

carried out in Canada reported an increasing rate of induction of labor accompanied by a reduction in FMR from 2.8 to 0.9 in FDs (per 1,000 total births) among postterm pregnancies from 1980 to 1995 (Sue-A-Quan et al, 1999). However, this study is flawed not only by its lack of control for contemporaneous changes in covariates but also by the use of different data sources for induction of labor and FMR; the rate of induction of labor was based on hospital samples, while the FMR was from national vital statistics. A more recent study using the Canadian Birth Database investigated the fetal mortality trend between 1985-87 and 1992-94 among postterm pregnancies (Wen et al, 2001). Unfortunately, this study was unable to specifically examine the effect of induction of labor due to an absence of data on induction in the Canadian birth registry. Therefore, a large population-based study with information on induction in individual woman is desirable to address a pressing issue concerning the effect of routine induction of labor on risk of FD postterm.

2.4.4 Temporal changes in obstetric practice

According to the United States National Vital Statistics Report, about 83% of women who gave birth in 1997 had recorded EFM, a 22% increase over 1989 (National Vital Stat Rep, Vol. 47, No. 27, 1999). The use of EFM rose for the seventh consecutive year in all age groups until 1997 and has become the most prevalent obstetric procedure in the United States. About two-thirds of mothers (64%) had at least one ultrasound examination during pregnancy in 1997, a 35% increase over 1989. Induction of labor was used in 18% of births in 1997, twice the 1989 level of 9%. Stimulation of labor was used in 11% of births in 1989 and increased to 17% in 1997 (a relative increase of 55%). Although the rate of induction or stimulation of labor was much lower than the rate of EFM or ultrasound, the percent increases were much greater. Altogether, one-third of births in 1997 were induced or stimulated; about 2% of births were both induced and stimulated.

One U.S. study found that, during the 1980s, the increase in EFM among pregnancies at low risk (i.e., term gestation, absence of medical or obstetric problems) was twice as high as the increase among pregnancies at high risk (Albers and Krulewitch, 1993). Using U.S. 1990 birth certificate data, Brett et al reported that the use of certain obstetric procedures (i.e., amniocentesis, tocolysis) was more frequent in Whites than in Blacks (Brett et al,

1994). However, differences between Whites and Blacks in the use of EFM, induction of labor, and ultrasound have not been studied.

In contrast to the increases in obstetric procedures, method of delivery underwent only a slight change during the same time period. Cesarean births fell 9% between 1989 and 1996, from 22.8% of births to 20.7%, but then increased marginally to 20.8% in 1997. Similarly, the rate of primary cesarean births (first cesareans for women with no previous cesarean) also fell 9% between 1989 and 1996, from 16.1 to 14.6, and remained at 14.6 in 1997. During the same period, the percent of births that were vaginal births after a previous cesarean increased by 50%, from 18.9% in 1989 to 28.3% in 1996, but decreased slightly to 27.4% in 1997 (National Vital Stat Rep, Vol. 47, No. 27, 1999).

2.5 Critique of previous studies

2.5.1 Definitional and methodologic problems

Previous studies of fetal mortality trends (including the two U.S. studies) (Goldenberg et al, 1987; Hsieh et al, 1997) used the flawed conventional definition of fetal mortality rate (the number of FDs as a proportion of total births) as a measure of risk for FD in different GA or BW categories, which renders the study conclusions highly questionable. One methodologic problem is that the denominator used (live births + fetal deaths) in calculating fetal mortality rate includes total births at a GA but not all the fetuses at risk for FD at that GA. However, according to the definition of 'risk,' the denominator needs to include all the members of a closed population (no entry, no withdrawal) at risk of becoming diseased or dying during a given period of time (Rothman and Greenland, 1998). During that specific period, an individual may end up with the study outcome or remain unaffected. Likewise, at a given GA, a fetus may be live-born, stillborn or remain as an ongoing pregnancy. It is the latter fetuses (ongoing pregnancies) that have been ignored in the conventional definition of fetal mortality rate. Yet, pregnancies that continue until the end of the specified GA are at risk of FD and therefore need to be included in the denominator. Thus, in calculating the GA-specific fetal death risk, the correct definition of the denominator should include *all* fetuses at risk for FD at a specified GA. This is composed of live births, stillbirths, and all

ongoing (undelivered) pregnancies at that GA. It must be noted that this definitional problem occurs only when FDs are categorized by GA or BW (the latter is often used as a proxy for GA, see below); the conventional definition is still a valid measure of overall fetal death risk (all GA combined).

In 1987, Yudkin et al found that the GA-specific risk for FD differs remarkably according to which denominator is used. Specifically, if the number of total births (stillbirths + live births) at a given GA is used as the denominator (e.g., in calculating the conventional fetal mortality rate), the earliest GAs have the highest risk, whereas the risk is lowest at >=41 weeks (nineteen times lower than that at 33 weeks). In contrast, if the total number of fetuses at risk (i.e., all ongoing pregnancies at each GA) is used as the denominator, then early preterm GAs have the lowest risk, whereas the risk rises fourfold after 39 weeks to a maximum at 41 weeks and above. Therefore, the two definitions convey completely different perceptions of fetal death risk at different GAs. The conventional definition greatly underestimates the risk for FD at term and postterm, and overestimates the risk preterm. As a consequence, any changes in fetal mortality trends at different GAs, if measured by the conventional approach, cannot readily be interpreted as a rise or fall in the risk for FD in the population. Unfortunately, the flaw of this definition continues to be ignored by many perinatal researchers (Ingemarsson et al, 1997; Hsieh et al, 1997, Sheiner et al, 2000; Winbo et al, 2001; Buck et al, 2002).

Another methodologic problem has been categorizing FDs by weight (e.g., the concept of BW-specific fetal mortality rate). BW is a poor proxy for GA, particularly in studying FD. First, the delay in delivery after antepartum FD may result in maceration. Therefore, the stillbirth weight may be less than the weight at the time of fetal demise (Yudkin et al, 1987). Second, LBW may result from either short gestation or IUGR, each of which may have different etiologic implications for FD; short gestation is a consequence but not a cause of FD, whereas IUGR is an important cause for FD. Third, in applying a BW-specific approach, we have no way of including all fetuses of similar BW into the denominator for calculating risk, since fetal weight is unknown until delivery. Thus, the conventional BW-specific fetal mortality rate is even worse than the proposed GA-specific fetal death risk in

that it conditions on birth (including live birth) at a given BW and conflates gestational duration and fetal growth. Unfortunately, the BW-specific approach has been standard in FD research (as elsewhere in perinatal epidemiology), as a result, fetal death risks and trends continue to be misinterpreted.

The third methodologic problem concerns whether to treat FD as a binary reproductive outcome 'death or not' or as a 'time to event.' Most etiologic studies of FD have used a case-control study design. Study subjects are usually obtained from a hospital perinatal database, national survey, or birth registry. Cases are defined as FDs occurring at any time during the study period, while controls are often a random sample of total live births, and data are usually analyzed by logistic regression. However, such a study design ignores the important fact that FD can occur throughout the entire pregnancy; as noted, most FDs occur before 37 weeks and more than half are under 28 weeks, whereas most live births occur at term. Under such circumstances, the binary endpoint of 'death or not' is insufficient, and time to this endpoint is also important. Clearly, the average duration of GA to FD is much shorter than the average duration of GA to live birth. Therefore, the *in utero* survival of fetuses needs to be treated as 'time to event' to take into account the impact of *in utero* duration (survival time) on the risk of FD. For survival data, life-table methods (including the Cox proportional hazard model) are the natural option. This approach fits well with the proposed definition of GA-specific fetal death hazard (see Chapter 3).

2.5.2 Registration artifacts

Previous studies of fetal death trends have not taken into account potential registration artifacts (i.e., increasing registration of early FDs). In Goldenberg et al's study (1987), for example, the FMR for the LBW group fell by 20% during the study period, whereas the FMR dropped by 40% for the 2,500-3,999 g BW group and by 71% for the group of >= 4,000 g. It is likely that the decline in early FDs was underestimated in that study, especially for the BW group <750 g due to more complete reporting of births at the borderline viability. Therefore, the conclusion that heavier fetuses (>=2,500 g) had a more rapid fall may be questioned. Rather, a large decline in early FDs may have been missed.

2.5.3 Impact of obstetric practice

Previous studies of FD trends have not related the decline to important changes in antenatal and/or intrapartum obstetric practices. As a consequence, it remains unclear to what extent the decline can be attributed to medical or clinical interventions. In recent years, policies on elective labor induction have undergone important changes; the recorded induction rate was twice as high in 1997 as in 1989 in the United States (National Vital Stat Rep, Vol. 47, No. 27, 1999). However, whether such an increase has contributed to the decline in FDs, particularly at term and postterm, remains unknown (note: the rapid decline observed in the two U.S. studies was among fetuses with BW >=2,500 g, which roughly corresponds to GA at >=35 or 36 weeks). Such a hypothesis is very plausible, since the accumulated evidence from randomized controlled trials suggests a benefit of induction of labor (elective use at >=41 weeks GA) on FDs, specifically among the uncomplicated low-risk pregnancies. Yet, due to limited sample sizes, no firm conclusions can be drawn, even from the largest multi-centre Canadian trial (Hannah et al, 1992).

Uncertainties and limitations of studies of FD trends (based on vital statistics) are due not only to methodologic problems but also to a lack of information on key variables before the 1989 revision of the FD certificate (Tolson et al, 1989). Since 1989, information has been recorded not only on obstetric procedures, but also on woman's life-style risk factors (e.g., tobacco and alcohol use) and method of delivery (e.g., cesarean section vs vaginal delivery), as well as on maternal medical risk factors, obstetric history, and prenatal care. Clearly, without taking into account other contemporaneous changes, an appropriate assessment of the impact of any favorable change in clinical practice on the fall in FDs is not possible.

2.6 Summary

Fetal mortality has continued to decline in the United States. However, appropriate estimation and interpretation of the decline are still lacking. It is now clear that using the conventional definition of BW-specific fetal mortality rate vs the definition of GA-specific fetal death risk can yield completely different results in depicting FD trends. GA-specific fetal death risk is a more appropriate approach than BW-specific fetal mortality rate in FD

research (although the data quality of GA usually is not as reliable as that of BW). Using the correct approach, several studies have revealed a marked increase in risk for FD as pregnancy advances to 41 weeks and above (Ferguson et al, 1994; Hilder et al, 1998; Conde-Agudelo et al, 2000). However, whether this pattern of increase also exists with the U.S. population remains unclear. Nor do we have any knowledge about temporal changes in GA-specific fetal death risk in the United States.

In recent decades, the reporting of FDs was increasingly complete in Alabama. However, no study has examined the completeness of reporting across the United States. Such knowledge is of key importance in properly interpretation of the temporal changes in fetal death risk at early GAs. As for the data quality of the U.S. vital statistics, most data items are underreported. The extent of underreporting varies. It seems that after 28 weeks GA, data completeness is better than that at 20-27 weeks. The reporting on basic items such as maternal sociodemographic characteristics is complete at all GAs.

Induction of labor has increased markedly over the last decade in the United States. Yet the effectiveness of this intervention on improving the fetal survival remains inconclusive. Considerable knowledge has been obtained about the effect on FD of maternal sociodemographic characteristics (e.g., maternal age), life style risk factors (e.g., cigarette smoking), and chronic diseases (e.g., chronic hypertension, diabetes). However, less is known whether these effects are modified by advancing GAs. The importance of separating intrapartum deaths from antepartum deaths has been stressed for years. However, very few studies have made such a separation. Unfortunately, data on the timing of FD are missing from U.S. vital records.

To overcome many of these above limitations and insufficiencies, this thesis specifically addresses the following questions: Does the fetal mortality trend revealed by GA-specific fetal death risk show important changes over time (1997 vs 1991) in the U.S.? What are the roles of registration artifacts in changes in the early fetal death risk (particularly close to the 20 weeks cut-off)? What is the impact of increased use of labor induction on changes in

fetal death risk at and after term? Do the changes and underlying determinants of the changes differ between Whites and Blacks, and between low- and high-risk pregnancies?

Chapter 3. SUBJECTS AND METHODS

3.1 Data Collection and Processing

3.1.1 U.S. vital statistics system

The vital statistics of the United States are collected, compiled, and published annually by NCHS at Centers for Disease Control and Prevention (CDC) of the U.S. Public Health Service, through a decentralized, cooperative system. Registration of live births, fetal deaths, and induced terminations of pregnancies is based on state law, and reports are filed and maintained in state vital statistics offices. NCHS is responsible for the development of national standards, instruction manuals, and data processing procedures. NCHS also provides training and technical assistance to individual states. These standards take the forms of recommended laws and regulations (Model State Vital Statistics Act and Regulations), definitions (live birth, fetal death, etc), and reporting forms (U.S. Standard Certificates and Reports). NCHS is also in charge of data quality control. The registration system comprises 57 registration areas: each state, the District of Columbia, New York City, American Samoa, Guam, Northern Mariana Islands, Puerto Rico, and the Virgin Islands. The cooperation between NCHS and state vital statistics offices proceeds under a joint agreement known as the Vital Statistics Cooperation Program.

3.1.1.1 Standard forms

The U.S. Standard Certificate of Live Birth and the U.S. Standard Report of Fetal Death (Appendices A and B) are used as models for the development of state forms for registration of vital events. The U.S. standard forms represent the minimum basic elements necessary for the collection and publication of national live birth and fetal death data. These include maternal sociodemographic characteristics (age, race, Hispanic origin of mother, education, and marital status), pregnancy history, prenatal visits (timing and number), date of birth, birth weight, sex, plurality, date that last normal menses began, and clinical estimate of gestational age.

The 1989 revision of the U.S. Standard Certificate of Live Birth and Standard Report of Fetal Death introduced significant changes in content and in format of data collection. New items were added under the section "medical and health information" to obtain information on "obstetric procedures" (7 categories) and "method of delivery" (7 categories). The item "obstetric procedures" comprises amniocentesis, EFM, induction of labor, stimulation of labor, tocolysis, and ultrasound. Data on maternal life-style risk factors such as tobacco (average number of cigarettes per day) and alcohol use (average number of drinks per week) during the pregnancy were collected for the first time. The item "medical risk factors for this pregnancy" (17 categories) includes diabetes, chronic hypertension, pregnancy-induced hypertension, anemia (Hct. <30/Hgb.<10), cardiac diseases, acute or chronic lung diseases, renal diseases, eclampsia, and Rh sensitization. The item "complications of labor and/or delivery" (16 categories) includes febrile (>100° F or 38° C), meconium (moderate/heavy), premature rupture of membranes (>12 hours), abruptio placentae, placenta previa, seizure during labor, precipitous labor (<3 hours), prolonged labor (>20 hours), dysfunctional labor, breech/malpresentation, cephalopelvic disproportion, cord prolapse, and fetal distress. The item "congenital anomalies of fetus or child" (22 categories) includes anencephaly, spina bifida/meningocele, hydrocephalus, Down's syndrome, and heart malformations. Data on complications of labor/delivery and congenital anomalies were collected in an open-end format in previous versions. Since 1989, all 5 items for the "medical and health information" section on the live birth certificate and fetal death report have been constructed in checkbox format, with one checkbox for each category of items. Information on frequency and time of use of the obstetric procedures, as well as severity of medical conditions, is not documented. For example, even if ultrasound was used both at 22 and 34 weeks of gestation, it can be checked only once on the form, and no data are recorded on when it was used. For each of the 5 items, a separate checkbox is provided in case none of the listed categories applies.

3.1.1.2 Quality control

The uniformity in data collection of U.S. vital statistics has been promoted by periodic issue of recommended standards from NCHS and by co-operative adoption of these standards by individual states. Most states conform closely in content to the standards. Reporting of live

birth and fetal death is guided by the 'Hospital's and Physician's Handbook' provided by NCHS (1987). Moreover, NCHS conducts data quality control while compiling data from individual states.

Quality control of FD data takes place in a number of ways. Some states have their own procedures and regular query reports with problem data back to the original data source. NCHS encourages these state-level efforts and provides guidelines for such queries. In addition, FD data are subjected to NCHS quality control procedures at several processing stages to check for the completeness, coding validity, and consistency of data items. First, problems or inconsistencies are checked against the original source and are corrected if possible. Second, for each state, the percentages of nonresponse for each item are compared with the state's previous year percentages and the U.S. average percentages. States are contacted when a very high percentage or large change in nonresponse is noted. Counts and percentages of records with impossible or out-of-range codes are also reviewed and compared with the previous year's performance. Third, according to written procedures, invalid or inconsistent values may be modified or assigned as unknown. Selected missing items may be imputed, either by using data from a previous record, or by assigning a standard value (see Vital Statistics of the United States, Technical Appendix, 1994 and 1997).

3.1.2 Study population

The U.S. live birth and fetal death data are limited to births or deaths occurring within the United States. Live births or fetal deaths occurring to U.S. citizens outside of the United States are not included in U.S. vital statistics. In compiling the data files, NCHS excludes fetal deaths <20 complete weeks in gestation.

3.1.2.1 Study period

This study includes live births and fetal deaths (stillbirths) that occurred in 1991 or 1997, and that were recorded on the U.S. live birth and fetal death files for the two years. No data were available on obstetric procedures (i.e., labor induction) before the 1989 revision of

U.S. vital statistic files and were incomplete until 1991. The 1997 data was the most available when the study was initiated.

3.1.2.2 Study subjects for description of fetal death risk and changes (full sample)

Live births and stillbirths from all 50 states and District of Columbia (New York City is included with New York state) were used for a descriptive analysis of changes in distribution of maternal sociodemographic characteristics (age, race, educational attainment, and marital status), obstetric procedures (EFM, ultrasound, induction of labor and stimulation of labor), medical (diabetes, chronic hypertension, and PIH) and life-style risk factors (cigarette smoking and alcohol consumption), as well as for estimation of fetal death hazards in the United States in 1991 and 1997. All analyses were limited to singleton pregnancies (for multiple pregnancies, fetal death risks are quite different).

There were a total 8,048,157 births (7,834,328 singleton; 213,829 multiple) for the two study years. Of which, 4,011,828 were singleton live births and 29,231 were singleton FDs for the 1991 data year. There were 3,769,139 singleton live births and 24,130 singleton FDs for the 1997 data year. Data from Puerto Rico, Virgin Island, Guam, and foreign residences were excluded.

3.1.2.3 Study subjects for analysis of determinants of fetal deaths (restricted sample)

Data from a restricted sample (the 39 states and District of Columbia) were included in the analytic study of determinants underlying the change in fetal mortality. The main reason for this restriction was to exclude states with incomplete data. Specifically, we included only those states in which data reporting was at least 80% complete for each of the following items: maternal life-style risk factor (cigarette smoking), obstetric procedures (induction of labor) and maternal severe medical conditions (chronic hypertension, diabetes, and PIH). These three items were chosen because of their importance as covariates for the present study (Little et al, 1993; Raymond et al, 1994; Sibai et al, 1984; Abdella et al, 1984; Mabie et al, 1986; Ananth et al, 1995; Yadav et al, 1997; Martin et al, 1999; Cunndy et al, 2000). Moreover, previous studies show that data on these items, and particularly on cigarette smoking and induction of labor, are most likely to be underreported; in contrast, data

reporting on maternal sociodemographic characteristics (maternal age, race, educational attainment and marital status) is fairly complete (Piper et al, 1989; Parrish et al, 1993; Buescher et al, 1993).

As noted earlier, the incompleteness of data can be due either to the fact that the items are not included on the state certificate or report form (therefore, data are completely missing from that state) or to the fact that the items are left unchecked on a portion of the records. Using the above inclusion criterion, a total of 11 states were excluded. In 9 states, the data item for maternal life-style risk factors (cigarette smoking) was not included on the state FD report form for 1991 (100% missing rate on cigarette smoking in these states). These 9 states are: California, Hawaii, Indiana, Louisiana, Maryland, Massachusetts, New York, Oklahoma, and South Dakota. Texas was excluded because of a very high missing rate on smoking, while Illinois was excluded because data were absent on induction of labor for 51% of records in 1991. The restricted sample includes a total of 4,411,365 singleton births, including 2,236,352 singleton live births and 16,880 singleton fetal deaths for 1991 and 2,144,266 singleton live births and 13,867 singleton fetal deaths for 1997.

3.1.3 Alexander's approach for correcting GA errors

NCHS computes GA in completed weeks by subtracting the date of birth from the date of onset of the last menstrual period (LMP). When the date of LMP is incomplete, e.g., missing day when there is a valid month and year (a major type of missing date on LMP), GA is imputed with the value of the preceding birth record that has a complete LMP date with the same computed month of gestation and the same 500 g BW interval. The clinical estimate of GA is used (for less than 5% of births) when information on the date of LMP is completely missing, invalid, or inconsistent with BW. The clinical estimate of GA is based on the clinician's pediatric assessment of the physical or neurological development of the newborn, early ultrasound dating, or combinations of various measures. For more than 95% of births, the GA assignment on the U.S. vital statistics data is based on the LMP date (Vital Statistics of the United States: Natality, 1997; Technical Appendix).

Records with missing values on GA have been largely reduced (i.e., the missing rate is under 1%) when NCHS uses the above algorithm to create a variable for GA in the U.S. vital statistics data. However, it can be anticipated that a large number of errors remain undetected, i.e., implausible BW for GA (Gaudino et al, 1997). Since GA is a pivotal variable for the estimation of GA-specific fetal death risk in the present study, the validity of GA values requires further scrutiny.

BW is thought to be more reliably recorded than GA in U.S. vital statistics. Therefore, Alexander et al constructed a set of BW-GA inclusion criteria (see Appendix C) to identify and delete cases with implausible BW-GA data by examining the distributions of weight (grouped into 125-g intervals) for each GA week. A distinct feature of this approach is that it is based on the clinical plausibility of the values (by consulting neonatologists), instead of using, for example, a set of statistically defined cut-points such as BW plus and minus 2.5 standard deviation (the first vs 99th percentile) from the mean for the GA (Alexander et al, 1996). The statistically defined cut-points were found to include records that clearly represent inaccurate GA values. Therefore, Alexander's approach is intended to find errors that have been largely ignored by the simple statistical approach, particularly at early GAs (20-27 weeks). Based on this method, a United States national reference for fetal growth has been developed using all singleton live births that occurred in 1991 (Alexander et al, 1996).

In the present study, Alexander's approach (SAS procedures provided by Dr. Robert Platt, see Appendix D) was used to examine data for all 50 states and the District of Columbia. Subjects with implausible BW-GA values according to this approach were deleted. For live births (>=20 weeks GA), proportions of deleted records were 0.54% for 1991 and 0.38% for 1997. For FDs (>=20 weeks GA), proportions of deleted records are 21.1% for 1991 and 13.1% for 1997. For live births at and after term (>=37 weeks GA), these proportions were 0.06% for 1991 and 0.01% for 1997. For FDs at and after term, these proportions were 7.0% for 1991 and 6.8% for 1997. Unsurprisingly, the error rates on GA were substantially higher in FDs than in live births. Most of the errors occurred at earlier GAs. After 37

weeks, these errors were largely reduced. Over time, it seems that GA reporting, particularly on FD, was improved.

The final data excluded a) multiple pregnancies, b) subjects with implausible BW-GA values, c) other races (except non-Hispanic Whites and Blacks) (see Appendix Figure a.1. for flow chart of data inclusion). This approach resulted in 3,664,054 singleton live births and 21,396 singleton fetal deaths for 1991 and 3,445,448 singleton live births and 19,089 singleton fetal deaths for 1997. These are the data upon which the description of the fetal death hazard in the U.S. (50 states and D.C.) and analyses of determinants for changes in fetal death hazard (39 states and D.C.) were conducted. However, to identify possible impact on the estimate of fetal death hazard, a comparison was also made before and after deletion of implausible BW-GA values (see Section 3.2.1.3).

3.1.4 Outcome measures

3.1.4.1 Registration artifact

3.1.4.1.1 Early FD at 20-22 weeks as a proportion of total births (>=20 weeks in GA) for the year. This proportion is used to identify whether there has been an increased registration of FDs at the borderline of viability over the study period.

3.1.4.1.2 Early FD at 20-22 weeks as a proportion of perinatal deaths for the year. Perinatal deaths refers to fetal deaths (>=20 weeks) + early neonatal deaths (<7 days of age). This proportion is used to identify any change in registration of early FDs as neonatal deaths (or vice versa) over the study period.

3.1.4.2 Fetal death hazard

3.1.4.2.1 Definition

Fetal death hazard refers to the number of FDs per 10,000 fetuses (ongoing singleton pregnancies) at a specific GA.

3.1.4.2.2 Computation

In actual computation, the numerator is the number of FDs occurring at a specific completed week of gestation, and the denominator is the number of undelivered (ongoing) singleton pregnancies at the beginning of that specific gestational week. Fetal death hazards for each completed week of gestation (from 20 to 43 weeks) were calculated.

The computation algorithm is as follows:

$$HD_i = \frac{FD_i}{TB - ND_{i-1}}$$

HD_i = fetal death hazard at specific completed week of gestation;
FD_i = no. of fetal deaths at a specific completed week of gestation;
TB = no. of total births (live births + fetal deaths) >=20 weeks of gestation;
ND_{i-1} = no. of accumulated births (live births + fetal deaths) from >=20 weeks of gestation until the end of the previous specific completed week of gestation.

For example, to calculate the fetal death hazard at 28 completed weeks GA, first determine the total number of FDs that occurred at the 28 weeks, then compute the total number of pregnancies that have reached at least 28 completed weeks by subtracting total number of live births and stillbirths =<27 completed weeks in GA from the total number of live births

and stillbirths >=20 completed weeks in GA. These two numbers are then used as the numerator and denominator in calculating the fetal death hazard at 28 weeks.

3.2 Data Analyses

3.2.1 Descriptive Analyses

3.2.1.1 Frequency distribution

3.2.1.1.1 Percentages of live births and fetal deaths at 20-36, and 37-43 weeks GA, Whites and Blacks, 1991 and 1997 were generated in the full sample (all 50 states and D.C.) and the restricted sample (the 39 states and D.C.), respectively. This analysis is intended to demonstrate that the majority of FDs were preterm while the majority of live birth occurred at and after term.

3.2.1.1.2 Frequency distributions were generated for maternal sociodemographic characteristics (maternal age, race, educational attainment and marital status), medical and life-style factors (onset of prenatal care, parity, diabetes, chronic hypertension, PIH, cigarette smoking and alcohol consumption), and obstetric procedures (EFM, induction of labor, stimulation of labor and ultrasound). Records with unknown data were excluded. No statistical significance test was conducted. This analysis was performed for each of the following groups.

a) Full sample (50 states and D.C.) and restricted sample (39 state and D.C.), 1991 vs 1997.
b) Restricted sample (39 states and D.C.), Whites and Blacks, 1991 vs 1997.

Group a) contrasts the full sample and the restricted sample to determine the extent to which the restricted sample represents the full sample with regard to maternal sociodemographic characteristics, prenatal care and medical risk factors. As elaborated above, data from eleven states were excluded because of the incompleteness of data. However, an important concern for restricting the analyses to more complete data is

whether representativeness has been compromised. Accordingly, a comparison between the full sample and the restricted sample is necessary.

Group b) is to examine differences in the frequency distributions between Whites and Blacks. Distinct racial gaps have been recognized regarding socioeconomic status (SES), women's access to prenatal care and life-style risk factors (Brett et al, 1994; Tossounian et al, 1997). Moreover, as reported in previous studies, U.S. Whites and U.S. Blacks underwent significantly different temporal trends in fetal and neonatal mortality (Gaudino et al, 1995; Demissie et al, 2001). For these reasons, Whites were separated from Blacks for analysis, while no analysis was carried out for other racial groups in the present study.

When generating the frequency tables, maternal age and educational attainment (reported in years) were categorized as maternal age =<19, 20-34, >=35 (years), and maternal educational attainment 0-8, 9-12, 13-15, >=16 (completed years). Maternal diseases such as diabetes, chronic hypertension or PIH were reported separately, while other medical conditions such as anemia (HCT.<30/Hgb.<10), cardiac diseases, acute or chronic lung disease, renal diseases and Rh sensitization were reported in one group. Maternal diabetes, chronic hypertension and PIH have been frequently reported as the most significant medical risk factors for FD (Sibai et al, 1984; Abdella et al, 1984; Mabie et al, 1986; Ananth et al, 1995; Yadav et al, 1997; Martin et al, 1999; Cunndy et al, 2000). For the same reason, we have divided pregnancies into high- vs low-risk pregnancies based on the presence or absence of these above three medical conditions and/ or maternal age <20 or >=35 years (see Section 3.2.2.2). Since the present study is not intended to identify specific medical risk factors for FD, no analysis was carried out for other maternal medical conditions or disorders.

The frequency distribution was performed for 1991 and 1997, separately. Temporal changes in maternal sociodemographic characteristics, medical and life-style risk factors were examined. An increasing trend as suggested by previous report (National Vital Stat Rep, Vol. 47, No. 27, 1999) in the use of obstetric procedures (EFM, induction of labor, stimulation of labor, and ultrasound) was demonstrated. Disparities between Whites and

Blacks in the use of these procedures, and their changes over time were also presented. To explore possible effect of induction labor on FD is the focus of this study. Therefore, we further examined the rate of this procedure according to GA in the following analysis.

3.2.1.1.3 Rate of induction of labor by GA (from 28 to 43 weeks) in the 39 states and D.C. was examined for:

a) U.S. Whites, 1997 vs 1991
b) U.S. Blacks, 1997 vs 1991

The rate of induction of labor as a proportion of total fetuses at risk (ongoing pregnancies) at given GA weeks was calculated. As a result, variations in the use of this procedure according to GA and possible changes over time (1997 vs 1991) were presented. This analysis is intended to examine evidence of increased use of induction of labor as GA advanced. A significantly higher rate of induction was anticipated at 41 to 43 weeks than at 28 to 36 or 37 to 40 weeks (as a consequence of elective labor induction between 41 to 42 weeks in the management of postterm pregnancy in the United States (Maternal Fetal Medicine, 4th edition, 1999)). This analysis was limited to >=28 weeks GA, partly because the reported missing rate is high for obstetric procedures (including induction) at 20-27 weeks (7.1 vs 4.9% at >=28 weeks) (Martin and Hoyert, 2002), and partly because our focus in the present study is on the possible effect of increased use of routine labor induction (e.g., at and after term) on the decrease in fetal death risk. In fact, our entire analyses of determinants of FD was restricted to >=28 weeks because of the concern of incomplete registration of FD at 20-27 weeks (Goldenberg et al, 1989; Phemlan et al, 1998). Log transform of the induction rate was conducted for better graphic display of changes at lower GAs.

3.2.1.1.4 Frequency of total live births by GA (28 to 43 weeks) for Whites and Blacks in the 39 states and D.C., 1991 vs 1997.

This analysis examines whether there was a change in GA distribution between 1991 and 1997 in Whites and Blacks in the United States. If the marked increase in labor induction (as reported by NCHS, see Chapter 2 Section 2.4.4) occurred at 41 to 43 weeks or earlier (perhaps due to more frequent use of elective labor induction in 1997 than in 1991 for the treatment of postterm pregnancies), it should have resulted in a marked decrease in the proportion of births at >=41 weeks (assuming no substantial change in the estimation of GA during the same time period). Accordingly, changes in labor induction (as showed in the above analysis) were compared to the relevant changes in GA distribution at different GA (e.g., 41-43 weeks). The analysis was restricted to the 39 states and D.C. in order to compare directly with the results for induction.

Since the rate of labor induction was significantly higher in Whites than in Blacks (as showed in the above analysis), we also anticipate that the change in GA distribution (if due to the increased use of induction of labor) should have been different between the two racial groups. Because of this, a contrast in GA distribution was made between Whites and Blacks. Since the number of live births =<27 weeks is very small, this analysis was limited to >=28 weeks GA.

3.2.1.2 Crude fetal death risk

The unadjusted crude fetal death risk was calculated within each category of maternal sociodemographic characteristics, medical and life-style risk factors. These include maternal age (<20, 20-34, >=35 years), educational attainment (0-8, 9-12, 13-15, >=16 completed years), marital status (yes, no), race (Whites, Blacks), onset of prenatal care (1^{st}-, 2^{nd}- or 3^{rd}-trimester), parity (1 or >=2), fetal gender (male, female), cigarette smoking (yes, no), alcohol consumption (yes, no), diabetes (yes, no), chronic hypertension (yes, no), pregnancy-induced hypertension (yes, no) and other maternal medical conditions (yes, no). Crude risk ratio (RR) and 95% confidence interval (CI) were obtained. When calculating the RR, onset of prenatal care in the 2^{nd}- or 3^{rd}-trimester was combined (owing to the small

number with 3rd-trimester onset), and used as reference to show possible protective effect of 1st-trimester prenatal care. When calculating the 95% CIs, Woolf's method (Taylor series or empirical logit) was used.

This analysis aims to show the crude effect of risk factor on FD, which provides a list of potential determinants for FD. Further analysis included an adjustment for confounding variables using the Cox proportional hazards model (see Section 3.2.2). Owing to incomplete reporting on FD at early GAs, the crude and multivariate analyses were restricted to FD >=28 weeks, for which reporting is believed to be complete (Martin JA and Hoyert DL, The National Fetal Death File, 2002). These analyses were performed separately for 1991 and 1997 (39 states and D.C.) to show the possible change in effect over the study period.

3.2.1.3 Fetal death hazard

Fetal death hazard (or GA-specific fetal death risk) was computed by year for each following group:

a) The full sample
b) The restricted sample
c) The full sample, Whites vs Blacks
d) The restricted sample, Whites vs Blacks

Fetal death hazard trends by GA (20-43 weeks) were depicted (1991 vs 1997) using line charts (using Microsoft Excel 2000). Differences in fetal death hazard were compared between the full sample and the restricted sample, and between U.S. Whites and U.S. Blacks. It is anticipated that the restricted sample would present a similar pattern as the full sample in the changes in fetal death hazard. Comparisons were also made before and after deletion of improbable GA records for each group (using Alexander's approach) to identify the possible impact of such deletions on the fetal death hazard trends.

3.2.1.4 Analysis of registration artefacts

Annual total number of live births, FDs, and early neonatal deaths for all 50 states and the District of Columbia (singleton, all ethnic groups) were analyzed to identify a trend toward increasing registration of FDs at the borderline of viability (close to 20-week cut-off) and/or classification of FDs as early neonatal deaths. FDs in early GA categories (20-22, 23-25 and 26-28 weeks) as a proportion of total births and as a proportion of perinatal deaths (fetal deaths + early neonatal deaths <7 days >=20 weeks GA) were calculated for 1991 and 1997, respectively. The overall fetal mortality rate (at all GAs) was calculated to identify temporal changes during the study period. To identify whether the reporting of early live births also underwent similar trends as the reporting of early FDs, live births at the 3 early GA categories as a proportion of total births were also calculated.

Newborn infants at 20-22 weeks are generally nonviable. To ensure an identical risk period, the rest of the early GAs (23-28) was also grouped by 3 weeks for each. The rate ratio (RR) was used to estimate the changes in these proportions and the changes in overall FMR from 1991 to 1997 (reference: 1991). The 95% confidence intervals (95% CIs) for the estimated RRs were computed using Woolf's method (Taylor series or empirical logit).

To identify possible racial differences in the registration practices in the United States, the above computations were carried out separately for Whites and Blacks of all 50 states and District of Columbia.

3.2.2 Multivariable Analyses

3.2.2.1 Strategy for statistical modeling

Fetal death as a binary reproductive endpoint can occur throughout the entire process of a woman's pregnancy. As GA approaches 37 or more weeks, fetal death risk increases dramatically. Moreover, this is accompanied by a large degree of censoring, as the majority of pregnancies end with live births at term. Accordingly, live birth and fetal death data need to be treated as censored event-time data. Each individual subject has been followed for a

varied amount of time, and data collection comprises an event time (GA for fetal death) or censoring time (GA for live birth), a censoring indicator (fetal death or live birth), and a set of covariates. Under this data structure, an appropriate form for analysis is Cox's semi-parametric proportional hazards model (Cox DR, 1972; Kalbfleich et al, 1980; Breslow and Day, 1987; Samet et al, 1998; Thomas D, 1998). Using the Cox model, comparison is made by risk set. At a specific time point during follow-up, a risk set is a set of subjects at risk for FD. For the risk set at 40 weeks GA, for example, comparison is made between FDs that occurred at that week and all fetuses at risk (ongoing singleton pregnancies that entered 40 weeks of gestation), including those who were live births at or after 40 weeks.

The goal of the Cox modeling was to determine whether the observed temporal change in fetal death hazard from 1991 to 1997 persisted after controlling for concomitant changes in relevant factors during the same time period. As a first step, a full Cox model was created to identify and quantify determinants for FD while controlling for potential confounding variables. As first reported by Raymond et al in 1994 (see Chapter 2, Section 2.3.1.1), the effect of advanced maternal age (>=35 yrs) and cigarette smoking varies by GA (>=28 weeks). Therefore, instead of treating all FDs as etiologically homogeneous, this analysis was carried out separately for subjects at 28 to 36 weeks, 37 to 41 weeks, and 42 to 43 weeks of gestation to determine if the estimated effect changes from preterm to term to postterm.

As a second step, a Cox model with only one dummy variable representing the 'period effect' for 1991 and 1997 (reference: 1991) was created. Next, all potential determinants revealed by the first step were sequentially added to the crude 'period effect' model to determine whether temporal changes in maternal sociodemographic characteristics or in medical or life-style risk factors contributed to the decrease in fetal death hazard. Impact on the 'period effect' from all the concomitant changes was represented by changes in point estimate for the period term.

Unfortunately, data limitations of the U.S. vital statistics prevented us from using the same approach to evaluate the effect of induction of labor. As mentioned in Chapter 3, Section

3.1.1.1, the live birth and fetal death files contain boxes to be checked for the use of all obstetric procedures, including induction of labor. However, no data are available on the time sequence for FD and induction of labor. This leads to a 'reverse causality' problem. In clinical practice, almost all antepartum FDs (representing more than 85% of total FDs) are delivered by induction. Under such circumstances, the outcome does not, as usual, follow the obstetric intervention; instead, intervention follows the outcome. It is therefore impossible to use individual-level data to analyze the effect of labor induction on fetal death risk.

Another limitation is that no information is available on indication for labor induction, which therefore prevents adjustment for confounding by indication. Specifically, indications (such as diabetes, chronic hypertension or PIH) may be associated with FD but do not lie on the causal pathway between induction and FD. Without controlling for these variables, it is difficult to determine the causal effect of induction of labor on FD, as these confounding variables may be unevenly distributed between those induced and those not induced. This has strongly affected those pregnancies between 37 and 40 weeks but probably not those ending at 41 weeks or above, as one can predict that at this stage there are perhaps more elective labor inductions, simply because of postterm gestation (Maternal-Fetal Medicine: 4th edition, 1999).

One alternative is group-level analysis, namely, an ecologic level study with Poisson regression. To this end, the data are reconstructed by using % to represent the use of induction of labor over time and across geographic regions. The effect of confounding by indication at the individual-level may not appear at the ecologic level (Greenland et al, 1989; 1994; Wen et al, 1999). This premise depends on whether, over time and across regions, the distribution in use of induction of labor is associated with the joint distributions of various indications (for intervention), such as premature rupture of membrane, IUGR, or diabetes. It is unlikely, however, that the marked increase in labor induction as reported by NCHS (see Chapter 2, Section 2.4.4) is due to large increases in the incidence of maternal medical conditions and/or pregnancy-related complications that led to the use of this intervention. Rather, the increase is likely due to a more liberal application of this

procedure (i.e., to reduce the incidence of postterm pregnancies), or to increased recording. Moreover, with an ecologic approach, the 'reverse causality' problem can be avoided because the grouped (%) data do not necessarily reflect the individual-level time sequence between exposure and outcome. Note that labor induction due to FD represents only a very small proportion of total induction use, our ecologic analysis should not be affected by such a 'noise' that in states with higher frequency of FDs would also have more labor inductions.

Ecologic analysis using Poisson regression has been widely recognized as an appropriate choice in analyzing geographic variations and time trends in studies of the incidence of rare events (Kuhn et al, 1994). However, the 'ecologic fallacy'-- a source of special bias that derives from lack of direct linkages among the exposure of interest, covariates, and outcome at the individual-level, can prevent inference of an effect found at the group-level to the individual-level (Piantadosi et al, 1988, 1994; Greenland et al, 1989, 1994). Specifically, when the analysis of the effect is based on the rate of labor induction in each individual state, a state-level effect, if revealed, implies only that an increased use of this obstetric procedure is associated with a decreased fetal death hazard at the state level. Yet, we cannot therefore conclude that induction of labor prevent FD, as the induction rate alone cannot specify which women did or did not experience labor induction, nor whether women whose labor was induced did or did not experience a FD. Perhaps, a decrease in fetal death hazard in individual states is due to other contemporaneous changes (e.g., decrease in maternal cigarette smoking), despite of the increased use of labor induction in these states. It may therefore be good practice to conduct both individual- and group-level analyses. The basic idea is to use the Cox proportional hazards model to evaluate and adjust for contemporaneous changes in all individual-level covariates, and to evaluate the impact of induction of labor on the 'period effect' (1997 vs 1991) at the ecologic (state)-level (%). Using a combined approach may not necessarily eliminate the problem of 'ecologic fallacy' but should help increase the robustness of our findings.

Briefly, for these analyses, three main modelling strategies were applied. First, the Cox proportional hazards model was used to identify and quantify determinants for FD. Second, a crude Cox regression model was created to specifically estimate the 'period effect', and

was then sequentially adjusted for all individual-level covariates to estimate their impact on the 'period effect'. The Cox model analyses were applied to the restricted sample (the 39 states and D.C.) because of more complete data in that sample (see Chapter 3, Section 3.1.2.3). Third, a Poisson regression model was created with an indicator variable for individual states, a binary variable for fetal sex, and a period term using 1991 as the reference. The Poisson model analyses were applied to the 49 states and D.C. (as mentioned in Chapter 3, Section 3.1.2.3, Ilinois was excluded because of the high missing rate for induction). The dataset was stratified according to state (plus D.C., 50 categories), birth year (1991 vs 1997), and fetal sex to create 50 x 2 x 2 = 200 strata. Impact on the period effect from induction of labor is represented by the change in point estimate for the period term, before and after adjustment for labor induction.

3.2.2.2 Data manipulation

For these analyses, subjects were further divided into high- vs low-risk pregnancies. As in previous study (Hannah et al, 1992), low-risk pregnancies were defined as maternal age 20-34 years and absence of diabetes, chronic hypertension, and pregnancy-induced hypertension; high-risk pregnancies were defined as maternal age <20 or >=35 years and/or presence of any of the above chronic conditions. Because of the specific interest in postterm induction, modelling analyses focused on pregnancies ending between 40 to 43 weeks in gestation, and were applied separately to high- and low-risk pregnancies in non-Hispanic Whites and Blacks.

3.2.2.3 Model specification

3.2.2.3.1 Cox proportional hazard model

In survival analysis, the choice of a time variable largely depends on whether it has strong effect on the hazard (Korn et al, 1997). We have such time variables as calendar time (year), time on study, and age. In mortality study, age is often used as the time variable for survival analysis. By definition, GA is the time interval between a woman's LMP and the

end of pregnancy. It measures the *in utero* survival time of an individual fetus. As reported, the fetal death hazard increases exponentially as GA advances (Yudkin et al, 1987). Interestingly, this is quite similar to the effect of age on the incidence of death (i.e., adults), wherein age is used as the time variable in the survival analysis of human life. Likewise, in the survival analysis of fetal life, GA is a natural time scale for modeling the fetal death hazard.

To test the proportional hazards assumption, two alternative approaches were used. First, the consistency of hazard ratios across each GA week [for example, from 40 to 43 weeks (HRw40, HRw41, HRw42, HRw43)] was examined. The regression analysis (with exactly the same original risk factors in each model) was repeated at each GA week. In particular, at 40 weeks, the dataset includes subjects who were at risk for FD at 40 weeks (no censoring, no death). The outcome was designated as 1 = FD occurred through 40 weeks; 0 = no FD or FD occurred after 40 weeks. Then, at 41 weeks, the dataset excludes all fetuses who died or were live-born at 40 weeks. The analysis was similarly repeated at 42 and 43 weeks. Finally, the estimated hazard ratios for each risk factor were compared across each GA week. If all point estimates are similar, then the proportional hazards assumption holds. As a second approach, we tested the proportionality on all covariates at once using test statement in the Cox model (in SAS), in which an interaction term, e.g., X*GA was created for each covariate X in the model. If any of the interaction terms are statistically significant, then those hazards are not proportional.

In this study, ties refer to the simultaneous occurrence of two or more deaths at a given GA. In the Cox model analyses (in SAS), ties can be dealt with by the following four methods (Ties= option): Breslow, Efron, Discrete and Exact. If there are no ties, all four methods produce identical parameter estimates. The Breslow method using the approximate likelihood of Breslow (1974) is the most efficient, when the sample size is large (i.e., less computationally intensive). However, when there are many ties, this approach can give biased estimates. The exact method computes the exact conditional likelihood under the proportional hazards assumption. This method, however, requires considerable computer resources. The discrete method is often applied when the time scale is discrete. This is

likely the case in our analysis since GA (week) is fairly discrete. However, this method is also extremely computationally intensive. The Efron method is another approximation (Efron B, 1977), which provides results that are much closer to the exact method results than does the Breslow approximation. In our analysis, the Breslow method is not an appropriate choice because of many ties at each GA. The Efron method is preferred, since the other two are computationally intensive (in both cases, there were insufficient computer resources in actual performance). Therefore, in this analysis, we have used the Efron method, but have examined the possible bias in parameter estimates by using different methods in a small random sample.

No automated model selection procedures (either stepwise or backward) were applied, as these selection procedures are based on statistical significance testing (P values); a confounding effect is not determined by statistical significance level. Specifically, in this analysis, no variable was removed from the model due simply to statistical nonsignificance (P >0.05). The determinants in the final model included maternal age (<20, 20-34, >=35 years), race (White vs Black), educational attainment (=<12 vs >12 completed years), unmarried status, nulliparity, fetal gender, maternal cigarette smoking (yes or no), onset of prenatal care during the 1st-trimester (yes or no), and presence vs absence of maternal medical conditions (diabetes, chronic hypertension, or PIH). These determinants were then sequentially added to the crude model with only a 'period term' (1997 vs 1991) to estimate the impact of each variable on the change in fetal death risk over time. Other pregnancy outcomes (e.g., IUGR, lethal congenital anomalies) and/or complications (e.g., premature rupture of membrane, abruptio placentae) are believed to be on the causal pathway between risk factors and FD (i.e., prior to or simultaneous with the occurrence of FD). However, many are indications or contraindications for labor induction. These variables therefore have not been included in the regression model.

Indications and contraindications for induction of labor, as recommended by the American College of Obstetricians and Gynecologists (ACOG) in 1991 are as follows. Indications include 1) pregnancy-induced hypertension; 2) premature rupture of membranes; 3) chorioamnionitis; 4) suspected fetal jeopardy, e.g. fetal growth restriction or

isoimmunization; 5) maternal medical problems, e.g. diabetes mellitus, renal disease, chronic hypertension, or chronic obstructive pulmonary disease; 6) fetal demise; 7) logistic factors, e.g. risk of rapid labor or long distance from hospital; and 8) postterm gestation. Contraindications include 1) placenta or vasa previa; 2) abnormal fetal lie; 3) cord presentation; 4) presenting part above the pelvic inlet; 5) prior classical uterine incision; 6) active genital herpes infection; 7) pelvic structural deformities; and 8) invasive cervical carcinoma.

3.2.2.3.2 Poisson regression model

Poisson regression has often been used to examine geographic variation and time trends in ecologic studies (Kuhn et al, 1994). When the expected binomial count is rare relative to the population size, the Poisson distribution provides a good approximation to the binomial distribution. In this regard, using Poisson regression to analyze the effect of induction of labor on FD at the ecologic (state)-level is appropriate, since FD is an extremely uncommon event relative to the total number of pregnancies (<1%).

Predictor variables in the Poisson regression model included an indicator variable for the 49 individual states and D.C. (50 categories), birth year (2 categories) and fetal gender (2 categories). For this ecologic analysis, the unit of analysis is the individual state. Fetal gender is included to create more units of analysis (lines of data). The data stratification therefore yielded a total of 50 x 2 x 2 = 200 lines of data. The dependent (outcome) variable is FD count in each stratum defined by a set of covariates (state, birth year, and fetal gender). The crude period effect models were first generated using an indicator variable for 1991 (reference) and 1997, and then were adjusted by adding induction of labor (%) to the crude model:

$$\log (Y) = ß0 + ß1 \text{ (state)} + ß2 \text{ (fetal gender)} + ß3 \text{ (year)} + ß4 \text{ (induction)} + \log (N)$$

In this case, Y is the count of the number of deaths occurring in each state in each year and in each fetal gender group. N is the amount of person-time (weeks) ongoing pregnancies at

risk. This amount was calculated by adding, for example, the number of births at 40 weeks + the number of births at 41 weeks multiplied by 2 + the number of births at 42 weeks multiplied by 3, for the analysis restricted to 40-43 weeks (i.e., for our interest of the effect of routine induction in the postterm period). The multiplier is the number of weeks of follow-up, i.e., those pregnancies that ended at 41 weeks therefore are followed by two completed weeks since the beginning of 40 weeks GA. The goodness of fit of the Poisson regression model was assessed using deviance statistics, with appropriate degrees of freedom. The deviance is a measure of the discrepancy between observed and fitted values, and a comparison of it with its degrees of freedom provides a measure of goodness of fit.

Chapter 4. RESULTS

4.1 Description of Data

Tables 1 and 2 show the total number and percentage of live births and fetal deaths at 20-36 and 37-43 weeks, separately for Whites and Blacks, in the full sample (50 states and D.C.) and the restricted sample (39 states and D.C.) after deletion of improbable GA records. In the two samples, a similar pattern of change was observed in the proportion of live births and fetal deaths before and after term between 1991 and 1997. In the 50 states and D.C., the total number of live births decreased during the study period, as did the total number of fetal deaths (for both Whites and Blacks). Among Whites, about 8% of total live births were preterm, while in Blacks this proportion was nearly 18% in 1991. In both races, the majority of FDs occurred before 37 weeks (70% in Whites; 83% in Blacks).

Table 1. Number and percentage of live births and fetal deaths, Whites and Blacks, 50 States and D.C., after deletion of improbable GA records

	1991				1997			
Whites								
GA (weeks)	Live births	(%)	Fetal deaths	(%)	Live births	(%)	Fetal deaths	(%)
20-36	244,595	(8.1)	10,498	(70.2)	251,697	(8.7)	9,894	(74.3)
37-43	2,788,280	(91.9)	4,465	(29.8)	2,633,435	(91.3)	3,415	(25.7)
Total	3,032,875		14,963		2,885,132		13,309	
Blacks								
GA (weeks)	Live births	(%)	Fetal deaths	(%)	Live births	(%)	Fetal deaths	(%)
20-36	110,303	(17.5)	5,329	(82.8)	88,907	(15.9)	4,824	(83.5)
37-43	520,876	(82.5)	1104	(17.2)	471,409	(84.1)	956	(16.5)
Total	631,179		6,433		560,316		5,780	

Table 2. Number and percentage of live births and fetal deaths, Whites and Blacks, 39 States and D.C., after deletion of improbable GA records

	1991				1997			
Whites								
GA (weeks)	Live births	(%)	Fetal deaths	(%)	Live births	(%)	Fetal deaths	(%)
20-36	136,059	(8.0)	6,059	(70.9)	145,216	(8.7)	5,838	(74.1)
37-43	1,570,596	(92.0)	2,491	(29.1)	1,522,345	(91.3)	2,041	(25.9)
Total	1,706,655		8,550		1,667,561		7,879	
Blacks								
GA (weeks)	Live births	(%)	Fetal deaths	(%)	Live births	(%)	Fetal deaths	(%)
20-36	67,722	(17.9)	3,504	(83.8)	54,962	(16.2)	3,118	(84.3)
37-43	310,384	(82.1)	680	(16.3)	284,061	(83.8)	579	(15.7)
Total	378,106		4,184		339,013		3,697	

4.1.1 Comparison of full sample and restricted sample

The frequency distribution of maternal sociodemographic characteristics was similar between the total 50 states and the restricted 39 states (Table 3). The percentage of mothers >=35 years of age was slightly higher in the full sample than in the restricted sample. However, from 1991 to 1997, a marked increase in maternal age >=35 years was observed in both samples (from 9.1 to 12.3 in the 50 states and from 8.6 to 11.8 in the 39 states). The percentage of mothers with less than high school education was slightly higher in the 50 states than in the 39 states. However, marked decreases in low maternal educational attainment (<=12 completed years) were observed in both samples. The proportion of mothers with unmarried status was much higher in 1997 than in 1991 both in the 50 states and the 39 states.

From 1991 to 1997, the use of obstetric procedures increased both in the 50 states and in the 39 states (Table 4). The magnitude of the increase was nearly identical in the two samples, despite the slightly higher prevalence in the restricted sample. During the 6-year period, labor induction increased by more than 70% in both samples, which is the most significant among the four obstetric procedures. The second largest increase is in stimulation of labor (about 40%). EFM and ultrasound also increased but not as substantially as the increase in labor induction and stimulation.

Table 3. **Frequency distribution of maternal sociodemographic chracteristics: 50 States and 39 States (District of Columbia included), 1991 vs 1997**

	1991		1997	
	50 States	**39 States**	**50 States**	**39 States**
Characteristics (%)	n=3,177,194	n=1,908,417	n=3,287,665	n=1,904,670
Maternal age (yrs)				
<=19	13	13.3	12.9	13
20-34	77.9	78.1	74.8	75.3
>= 35	9.1	8.6	12.3	11.8
Education (yrs)				
0~8	6.4	3.4	5.9	3.8
9~12	54.9	56.6	49.3	49.3
13~15	20.8	21.7	22.4	23.5
>=16	17.9	18.3	22.5	23.4
Marital status				
married	70.9	71.4	67.8	68.4
unmarried	29.1	28.6	32.2	31.6
Race				
White	83.3	81.7	84.2	83.4
Black	16.7	18.4	15.8	16.6

Table 4. **Frequency distribution of obstetric procedures: 50 States and 39 States (District of Columbia included, 1991 vs 1997**

	1991		1997	
Reported Use (%)	**50 States** n=3,177,194	**39 States** n=1,908,417	**50 States** n=3,287,665	**39 States** n=1,904,670
EFM				
yes	75.4	79.6	83.9	86.4
no	24.6	20.4	16.1	13.6
Induction				
yes	10.8	12.3	19.2	20.8
no	89.2	87.7	80.9	79.2
Stimulation				
yes	12.2	12.9	17.9	18.1
no	87.8	87.1	82.1	81.9
Ultrasound				
yes	56.6	62.1	65.1	68.5
no	43.4	37.9	34.9	31.5

EFM = electronic fetal monitoring

Table 5 shows that the frequency distribution of onset of prenatal care, parity, cigarette smoking, and maternal medical conditions (diabetes, chronic hypertension and PIH) was roughly identical between the restricted and full samples. The proportion of women whose onset of prenatal care occurred during the 1st-trimester increased, whereas the rate of cigarette smoking decreased during the study period. No temporal change was observed in the prevalence of nulliparity, diabetes, chronic hypertension and PIH. Note that the proportion of unknown data on cigarette smoking and/or alcohol consumption was extremely high in the 50 states.

When generating the frequency distributions (Tables 3 to 5), records with unknown data on other variables were deleted, except for cigarette smoking (9 states with no data collection on cigarette smoking). The results presented in these Tables are only for Whites (non-Hispanic) and Blacks combined. All other ethnicities were excluded.

Table 5. **Frequency distribution of maternal medical and life-style risk factors: 50 States and 39 States (District of Columbia included), 1991 vs 1997**

	1991		1997	
	50 States	**39 States**	**50 States**	**39 States**
Risk Factor (%)	n=3,177,194	n=1,908,417	n=3,287,665	n=1,904,670
Onset of prenatal care				
none	1.6	1.3	1.1	1
1st	77.1	78.8	83.1	84
2nd	17.6	16.6	13.2	12.6
3rd	3.7	3.3	2.6	2.4
Parity				
1	33.4	33	33.4	33.4
>=2	66.6	67	66.6	66.6
Cigarette smoking				
yes	13.3	18.8	10.9	14.9
no	60.7	81.2	70.3	85.2
unknown	26.1	0	18.9	0
Diabetes				
yes	2.3	2.4	2.5	2.7
no	97.7	97.6	97.5	97.4
Chronic hypertension				
yes	0.7	0.7	0.7	0.8
no	99.4	99.3	99.3	99.2
PIH				
yes	2.7	3	3.7	4
no	97.3	97	96.4	96
Other diseases*				
yes	3.3	3.5	4.2	4.2
no	96.7	96.6	95.8	95.8

PIH = pregnancy-induced hypertension

*Other diseases include anaemia (HCT.<30/Hgb.<10), cardiac diseases, acute or chronic lung diseases, renal diseases, and Rh sensitization

4.1.2 Comparison of U.S. Whites and U.S. Blacks

The descriptive analysis was also carried out in Whites and Blacks, separately (39 states and D.C.). We observed a significantly higher proportion of teenage mothers among Blacks than in Whites (25 vs 11%). In contrast, a higher percentage of White mothers were >=35 years old. The proportion of maternal educational attainment <=12 years was higher in Blacks than in Whites, and the percentage of unmarried mothers was also higher in Blacks. The proportion of mothers whose onset of prenatal care occurred during the 1st-trimester was higher in Whites than in Blacks. Yet, Black mothers had a lower prevalence of cigarette smoking.

Over time, in both Whites and Blacks, the prevalence of advanced maternal age (>=35 years) and 1st-trimester prenatal care increased, whereas the frequency of maternal cigarette smoking and educational attainment <=12 years decreased. No temporal change was observed in other risk factors such as diabetes, chronic hypertension and PIH (see Tables 6 and 7).

Table 6. **Frequency distribution of maternal sociodemographic characteristics: Whites and Blacks, 1991 vs 1997**

	1991		1997	
	Whites	**Blacks**	**Whites**	**Blacks**
Characteristics (%)	1,558,275	350,142	1,587,740	316,930
Maternal age (yrs)				
<=19	10.8	24.6	10.9	23.6
20-34	80	69.6	76.7	68.3
>= 35	9.2	5.8	12.5	8.1
Education (yrs)				
0~8	3.4	3.7	3.9	3
9~12	53.4	70.9	46.3	64.7
13~15	22.4	18.5	23.8	22.4
>=16	20.9	6.9	26.1	9.9
Marital status				
married	80.6	30.5	76.1	29.8
unmarried	19.4	69.5	23.9	70.2

Table 7. **Frequency distribution of maternal medical and life-style risk factors: Whites and Blacks, 1991 vs 1997**

	1991		1997	
	Whites	**Blacks**	**Whites**	**Blacks**
Risk Factor (%)	1,558,275	350,142	1,587,740	316,930
Onset of prenatal care				
none	0.8	3.6	0.7	2.4
1st	82.6	61.9	86.4	72.2
2nd	14	28.2	10.9	20.8
3rd	2.7	6.3	2	4.5
Parity				
1	33.7	29.7	33.8	31
>=2	66.3	70.3	66.2	69
Cigarette smoking				
yes	19.7	14.8	15.8	10.1
no	80.3	85.2	84.2	89.9
Diabetes				
yes	2.5	2.1	2.7	2.5
no	97.5	98	97.3	97.5
Chronic hypertension				
yes	0.6	1.1	0.7	1.3
no	99.4	98.9	99.3	98.7
PIH				
yes	3	2.9	4	4.1
no	97	97.1	96	95.9
Other diseases*				
yes	3.2	4.6	4	5.3
no	96.8	95.4	96	94.7

PIH = pregnancy-induced hypertension

*Other diseases include anaemia (HCT.<30/Hgb.<10), cardiac diseases, acute or chronic lung diseases, renal diseases, and Rh sensitization

Table 8 shows the significant racial disparities between Whites and Blacks in the use of obstetric procedures, and their temporal changes during the 6-year period. Labor induction was used in 13% of White mothers in 1991 vs about 8% in Blacks. In 1997, this percentage increased to 22 and 15% for Whites and Blacks, respectively. The magnitude of increase was similar in both racial groups. Consequently, the racial gap in this obstetric procedure remained nearly unchanged (about 50% lower in Blacks than in Whites). Similar racial disparities were also observed in EFM, stimulation of labor and ultrasound. However, the magnitude of difference in labor induction is the most pronounced. By stratification, this difference was further demonstrated according to GA (see Section 4.1.3).

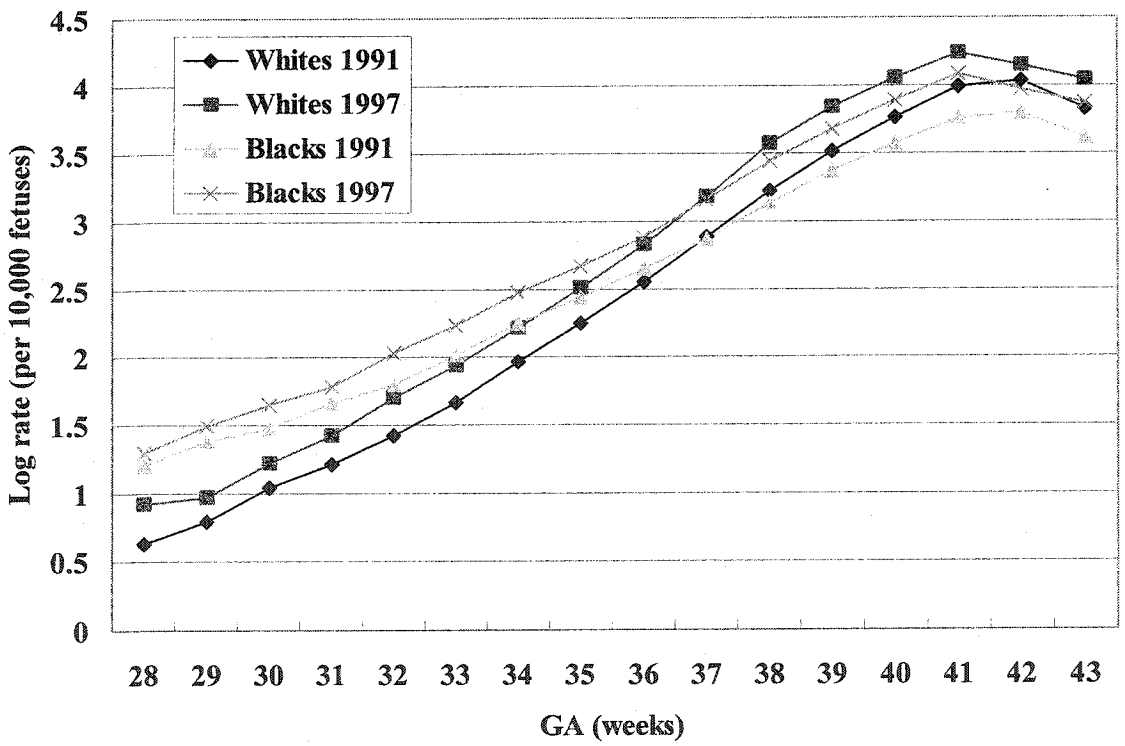
Table 8. **Percentage of obstetric procedures: Whites and Blacks, 1991 vs 1997**

	1991		1997	
	Whites	**Blacks**	**Whites**	**Blacks**
Reported Use (%)	1,558,275	350,142	1,587,740	316,930
EFM				
yes	80.5	75.9	86.6	85.4
no	19.5	24.1	13.4	14.6
Induction				
yes	13.2	8.3	22	14.9
no	86.8	91.7	78	85.1
Stimulation				
yes	13.3	11.2	18.4	16.9
no	86.7	88.9	81.6	83.1
Ultrasound				
yes	63.7	54.7	69.7	62.5
no	36.3	45.3	30.3	37.5

4.1.3 Rate of induction of labor by GA in the 39 states and D.C., Whites and Blacks, 1997 vs 1991

Figure 1 summarizes the changes in use of labor induction over time and across GA (28 to 43 weeks) and the differences between Whites and Blacks. For both Whites and Blacks, there was a greater increase at 37-41 weeks than at 28-36 weeks. For both races in 1991, the highest rate of induction was at 42 weeks, whereas in 1997 the highest rate occurred at 41 weeks, suggesting not only that induction of labor was used more frequently but also that it was used earlier. For both Whites and Blacks, the rate of labor induction increased as GA advanced from 28 to 41 weeks. However, at 28-36 weeks, the induction rate was lower in Whites than in Blacks, whereas after 37 weeks it was higher in Whites than in Blacks.

Figure 1. Induction of labor at each completed week of gestation



4.1.4 Frequency of total live births by GA in the 39 states and D.C., Whites and Blacks, 1997 vs 1991

Figures 2 and 3 show the changes in GA distribution between 1991 and 1997 in Whites and Blacks. The proportion of total live births at 40-43 weeks decreased in Whites, whereas it increased at 36-39 weeks. In Blacks, however, a decrease was observed both at 33-36 weeks and at 41-43 weeks, while an increase was seen at 37-40 weeks. In Whites, a significant shift toward lower GAs was observed; in 1991, the largest proportion of births occurred at 40 weeks, whereas in 1997, the largest proportion of births was at 39 weeks (Figure 2). In Blacks, however, no such shift was observed in the GA distribution of total live births (Figure 3).

Figure 2. GA distribution in Whites, 1997 vs 1991

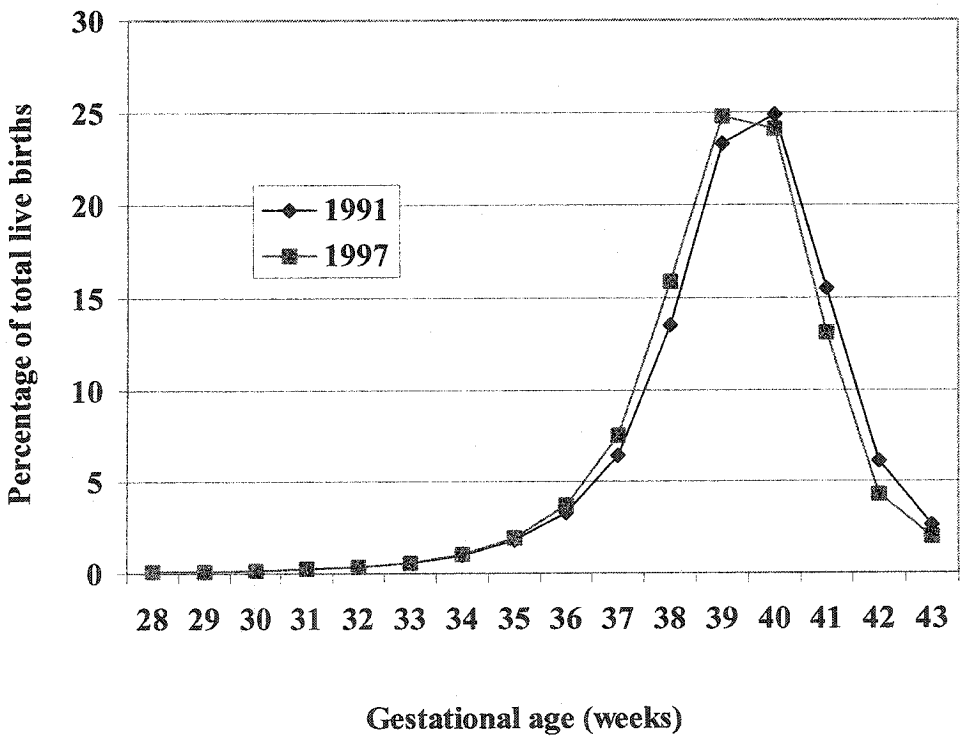
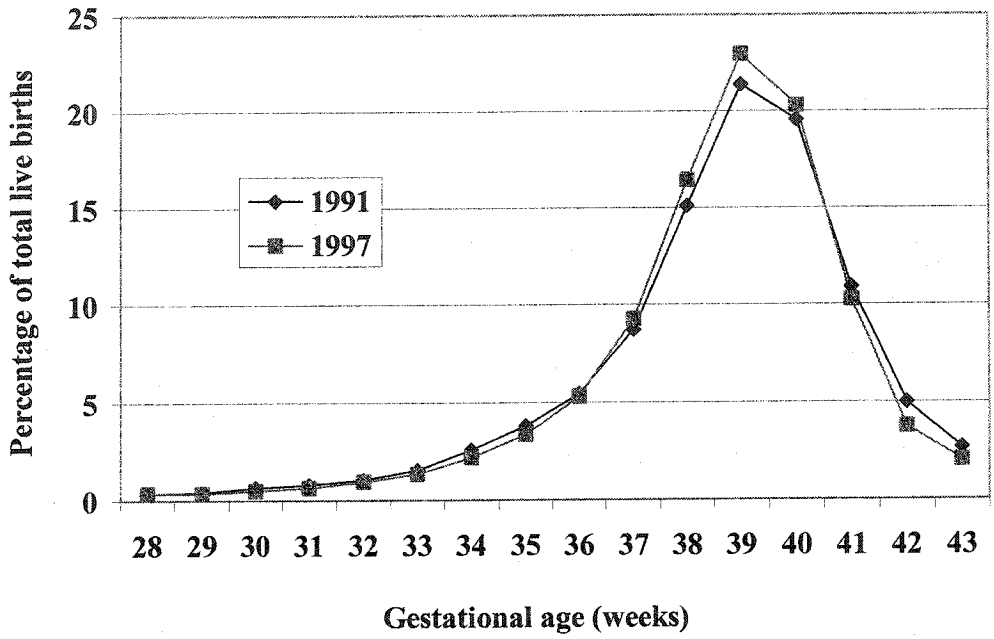


Figure 3. GA distribution in Blacks, 1997 vs 1991



4.1.5 Crude fetal death risk

Table 9 shows that a significantly higher risk of FD occurred among mothers who were < 20 or >=35 years of age, had education attainment <=12 complete years, or were unmarried or of Black race. A trend was observed in FD risk by educational attainment; the lower in educational level, the higher in risk.

Table 10 shows that women who began prenatal care during the 1st-trimester were at significantly lower risk for FD compared with those who began in the 2nd - or 3rd-trimester. It seems that nulliparity imposed no higher risk of FD (compared with parity >=2). Maternal cigarette smoking during pregnancy increased the risk of FD. Maternal diseases such as diabetes, chronic hypertension and PIH showed strong associations with FD. We also observed marginal female excess in FD in both years. No significant temporal changes

in the effect were observed between 1991 and 1997, except for PIH (decreased) and cigarette smoking (increased). The crude analysis of fetal death risk was performed in the 39 states and D.C.

Table 9. Crude fetal death risk by maternal sociodemographic characteristics

	1991			1997		
Characteristic (%)	**Risk/10,00**	**RR**	**95% CI**	**Risk/10,00**	**RR**	**95% CI**
Maternal age (yrs)						
<=19	31.33	1.21	1.12-1.30	30.65	1.33	1.23-1.44
20-34	25.99	1	(reference)	22.97	1	(reference)
>=35	39.55	1.52	1.40-1.65	32.38	1.41	1.30-1,53
Education (yrs)						
0~8	35.08	1.77	1.53-2.03	32.64	1.97	1.70-2.25
9~12	31.93	1.61	1.49-1.75	30.33	1.83	1.68-1.98
13~15	22.9	1.16	1.05-1.24	21.26	1.28	1.16-1.38
>=16	19.8	1	(reference)	16.6	1	(reference)
Marital status						
unmarried	33.35	1.55	1.47-1.65	31.26	1.53	1.44-1.62
married	21.47	1	(reference)	20.41	1	(reference)
Race						
Black	41.3	1.66	1.56-1.77	38.18	1.7	1.59-1.81
White	24.85	1	(reference)	22.46	1	(reference)

RR = Risk ratio
CI = confidence interval

Table 10. Crude fetal death risk by maternal medical and life-style risk factors, 1991 and 1997

	1991			1997		
	Risk/10,000	RR	95%CI	Risk/10,000	RR	95%CI
Risk Factor (%)						
Onset of prenatal care						
1st (trimester)	25.58	0.7	0.66-0.75	23.2	0.66	0.62-0.71
2nd or 3rd	36.39	1	(reference)	34.92	1	(reference)
Parity						
1	28.17	1.02	0.96-1.08	25.49	1.02	0.97-1.09
>=2	27.72	1	(reference)	24.87	1	(reference)
Fetal gender						
male	27.55	0.98	0.93-1.03	24.26	0.94	0.89-0.99
female	28.17	1	(reference)	25.85	1	(reference)
Cigarette smoking						
yes	36.8	1.43	1.34-1.52	39.17	1.73	1.62-1.85
no	25.8	1	(reference)	22.62	1	(reference)
Diabetes						
yes	56.32	2.07	1.83-2.35	51.02	2.09	1.85-2.37
no	27.17	1	(reference)	24.37	1	(reference)
Chronic hypertension						
yes	114.05	4.18	3.56-4.92	82.09	3.33	2.78-4.00
no	27.26	1	(reference)	24.64	1	(reference)
PIH						
yes	53.96	1.99	1.78-2.24	37.18	1.51	1.34-1.71
no	27.06	1	(reference)	24.57	1	(reference)
Other diseases*						
yes	43.4	1.59	1.41-1.79	34.1	1.38	1.22-1.56
no	27.31	1	(reference)	24.68	1	(reference)

RR = Risk ratio
CI = confidence interval
PIH = pregnancy-induced hypertension
*Other diseases include anaemia (HCT.<30/Hgb.<10), cardiac diseases, acute or chronic lung diseases, renal diseases, and Rh sensitization

4.2 Fetal death hazard

4.2.1 50 states (with D.C.) and 39 states (with D.C.)

The fetal death hazard for the 50 states (with D.C.) was calculated, before and after deletion of improbable GAs (see Appendix Figures a.2 and a.3, respectively). The results show that the fetal death risk was relatively high at the low and high end of the GA distribution (20-43 weeks) but much higher at 41 weeks and above. In between, however, the hazard curve was relatively flat, and the risk remained at a low level of about 2 per 10,000 ongoing pregnancies from 25 to 35 weeks.

At 20-22 weeks, the fetal death hazard was significantly higher in 1997 than in 1991, whereas from 37 to 43, it was much lower. In examining the changes in the fetal death hazard by GA, it was found that in 1991, the risk increased after 37 weeks and reached the highest level at 43 weeks. In contrast, in 1997, the hazard decreased from 40 to 43 weeks, and at 43 weeks, it was about 5 per 10,000 ongoing pregnancies, compared with 8 per 10,000 in 1991, a relative decrease of 40 percent (see Appendix Figure a.3).

Using the same approach, the fetal death hazard for the 39 restricted states was calculated before and after deletion of improbable GAs in 1991 vs 1997 (see Appendix Figures a.4 and a.5). The changes in the fetal death hazard at 20-22 and 40-43 weeks observed in the 39 restricted states (plus D.C.) were similar to those in the 50 states (plus D.C.), although the magnitude of decrease at 40-43 weeks was slightly smaller in the 39 states.

After deletion of improbable GAs, the hazards at early GAs (20-24 weeks) were reduced substantially in the 39 states (as they were in the 50 states). Deletion of improbable GAs did not alter the overall GA patterns in the fetal death hazard, but it markedly lowered the hazard at 20-24 weeks, suggesting that reported GA estimates near the borderline of viability are often incorrect.

4.2.2 Whites vs Blacks

The fetal death hazard was computed separately for Whites and Blacks in the 50 states and D.C. (Figure 4); the hazards were higher in Blacks than in Whites throughout the entire GA range. For example, at 20-22 weeks, the hazard was nearly 3-fold higher in Blacks than in Whites. From 23 to 37 weeks, the hazard remained 2-fold higher in Blacks. Between 1991 and 1997, for both Whites and Blacks, a significant increase in fetal death hazard was observed at 20-22 weeks of gestation. On the other hand, a marked decrease was observed from 40 to 43 weeks in Whites. Such a decrease appears increasingly large as GA advances. However, for Blacks, a significant decrease was seen only at 42 and 43 weeks. Surprisingly, there was an increase in risk, rather than a decrease, at 41 weeks, for Blacks. For Blacks, however, the changes in fetal death hazard from 23 to 41 weeks were highly unstable. A similar pattern was observed in the 39 restricted states (plus D.C.) in the changes between Whites and Blacks in fetal death hazard (Figure 5).

Figure 4. Fetal death hazard in Whites and Blacks, 50 states and D.C., 1997 vs 1991

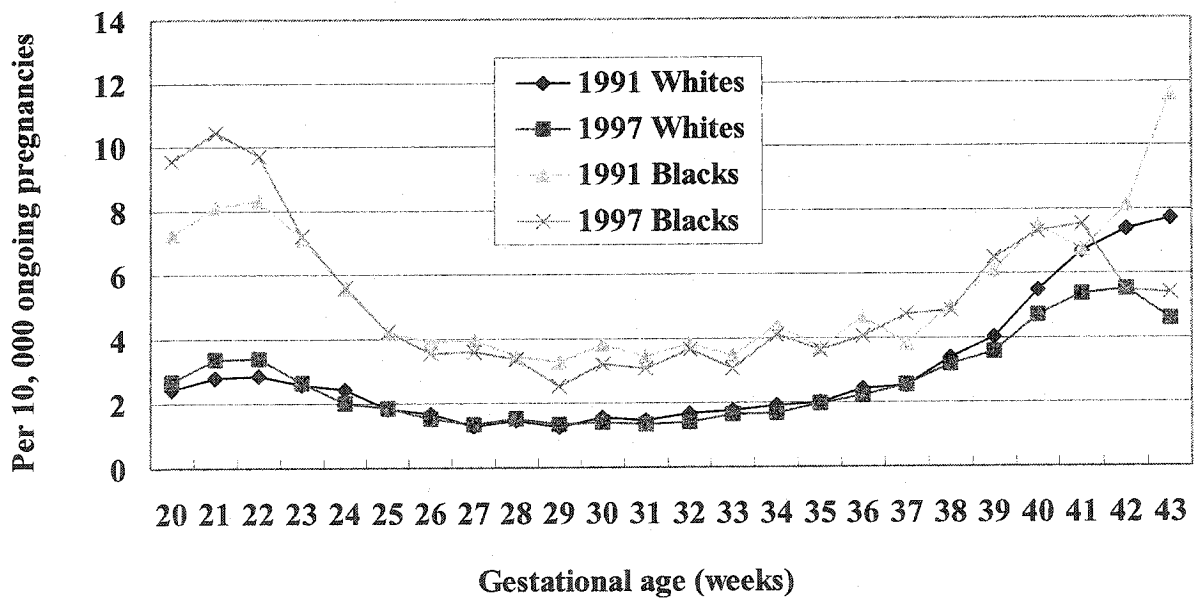
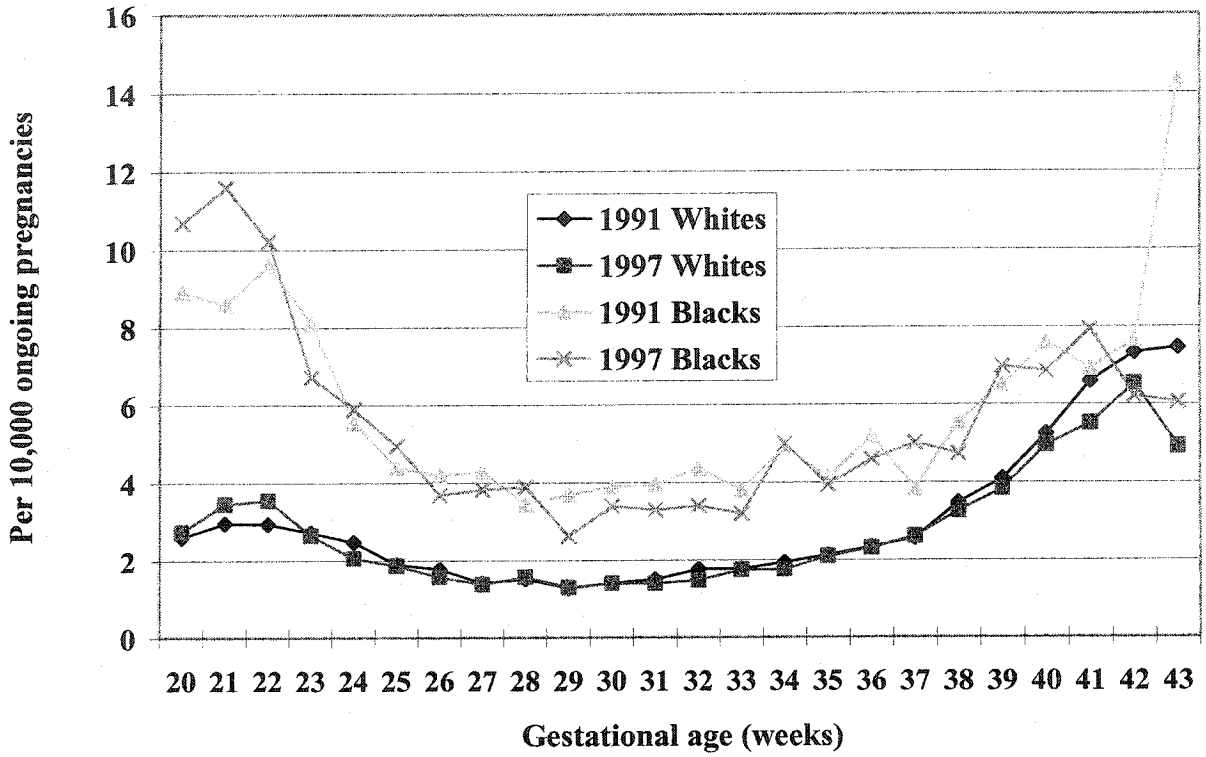


Figure 5. Fetal death hazard in Whites and Blacks, 39 States and D.C., 1997 vs 1991



4.3 Registration artifacts

4.3.1 50 states and D.C., all ethnicities

Table 11 shows the proportions of FDs in the 3 early GA categories (20-22, 23-25, and 26-28 weeks) relative to total births (all GAs) in the 50 states and D.C. From 1991 to 1997, the total number of live births decreased, as did the total number of fetal deaths. The overall fetal death rate fell from 77.7 (per 10,000 total births) in 1991 to 67.8 in 1997, a relative decrease of 14.6%, whereas fetal deaths at 20-22 weeks as a proportion of total births (live births and stillbirths >=20 weeks) increased from 14.5 to 16.9 (per 10,000 total births), a relative increase of 17% (reference: 1991, RR: 1.17; 95% CI: 1.12-1.21). Other early GA categories, however, did not show a similar increase. In fact, there were slight but statistically significant decreases at 23-25 and 26-28 weeks.

Table 11. Fetal deaths in the three early GA categories as a proportion* of total births, 50 States and D.C., all ethnicities

GA (weeks)	1991	1997	RR (reference: 1991)	95% CI
20-22	14.52	16.94	1.17	1.12-1.21
23-25	10.49	10.06	0.96	0.92-0.99
26-28	6.9	6.56	0.95	0.90-0.99
Total	77.57	67.8	0.87	0.86-0.88
Total fetal deaths	32,129	26,486		
Total births	4,141,862	3,906,295		

CI = confidence interval
RR = relative risk
*Proportions are expressed per 10,000 total births

Table 12. **Fetal deaths in the three early GA categories as a proportion* of perinatal deaths, 50 States and D.C., all ethnicities**

Gestational age (weeks)	1991	1997	RR (reference:1991)	95% CI
20-22	11.91	16.17	1.36	1.30-1.41
23-25	8.61	9.6	1.12	1.08-1.15
26-28	5.66	6.26	1.11	1.08-1.13
Total	63.63	64.71	1.02	1.00-1.04
unknown	7.71	2.7	0.35	0.34-0.36
Total fetal deaths	32,129	26,486		
Early neonatal deaths	18,362	14,435		
Perinatal deaths	50,491	40,933		

CI = confidence interval
RR = rate ratio
*Proportions are expressed per 100 perinatal deaths

Table 12 shows that FDs at 20-22 weeks as a proportion of perinatal deaths (fetal deaths + early neonatal deaths <7 days) increased from 11.9 to 16.2 percent, a 36% increase. An increase was also observed in the two other early GA categories, somewhat smaller but statistically significant (12 and 11% at 23-25 and 26-28 weeks, respectively). The total number of early neonatal deaths decreased from 18,362 to 14,435 during the period, while total FDs as a proportion of perinatal deaths increased by only 2% (95% CI: 1.00-1.04).

4.3.2 Whites vs Blacks

Appendix Tables a.1 and 2 show the 3 types of proportions separately for Whites and Blacks. FDs as a proportion of total births in the 3 early GA categories were about 2- to 3-fold higher in Blacks than in Whites in 1991 and 1997. For both races, a marked increase (from 1991 to 1997) was observed at 20-22 weeks. The relative increase was nearly 2 times as high for Blacks as for Whites (26 vs 14%). No increase was observed in the other two early GA categories.

For both races, the percentages of FDs at early GAs relative to perinatal deaths increased in almost all the 3 early GA categories (20-22, 23-25, and 26-28 weeks) from 1991 to 1997, while the relative increase was about 2- to 3-fold higher at 20-22 weeks than in the other two GA categories. Live births in the three early GA categories as a proportion of total births were about 3- to 4-fold higher in Blacks than in Whites in 1991 and 1997. Over time, this proportion decreased in Blacks but increased in Whites (slightly but statistically significantly in all the 3 early GA categories).

4.4 Analysis on risk factors of fetal death

4.4.1 Cox proportional hazards model analysis on risk factors of fetal death

In this study, a number of (risk or protective) factors were associated with FD in the United States (39 states and D.C.). The incidence of FD varied according to maternal age, with a significantly increased risk among mothers aged 35 years or older. Unmarried mothers had a slight but statistically significant increase in risk as well. An elevated risk was also seen among mothers who smoked during pregnancy. Maternal educational level at or under high school was associated with FD. Women with diabetes were at significantly increased risk, as were those with chronic hypertension or PIH. Early onset of prenatal care (during the 1st-trimester) was associated with a significantly lower risk.

As presented in Section 4.2.1, the fetal death risk remained relatively constant between 25 to 36 weeks, whereas it increased exponentially from 37 to 43 weeks. Because some risk

factors may have different impacts on FD at different GAs, separate analyses were performed for three distinct GA groups: 28-36 weeks, 37-40 weeks, and 41-43 weeks.

Appendix Tables a.3, 4, and 5 summarize the associations between various factors and FD (hazard ratios and their 95% CIs) in each of the three GA groups. Significant variations in the effect across GA were observed for several factors. The effect of maternal age >=35 years appeared increasingly strong as GA advanced; in particular, at 28 to 36 weeks, the HR was 1.23 (95% CI 1.15-1.30) but increased to 2.21 (95% CI 2.02-2.40) at 41 to 43 weeks. Maternal age <20 years showed a protective effect at 41-43 weeks (HR 0.71, 95% CI 0.50-0.92), whereas from 28 to 40 weeks, no such protective effect was observed. Conversely, nulliparity increased the risk for FD at 41 to 43 weeks (HR 1.28, 95% CI 1.08-1.57) but not =< 40 weeks. Maternal educational attainment =<12 years and unmarried status were both associated with an increased risk for FD at 37 to 43 weeks but not at 28-36 weeks. Maternal diabetes and PIH showed a much stronger effect at 37-43 weeks than at 28-36 weeks. Chronic hypertension demonstrated a strong impact throughout the entire GA range from 28 to 43 weeks. A reduced risk of FD among male fetuses was observed at 41-43 weeks (HR 0.85, 95% CI 0.72-0.98), whereas at 28-36 weeks, male and female fetuses had a similar risk. Blacks were at a significantly increased risk for FD as compared to Whites. Maternal cigarette smoking during pregnancy was associated with FD. Mother's onset of prenatal care during the 1st-trimester showed a protective effect in each GA group. However, the effects of maternal race, early prenatal care, and maternal cigarette smoking did not vary by GA. Clearly, most risk factors impacted on FD at >=37 weeks and had their strongest effect at 41 to 43 weeks, whereas few were associated with FD under 37 weeks.

4.4.2 Cox proportional hazards model analysis for period effect

Table 13 shows the results of the Cox proportional hazard model analyses of the crude and adjusted period effect (1997 vs 1991) at 40-43 weeks in the 39 states and D.C. In the crude model, only one dummy variable denoting the period effect was included. The crude period effect was 0.87 (95% CI 0.80-0.94), representing a 13% decrease in the fetal death hazard at 40 to 43 weeks (Whites and Blacks combined). As demonstrated in the descriptive analysis, the frequency of maternal age >=35 years, unmarried status, and 1st-trimester

onset of prenatal care increased over the study period, whereas the prevalence of maternal cigarette smoking and maternal education level <=12 years decreased. These are important contemporaneous changes that may have contributed to the decrease in fetal death hazard. As shown in Table 14, however, after sequentially adding these covariates into the crude model, the period effect remained virtually unchanged (HR 0.88, 95% CI 0.81-0.96), suggesting that the temporal changes in maternal sociodemographic characteristics, life style risk factors, and onset of prenatal care did not explain the observed decrease in fetal death hazard at 40 to 43 weeks in the United States. Table 14 also shows the change in period effect when each variable was added sequentially into the model.

Table 13. Cox proportional hazards model: 40-43 weeks, 39 States and D.C., crude and full adjusted period effect (1997 vs 1991)

	HR	**95% CI**
Crude	0.87	0.80-0.94
Adjusted	0.88	0.81-0.96
Maternal age (yrs)		
<20	0.83	0.72-2.26
>=35	2	1.76-2.26
Black race	1.29	1.14-1.45
Male gender	0.95	0.87-1.03
Maternal education <=12 yrs	1.12	1.02-1.24
Onset of 1st-trimester prenatal care	0.6	0.54-0.66
Unmarried status	0.98	0.88-1.09
Nulliparity	1.19	1.08-1.31
Cigarette smoking	1.3	1.17-1.45
Diabetes	2.23	1.81-2.75
Chronic hypertension	2.76	1.95-3.90
PIH	1.7	1.38-2.10

HR = hazard ratio
CI = confidence interval
PIH = pregnancy-induced hypertensio

Table 14. Cox proportional hazards model: 40-43 weeks, 39 States and D.C., crude and sequentially adjusted period effect (1997 vs 1991)

Variables	Period effect	95% CI
Crude HR	0.87	0.80-0.94
Plus maternal age (yrs)		
<20	0.87	0.80-0.94
>=35	0.85	0.78-0.92
Plus Black race	0.85	0.78-0.93
Plus fetal gender	0.85	0.78-0.93
Plus maternal education=<12 yrs	0.86	0.79-0.93
Plus onset of 1st-trimester prenatal care	0.88	0.80-0.96
Plus unmarried status	0.88	0.80-0.95
Plus nulliparity	0.88	0.80-0.95
Plus cigarette smoking	0.88	0.81-0.96
Plus diabetes	0.88	0.80-0.96
Plus chronic hypertension	0.88	0.81-0.96
Plus PIH	0.88	0.81-0.96

HR = hazard ratio
CI = confidence interval
PIH = pregnancy-induced hypertension

Appendix E shows the SAS output of testing proportional hazard assumption using the two alternative approaches (see Chapter 3, Section 3.2.2.3). By global testing (using the proportionality test statement in SAS), it was found that the effect of some variables (age, prenatal care and diabetes) varied by GA (statistically significant) from 28 to 36 weeks, whereas from 37 to 43 weeks the testing results are not significant. As our focus in these analyses is at 40-43 weeks, we specifically examined the effect of each variable at these GA weeks. It seems that the proportionality assumption roughly holds.

Appendix F shows the results of analyzing the effects of various determinants using a small sample with different approaches to handle ties (Exact, Discrete, Efron and Breslow). The Efron approximation produced results that are closer to the Exact method results than did the Breslow approximation. The differences in parameter estimates among the four approaches are small, however.

4.4.3 Poisson regression model analysis for the effect of induction of labor

Table 4 summarizes the results of the Poisson regression analysis of the ecologic- (state)-level effect of induction of labor on risk of fetal death at 40-43 weeks in Whites and Blacks (49 states and D.C.). Among Whites, the crude period effect (rate ratio, RR) for 1997 vs 1991 was 0.79 (95% CI 0.74-0.84). After adjusting for induction of labor, however, the period effect entirely disappeared (RR 0.98, 95% CI 0.82-1.16), suggesting that induction was responsible for the decrease. For White mothers, these results were similar among both risk strata. Among Blacks, the crude period effect was 0.76 (95% CI 0.67-0.87) and actually became slightly stronger (RR 0.67, 95% CI 0.50-0.88) after adjusting for induction of labor. In both racial/ethnic groups, confidence intervals widened after adjustment, as expected from the collinearity between year and induction at the state level.

Because in Blacks the reduction in fetal death risk was only observed at 42 and 43 weeks, we carried out a separate Poisson regression analysis restricted to these gestational ages. The results show that a crude period effect of 0.69 (95% CI 0.56-0.84) changed little (RR 0.69, 95% CI 0.51-0.94) after adjusting for induction of labor. Similar results were observed among Black mothers at low risk [crude RR 0.58 (95% CI 0.43-0.79), adjusted RR 0.58 (95% CI 0.39-0.88)]. For Black mothers at high risk, however, the period effect at 42-43 weeks fell from RR 0.81 (95% CI 0.58-1.13) before adjustment to RR 1.06 (95% CI 0.64-1.73) after adjustment.

Table 15 also shows the results of induction effect in Whites and Blacks in the Poisson regression model. In White mothers at low risk, the induction effect was 0.96 (95% CI

0.94-0.98), representing a 4% reduction in fetal death risk for every 1% of increase in induction rate at each state. For Black mothers, however, no such a protective effect was observed in either risk stratum. Appendix G shows the SAS output for the Poisson regression analysis results.

Table 15. Poisson regression model for period effect at 40-43 weeks in Whites and Blacks, before and after adjustment for induction of labor, 49 states and D.C., 1997 vs 1991

	Whites		Blacks	
	Crude RR	Adjusted RR	Crude RR	Adjusted RR
All pregnancies	0.79	0.98	0.76	0.67
	[0.74-0.84]	[0.82-1.16]	[0.67-0.87]	[0.50-0.88]
Low-risk pregnancies*	0.82	1.19	0.70	0.63
	[0.75-0.90]	[0.95-1.49]	[0.58-0.85]	[0.44-0.93]
High-risk pregnancies**	0.78	0.96	0.84	0.77
	[0.70-0.87]	[0.71-1.27]	[0.68-1.03]	[0.49-1.17]

The adjusted induction effect RR [and 95% CI]

	Whites	Blacks
All pregnancies	0.98	1.02
	[0.96-1.00]	[0.98-1.05]
Low-risk pregnancies*	0.96	1.01
	[0.94-0.98]	[0.97-1.06]
High-risk pregnancies**	0.98	1.01
	[0.95-1.00]	[0.97-1.06]

RR = rate ratio
Number in brackets is the 95% confidence interval.
Low-risk pregnancy defined as maternal age 20-34 yrs and absence of diabetes, chronic hypertension, and pregnancy-induced hypertension.
High-risk pregnancy defined as maternal age <20 or >=35 yrs and/or presence of any of the above medical conditions.

Chapter 5. DISCUSSION

This study has estimated fetal death hazard changes in the United States between 1991 and 1997. For Whites, a consistent decrease was seen from 37 to 43 weeks; for Blacks, a marked decrease was observed only at 42 and 43 weeks. On the other hand, a considerable increase at the extremely early GA of 20 to 22 weeks was noted for both Whites and Blacks, although for Blacks the increase was more substantial. To fully understand these findings, we examined contemporaneous changes in registration practices, maternal sociodemographic characteristics, medical and life-style risk factors, and obstetric interventions, as well as improvements in prenatal health care during the study period.

5.1 Registration Artifact

The study results suggest that registration practices in the United States have experienced important changes during the last decade with regard to the reporting of FDs at extremely early GAs, i.e., increasing registration of FDs near the borderline of viability (close to 20 weeks cut-off). Moreover, these changes appear to have occurred to different degrees in Whites and Blacks.

In the United States, the total number of births (live births + stillbirths >=20 weeks GA) decreased from 1991 to 1997. In constrast, FDs at 20-22 weeks GA as a proportion of total births in 1997 increased by 17% over 1991 (RR: 1.17; 95% CI: 1.12-1.21). No similar increase was observed in the other two early GA categories (23-25 or 26-28 weeks); rather, there was a slight but statistically significant decrease in these other categories. These findings are consistent with two previous investigations in the state of Alabama (Goldenberg et al, 1989; Phelan et al, 1998). The Alabama studies used the state vital statistics data during the period 1974-84 and 1974-94, respectively. In the two Alabama studies, FDs recorded as weighing <1,500 g were divided into three BW categories: <500 g, 500-999 g and 1,000-1,499 g. A marked increase was observed in FDs <500 g as a proportion of total births (each year) both for 1974-84 and 1984-94. However, FDs in the

500-999 g and in the 1,000-1,499 g BW categories as a proportion of total births decreased during the same period. Although the BW cut-offs do not exactly correspond to our GA cut-offs in classifying early FDs into 3 categories, both capture a similar pattern of changes; an upward trend in fetal death rate at and before 22 weeks cut-off (note: BW 500 g corresponds approximately to GA 22 weeks) was confirmed both at the individual state-level and nationwide in the United States.

Given that the increase was limited to 20-22 weeks, whereas the decrease was confined to 23 weeks onwards, it is difficult to postulate extrinsic risk factors (e.g., exposure to environmental toxins) that could account for this pattern of changes. The hazardous effect, if any, should not necessarily have been restricted to the extremely early GAs (i.e., impact only on pregnancies at 20-22 weeks, but not on those at 23-25 or 26-28 weeks). To date, no data suggest an increase in environmental toxins (e.g., domestic pesticide use) during the study period that would specifically target extremely early pregnancies, or that exposure to such toxins was prevalent among pregnant women in the United States.

It is also unlikely that the increase in FDs at 20-22 weeks can be attributed to increased termination of pregnancies (due to early diagnosis of lethal congenital anomalies such as anencephaly, spina bifida). The latter was suggested to be responsible for the increase in congenital anomaly-related FDs at 20-25 weeks from 1985 to 1996 in Canada (using Statistics Canada's birth and death databases) (Liu et al, 2001). In the United States, however, pregnancy terminations (i.e., induced abortions) are documented separately from FDs (using a different standard form developed by NCHS). Under the U.S. jurisdiction, a fetus with a lethal congenital anomaly, if terminated, should not be registered as a FD. Thereby, a decrease (rather than an increase) should have been observed in congenital anomaly-related FDs (based on the FD reports) had there been a similar increase (as in Canada) in pregnancy terminations in the United States. Nevertheless, such a reduction, if any, could not be substantial due to the fact that congenital anomaly-related FDs (e.g., anencephaly and spina bifida) represent only a small proportion (10-20%) of total FDs. This perhaps explains the slight decrease in FDs in the other two early GA categories (at 23-25

and 26-28 weeks), but it obviously cannot account for the marked increase in FDs close to the 20-week cut-off for registration.

A more likely explanation for the increase in FDs at 20-22 weeks is that the registration of FDs near the borderline of viability was becoming more complete from 1991 to 1997 in the United States. In fact, similar results have been reported from Canada (Joseph et al, 1999) and other developed countries (Kramer et al, 2001). Such a registration artifact may have masked an otherwise downward trend in FDs at 20-22 weeks (as was observed in the other two early GA categories), which may have been attributable to better prenatal surveillance and care over the study period (e.g., increasing use of early ultrasound scanning and subsequent termination of pregnancies with the diagnosis of severe congenital anomalies).

The existence of second potential registration artifact (FDs increasingly classified as neonatal deaths) was not supported by the data. FDs in all the three early GA categories increased as a proportion of perinatal deaths (FDs >=20 weeks + early neonatal deaths <7 days): by 36 percent at 20-22 weeks, 12 percent at 23-25 weeks, and 11 percent at 26-28 weeks, respectively. If this artifact was pronounced, a decrease rather than an increase in this proportion (particularly near the borderline of viability) should have been observed, assuming no true change in occurrence of either total FDs or early neonatal deaths.

With the large increase in FDs near the borderline of viability, an increase in early preterm live births (at 20-22 weeks in particular) should have also been observed if many deaths formerly registered as FDs were now registered as live births and then died and were recorded as neonatal deaths (since at 20-22 weeks, virtually all live births result in neonatal deaths). However, live births in all three early GA categories increased only marginally in Whites, whereas a decrease of similar magnitude was seen in Blacks.

It is therefore likely that the marked increase in the proportions of FDs in all the 3 early GA categories (relative to perintal deaths) is a result of a decrease in early neonatal deaths. This is particularly true at 23-25 and 26-28 weeks, since no increase in FDs was observed in these GA categories. Live born infants at 20-22 weeks remain nonviable in 1997, but the

increased registration of early FDs resulted in a relatively higher increase in the proportion (36%) than in the other two early GA categories (12 and 11%, respectively).

Nevertheless, as viability increases at early GAs (<28 weeks) and as the dividing lines between FDs and neonatal deaths at extreme early GAs (close to the 20-week cut-off) are often obscure and highly subject to the physician's judgment, we still cannot completely exclude the likelihood of an increased registration of FDs as early neonatal deaths. The magnitude of such a change in registration is probably too small to be detected by the proposed index of early FDs relative to perinatal deaths. It is also possible that an increase in registering FDs as early neonatal deaths was masked by the decrease in early neonatal deaths during the study period.

It is worth highlighting that the present study shows significant racial differences in the occurrence of preterm live births and FDs in the United States. There was a striking 2- to 4-fold disparity in all three early GA categories between Whites and Blacks. Over time, for both Whites and Blacks, the increase in FDs was restricted to 20-22 weeks. Yet, the magnitude of increase was nearly twice as high for Blacks than for Whites. On the other hand, preterm live births in all the three early GA categories increased for Whites, but decreased for Blacks; the magnitude of these changes was small but statistically significant for Whites and marginally significant for Blacks.

Identifying possible registration artifacts is important not only for properly interpreting temporal changes in fetal mortality, but also for appreciating racial disparities in the occurrence of early FDs between Whites and Blacks. At 20 to 36 weeks, the fetal death hazard was much higher for Blacks than for Whites. Over time, the magnitude of increase in the hazard at 20-22 weeks was more pronounced for Blacks than for Whites (see Chapter 4, Section 4.2.2). However, this estimate may have been biased by racial differences in registration. The fact that the increase in reporting FDs at 20-22 weeks (as a proportion of total births) was twice as high in Blacks, and that FDs relative to perinatal deaths was also higher for Blacks than for Whites in this GA category, suggests that over time, the changes in registration practices may have differed between Whites and Blacks. The more rapid

increase in Blacks may be due to either much poorer underreporting in 1991 or greater improvement thereafter or both. It is also possible that neonatal deaths near the borderline of viability were more likely classified as FDs for Blacks than for Whites. In fact, differences in registration by race in the U.S. have been reported in the past (David RJ, 1986; Kramer et al, 2001). Therefore, apparent racial disparities in the fetal death hazard may be biased by differences in FD reporting, particularly at extremely early GAs.

In conclusion, from 1991 to 1997, the increase in fetal death hazard at 20-22 weeks was probably due to more complete reporting of FDs near the borderline of viability in the United States. No clear evidence was obtained concerning an increased classification of FDs as early neonatal deaths during the study period. Substantial disparities were observed in the fetal death hazard between Whites and Blacks, particularly at extremely early GAs. However, the magnitude of the racial disparities may have been biased by registration artifacts.

5.2 Fetal Death Hazard

5.2.1. Comparison to other countries

As shown, the fetal death hazard in the United States was relatively low in preterm pregnancies (from 25 to 36 weeks), whereas it increased at term, and especially postterm. This pattern of changes is consistent with previous observations in a variety of population settings from Northern Europe to South America (Yudkin, 1987; Ferguson et al, 1994; Hilder et al 1998; Conde-Agudelo et al, 2000). The only exception is that, in the present study, a higher risk (vs at 26-36 weeks) was also observed near the borderline of viability (from 20 to 25 weeks), particularly among U.S. Blacks. The increased risk at early GAs has often been ignored by previous studies, who have often limited their analysis of GA-specific FDR to >=28 weeks, perhaps because of the concern about the incomplete reporting on FDs at extremely early GAs. FDs under 28 weeks are not registered in many European countries (Kramer et al, 2001).

To my knowledge, no international or regional (within a country) comparisons of fetal death hazards have been published. It can be anticipated that such a comparison would be strongly influenced by varied registration policies and/or practices across countries or regions at extremely early GAs. However, at >=28 weeks GA, FD registration appears complete (Harter et al, 1986; Kleinman et al, 1986; Goldhaber MK, 1989). Therefore, distinct disparities observed at 28 weeks and above are certainly worthy of note. Hilder et al (1998) reported the fetal death hazard at >=28 weeks for 1989-1991 in the North East Thames Regions (data from 18 hospitals, 1989-1991). It was quite comparable to the hazard among U.S. Whites in 1991 obtained in the present study at 28 to 40 weeks; however, from 41 to 43 weeks, the hazard was much lower in U.S. Whites. Given that these two countries are similar in socioeconomic development and cultural and ethnic background, it would be intriguing to further explore the disparities at 41 to 43 weeks which, to a large extent, may reflect differences between the two countries in obstetric policy and/or clinical practice regarding the management of postterm pregnancy.

The fetal death hazard in South America (data from 18 countries from 1985 to 1997) (Conde-Agudelo et al, 2000) was 2-3 times higher than the hazard among U.S. Whites in 1991 at 28 to 40 weeks. At 41 to 43 weeks, it was about 10-25 times as high. Certainly, such large disparities may not only reflect differences in registration practices, prenatal health care, or obstetric practices, but also differences in culture, ethnicity, and socioeconomic development between the United States and South American countries. The extremely high fetal death hazard in the postterm period among Latin American populations is particularly striking and warrants further investigation.

5.2.2 Differences according to GA

Apart from the relatively high increase (from 1991 to 1997) at 20 to 22 weeks, which (as discussed above) was probably due to more complete reporting, no reduction was observed in the fetal death hazard from 23 to 36 weeks (before term). Although a trend toward a decrease could be seen from 37 to 39 weeks in Whites, no significant decrease occurred until 40 weeks and later. Strikingly, in terms of absolute numbers, the majority of total FDs (>=20 weeks) occurred before term (<37 weeks). For Whites, about 70% of total FDs were

preterm; for Blacks, this proportion was more than 80% (Tables 1 and 2). Therefore, at term and postterm, the hazard is high but the total number of deaths is small, whereas before term the hazard is low (except at 20-24 weeks) but the total number of deaths is large.

To understand these 'contradictions,' it may be necessary to briefly review delivery patterns by GA. It has been well recognized that the majority of pregnancies are delivered at term, and that the proportion of preterm births is small (<10%). The number of fetuses at risk for FD in the postterm period becomes much smaller than before term (20-36 weeks). Before 37 weeks, the duration of follow-up can be up to 16 weeks (from 20 to 36 weeks) until a pregnancy outcome (live birth or stillbirth) is known, while at term and postterm this duration is no more than 6 weeks (from 37 to 43 weeks). Thus, before 37 weeks, there are a relatively larger number of fetuses at risk for a much longer time than at and after term. This explains why the total number of FDs preterm (20-36 weeks) is much greater than at term and postterm, despite the fact that fetal death risk is relatively low throughout most of the preterm period, while high term and postterm. Certainly, the large proportion of total FDs occurring <37 weeks, with no decrease from 1991 to 1997, suggests that future research, fetal surveillance, and prevention efforts should be focused on preterm FDs.

5.3 Etiology of Fetal Death

The distinct divergence in the temporal trends of fetal death risk (FDR) preterm, term and postterm has important etiologic implications. It is likely that unknown factors responsible for the marked decrease at >=40 weeks did not occur, or did not have the same impact, among pregnancies under 37 weeks. Factors associated with FD preterm may not necessarily pose equivalent influences on FD at term or postterm. Conversely, obstetric interventions effective in preventing FD at term or postterm may not exert a similar impact on FD preterm.

5.3.1 Pathophysiologic mechanism

One may speculate that the etiology of preterm FD may differ from that of term FD, and that the etiology of term FD may differ from that of postterm FD. This hypothesis is suggested by the fact that FDR varied substantially with advancing GA. As noted above, FDR increased exponentially at term and appeared very high postterm, while it was low preterm (25-35 weeks). The underlying pathophysiologic mechanisms are in line with a markedly increased risk of placental-fetal complications (i.e., placental abnormalities, IUGR) as GA advances into the postterm period. The elevated risk is believed to derive primarily from so-called 'placental insufficiency' (Vorherr H, 1975), a consequence of failing placental capability coupled with increased demand for nutrient supply and oxygenation due to continued fetal growth.

This problem of 'placental insufficiency' perhaps can occur throughout late pregnancy (after 37 weeks). Nevertheless, it appears to worsen in the postterm period, i.e., the placenta may reach its limit of capability, while delivery has not yet been initiated and the fetus continues to grow. This problem is less likely to occur at early term or preterm, simply because continued fetal growth at this stage is still within the placenta's capability. It is likely that 'placental insufficiency,' which finally leads to an increased risk of FD, may further deteriorate in the presence of extrinsic risk factors, such as older maternal age (>=35 years), maternal cigarette smoking, or diabetes. These risk factors may further compromise the capability of the placenta (e.g., cigarette smoking may jeopardize placental oxygenation). In other words, extrinsic risk factors may interact with an aging maternal placenta in the postterm period, thereby strengthening the effect of these risk factors vs their impact at or before term.

Thus, the etiology of postterm FD may differ from that of preterm or term FD. Unfortunately, most previous etiologic studies investigated FDs as a single identity, e.g., in a case-control study, comparing live births and fetal deaths regardless of GA. As a consequence, not only may important etiologic differences have been obscured but also effect modification by GA would have been missed.

5.3.2 Maternal age, cigarette smoking, and parity

The present study confirmed the effects on FD of advanced maternal age (>=35 years), cigarette smoking, and nulliparity, which have been recognized for decades. More interestingly, differential impacts were revealed at different GAs. The results show that the effect of advanced maternal age increased substantially from preterm to term to postterm. This finding is in accordance with a single previous study reported in the literature, which investigated the differential impacts of older maternal age (>=35 years), cigarette smoking, and nulliparity within three GA categories (28-36, 37-41, and >=42 weeks) using data (1983 to 1989) from the Swedish Medical Birth Registry (Raymond et al, 1994).

Surprisingly, the present study also demonstrates that at 41 to 43 weeks GA, teenage mothers (<20 years) were at lower risk of FD than mothers 20-34 years old. However, no similarly reduced risk was seen at 40 weeks or earlier. This finding, combined with the finding of an increasing effect of advanced maternal age (>=35 years) with advancing GA (the largest effect at 41 to 43 weeks), suggests a strong interaction between maternal age and GA on the risk of FD. Such an interaction may reflect deteriorating maternal physiological or placental function with advancing maternal age coupled with an increasing placental demand (for continued fetal growth) as GA progresses. Note that teenage mother showed increased rather than decreased risk for FD in the crude analysis (see Table 9). Therefore, without stratification, no such differentials in effect by GA would have been revealed.

In the present study, no substantial variations by GA were observed in the effect of maternal cigarette smoking, although a statistically significant association was seen throughout gestation. In contrast, in the above-mentioned Swedish study (Raymond et al, 1994), the effect of maternal cigarette smoking decreased as pregnancy advanced, and became statistically nonsignificant at >=42 weeks. As to nulliparity, the Swedish study reported an increase in FDR at 28-36 weeks, whereas in the present study, no such effect was found. However, for both studies, nulliparity was associated with an increased risk at >=41 weeks but not at 37 to 40 weeks.

It is unknown to what extent poor data quality may have affected our analysis of the effect of cigarette smoking and its variation by GA. As noted, maternal cigarette smoking is underreported on U.S. birth certificates (Paper et al, 1993; Master's dissertation, 1996). If the degree of underreporting varies by GA and, moreover, is differential between mothers with live births and mothers with fetal deaths, bias would be introduced (toward the null if cigarette smoking is more likely to be underreported among mothers with FDs). In the Swedish study, data quality on smoking is perhaps better; however, no statistically significant effect was observed at >=42 weeks, despite an effect at 28-41 weeks. Therefore, whether the effect of maternal cigarette smoking varies with GA remains an open question.

It is unlikely that a bias due to underreporting would have occurred in assessing the effect of maternal age and nulliparity, because information on maternal age and nulliparity are often obtained from medical records, while data on maternal cigarette smoking are based on recall. If the latter are obtained when the pregnancy outcome is known (e.g., at the time of completing the live birth or fetal death certificate), then women's recall might be strongly affected by an unexpected tragedy (e.g., smoking women may relatively underreport because of guilt over the fetal loss).

5.3.3 Maternal chronic diseases, educational attainment, fetal gender, marital status, and onset of prenatal care

Maternal chronic diseases such as diabetes, chronic hypertension, and pregnancy-induced hypertension (PIH) have been consistently associated with the risk of FD (Sibai et al, 1984; Abdella et al, 1984; Mabie et al, 1986; Ananth et al, 1995; Yadav et al, 1997; Martin et al, 1999; Cunndy et al, 2000). The present study confirms these findings. Moreover, we observed much stronger effects of these factors on FD at >=37 weeks than at 28 to 36 weeks (except for the effect of chronic hypertension, which had no substantial variation across GA). Elevated risk was also seen among socioeconomically disadvantaged mothers (e.g., maternal educational attainment <=12 years, unmarried status) and among mothers with Black race. However, the effect of maternal educational attainment <=12 years and unmarried status appeared only at term and after term, not before term. The effect of Black

race did not show significant variations from preterm to term to postterm. A protective effect associated with early onset of prenatal care was noted from 28 to 43 weeks, indicating that the benefit of 1st-trimester onset of prenatal care may not be limited to preterm pregnancies, but also extend to those at term and postterm. On the other hand, early onset of prenatal care may merely serve as a marker for 'healthy' health behavior, and a planned and desired pregnancy, which themselves are responsible for the reduced FD risk.

Male gender showed a protective effect on FDR at 41 to 43 weeks, whereas no such an effect was observed at 37-40 or 28-36 weeks. Interestingly, a recent study showed that among term pregnancies, male fetal gender was associated with an increased risk of FD in the lower BW quintile, whereas in the upper BW quintile, the risk was lower (Smith GC, 2000). In other words, male gender showed an adverse effect among lighter fetuses, but a protective effect among heavier fetuses. The BW-specific approach is likely to have underestimated the true FDR at term and postterm in Smith's study, however (as discussed in Chapter 2, Section 2.5.1). In the present study, the protective effect of male fetal gender found at >=41 weeks is perhaps due to the fact that most fetuses born in this GA range are in the upper BW quintile. Therefore, the results on fetal gender from Smith's study are in accordance with the present study, suggesting that male fetus is less likely to die in the postterm period compared to the female fetus.

5.3.4 Causal pathway and adjustment considerations

In the present analysis, no adjustment was undertaken for placental complications, including abruptio placentae, placenta previa, or prelabor rupture of membranes, nor was there adjustment for fetal abnormalities such as IUGR or congenital anomalies. These complications or disorders are likely an intermediate step on the causal pathway between risk factors such as older maternal age or cigarette smoking and FD. In fact, previous studies have consistently demonstrated that the association between maternal cigarette smoking and FD is eliminated or sharply reduced when placental complications and IUGR are adjusted for in multivariate regression analyses (Meyer et al, 1977; Callan et al, 1990; Raymond et al, 1994; Conde-Agudelo et al, 2000). Those results suggest that the effect of maternal cigarette smoking on FD may be mediated by placental or fetal complications.

In contrast, maternal age >=35 years is likely to have an effect on FD that is independent of placental or fetal complications. Older women (>=35 yrs) are more likely than younger women to have such medical disorders as diabetes, chronic hypertension, or PIH. Older women are also at significantly increased risk for placental/fetal complications such as placental abruption (Kramer et al, 1997) and IUGR, while the latter complication appears to be independently associated with FD (Cnattingius et al, 1998). However, after simultaneously adjusting for placental complications, IUGR, and maternal chronic diseases (diabetes, chronic hypertension and PIH), the significantly elevated risk among older women appears to persist (Raymond et al, 1994; Fretts et al, 1995; 1997), suggesting at least two causal pathways between advanced maternal age (>=35 years) and FD. Thus, some fetal deaths may be mediated or accompanied by severe placental and/or fetal complications, while others are a direct consequence of some other unrecognized effect of advanced age. Accordingly, to properly evaluate the effect on FD of major risk factors such as advanced maternal age or cigarette smoking, the present study did not adjust for other adverse pregnancy outcomes involving placental or fetal complications.

5.3.5 Conclusions

The present study confirms previous findings of the associations between FD and maternal sociodemographic characteristics (age, race, marital status, and educational attainment), fetal gender, maternal medical conditions (chronic hypertension, PIH, and diabetes), and cigarette smoking, as well as early onset of prenatal care. Furthermore, a marked increase was revealed from preterm to term to postterm in the strength of the associations. Nearly all the factors impacted on FD at >=37 weeks (with the strongest impact at 41-43 weeks), whereas only a few were associated with FD preterm (28-36 weeks). Such differentials parallel the increasing trend in fetal death hazard as GA advances to 41 weeks and above, i.e., low risk preterm and high risk at and after term.

5.4 Impacts of Various Factors on the Temporal Decrease in Fetal Death Risk

To understand the temporal changes in fetal death hazard, we need to identify not only the potential risk and protective factors for FD, but also their changes (decrease or increase) in prevalence over time, and to quantify the possible impact of such changes on the fall in fetal death risk. Certainly, if a factor is found not to be associated with FD, no impact on the decrease should be attributed to this factor. However, if such an association exists but no contemporaneous change occurs in the prevalence of that factor, it would still be difficult to attribute the decrease in FDs in the population to that factor.

5.4.1 Temporal changes

Our analyses examined the distributions of various maternal sociodemographic characteristics and medical and life-style risk factors among live births and fetal deaths in 1991 and 1997, respectively. Important changes over time were noted: the prevalence of maternal cigarette smoking decreased, whereas the proportion of mothers aged >=35 years increased; more women initiated their prenatal care during the first trimester of the pregnancy, while the percentage of unmarried mothers increased.

Although no similar report has been published for the same period of time in the United States, these temporal changes nevertheless are consistent with findings from a hospital-based cohort study (i.e., for the period 1991-1996) in Canada, based on systematically collected data since 1978 (Kramer et al, 1998). Therefore, it is unlikely that such changes are simply due to changes in reporting over time. Rather, the increase in the percentage of women who gave birth at >=35 years and the decrease in smoking probably reflect population trends during the study period. Risk factors such as cigarette smoking, if reduced in prevalence, may have had a positive influence on the fall in fetal death hazard, whereas the increase in advanced maternal age may have had a negative impact.

5.4.2 Influence of temporal changes in determinants on the crude period effect

Cox proportional hazard models were used to further identify and quantify the impact of the temporal changes of determinants on the decrease in FDs. A dummy variable was created to

indicate the crude period effect (reference: 1991), which was 0.87, 95% CI 0.80-0.94. Surprisingly, after sequentially adjusting for important covariates, the period effect remained virtually unchanged (HR 0.88, 95% CI 0.81-0.96), indicating that the observed decrease cannot be explained by the effects of the variables included in the model (see Table 14).

A decrease in cigarette smoking contributed somewhat to the decrease in fetal death hazard at 40 to 43 weeks, as did the increase in proportion of women with the 1st-trimester onset of prenatal care. As shown in the sequential adjustment, however, the beneficial effects of the decrease in cigarette smoking and the increase in early prenatal care were marginal, and to a large extent were counterbalanced by the adverse effects (of similar magnitude) due to the increases in advanced maternal age and unmarried status (see Table 14). As a consequence, the net effect of the temporal changes of these factors on the decrease in FDs was negligible. Partly, this is because the strength of association between these factors and FD was not strong (HR 1-2.0), and partly, due to the fact that the prevalence of these factors was not very high and did not change sufficiently over time to produce any appreciable impact. For example, maternal cigarette smoking affected 18.5% of pregnant women in 1991, while this proportion was 14.6% in 1997, an absolute decrease of only 3.9%. Similarly, advanced maternal age represented 8.8% of the population in 1991, while in 1997 this proportion was 12%, an absolute increase of 3.2%. Other important risk factors, such as nulliparity and maternal medical conditions (diabetes, chronic hypertension, and PIH), were associated with FD at 41 to 43 weeks. However, the prevalence of these risk factors did not change over time. As a result, no appreciable impact was observed from these variables on the decrease in FDR.

In conclusion, it is unlikely that the observed decrease in fetal death hazard at 40 to 43 weeks can be attributed to the changes in maternal sociodemographic characteristics, life-style risk factors, or earlier onset of prenatal care, nor can it be attributed to the changes in prevalence in maternal medical conditions during the study period.

5.5 Impact of Obstetric Care on the Temporal Decrease in Fetal Death Risk

As evidenced by the dramatic increase in induction of labor over time and across GA (larger increase after 40 weeks) and the results of ecologic-level analyses, the marked decrease in fetal death risk at 40-43 weeks can be largely attributed to the increased use of induction of labor. Such an effect is perhaps due to the fact that earlier and more frequent use of labor induction prevented more pregnancies from being delivered at >=40 weeks and thereby averted the high risk for FD in this gestational period.

5.5.1 Effects of ultrasound, EFM, and stimulation of labor

Before discussing the effect of induction of labor, it may be helpful to review the possible effect of other obstetric procedures on FDs, since these procedures also increased during the study period. It is worth highlighting that among the four obstetric procedures, ultrasound and induction of labor may theoretically impact on antepartum FDs, whereas the effects of EFM or stimulation of labor, if any, should be limited to intrapartum FDs.

Routine ultrasound scanning may aid the early detection of severe congenital anomalies (e.g., anencephaly, spina bifida). The increase in ultrasound, therefore, may have resulted in an increase in the detection of fetal abnormalities. In the United States, FDs are reported separately from pregnancy terminations (induced abortions). A fetus with severe congenital anomalies, if terminated, would have no chance to be reported as a FD. Therefore, an increased detection and subsequent abortion or termination of pregnancies with severe congenital anomalies may have contributed to the decrease in FDs in the United States. Yet, the proportion of FDs caused by severe congenital anomalies such as anencephaly or spina bifida is relatively small (under 15%). Moreover, no substantial increase in ultrasound use was observed during the study period (for Whites, it increased from 62 to 68%; for Blacks, it increased from 54 to 62%). Therefore, it is unlikely that the marked decrease in FDs at >=40 weeks can be attributed to the slight increase in use of ultrasound and the early detection and termination of fetuses with severe congenital anomalies. Moreover, even if there was such an effect, it should also have occurred before 37 weeks, as the affected

fetuses should be equally, if not more likely, to die preterm. However, at 28 to 36 weeks, as noted, no reduction was observed.

Is it possible that EFM was responsible for the decrease in FDs observed at >=40 weeks? On the one hand, EFM may be superior to intermittent auscultation in continuously depicting variations in fetal heart rate patterns, which is thought to be critical in indicating the adequacy of fetal oxygenation, as well as the timely detection of fetal distress and subsequent cesarean section to avoid FD. On the other hand, as GA advances to postterm, the incidence of fetal hypoxia may increase due to placental insufficiency. Therefore, an effect of EFM on the decrease in FDs seems plausible (provided that the decrease was accompanied by an increase not only in EFM but also in cesarean section). Nevertheless, the magnitude of the impact should be very small, given that EFM is an obstetric intervention that is primarily applied during labor. Therefore, such an effect, if any, would be limited to intrapartum FDs, which represents only a small proportion of total FDs (10-15%), too small to account for the marked decrease observed at >=40 weeks. Such an effect seems unlikely, however, since no increase was observed in cesarean section (the cesarean section rate was 22% in 1991 vs 21% in 1997). Certainly, if EFM is effective in preventing FD, the effect should come from timely delivery of the compromised fetus by cesarean section.

As an instrument useful in monitoring fetal oxygenation, EFM may have been responsible for the reduction in asphyxia-associated FDs when EFM rapidly gained its popularity after its introduction in the 1960s. In fact, some decreases in perinatal deaths due to the increased use of EFM had been reported by observational studies in the 1980s (Mueller-Heubach et al, 1980; Erkkola et al, 1984). However, during the last decade when EFM has become nearly universal (reported in about 80% of White women in 1991 and more than 85% in 1997), such an effect may no longer be detectable. Unfortunately, owing to absence of data on timing of deaths, the present study cannot demonstrate whether there was a trend towards fewer intrapartum fetal deaths (e.g., due to fetal asphyxia).

Stimulation of labor increased markedly during the study period. However, if compared to the proportion of mothers with EFM or ultrasound, the proportion of pregnancies with stimulated labor remained low (<20%). It remains unclear whether a decrease in labor dystocia due to more frequent use of stimulation has helped to reduce fetal mortality. As for EFM, however, such a beneficial effect is unlikely to account for the observed decrease at >=40 weeks, since the effect would be restricted to intrapartum deaths. While prolonged labor may pose an increased risk for *in utero* fetal well-being, stimulation of labor (by oxytocin) may cause severe obstetric complications, including fetal distress (Rooks JP, 1999). If, however, both stimulated and nonstimulated prolonged labors are under continuous EFM, and cesarean section is performed once fetal compromise is evidenced, then there should be no differential impact of stimulation vs nonstimulation on FD. This seems highly likely, since EFM is widely used (>80%) even among uncomplicated, low-risk pregnancies.

In summary, the marked decrease in FDs at >=40 weeks is probably not attributable to the slight increase in use of ultrasound. Nor can it be attributable to the increase in EFM or stimulation of labor, because the beneficial effects should be due to prompt delivery by cesarean section, whereas the latter showed no increase over the study period. Moreover, even if there is a protective effect of EFM or stimulation of labor, the effect would clearly be limited to intrapartum FDs, representing only a small fraction of total FDs, and thus be too small to account for the marked decrease in FDR at >=40 weeks.

5.5.2 Temporal changes in induction of labor

As noted, induction of labor has experienced the most pronounced increase among the four obstetric procedures reported in the United States. In Whites, it increased from 13 to 22%, a relatively 66% of increase; in Blacks, it increased from 8.4 to 15%, a relative increase of 79% (note: the induction rate for Blacks in 1997, even after the marked increase, was similar to the level of Whites in 1991). The induction rate in Blacks was about half that of Whites; over time, the Black-White gap remained nearly unchanged.

The dramatic increase in labor induction, which occurred within a 6-year period in both Whites and Blacks, is unlikely to be attributable to an increased incidence of indications that require more frequent induction (no evidence of a sharp increase in maternal or fetal complications). Rather, such an increase in both Whites and Blacks is more likely due to increased use of elective labor induction in treatment for post-datism, particularly among uncomplicated low-risk pregnancies. Unfortunately, in the present study, no information is available on the indication for induction. Yet, it can be anticipated that more pregnancies would have been delivered earlier than previously, if there has been an increased use of routine elective labor induction. Such an effect would have substantially reduced the incidence of postterm pregnancies.

5.5.3 Impact of the increased use of induction of labor on changes in the GA distribution of total live births

Current obstetric guidelines for the management of postterm pregnancies recommend that labor be induced in the presence of a favorable cervix between 41 and 42 weeks in gestation; if the cervix is unfavorable, either induction of labor or antenatal fetal monitoring is an option (Maternal-Fetal Medicine, 4th edition, 1999). However, this recommendation may not necessarily represent the viewpoints or clinical practices of all obstetricians across different countries or regions in the United States.

Our study results show that the proportion of births delivered by induction of labor was much higher for both Whites and Blacks in the United States at 41-43 weeks compared with 37-40 weeks. Such a disparity is almost certainly a consequence of a policy of routine elective labor induction for post-datism. More strikingly, for both races in 1991, women who gave birth at 42 weeks had the highest rate of labor induction, whereas in 1997, the highest rate was at 41 weeks, indicating important changes in obstetric management of postterm pregnancy in recent years in the United States. In particular, not only was induction of labor more frequently employed, but the timing of its use also appeared earlier.

The observed Black-White differences in the use of induction of labor deserve further discussion. From 1991 to 1997, for both races, an increase of this intervention occurred in

each GA week (from 28 to 43 weeks). However, in Whites, the use of induction of labor (compared with Blacks) was more frequent after 37 weeks and the disparity increased as GA advanced to 41 weeks (see Figures 1). For both races, over time, the largest increase was at 41 weeks, however. Among Whites, a direct consequence of the trend toward increasing use of induction across GA was a downward shift in the GA distribution. As shown in Figure 2, for Whites, a marked decrease in the proportion of births occurred from 40 to 43 weeks, whereas at 35 to 39 weeks, a relative increase of virtually the same magnitude was observed. In 1991, the highest percentage of births occurred at 40 weeks, whereas in 1997, it was at 39 weeks, i.e., one week earlier.

In contrast, no such clear change in the GA distribution was observed among Blacks (as shown in Figure 3). Rather, a slight decrease in the proportion of births was seen both at 33 to 36 weeks and at 41 to 43 weeks, with a relative increase noted from 37 to 40 weeks. Therefore, unlike the distinct downward shift in Whites, the GA distribution among Blacks was more concentrated at term (with a decrease on both tails of the distribution: preterm and postterm). Note that an earlier and more frequent use of induction of labor paralleled the trend toward earlier delivery in Whites but not in Blacks, indicating there may have been differential impacts of induction of labor on the GA distribution in Whites vs Blacks. Such differential impacts are probably a consequence of a White-Black gap in the use of this obstetric intervention; the induction rate in Whites nearly doubled that in Blacks, even though it increased substantially in both racial groups over the study period.

It is of interest that in the present study, an increase in the preterm birth rate (<37 weeks) was noted in Whites, in contrast with a decrease in Blacks. This pattern of change was also reported in a study based on U.S. vital statistics in 1989 and 1997 (Demissie et al, 2001). Obstetric interventions, i.e., preterm induction of labor, preterm cesarean delivery, and early ultrasound dating have been associated with an increasing trend in preterm birth, of which preterm induction of labor accounted for a major portion of the increase (Kramer et al, 1998; Demissie et al, 2001). The impact of preterm induction of labor was observed in Whites but not in Blacks (or perhaps the impact was outweighed by other unknown

favorable changes in Blacks). Thus, the determinants underlying the different trends in preterm births between Whites and Blacks deserve further investigation.

It is noteworthy that in Whites, a large decrease in proportion of births occurred from 40 to 43 weeks, whereas in Blacks, a decrease was seen only at >=41 weeks. Although no comparable report is available on the trend of postterm births and the underlying role of induction of labor in the U.S., the recent Canadian Perinatal Health Report shows a dramatic decrease in the postterm birth rate in Canada, from 4.4% in 1991 to 1.8% in 1997 (Canadian Perinatal Health Report, 2000). That report suggested that the decrease was due partly to more frequent labor induction and partly to increased use of ultrasound dating and subsequent reduction of GA errors.

As indicated by previous studies, early ultrasound scanning is likely to impact on the dating of GA (Joseph et al, 1996; Kramer et al, 1998). Therefore, before a conclusion can be drawn on induction of labor and the changes in the GA distribution, a brief review of the possible effect of ultrasound is necessary. Ultrasound-based GA is more accurate than LMP-based GA (even in cases of well-recorded LMP and normal menses). LMP-based GA appears to have largely overestimated the incidence of postterm birth (Kramer et al, 1988; Meir et al, 1999), whereas ultrasound-based GA, to some extent, may have caused an artificial temporal increase in preterm birth (Kramer et al, 1998). Due largely to the rapid increase in the routine use of early ultrasound, the overall GA distribution, as reported, has been shifted toward the low end (Kramer et al, 1988; Goldenberg et al, 1989). Yet, in the present study, on the one hand, no substantial increase in ultrasound use was observed during the 6-year period; on the other, more than 95% of the U.S. vital statistics records have LMP-based GA (NCHS technical appendix, 1996). Therefore, it is unlikely that the changes in the GA distributions observed in the present study can be attributed to the slightly increased use of early ultrasound. Rather, these changes, particularly the decrease in the proportion of births at >=40 weeks (based on LMP), is mostly likely the result of increased use of induction of labor, which as discussed in the following section, also contributed to the decrease in FDs in this GA period.

5.5.4 Impact of the increased use of induction of labor on the decrease in FDs

In the present study, induction of labor seems responsible for the marked decrease in fetal death hazard at 40 weeks and above. The plausibility of this inference can be demonstrated in several ways. Most of all, the dramatic increase in use of induction of labor, particularly at and before 41-43 weeks, caused more pregnancies that would otherwise have been delivered by spontaneous labor at 42 or 43 weeks (or even later) to be terminated earlier at term, and thereby avoided the high risk for FD in the postterm period. In fact, the marked decrease in the proportion of total live births at 40-43 weeks was accompanied by a marked decrease in FDs; both occurred exactly within the same GA range in Whites. It seems likely that by shifting deliveries from the high-risk period to the relatively low-risk period, the increased use of induction of labor improves fetal survival. Such a benefit therefore depends on the magnitude of difference in risk across GA, the greater the difference, the larger the effect. In other words, had there not been an increase in risk in postterm period, an earlier delivery by induction would not have reduced the incidence of FD.

Following this line of argument, it is not surprising to see that in Whites, as the risk increased, the decrease (1997 vs 1991) from 40 weeks onward appeared increasingly large with advancing GA (Figures 4 and 5). In contrast, before 37 weeks, no appreciable decrease was seen, which is likely due to the fact that there was no significant gradient in risk from 28 to 36 weeks, even if induction of labor also increased substantially at these GAs. Therefore, a more evident decrease in fetal death hazard at 40-43 weeks in Whites (compared to that at 37-39 weeks) may be due partly to more frequent use of induction at >=40 weeks (i.e., at 40-43 weeks, it was about 50% higher in 1991 than that at 37-39 weeks in 1997), and partly to the inherently greater risk at 40-43 weeks.

Our inference concerning the protective effect of induction of labor on FD is substantiated by the results of the multivariate Poisson regression analyses. Between 1991 and 1997, the decrease at 40 to 43 weeks among Whites appears attributable to the increased use of induction of labor (before adjustment for induction of labor, the period effect RR was 0.79, 95% CI 0.74-0.84; after adjustment, the RR was 0.98, 95% CI 0.82-1.16). Such an effect in U.S. Whites is consistent with the findings from a nationwide study in Canada, which

reported an increasing rate of induction of labor accompanied by a significant reduction in FDs from 1980 to 1995 among postterm pregnancies (Sue-A-Quan AK et al, 1999). Unfortunately, randomized controlled trials have been unable to detect such a beneficial effect (induction of labor vs serial fetal monitoring). This is partly due to the limited sample size of the trials, and partly due to the use of a different measure of outcome, i.e., perinatal mortality. If induction of labor has reduced the incidence of FD, there is no reason to suggest a similar effect on early neonatal death. In fact, it is possible that use of labor induction results in earlier delivery of some moribund infants who would have otherwise died *in utero* but are born alive and die as newborns. Therefore, a possible effect of induction of labor on the decrease in FDs may have been offset by an increase in neonatal deaths when combining the two as perinatal deaths. This seems unlikely, however, in the light of persistent decline in early neonatal mortality both at term and postterm (Vital and Health Statistics, 1995).

To date, the largest randomized controlled trial studied 3,407 women with singleton uncomplicated pregnancies (i.e., absence of maternal diseases e.g., diabetes mellitus or complications of labor/delivery e.g., placenta previa, PROM, malpresentation) at 41 or more weeks of gestation. Only 2 cases of FDs were observed in the monitoring group (n=1,706) and none in the induction group (n=1,701) (Hannah ME et al, 1992). Meanwhile, a meta-analysis of 11 trials reported in the literature has revealed a beneficial effect of induction on perinatal death at >=41 weeks in GA (Grant JM, 1994). Therefore, it is likely that if a randomized controlled trial were large enough, a statistically significant effect on FD would be observed.

It is of interest that the protective effect of labor induction in the present study was observed among White pregnancies either at high or low risk for adverse pregnancy outcomes. In modern obstetric practice, high-risk pregnancies (defined in the present study as maternal age >=35 years and/or the presence of diabetes, chronic hypertension, or PIH) are under closer monitoring and special care, including more frequent use of antenatal fetal monitoring. Once maternal or fetal complications are evidenced, induction or cesarean section is often used. Therefore, it is not surprising to see a protective effect of induction of

labor among high-risk pregnancies. As discussed earlier, the uncertainty is about its use in low-risk pregnancies. Our results suggest that increased use of labor induction is also beneficial in preventing postterm FDs among pregnancies apparently at low risk (defined as maternal age 20-34 years, and absence of diabetes, chronic hypertension, and PIH).

No statistically significant beneficial effect of induction of labor on FD was observed in U.S. Blacks, especially in low-risk pregnancies. The results of the multivariate Poisson regression show that before adjustment for induction of labor, the period effect RR was 0.69, 95% CI 0.56-0.84; after adjustment, the RR was 0.69, 95% CI 0.51-0.94. Although the fetal death hazard was slightly higher in Blacks than in Whites (at term and postterm), the induction rate among Blacks was much lower. The induction rate for Blacks in 1997, even after a rapid increase, was similar to the level in Whites in 1991. As discussed above, the effect of induction of labor in reducing FDs is achieved by earlier delivery to avoid the high-risk postterm period. Because of the relatively low induction rate in Blacks, the decrease in proportion of births at >=41 weeks might be too small to produce a noticeable impact on FD, especially among those who were apparently at low risk.

In conclusion, between 1991 and 1997, the decrease in FDs at 40 to 43 weeks among Whites appears attributable to the markedly increased use of induction of labor, either in high- or low-risk pregnancies, whereas no significant effect of induction was observed in U.S. Blacks, particularly in low-risk pregnancies.

5.6 Postterm Pregnancy: Evaluation and Management

As long ago as 399 BC, Aristotle appreciated that the gestation period for human pregnancy varies considerably and that prolonged pregnancy is not uncommon (Aristotle, Works, Vol II). In 1902, Ballantyne described the problem of postterm pregnancy for the first time in modern obstetric terms (Ballantyne JW, 1902). Twenty years later, he recommended induction of labor as the best method of preventing postterm pregnancy (Ballantyne and

Brown, 1922). By definition, a postterm pregnancy is one that is prolonged to 42 weeks (294 days) or beyond (Maternal-Fetal Medicine, 4th edition, 1999).

Although it has been recognized for decades that prolonged pregnancy poses an increased risk to fetal survival, the magnitude of the risk was not well established until 1987, when Yudkin et al (1987) correctly defined the fetal death risk. The risk is largely underestimated (and consequently, the temporal trend has been missed) by using either the GA- or BW-specific fetal mortality 'rate' or perinatal mortality 'rate.' As discussed above, the major problem derives from an inappropriate definition of the denominator, which includes only live births and stillbirths at given GA or BW but excludes ongoing pregnancies at risk for FD (see Chapter 2 Section 2.5.1). The BW- or GA-specific perinatal mortality rate carries the same methodological flaw as BW- or GA-specific fetal mortality rate (Kramer et al, 2002). Moreover, perinatal mortality combines FDs and early neonatal death into a single category. Such a combination in the past may have facilitated international or regional comparisons, but it is inappropriate for evaluating the effect of induction of labor.

Even with these above limitations, some important findings from previous studies still merit discussion. In the absence of maternal/fetal disorders or complications such as heart disease, diabetes, hypertension, congenital anomalies, placenta previa, or premature rupture of membrane, perinatal deaths postterm remains 2- to 3-fold higher than at term (Lucas et al, 1965). This finding helps in interpreting our findings that a reduction in FDs (due to increased use of induction of labor) was observed among pregnancies which were apparently at low risk for FD (maternal age at 20-34 years and absence of maternal medical conditions). Pathophysiologic studies suggest that the increased risk in the postterm period can be attributed to 'placental insufficiency.' In particular, the postterm fetus may outgrow the ability of its placenta to provide sufficient nutrients and adequate oxygenation for continued fetal growth, and therefore is at increased risk for adverse perinatal outcomes including FD (resulting from either malnutrition or hypoxia) (Cunningham et al, 1997). Therefore, GA alone may be an independent determinant of FDR, even among uncomplicated, low-risk pregnancies.

Important manifestations of the increased risk of FD, among postterm pregnancies may include aberrations in fetal growth, fetal distress, meconium staining and meconium aspiration syndrome, oligohydramnios, and shoulder dystocia. In 1954, Clifford first noted that undernourished postterm fetuses often demonstrated signs of chronic hypoxemia and starvation (Clifford et al, 1954). The prevalence of IUGR is significantly higher among postterm pregnancies and, moreover, is independently associated with the increased risk of FD (Campbell et al, 1997; Divon et al, 1998). Macrosomia is also a common complication of postterm birth and it has been estimated that twice as many postterm fetuses weigh more than 4,000 g compared to term infants (Eden et al 1987). Virtually all studies of postterm pregnancies report a significantly higher incidence of meconium-stained amniotic fluid and a greater risk of meconium aspiration syndrome (Eden et al, 1987; Crowley P, 1989).

In current obstetric practice, the management of postterm pregnancy that is otherwise uncomplicated remains controversial. Central to this controversy is whether the fetus is at increased risk of adverse perinatal outcome as the pregnancy advances. From the results of our study and of previous studies, the markedly increased risk of FD is clearly demonstrated when GA advances to >=41 weeks. The results of our study further suggest that earlier and more frequent use of labor induction help reduce the risk of FDs. Therefore, to date, the accumulated evidence favors a policy of routine labor induction at >=41 weeks or even earlier. In current obstetric practice, however, two management schemes are recommended and used. In one, pregnancy is allowed to progress to 41 weeks and beyond. Labor is induced only if the cervix is well effaced or dilated or both, or if fetal compromise occurs. In the second scheme, labor is routinely induced at >=41 weeks or even earlier. The results of our study suggest that the second approach has been increasingly applied in recent years.

Since the early 1990s, advances in knowledge concerning the physiology of cervical ripening (Leppert PC, 1995) and the subsequent wide availability of new drugs, e.g., prostaglandin (PG) E_2 gel, may have largely facilitated the induction of labor in the United States. Unlike more traditional techniques for labor induction, e.g., oxytocin and amniotomy, which often increase the likelihood of dystocia (particularly when the cervix is

unripe) and thus of cesarean section, PG E_2 promotes cervical ripening and therefore makes the intervention safer and more efficient. It is now well established that PG E_2 reduces the risk of cesarean section compared with traditional induction techniques, especially in the presence of an unripe cervix (Keirse MJNC, 1991).

The largest randomized controlled trial of postterm pregnancy management reported a slightly lower cesarean section rate in the induction group compared to the serial fetal monitoring group (Hannah et al, 1992). The researchers later suggested that this benefit was largely due to the use of PG E_2 gel for labor induction (Hannah et al, 1996). Similar reports have also been seen in other studies (Grant JM, 1994). In fact, in the present study, the cesarean section rate decreased slightly during the 6-year period (from about 22% in 1991 to 21% in 1997), while induction of labor increased substantially.

Early application of induction of labor prior to the postterm period may not only help reduce FDs but also have other benefits. For example, it may reduce the high incidence of meconium-stained amniotic fluid and meconium aspiration syndrome. These complications may be associated with an increased risk for fetal acidosis, neonatal seizures, and early neonatal deaths (Minchom et al, 1987). These findings provide additional justification for a policy of earlier (prior to the postterm period) routine labor induction among low-risk pregnancies.

5.7 Limitations of the Study

The data quality of U.S. live birth and fetal death files has been frequently questioned, particularly the underreporting of obstetric procedures and of medical and life-style risk factors. Reporting of maternal medical conditions (diabetes, chronic hypertension, and PIH) is relatively complete, as is the reporting of maternal sociodemographic characteristics (maternal age, educational attainment, and marital status), fetal gender, parity, and GA (Piper et al., 1993; Parrish et al., 1993; Buescher et al., 1993; Watkins et al., 1996).

In the present study, the completeness of reporting on induction of labor is of major concern. A number of studies show that labor induction has been underreported on the U.S. birth certificates (e.g., the sensitivity is only about 60%) (Parrish et al., 1993; Buescher et al., 1993). Certainly, incompleteness of data would be a significant problem if the analysis of the effect were based on data of individual woman. However, in the present study, the analysis of the effect is at the ecologic level. In particular, the impact of temporal changes in the use of induction of labor on FDs was estimated at individual state using Poisson regression. Therefore, it is the data on the changes over time in the prevalence of induction of labor (%) in each state (not the data on 'use' vs 'not use' in an individual woman) that is of key importance for the success of the ecologic approach. In other words, if labor induction is underreported, but over time the extent of underreporting remains the same and the changes in the rate of labor induction are valid, then the ecologic approach would at least partly circumvent the problem of incompleteness of data.

A sharp increase in the use of induction of labor was documented over the 6-year study period. In contrast, the use of amniocentesis remained nearly unchanged (31.7 in 1991 vs 30.7 in 1997) (National Vital statistics Report, 1994; 1999). Since both are important obstetric interventions, it is unlikely that the underreporting would be differential depending on which intervention is used. In other words, if the observed increase in labor induction is an artifact of improved reporting, a similar increase should have also been seen in amniocentesis (or cesarean section, see Chapter 2, Section 2.4.4). Therefore, it is unlikely that the observed increase in labor induction is simply a result of better reporting. Underreporting is a significant problem in the U.S. vital statistics report. Yet, there is no evidence that this problem substantially improved over the 6-year period. In other words, it is reasonable to believe that the trend of increase in labor induction should be the result of increased use, rather than the consequence of improved reporting. It is likely that in both years (1997 and 1991), the rate of labor induction was underreported, yet the extent of underreporting remained unchanged and the estimated magnitude of the increase is therefore unbiased. In fact, if the temporal increase in labor induction were merely reporting artifact, no association should have been observed between states with increased induction rate and those with lower fetal death risk. In other words, the period effect for the

fetal death hazard should have remained unchanged after adjustment. Therefore, the validity of the study results, i.e., the ecologic (state) level effect of induction of labor, does not appear 'fatally flawed' by the incompleteness of data.

A problem that is more likely to threaten the validity of our results is the lack of information on the indications for labor induction. Because of this data limitation, individual data cannot be used. Rather, only the state-level effect could be evaluated. As always, an effect observed at the ecologic level cannot necessarily be inferred at the individual-level. In addition to incomplete control for confounding, a major problem of the ecologic approach is the so-called 'ecologic fallacy.' In this study, the analysis of the induction effect was based on the rate of labor induction in each individual state, rather than the use of induction in individual women. Obviously, the induction rate alone cannot specify who did or did not use labor induction, nor whether women with induction of labor did or did not experience a FD. The ecologic approach has the advantage (in this study in particular) in dealing with the incompleteness of data as discussed above. However, the absence of data on the joint distribution of the intervention and FD prevents the effect observed at the state-level from being interpreted as an association between induction of labor and FD at the individual-level.

We conclude that the observed reduction in FDR is likely attributable to induction of labor. Yet other possibilities cannot be completely excluded. Fortunately, by excluding the impact of contemporaneous changes in maternal sociodemographic characteristics (maternal age, race, educational attainment), cigarette smoking, nulliparity, and maternal medical conditions, the robustness of the study conclusions should be improved (note: the impact of these factors was evaluated from data on individual women). Moreover, by using the ecologic approach, confounding by indication, often an intractable problem in observational studies at the individual level is largely reduced (Greenland et al, 1996; 1998, Wen and Kramer, 1999). One can predict that the effect of induction of labor is most likely affected by confounding by indication for pregnancies induced at 37-40 weeks but probably not for those at 41 weeks or above, because induction of labor in the postterm period is usually

elective. Nevertheless, those women who accepted this intervention may differ in some unrecognized ways from those who did not.

Unfortunately, data on many other risk factors for FD are not contained in U.S. vital statistics. These other risk factors include women's previous medical or obstetric history (i.e., medical treatment, induced abortion, previous FD), illegal drug use, genetic or chromosomal traits, family history of adverse perinatal outcomes, genital tract infection (such as chorioamnionitis or bacterial vaginosis), HIV, hepatitis B, radiation, mental or behavioral disorders (e.g., depression), as well as social factors such as family violence. Therefore, incomplete control of confounding variables may still be a problem for this study. Nevertheless, the impact of these risk factors on the decrease in FD risk may not be large, as it seems unlikely that these risk factors decreased markedly over the 6-year period.

Another problem concerns the lack of data on the timing of FD. Induction of labor, if successful, may help prevent antepartum FD (before labor). Ideally, we should separate antepartum FD from intrapartum FD for evaluation, because the two have distinct etiologic determinants. For example, intrapartum FD largely reflects the quality of intrapartum care, whereas antepartum FD is associated not only with the quality of prenatal care but also with maternal sociodemographic characteristics. Since antepartum FDs (in developed countries) represent the majority of total FDs (more than 85 percent), the etiologic differences revealed in the present study probably apply mostly to antepartum FD rather than intrapartum FD.

Finally, GA measurement, as noted earlier, is primarily based on woman's LMP date in U.S. vital statistics records. Although specific measures have been taken to reduce large errors, some errors undoubtedly remain in the data. These errors, even though within the range of appropriateness for BW, and therefore unrecognizable by the data error check procedures of NCHS, may exert an important impact on the measured fetal death hazard. In fact, after deleting inappropriate GA-BW records (using Alexander's approach), the fetal death hazard at 20 to 25 decreased substantially, suggesting these errors are more frequent at early GAs than at late GAs (>=28 weeks). Therefore, without deleting these errors, the

fetal death hazard at early GAs would have been overestimated. Further investigation of the impact of GA errors on the estimate of fetal death hazard is warranted.

The logistic regression model provides an alternative analytic approach to the Cox proportional hazards model used in our study to adjust the period (year) effect on FD risk for individual-level covariates. If the overall incidence of FD is what counts to women and their fetuses, then a FD at 22 weeks should not be weighted more heavily (i.e., as 'worse') than a FD at 40 weeks. In fact, the latter is often emotionally more difficult for women and their families than the former. The Cox procedure does precisely that, however: earlier FD carries a higher risk than later FD. Nonetheless, it is unlikely that risk factors for FD operate differentially over time, and thus adjustment for individual-level covariates should yield very similar estimates for the period (year) effect using either the logistic or Cox regression approach.

The Cox regression model also has limitations in handling ties (see Section 3.2.2.3.1 for definition). In our Cox model analyses, we compared the results using four different options (Breslow, Efron, Discrete, and Exact) in dealing with ties. A piecewise exponential regression model may be the best choice when there are many ties (at each GA week). Further study with a comparison between the two approaches would help highlight the potential impact of this limitation of the Cox regression model for studying FD.

5.8 Summary, Relevance, and Implications

Using the U.S. vital statistics data files, the present study has estimated changes in GA-specific FDR (20-43 weeks) between 1991 and 1997 and assessed the impact of changes in registration practices and of the increased use of induction of labor on changes in GA-specific FDR in the United States. To identify whether there has been an increased registration of early FDs and/or classification of early FDs as neonatal deaths at the borderline of viability over the study period, two indices were used: FDs at 20-22 weeks as a proportion of total births (>=20 weeks in GA) and as a proportion of perinatal deaths (FDs

+ early neonatal deaths). The determinants for the risk in FDs were analyzed using the Cox proportional hazard model, as were the impacts of temporal changes in the prevalence of these determinants on the decrease in FDs. Due to the data limitations, the effect of induction of labor on FDs was assessed at the ecologic (state) level using Poisson regression. All analyses were carried out in Whites and Blacks separately.

The main findings from the present study are as follows:

a) In the United States, the fetal death hazard was relatively low in preterm pregnancies (from 25 to 36 weeks), whereas it increased at term and was very high among postterm pregnancies.

b) The fetal death hazard was markedly higher for Blacks than for Whites, particularly at early GAs (<28 weeks).

c) Between 1991 and 1997, the fetal death hazard changed significantly. For Whites, a consistent decrease was observed from 37 to 43 weeks; for Blacks, a marked decrease was seen only at 42 and 43 weeks. For both races, a considerable increase at 20-22 weeks was noted, although for Blacks the increase was more substantial.

d) Between 1991 and 1997 for both Whites and Blacks, the increase in fetal death hazard at 20-22 weeks was probably due to more complete registration of FDs. No clear evidence of a change was observed in classification of death in the extreme preterm period from FD to early neonatal death.

e) The etiologic determinants for FD include maternal sociodemographic characteristics (age, race, marital status and educational attainment), fetal gender, maternal medical conditions (diabetes, chronic hypertension and PIH), cigarette smoking and early onset of prenatal care. Most etiologic determinants were associated with FD at >=37 weeks (with the strongest impact at 41 to 43 weeks). Only a few were associated with FD preterm (28-36 weeks).

f) During the study period, pronounced changes were observed in the prevalence of maternal cigarette smoking, advanced maternal age (>=35 years), unmarried status, and early onset of prenatal care. However, the net impact of these changes on the decrease in FDs was negligible.

g) For both Blacks and Whites, the frequency of labor induction was much higher at 41-43 weeks than at 37-40 weeks. Over time, significant trend was observed toward earlier and more frequent use of labor induction. Yet in Blacks, the induction rate remained only half that in Whites.

h) Between 1991 and 1997, the decrease in FDs at 40-43 weeks among U.S. Whites appears attributable to the increased use of induction of labor. Such an effect was observed both in high- and low-risk pregnancies. However, no significant effect of induction was observed in U.S. Blacks, either in high- or low-risk pregnancies.

The results of our study have several important implications relevant to clinical practice, public health policy, and epidemiologic research:

a) Current obstetric guidelines recommend that labor be induced in the presence of a favorable cervix between 41 and 42 weeks gestation. If the cervix is unfavorable, either induction of labor or antenatal fetal monitoring is an option (Maternal-Fetal Medicine, 4th edition, 1999). However, the results of the present study suggest an earlier (at or before 41 weeks) and routine use of labor induction to reduce the high risk in FD among postterm pregnancies. Meanwhile, with the increased availability of PG E_2, labor induction may not necessarily be conditional on a favorable cervix. Therefore, current obstetric guidelines regarding the use of labor induction should be re-evaluated.

b) Registration of FDs at extremely early GAs remains incomplete in the United States. State vital statistics offices therefore need to take further steps to improve

reporting. Meanwhile, public health surveillance and interpretation of fetal mortality trends need to take account of possible registration artifacts at early GAs.

c) In epidemiologic studies of FD, GA-specific FDR (fetal death risk or hazard) is the most appropriate measure of outcome. This definition should also be introduced into public health surveillance to facilitate the proper interpretation of temporal changes.

d) It is now clear that in etiologic studies of FD, the effect of potential determinants should be examined at different GAs. The potential modification of the effect of these determinants by GA may be masked if FDs are analyzed only as a whole.

e) To further reduce the incidence of FDs, future etiologic research, fetal surveillance, and prevention efforts should focus on unexplained preterm FDs. Risk factors such as intrauterine infections that may be responsible both for preterm labor and preterm FD are of particular concern.

f) International or regional (within-country) comparisons of fetal death hazards are warranted. Disparities between countries or regions with similar socioeconomic development and cultural and ethnic background may reflect differences in obstetric practice (e.g., policy of labor induction). Such comparisons should be limited to >=28 weeks GA to reduce the potential impact of incomplete registration of early FDs.

g) To overcome the limitations in our study, especially the lack of data on indication for labor induction, future epidemiologic research on the effect of labor induction is desirable, e.g., using hospital perinatal databases that have systematically collected data on covariates such as indication for labor induction.

h) As mentioned above, further methodologic exploration in multivarable modeling analyses in FD study are also warranted. At least three modeling approaches are

avaiable for FD study: logistic regression, Cox proportional hazards model, and piecewise exponential regression. Each applies under different assumptions and with its own limitations. A comparison of the three modeling appraoches might be revealing in regard of a proper estimate of FD risk and its determinants. For example, by examing the parameter estimates, it will help understand the extent to which a logistic regression approach biases the estimates compared with Cox regression model.

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APPENDIX: Figures (a.1-5) and Tables (a.1-5)

Figure a.1. Flow chart for study subjects exclusion in 50 States and D.C.

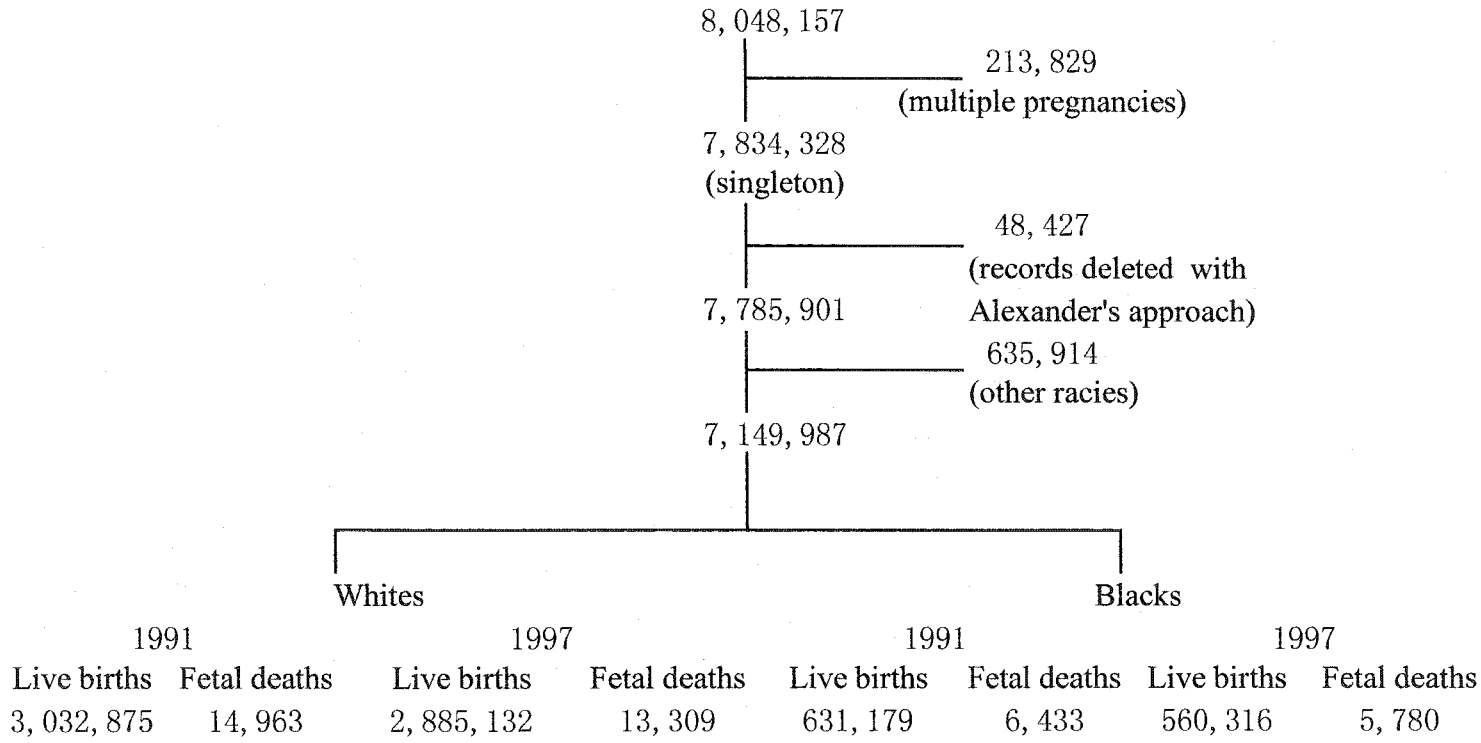


Figure a.2. Fetal death hazard: 50 States and District of Columbia, 1991 vs 1997 (before deletion of improbable GA records)

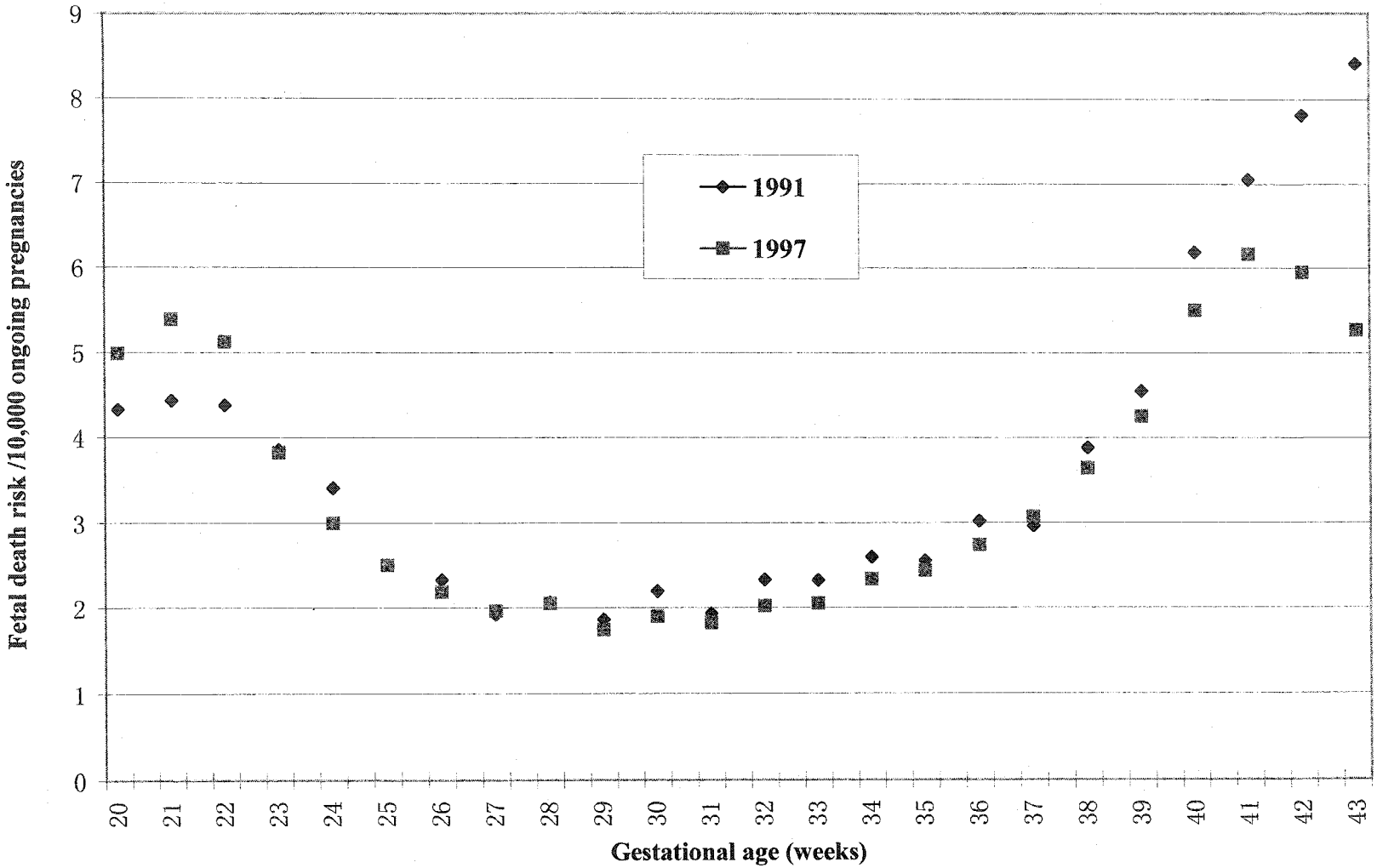


Figure a.3. Fetal death hazard: 50 States and District of Columbia, 1991 vs 1997 (after deletion of improbable GA records)

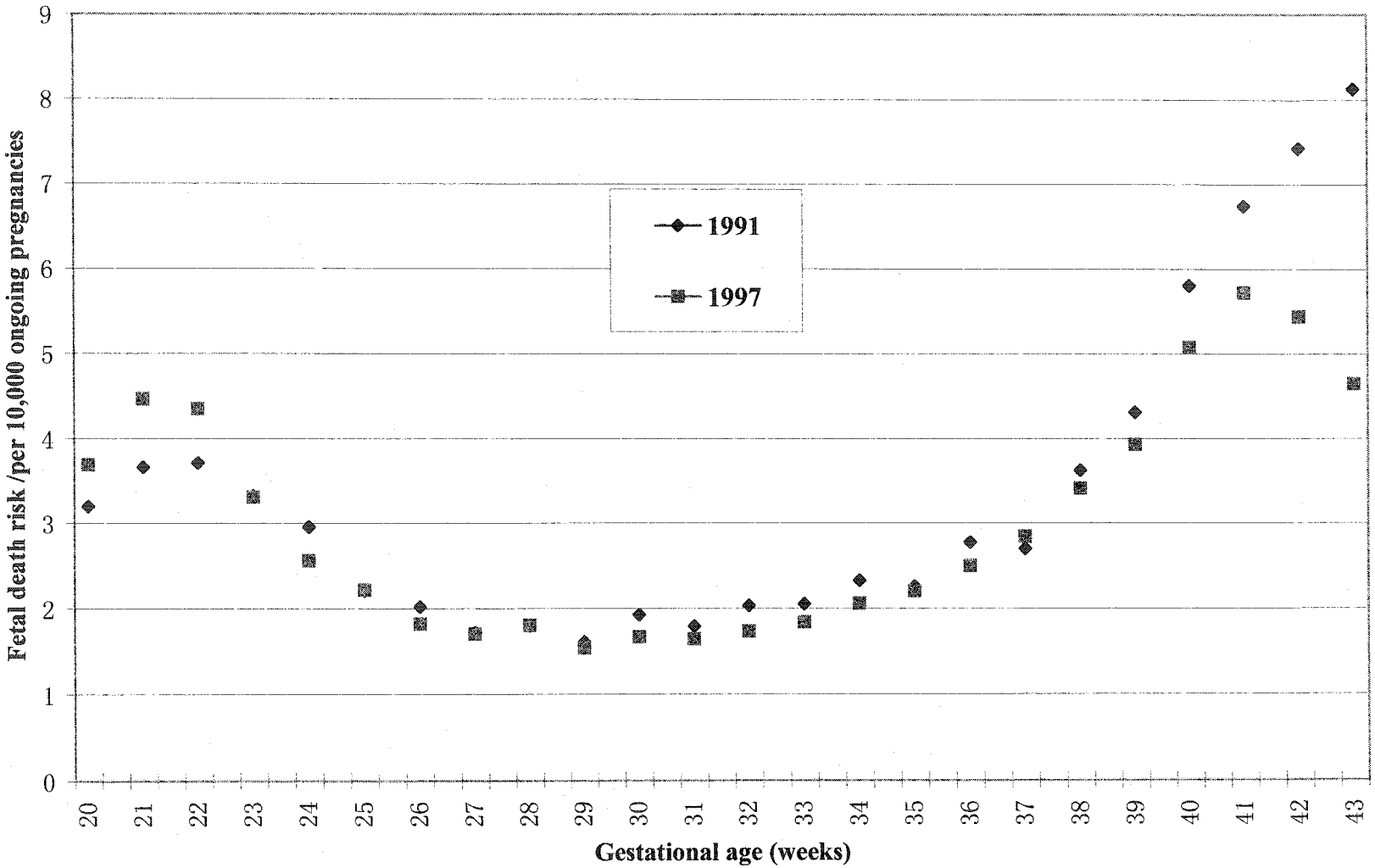


Figure a.4. Fetal death hazard: 39 States and District of Columbia, 1991 vs 1997 (before deletion of improbable GA records)

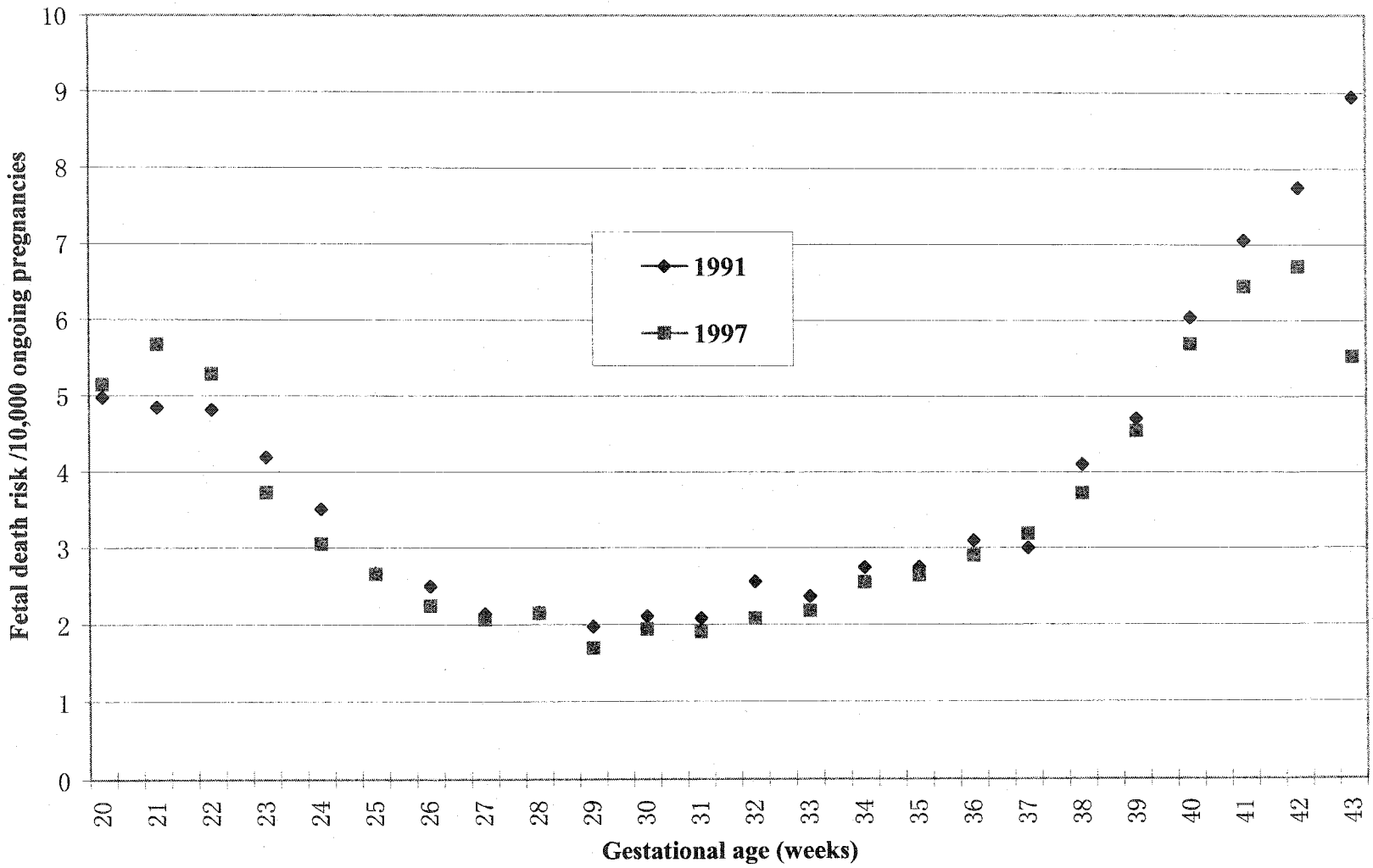


Figure a.5. Fetal death hazard: 39 States and District of Columbia, 1991 vs 1997 (after deletion of improbable GA records)

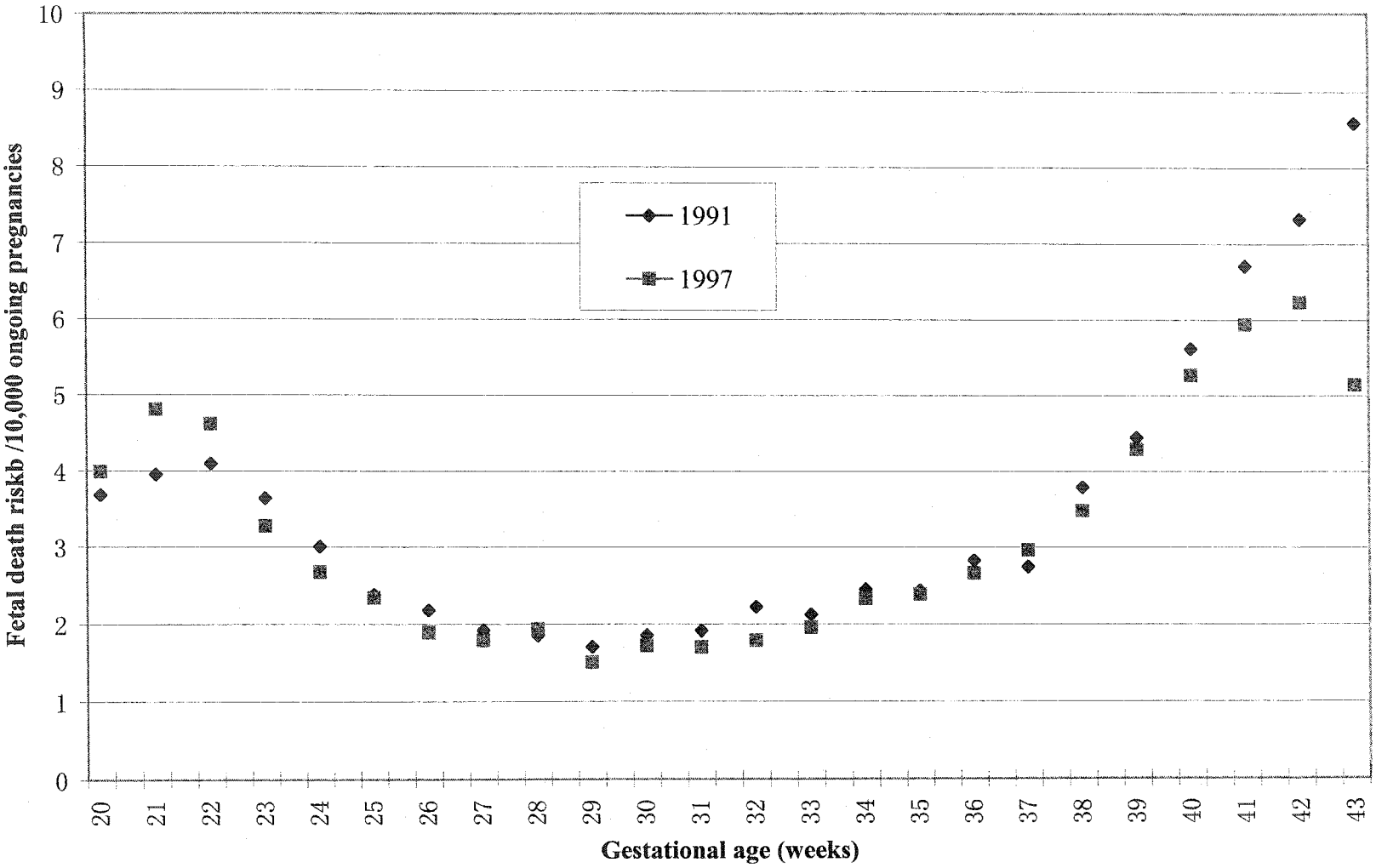


Table a.1. **Fetal deaths in the three early GA categories as a proportion* of total births and as proportion of perinatal deaths, and live births in the three early GA categores as a proportion* of total births: U.S. Whites, 1991 vs 1997**

	fetal/total			fetal/perinatal			live/total		
GA	1991	1997	RR[95% CI]	1991	1997	RR[95% CI]	1991	1997	RR[95% CI]
20-22	11.44	13.07	1.14 [1.19-1.09]	11.22	14.83	1.32 [1.39-1.26]	8.37	8.90	1.06 [1.12-1.01]
23-25	8.63	8.23	0.95 [1.01-0.90]	8.46	9.34	1.10 [1.17-1.04]	18.42	20.51	1.11 [1.15-1.07]
26-28	5.59	5.56	0.99 [1.06-0.93]	5.49	6.30	1.15 [1.23-1.07]	34.37	37.25	1.08 [1.11-1.06]
unknown	7.87	2.41	0.31 [0.56-0.17]	7.71	2.74	0.36 [0.39-0.33]	97.53	93.04	0.95 [0.99-0.92]
total	66.27	57.73	0.87 [0.89-0.85]	64.99	65.48	1.01 [1.03-0.98]			
No. of early neonatal deaths(<7 days):				11,647		9,402			
No. of fetal deaths:				21,620		17,838			
No. of perinatal deaths:				33,267		27,240			
No. of total births:				3,262,322 {1991}		3,089,932 {1997}			

Perintal deaths = fetal deaths + early neonatal deaths (<7 days)

RR = relative risk or rate ratio

Reference : 1991

CI = confidence interval

*Proportions are expressed per 10,000 total births or percent of perinatal deaths

Table a.2. **Fetal deaths in the three early GA categories as a proportion* of total births and as proportion of perinatal deaths, and live births in the three early GA categores as a proportion* of total births: U.S. Blacks, 1991 vs 1997**

	feta/total			feta/perinatal			live/total		
GA	1991	1997	RR[95% CI]	1991	1997	RR[95% CI]	1991	1997	RR[95% CI]
20-22	30.62	38.45	1.26 [1.33-1.18]	13.64	19.35	1.42 [1.51-1.33]	36.98	35.32	0.96 [1.01-0.90]
23-25	19.97	20.54	1.03 [1.11-0.95]	8.90	10.34	1.16 [1.26-1.07]	70.19	69.46	0.99 [1.03-0.95]
26-28	13.73	12.32	0.90 [0.99-0.82]	6.11	6.20	1.01 [1.12-0.92]	114.92	106.15	0.92 [0.95-0.89]
unknown	17.04	4.99	0.29 [0.53-0.16]	7.59	2.51	0.33 [0.38-0.29]	115.18	86.81	0.75 [0.79-0.72]
total	135.95	124.65	0.92 [0.95-0.89]	60.57	62.71	1.04 [1.08-1.00]			
No. of early neonatal deaths(<7 days):				6,120		4,499			
No. of fetal deaths:				9,400		7,566			
No. of perinatal deaths:				15,520		12,065			
No. of total births:				691,420 {1991}		606,975 {1997}			

Perintal deaths = early neonatal deaths (<7 days) + fetal deaths

RR = relative risk

Reference: 1991

CI = confidence interval

*Proportions are expressed per 10,000 total births or percent of perinatal deaths

Table a.3. Cox Proportional hazard model for determinants at 28 to 36 weeks

Variables	Adjusted HR	95% CI
Maternal age (yrs)		
<20	0.97	0.90-1.05
20-34	1.00 (Reference)	
>=35	1.23	1.15-1.30
Black race	1.24	1.18-1.30
Male gender	1.00	0.95-1.05
Maternal education <=12 yrs	0.86	0.81-0.92
1st-trimester prenatal care	0.78	0.73-0.84
Unmarried status	1.07	1.01-1.13
Nulliparity	1.07	1.01-1.14
Cigarette smoking	1.19	1.17-1.20
Diabetes	1.21	1.10-1.33
Chronic hypertension	2.14	2.00-2.28
PIH	1.15	1.05-1.24

HR = hazard ratio
CI = confidence interval
PIH = pregnancy-induced hypertension

Table a.4. **Cox Proportional hazard model for determinants at 37 to 40 weeks**

Variables	Adjusted HR	95% CI
Maternal age (yrs)		
<20	0.91	0.81-01.01
20-34	1.00 (Reference)	
>=35	1.53	1.43-1.62
Black race	1.36	1.27-1.44
Male gender	1.02	0.96-1.08
Maternal education <=12 yrs	1.18	1.11-1.25
1st-trimester prenatal care	0.66	0.59-0.74
Unmarried status	1.24	1.17-1.32
Nulliparity	1.06	0.99-1.15
Cigarette smoking	1.21	1.20-1.23
Diabetes	2.39	2.25-2.52
Chronic hypertension	3.25	3.04-3.46
PIH	1.58	1.43-1.72

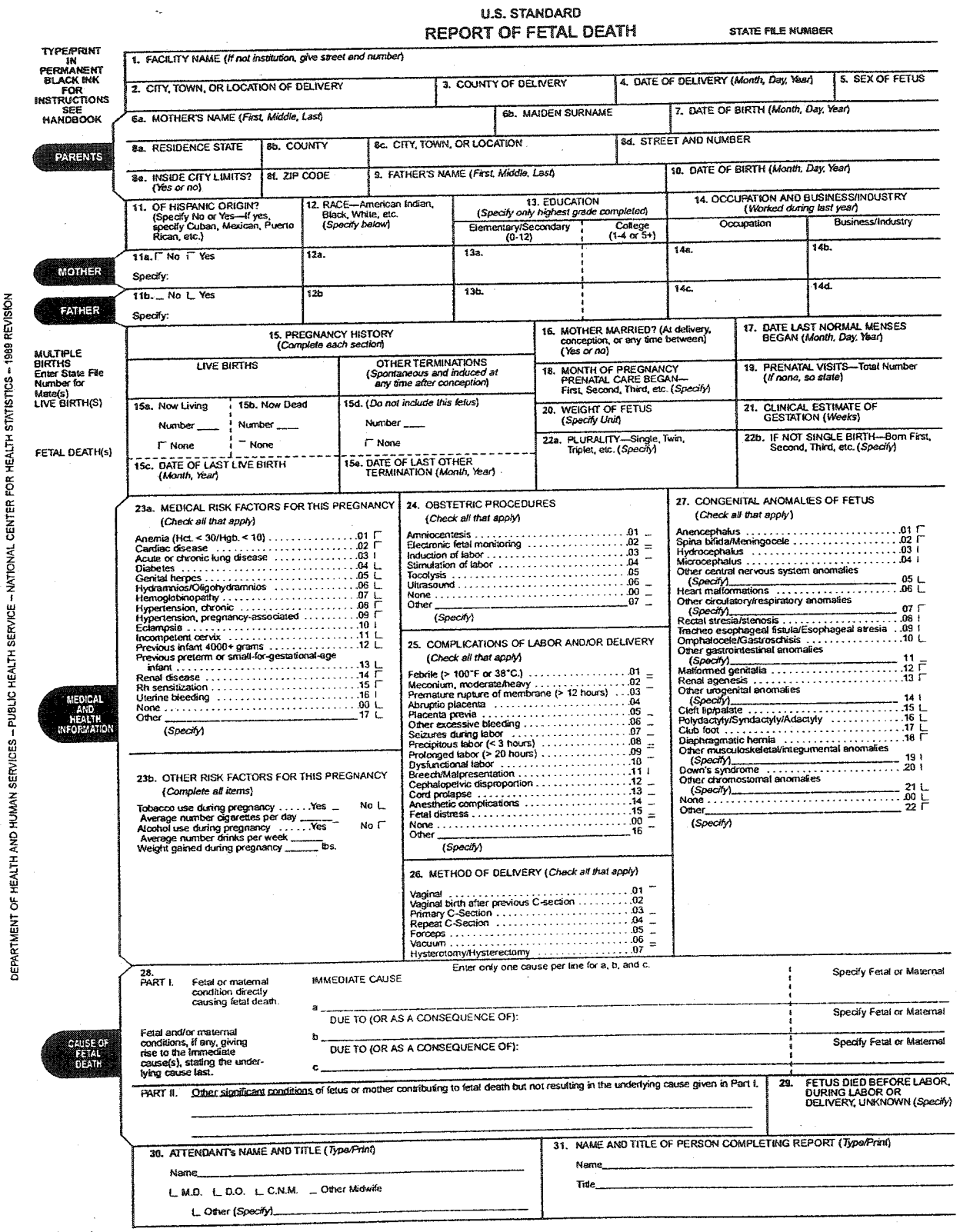
HR = hazard ratio
CI = confidence interval
PIH = pregnancy-induced hypertension

Table a.5. Cox Proportional hazard model for determinants at 41 to 43 weeks

Variables	Adjusted HR	95% CI
Maternal age (yrs)		
<20	0.71	0.50-0.92
20-34	1.00 (Reference)	
>=35	2.21	2.02-2.40
Black race	1.22	1.04-1.40
Male gender	0.85	0.72-0.98
Maternal education <=12 yrs	1.20	1.06-1.35
1st-trimester prenatal care	0.70	0.55-0.85
Unmarried status	1.20	1.05-1.36
Nulliparity	1.28	1.08-1.57
Cigarette smoking	1.20	1.17-1.24
Diabetes	2.14	1.81-2.47
Chronic hypertension	1.75	1.09-2.40
PIH	1.90	1.59-2.20

HR = hazard ratio
CI = confidence interval
PIH = pregnancy-induced hypertension

Appendix A.



U.S. STANDARD
REPORT OF FETAL DEATH

STATE FILE NUMBER

TYPE/PRINT IN PERMANENT BLACK INK FOR INSTRUCTIONS SEE HANDBOOK

DEPARTMENT OF HEALTH AND HUMAN SERVICES – PUBLIC HEALTH SERVICE – NATIONAL CENTER FOR HEALTH STATISTICS – 1989 REVISION

1. FACILITY NAME (*If not institution, give street and number*)

2. CITY, TOWN, OR LOCATION OF DELIVERY | 3. COUNTY OF DELIVERY | 4. DATE OF DELIVERY (*Month, Day, Year*) | 5. SEX OF FETUS

PARENTS

6a. MOTHER'S NAME (*First, Middle, Last*) | 6b. MAIDEN SURNAME | 7. DATE OF BIRTH (*Month, Day, Year*)

8a. RESIDENCE STATE | 8b. COUNTY | 8c. CITY, TOWN, OR LOCATION | 8d. STREET AND NUMBER

8e. INSIDE CITY LIMITS? (*Yes or no*) | 8f. ZIP CODE | 9. FATHER'S NAME (*First, Middle, Last*) | 10. DATE OF BIRTH (*Month, Day, Year*)

	11. OF HISPANIC ORIGIN? (Specify No or Yes—If yes, specify Cuban, Mexican, Puerto Rican, etc.)	12. RACE—American Indian, Black, White, etc. (*Specify below*)	13. EDUCATION (*Specify only highest grade completed*) Elementary/Secondary (0-12)	13. EDUCATION College (1-4 or 5+)	14. OCCUPATION AND BUSINESS/INDUSTRY (*Worked during last year*) Occupation	Business/Industry
MOTHER	11a. ☐ No ☐ Yes Specify:	12a.	13a.		14a.	14b.
FATHER	11b. ☐ No ☐ Yes Specify:	12b	13b.		14c.	14d.

MULTIPLE BIRTHS Enter State File Number for Mate(s) LIVE BIRTH(S)

FETAL DEATH(s)

15. PREGNANCY HISTORY (*Complete each section*)

LIVE BIRTHS		OTHER TERMINATIONS (*Spontaneous and induced at any time after conception*)
15a. Now Living Number ____ ☐ None	15b. Now Dead Number ____ ☐ None	15d. (*Do not include this fetus*) Number ____ ☐ None
15c. DATE OF LAST LIVE BIRTH (*Month, Year*)		15e. DATE OF LAST OTHER TERMINATION (*Month, Year*)

16. MOTHER MARRIED? (At delivery, conception, or any time between) (*Yes or no*)

17. DATE LAST NORMAL MENSES BEGAN (*Month, Day, Year*)

18. MONTH OF PREGNANCY PRENATAL CARE BEGAN—First, Second, Third, etc. (*Specify*)

19. PRENATAL VISITS—Total Number (*If none, so state*)

20. WEIGHT OF FETUS (*Specify Unit*)

21. CLINICAL ESTIMATE OF GESTATION (*Weeks*)

22a. PLURALITY—Single, Twin, Triplet, etc. (*Specify*)

22b. IF NOT SINGLE BIRTH—Born First, Second, Third, etc. (*Specify*)

MEDICAL AND HEALTH INFORMATION

23a. MEDICAL RISK FACTORS FOR THIS PREGNANCY (*Check all that apply*)

Anemia (Hct. < 30/Hgb. < 10) ..... .01 ☐
Cardiac disease ..... .02 ☐
Acute or chronic lung disease ..... .03 ☐
Diabetes ..... .04 ☐
Genital herpes ..... .05 ☐
Hydramnios/Oligohydramnios ..... .06 ☐
Hemoglobinopathy ..... .07 ☐
Hypertension, chronic ..... .08 ☐
Hypertension, pregnancy-associated ..... .09 ☐
Eclampsia ..... .10 ☐
Incompetent cervix ..... .11 ☐
Previous infant 4000+ grams ..... .12 ☐
Previous preterm or small-for-gestational-age infant ..... .13 ☐
Renal disease ..... .14 ☐
Rh sensitization ..... .15 ☐
Uterine bleeding ..... .16 ☐
None ..... .00 ☐
Other _____ .17 ☐
(*Specify*)

23b. OTHER RISK FACTORS FOR THIS PREGNANCY (*Complete all items*)

Tobacco use during pregnancy ..... Yes ☐ No ☐
Average number cigarettes per day _____
Alcohol use during pregnancy ..... Yes ☐ No ☐
Average number drinks per week _____
Weight gained during pregnancy _____ lbs.

24. OBSTETRIC PROCEDURES (*Check all that apply*)

Amniocentesis ..... .01 ☐
Electronic fetal monitoring ..... .02 ☐
Induction of labor ..... .03 ☐
Stimulation of labor ..... .04 ☐
Tocolysis ..... .05
Ultrasound ..... .06 ☐
None ..... .00 ☐
Other _____ .07 ☐
(*Specify*)

25. COMPLICATIONS OF LABOR AND/OR DELIVERY (*Check all that apply*)

Febrile (> 100°F or 38°C.) ..... .01 ☐
Meconium, moderate/heavy ..... .02 ☐
Premature rupture of membrane (> 12 hours) ..... .03 ☐
Abruptio placenta ..... .04
Placenta previa ..... .05 ☐
Other excessive bleeding ..... .06 ☐
Seizures during labor ..... .07 ☐
Precipitous labor (< 3 hours) ..... .08 ☐
Prolonged labor (> 20 hours) ..... .09 ☐
Dysfunctional labor ..... .10 ☐
Breech/Malpresentation ..... .11 ☐
Cephalopelvic disproportion ..... .12 ☐
Cord prolapse ..... .13 ☐
Anesthetic complications ..... .14 ☐
Fetal distress ..... .15 ☐
None ..... .00 ☐
Other _____ .16 ☐
(*Specify*)

26. METHOD OF DELIVERY (*Check all that apply*)

Vaginal ..... .01 ☐
Vaginal birth after previous C-section ..... .02
Primary C-Section ..... .03 ☐
Repeat C-Section ..... .04 ☐
Forceps ..... .05 ☐
Vacuum ..... .06 ☐
Hysterotomy/Hysterectomy ..... .07 ☐

27. CONGENITAL ANOMALIES OF FETUS (*Check all that apply*)

Anencephalus ..... .01 ☐
Spina bifida/Meningocele ..... .02 ☐
Hydrocephalus ..... .03 ☐
Microcephalus ..... .04 ☐
Other central nervous system anomalies (*Specify*)_____ 05 ☐
Heart malformations ..... .06 ☐
Other circulatory/respiratory anomalies (*Specify*)_____ 07 ☐
Rectal stresia/stenosis ..... .08 ☐
Tracheo esophageal fistula/Esophageal stresia ..09 ☐
Omphalocele/Gastroschisis ..... .10 ☐
Other gastrointestinal anomalies (*Specify*)_____ 11 ☐
Malformed genitalia ..... .12 ☐
Renal agenesis ..... .13 ☐
Other urogenital anomalies (*Specify*)_____ 14 ☐
Cleft lip/palate ..... .15 ☐
Polydactyly/Syndactyly/Adactyly ..... .16 ☐
Club foot ..... .17 ☐
Diaphragmatic hernia ..... .18 ☐
Other musculoskeletal/integumental anomalies (*Specify*)_____ 19 ☐
Down's syndrome ..... .20 ☐
Other chromostomal anomalies (*Specify*)_____ 21 ☐
None ..... .00 ☐
Other_____ 22 ☐
(*Specify*)

CAUSE OF FETAL DEATH

28. PART I. Fetal or maternal condition directly causing fetal death. Enter only one cause per line for a, b, and c.

IMMEDIATE CAUSE — Specify Fetal or Maternal

a _____

DUE TO (OR AS A CONSEQUENCE OF): — Specify Fetal or Maternal

b _____

DUE TO (OR AS A CONSEQUENCE OF): — Specify Fetal or Maternal

c _____

Fetal and/or maternal conditions, if any, giving rise to the immediate cause(s), stating the underlying cause last.

PART II. Other significant conditions of fetus or mother contributing to fetal death but not resulting in the underlying cause given in Part I.

29. FETUS DIED BEFORE LABOR, DURING LABOR OR DELIVERY, UNKNOWN (*Specify*)

30. ATTENDANT'S NAME AND TITLE (*Type/Print*)

Name_____

☐ M.D. ☐ D.O. ☐ C.N.M. ☐ Other Midwife

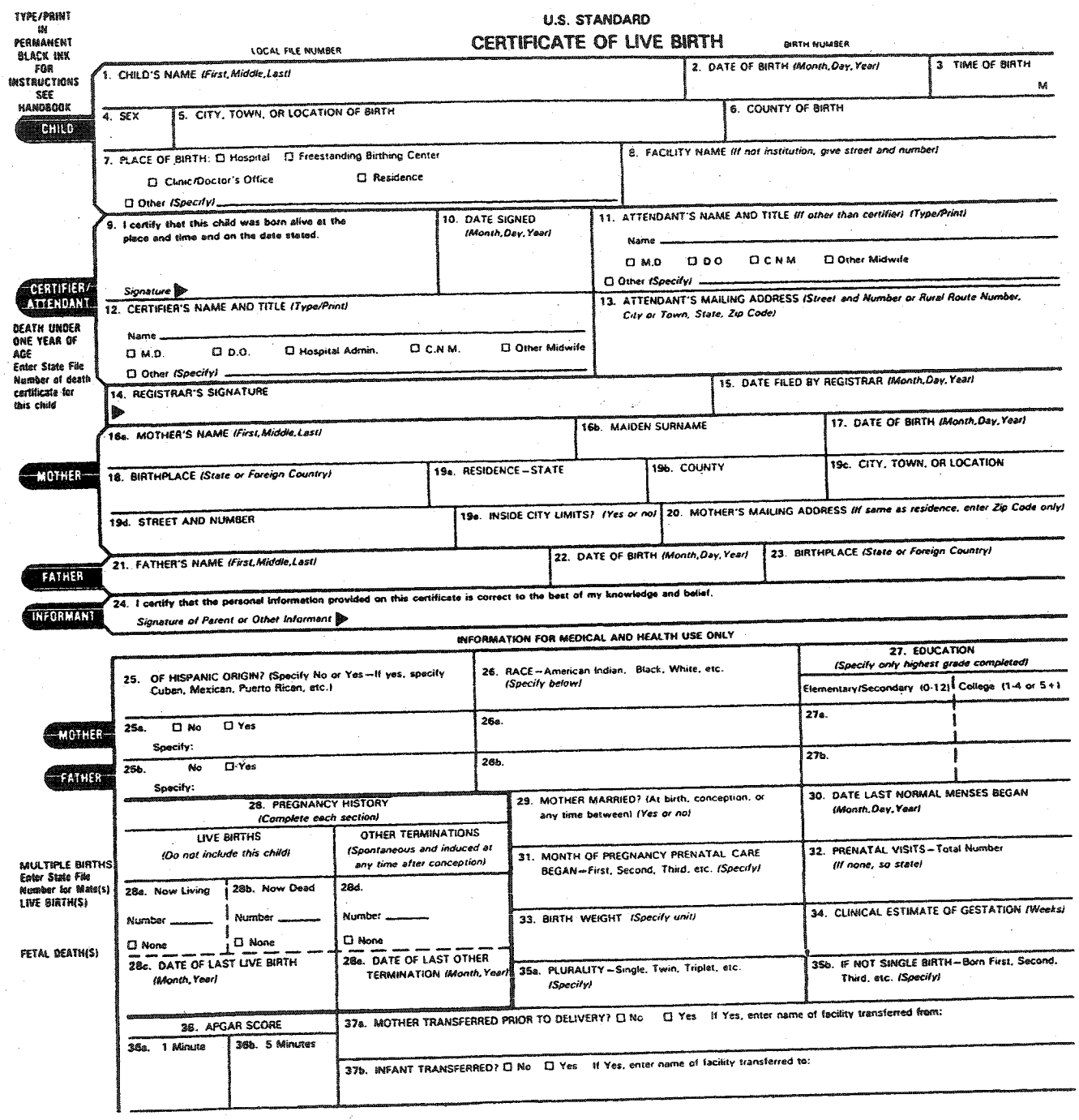
☐ Other (*Specify*)_____

31. NAME AND TITLE OF PERSON COMPLETING REPORT (*Type/Print*)

Name_____

Title_____

Appendix B.



TYPE/PRINT IN PERMANENT BLACK INK FOR INSTRUCTIONS SEE HANDBOOK

U.S. STANDARD

CERTIFICATE OF LIVE BIRTH

LOCAL FILE NUMBER

BIRTH NUMBER

CHILD

1. CHILD'S NAME (First, Middle, Last)
2. DATE OF BIRTH (Month, Day, Year)
3. TIME OF BIRTH
4. SEX
5. CITY, TOWN, OR LOCATION OF BIRTH
6. COUNTY OF BIRTH
7. PLACE OF BIRTH: ☐ Hospital ☐ Freestanding Birthing Center ☐ Clinic/Doctor's Office ☐ Residence ☐ Other (Specify)
8. FACILITY NAME (If not institution, give street and number)

CERTIFIER/ ATTENDANT

9. I certify that this child was born alive at the place and time and on the date stated. Signature ▶
10. DATE SIGNED (Month, Day, Year)
11. ATTENDANT'S NAME AND TITLE (If other than certifier) (Type/Print) Name ☐ M.D ☐ D O ☐ C N M ☐ Other Midwife ☐ Other (Specify)
12. CERTIFIER'S NAME AND TITLE (Type/Print) Name ☐ M.D. ☐ D.O. ☐ Hospital Admin. ☐ C.N M. ☐ Other Midwife ☐ Other (Specify)
13. ATTENDANT'S MAILING ADDRESS (Street and Number or Rural Route Number, City or Town, State, Zip Code)

DEATH UNDER ONE YEAR OF AGE Enter State File Number of death certificate for this child

14. REGISTRAR'S SIGNATURE ▶
15. DATE FILED BY REGISTRAR (Month, Day, Year)

MOTHER

16a. MOTHER'S NAME (First, Middle, Last)
16b. MAIDEN SURNAME
17. DATE OF BIRTH (Month, Day, Year)
18. BIRTHPLACE (State or Foreign Country)
19a. RESIDENCE – STATE
19b. COUNTY
19c. CITY, TOWN, OR LOCATION
19d. STREET AND NUMBER
19e. INSIDE CITY LIMITS? (Yes or no)
20. MOTHER'S MAILING ADDRESS (If same as residence, enter Zip Code only)

FATHER

21. FATHER'S NAME (First, Middle, Last)
22. DATE OF BIRTH (Month, Day, Year)
23. BIRTHPLACE (State or Foreign Country)

INFORMANT

24. I certify that the personal information provided on this certificate is correct to the best of my knowledge and belief. Signature of Parent or Other Informant ▶

INFORMATION FOR MEDICAL AND HEALTH USE ONLY

25. OF HISPANIC ORIGIN? (Specify No or Yes – If yes, specify Cuban, Mexican, Puerto Rican, etc.)	26. RACE – American Indian, Black, White, etc. (Specify below)	27. EDUCATION (Specify only highest grade completed) Elementary/Secondary (0-12) | College (1-4 or 5+)
MOTHER 25a. ☐ No ☐ Yes Specify:	26a.	27a.
FATHER 25b. ☐ No ☐ Yes Specify:	26b.	27b.

28. PREGNANCY HISTORY (Complete each section)		29. MOTHER MARRIED? (At birth, conception, or any time between) (Yes or no)	30. DATE LAST NORMAL MENSES BEGAN (Month, Day, Year)
LIVE BIRTHS (Do not include this child)	OTHER TERMINATIONS (Spontaneous and induced at any time after conception)		
MULTIPLE BIRTHS: Enter State File Number for Mate(s) LIVE BIRTH(S) 28a. Now Living Number ☐ None 28b. Now Dead Number ☐ None	28d. Number ☐ None	31. MONTH OF PREGNANCY PRENATAL CARE BEGAN – First, Second, Third, etc. (Specify)	32. PRENATAL VISITS – Total Number (If none, so state)
FETAL DEATH(S) 28c. DATE OF LAST LIVE BIRTH (Month, Year)	28e. DATE OF LAST OTHER TERMINATION (Month, Year)	33. BIRTH WEIGHT (Specify unit)	34. CLINICAL ESTIMATE OF GESTATION (Weeks)
		35a. PLURALITY – Single, Twin, Triplet, etc. (Specify)	35b. IF NOT SINGLE BIRTH – Born First, Second, Third, etc. (Specify)
36. APGAR SCORE 36a. 1 Minute 36b. 5 Minutes		37a. MOTHER TRANSFERRED PRIOR TO DELIVERY? ☐ No ☐ Yes If Yes, enter name of facility transferred from:	
		37b. INFANT TRANSFERRED? ☐ No ☐ Yes If Yes, enter name of facility transferred to:	

38a. MEDICAL RISK FACTORS FOR THIS PREGNANCY

(Check all that apply)

- Anemia (Hct. < 30/Hgb. < 10) . . . 01 ☐
- Cardiac disease . . . 02 ☐
- Acute or chronic lung disease . . . 03 ☐
- Diabetes . . . 04 ☐
- Genital Herpes . . . 05 ☐
- Hydramnios/Oligohydramnios . . . 06 ☐
- Hemoglobinopathy . . . 07 ☐
- Hypertension, chronic . . . 08 ☐
- Hypertension, pregnancy-associated . . . 09 ☐
- Eclampsia . . . 10 ☐
- Incompetent cervix . . . 11 ☐
- Previous infant 4000+ grams . . . 12 ☐
- Previous preterm or small-for-gestational-age infant . . . 13 ☐
- Renal disease . . . 14 ☐
- Rh sensitization . . . 15 ☐
- Uterine bleeding . . . 16 ☐
- None . . . 00 ☐
- Other _____ 17 ☐ *(Specify)*

38b. OTHER RISK FACTORS FOR THIS PREGNANCY

(Complete all items)

- Tobacco use during pregnancy . . . Yes ☐ No ☐
  - Average number cigarettes per day _____
- Alcohol use during pregnancy . . . Yes ☐ No ☐
  - Average number drinks per week _____
- Weight gained during pregnancy _____ lbs.

39. OBSTETRIC PROCEDURES

(Check all that apply)

- Amniocentesis . . . 01 ☐
- Electronic fetal monitoring . . . 02 ☐
- Induction of labor . . . 03 ☐
- Stimulation of labor . . . 04 ☐
- Tocolysis . . . 05 ☐
- Ultrasound . . . 06 ☐
- None . . . 00 ☐
- Other _____ 07 ☐ *(Specify)*

40. COMPLICATIONS OF LABOR AND/OR DELIVERY

(Check all that apply)

- Febrile (>100°F. or 38°C.) . . . 01 ☐
- Meconium, moderate/heavy . . . 02 ☐
- Premature rupture of membrane (>12 hours) . . . 03 ☐
- Abruptio placenta . . . 04 ☐
- Placenta previa . . . 05 ☐
- Other excessive bleeding . . . 06 ☐
- Seizures during labor . . . 07 ☐
- Precipitous labor (<3 hours) . . . 08 ☐
- Prolonged labor (>20 hours) . . . 09 ☐
- Dysfunctional labor . . . 10 ☐
- Breech/Malpresentation . . . 11 ☐
- Cephalopelvic disproportion . . . 12 ☐
- Cord prolapse . . . 13 ☐
- Anesthetic complications . . . 14 ☐
- Fetal distress . . . 15 ☐
- None . . . 00 ☐
- Other _____ 16 ☐ *(Specify)*

41. METHOD OF DELIVERY *(Check all that apply)*

- Vaginal . . . 01 ☐
- Vaginal birth after previous C-section . . . 02 ☐
- Primary C-section . . . 03 ☐
- Repeat C-section . . . 04 ☐
- Forceps . . . 05 ☐
- Vacuum . . . 06 ☐

42. ABNORMAL CONDITIONS OF THE NEWBORN

(Check all that apply)

- Anemia (Hct. < 39/Hgb. < 13) . . . 01 ☐
- Birth injury . . . 02 ☐
- Fetal alcohol syndrome . . . 03 ☐
- Hyaline membrane disease/RDS . . . 04 ☐
- Meconium aspiration syndrome . . . 05 ☐
- Assisted ventilation <30 min . . . 06 ☐
- Assisted ventilation ≥30 min . . . 07 ☐
- Seizures . . . 08 ☐
- None . . . 00 ☐
- Other _____ 09 ☐ *(Specify)*

43. CONGENITAL ANOMALIES OF CHILD

(Check all that apply)

- Anencephalus . . . 01 ☐
- Spina bifida/Meningocele . . . 02 ☐
- Hydrocephalus . . . 03 ☐
- Microcephalus . . . 04 ☐
- Other central nervous system anomalies *(Specify)* _____ 05 ☐
- Heart malformations . . . 06 ☐
- Other circulatory/respiratory anomalies *(Specify)* _____ 07 ☐
- Rectal atresia/stenosis . . . 08 ☐
- Tracheo-esophageal fistula/Esophageal atresia . . . 09 ☐
- Omphalocele/Gastroschisis . . . 10 ☐
- Other gastrointestinal anomalies *(Specify)* _____ 11 ☐
- Malformed genitalia . . . 12 ☐
- Renal agenesis . . . 13 ☐
- Other urogenital anomalies *(Specify)* _____ 14 ☐
- Cleft lip/palate . . . 15 ☐
- Polydactyly/Syndactyly/Adactyly . . . 16 ☐
- Club feet . . . 17 ☐
- Diaphragmatic hernia . . . 18 ☐
- Other musculoskeletal/integumental anomalies *(Specify)* _____ 19 ☐
- Down's syndrome . . . 20 ☐
- Other chromosomal anomalies *(Specify)* _____ 21 ☐
- None . . . 00 ☐
- Other _____ 22 ☐ *(Specify)*

Appendix C.

Birth Weight and Gestational Age Inclusion Criteria

Gestational Age (weeks)	Birth Weight (g)
20-21	125-1250
22	125-1375
23	125-1500
24	125-1625
25	250-1750
26	250-2000
27	250-2250
28	250-2500
29	250-2750
30	375-3000
31	375-3250
32	500-3500
33	500-3750
34	750-4000
35	750-4500
36	750-5000
37	1000-5500
>=38	1000-6000

Cases with a birth weight value within the stated range for their specific gestational age were included in the study.

Appendix D.

Dr. Robert W. Platt's SAS procedure for deleting GA errors using Alexander's Approach

```
data one;
infile 'f:\cohort.txt';
input gestage bwt mort;

ALEXA = 0;  ALEXB = 0;
IF GESTAGE LE 21 AND BWT GT 1250 THEN ALEXA = 1;
IF GESTAGE = 22 AND BWT GT 1375 THEN ALEXA = 1;
IF GESTAGE = 23 AND BWT GT 1500 THEN ALEXA = 1;
IF GESTAGE = 24 AND BWT GT 1625 THEN ALEXA = 1;
IF GESTAGE = 25 AND BWT GT 1750 THEN ALEXA = 1;
IF GESTAGE = 26 AND BWT GT 2000 THEN ALEXA = 1;
IF GESTAGE = 27 AND BWT GT 2250 THEN ALEXA = 1;
IF GESTAGE = 28 AND BWT GT 2500 THEN ALEXA = 1;
IF GESTAGE = 29 AND BWT GT 2750 THEN ALEXA = 1;
IF GESTAGE = 30 AND BWT GT 3000 THEN ALEXA = 1;
IF GESTAGE = 31 AND BWT GT 3250 THEN ALEXA = 1;
IF GESTAGE = 32 AND BWT GT 3500 THEN ALEXA = 1;
IF GESTAGE = 33 AND BWT GT 3750 THEN ALEXA = 1;
IF GESTAGE = 34 AND BWT GT 4000 THEN ALEXA = 1;
IF GESTAGE = 35 AND BWT GT 4500 THEN ALEXA = 1;
IF GESTAGE = 36 AND BWT GT 5000 THEN ALEXA = 1;
IF GESTAGE = 37 AND BWT GT 5500 THEN ALEXA = 1;
IF GESTAGE > 37 AND BWT GT 6000 THEN ALEXA = 1;

IF GESTAGE IN (20,21,22,23,24) AND BWT LT 125 THEN ALEXB = 1;
IF GESTAGE IN (25,26,27,28,29)      AND BWT LT 250 THEN ALEXB = 1;
IF GESTAGE IN (30,31)          AND BWT LT 375 THEN ALEXB = 1;
IF GESTAGE IN (32,33)          AND BWT LT 500 THEN ALEXB = 1;
IF GESTAGE IN (34,35,36)        AND BWT LT 750 THEN ALEXB = 1;
IF GESTAGE > 36               AND BWT LT 1000 THEN ALEXB = 1;

ALEX = 0; IF ALEXA = 1 OR ALEXB = 1 THEN ALEX = 1;

run;

libname test 'f:\';

data two;
set one;
if alex=1 then delete;
run;
```

Appendix E. Results of testing proportional hazard (PH) assumption

Table E.1. Results of testing PH assumption using SAS proportionality test statement (for pregnancies at 28-36 weeks GA)

Testing Global Null Hypothesis: BETA=0

Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	973.3143	26	<.0001
Score	1453.7340	26	<.0001
Wald	1312.1617	26	<.0001

Analysis of Maximum Likelihood Estimates

Variable	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio
birthyr	1	0.34835	0.30850	1.2750	0.2588	1.417
mage1	1	1.22392	0.46563	6.9091	0.0086	3.400
mage2	1	-0.57644	0.47520	1.4715	0.2251	0.562
race	1	0.30177	0.36734	0.6748	0.4114	1.352
meduct	1	-0.95529	0.34324	7.7458	0.0054	0.385
mprev1	1	0.73795	0.34976	4.4517	0.0349	2.092
marital	1	0.10950	0.37812	0.0839	0.7721	1.116
nullipar	1	0.57689	0.34636	2.7742	0.0958	1.780
sex	1	-0.16628	0.30549	0.2963	0.5862	0.847
tobacc	1	0.18248	0.07647	5.6948	0.0170	1.200
diabetes1	1	-4.11170	0.80362	26.1782	<.0001	0.016
chyper1	1	1.54300	0.85349	3.2684	0.0706	4.679
phyper1	1	1.01545	0.60533	2.8141	0.0934	2.761
birthyrt	1	-0.01123	0.00951	1.3942	0.2377	0.989
mage1t	1	-0.03882	0.01441	7.2527	0.0071	0.962
mage2t	1	0.02415	0.01459	2.7376	0.0980	1.024
racet	1	-0.00269	0.01134	0.0562	0.8127	0.997
meductt	1	0.02490	0.01058	5.5460	0.0185	1.025
mprev1t	1	-0.03040	0.01078	7.9521	0.0048	0.970
maritalt	1	-0.00140	0.01166	0.0144	0.9044	0.999
nullipart	1	-0.02004	0.01067	3.5255	0.0604	0.980
sext	1	0.00515	0.00942	0.2987	0.5847	1.005

tobacct	1	-0.0003599	0.00237	0.0232	0.8790	1.000
diabetes1t	1	0.13134	0.02419	29.4871	<.0001	1.140
chyper1t	1	-0.02415	0.02644	0.8345	0.3610	0.976
phyper1t	1	-0.02722	0.01877	2.1044	0.1469	0.973

Linear Hypotheses Testing Results

Label	Wald Chi-Square	DF	Pr > ChiSq
PROPORTIONALITY_TEST	55.7215	13	<.0001

Table E.2. Results of testing PH assumption using SAS proportionality test statement (for pregnancies at 37-40 weeks GA)

Testing Global Null Hypothesis: BETA=0

Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	1151.8914	26	<.0001
Score	1707.6240	26	<.0001
Wald	1523.0966	26	<.0001

Analysis of Maximum Likelihood Estimates

Variable	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio
birthyr	1	0.95436	1.13860	0.7026	0.4019	2.597
mage1	1	0.98448	1.87272	0.2764	0.5991	2.676
mage2	1	-2.65721	1.68885	2.4755	0.1156	0.070
race	1	0.54116	1.49283	0.1314	0.7170	1.718
meduct	1	-0.64640	1.25812	0.2640	0.6074	0.524
mprev1	1	-1.31351	1.32296	0.9858	0.3208	0.269
marital	1	-0.21038	1.42251	0.0219	0.8824	0.810
nullipar	1	2.08632	1.28658	2.6296	0.1049	8.055
sex	1	2.59354	1.13118	5.2568	0.0219	13.377
tobacc	1	0.22745	0.27912	0.6641	0.4151	1.255
diabetes1	1	5.08063	2.46589	4.2451	0.0394	160.875
chyper1	1	-0.22433	3.80434	0.0035	0.9530	0.799
phyper1	1	3.11935	2.69408	1.3406	0.2469	22.632
birthyrt	1	-0.02558	0.02958	0.7479	0.3872	0.975
mage1t	1	-0.02801	0.04865	0.3316	0.5647	0.972
mage2t	1	0.08013	0.04386	3.3386	0.0677	1.083
racet	1	-0.00618	0.03881	0.0254	0.8735	0.994
meductt	1	0.02103	0.03269	0.4139	0.5200	1.021
mprev1t	1	0.02355	0.03437	0.4693	0.4933	1.024
maritalt	1	0.01119	0.03695	0.0917	0.7620	1.011
nullipart	1	-0.05580	0.03340	2.7918	0.0947	0.946
sext	1	-0.06683	0.02939	5.1724	0.0229	0.935
tobacct	1	-0.0009184	0.00725	0.0161	0.8992	0.999

diabetes1t	1	-0.10982	0.06439	2.9091	0.0881	0.896
chyper1t	1	0.03656	0.09905	0.1362	0.7121	1.037
phyper1t	1	-0.06944	0.07028	0.9763	0.3231	0.933

Linear Hypotheses Testing Results

Label	Wald Chi-Square	DF	Pr > ChiSq
PROPORTIONALITY_TEST	15.5749	13	0.2729

Table E.3. Results of testing PH assumption using SAS proportionality test statement (for pregnancies at 41-43 weeks GA)

Testing Global Null Hypothesis: BETA=0

Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	256.5771	26	<.0001
Score	356.0744	26	<.0001
Wald	325.7079	26	<.0001

Analysis of Maximum Likelihood Estimates

Variable	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio
birthyr	1	6.21684	3.95991	2.4647	0.1164	501.117
mage1	1	12.41778	6.44146	3.7164	0.0539	247157.5
mage2	1	-0.11811	5.64503	0.0004	0.9833	0.889
race	1	-1.85062	5.01893	0.1360	0.7123	0.157
meduct	1	-2.91512	4.31784	0.4558	0.4996	0.054
mprev1	1	2.46457	4.22139	0.3409	0.5593	11.758
marital	1	-4.18115	4.50100	0.8629	0.3529	0.015
nullipar	1	-4.68698	4.24431	1.2195	0.2695	0.009
sex	1	1.07641	3.80293	0.0801	0.7771	2.934
tobacc	1	0.43571	1.02271	0.1815	0.6701	1.546
diabetes1	1	-17.74267	8.67610	4.1820	0.0409	0.000
chyper1	1	7.19501	19.04501	0.1427	0.7056	1332.760
phyper1	1	0.57306	8.65038	0.0044	0.9472	1.774
birthyrt	1	-0.15254	0.09535	2.5592	0.1097	0.859
mage1t	1	-0.30698	0.15518	3.9135	0.0479	0.736
mage2t	1	0.02218	0.13589	0.0266	0.8703	1.022
racet	1	0.04902	0.12056	0.1653	0.6843	1.050
meductt	1	0.07446	0.10395	0.5131	0.4738	1.077
mprev1t	1	-0.06766	0.10146	0.4447	0.5049	0.935
maritalt	1	0.10520	0.10821	0.9451	0.3310	1.111
nullipart	1	0.10694	0.10221	1.0949	0.2954	1.113
sext	1	-0.02994	0.09152	0.1070	0.7435	0.971

tobacct	1	-0.00607	0.02464	0.0607	0.8053	0.994
diabetes1t	1	0.44351	0.20731	4.5769	0.0324	1.558
chyper1t	1	-0.15960	0.45824	0.1213	0.7276	0.852
phyper1t	1	0.00180	0.20804	0.0001	0.9931	1.002

Linear Hypotheses Testing Results

Label	Wald Chi-Square	DF	Pr > ChiSq
PROPORTIONALITY_TEST	16.7977	13	0.2087

Table E.4. Results of testing PH assumption by examining parameter estimates at different GA (at 40 weeks)

Summary of the Number of Event and Censored Values

Total	Event	Censored	Percent Censored
1797369	879	1796490	99.95

Convergence Status

Convergence criterion (GCONV=1E-8) satisfied.

Model Fit Statistics

Criterion	Without Covariates	With Covariates
-2 LOG L	25318.425	25081.792
AIC	25318.425	25105.792
SBC	25318.425	25163.137

Testing Global Null Hypothesis: BETA=0

Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	236.6334	12	<.0001
Score	362.9438	12	<.0001
Wald	322.2371	12	<.0001

Analysis of Maximum Likelihood Estimates

Variable	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio

mage1	1	-0.10286	0.10999	0.8746	0.3497	0.902
mage2	1	0.53517	0.10187	27.6004	<.0001	1.708
race	1	0.26197	0.09202	8.1048	0.0044	1.299
meduct	1	0.12335	0.07521	2.6903	0.1010	1.131
mprev1	1	-0.40252	0.07808	26.5791	<.0001	0.669
marital	1	0.19678	0.08381	5.5121	0.0189	1.217
nullipar	1	-0.09637	0.07502	1.6504	0.1989	1.100
sex	1	0.01647	0.06747	0.0596	0.8071	1.017
tobacc	1	0.18948	0.01684	126.6672	<.0001	1.209
diabetes1	1	0.90467	0.15825	32.6799	<.0001	2.471
chyper1	1	1.37942	0.22859	36.4140	<.0001	3.973
phyper1	1	0.30915	0.18359	2.8356	0.0922	1.362

Appendix E.5. Results of testing PH assumption by examining parameter estimates at different GA (at 41 weeks)

Summary of the Number of Event and Censored Values

Total	Event	Censored	Percent Censored
846364	541	845823	99.94

Convergence Status

Convergence criterion (GCONV=1E-8) satisfied.

Model Fit Statistics

Criterion	Without Covariates	With Covariates
-2 LOG L	14767.899	14629.579
AIC	14767.899	14653.579
SBC	14767.899	14705.100

Testing Global Null Hypothesis: BETA=0

Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	138.3193	12	<.0001
Score	205.6711	12	<.0001
Wald	183.9110	12	<.0001

Analysis of Maximum Likelihood Estimates

Variable	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio

mage1	1	-0.19500	0.14015	1.9358	0.1641	0.823
mage2	1	0.79181	0.12569	39.6836	<.0001	2.207
race	1	0.22288	0.12189	3.3437	0.0675	1.250
meduct	1	0.12488	0.09584	1.6978	0.1926	1.133
mprev1	1	-0.33797	0.10057	11.2928	0.0008	0.713
marital	1	0.08923	0.10690	0.6968	0.4039	1.093
nullipar	1	-0.30990	0.09321	11.0547	0.0009	1.362
sex	1	-0.14311	0.08624	2.7535	0.0970	0.867
tobacc	1	0.19829	0.02115	87.8937	<.0001	1.219
diabetes1	1	0.46352	0.25566	3.2871	0.0698	1.590
chyper1	1	0.76210	0.41259	3.4118	0.0647	2.143
phyper1	1	0.69202	0.19837	12.1696	0.0005	1.998

Appendix E.6. Results of testing PH assumption by examining parameter estimates at different GA (at 42 weeks)

Summary of the Number of Event and Censored Values

Total	Event	Censored	Percent Censored
296660	246	296414	99.92

Convergence Status

Convergence criterion (GCONV=1E-8) satisfied.

Model Fit Statistics

Criterion	Without Covariates	With Covariates
-2 LOG L	6199.368	6150.741
AIC	6199.368	6174.741
SBC	6199.368	6216.805

Testing Global Null Hypothesis: BETA=0

Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	48.6268	12	<.0001
Score	56.6612	12	<.0001
Wald	55.1164	12	<.0001

Analysis of Maximum Likelihood Estimates

Variable	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio

mage1	1	-0.34961	0.20111	3.0220	0.0821	0.705
mage2	1	0.77889	0.19711	15.6145	<.0001	2.179
race	1	-0.04150	0.17793	0.0544	0.8156	0.959
meduct	1	0.29612	0.14771	4.0190	0.0450	1.345
mprev1	1	-0.28395	0.14318	3.9329	0.0473	0.753
marital	1	0.38216	0.14894	6.5837	0.0103	1.465
nullipar	1	-0.15376	0.14153	1.1802	0.2773	1.167
sex	1	-0.21668	0.12836	2.8494	0.0914	0.805
tobacc	1	0.11021	0.04498	6.0025	0.0143	1.117
diabetes1	1	0.83572	0.31126	7.2090	0.0073	2.306
chyper1	1	-0.33782	1.00419	0.1132	0.7366	0.713
phyper1	1	0.41849	0.32434	1.6648	0.1970	1.520

Appendix E.7. Results of testing PH assumption by examining parameter estimates at different GA (at 43 weeks)

Summary of the Number of Event and Censored Values

Total	Event	Censored	Percent Censored
93427	128	93299	99.86

Convergence Status

Convergence criterion (GCONV=1E-8) satisfied.

Model Fit Statistics

Criterion	Without Covariates	With Covariates
-2 LOG L	2929.904	2852.215
AIC	2929.904	2876.215
SBC	2929.904	2910.440

Testing Global Null Hypothesis: BETA=0

Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	77.6881	12	<.0001
Score	119.3969	12	<.0001
Wald	103.0813	12	<.0001

Analysis of Maximum Likelihood Estimates

Variable	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio

mage1	1	-0.98098	0.34004	8.3226	0.0039	0.375
mage2	1	0.82196	0.25838	10.1203	0.0015	2.275
race	1	0.48200	0.21663	4.9506	0.0261	1.619
meduct	1	0.23046	0.20029	1.3240	0.2499	1.259
mprev1	1	-0.56594	0.18888	8.9778	0.0027	0.568
marital	1	0.16141	0.20590	0.6145	0.4331	1.175
nullipar	1	-0.13223	0.20295	0.4245	0.5147	1.142
sex	1	-0.17515	0.17760	0.9726	0.3240	0.839
tobacc	1	0.22842	0.04099	31.0577	<.0001	1.257
diabetes1	1	1.32869	0.32179	17.0490	<.0001	3.776
chyper1	1	0.71841	0.71920	0.9978	0.3178	2.051
phyper1	1	0.79496	0.36842	4.6558	0.0309	2.214

Appendix F. Results of parameter estimates using different methods in handling ties (Exact, Discrete, Efron and Breslow) in a small sample

Table F.1. Results of parameter estimates using the Exact method

Summary of the Number of Event and Censored Values

Total	Event	Censored	Percent Censored
39667	74	39593	99.81

Testing Global Null Hypothesis: BETA=0

Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	45.3214	12	<.0001
Score	76.6978	12	<.0001
Wald	63.4850	12	<.0001

Analysis of Maximum Likelihood Estimates

Variable	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio
mage1	1	-0.29263	0.40641	0.5185	0.4715	0.746
mage2	1	0.97593	0.32132	9.2248	0.0024	2.654
race	1	0.11842	0.28248	0.1757	0.6751	1.126
meduct	1	-0.58734	0.26354	4.9670	0.0258	0.556
mprev1	1	-0.68916	0.26575	6.7252	0.0095	0.502
marital	1	0.02354	0.30687	0.0059	0.9388	1.024
nullipar	1	-0.26004	0.25022	1.0800	0.2987	0.771
sex	1	-0.18018	0.23347	0.5956	0.4402	0.835
tobacc	1	0.26493	0.05664	21.8751	<.0001	1.303
diabetes1	1	1.04258	0.52150	3.9968	0.0456	2.837
chyper1	1	0.76129	1.02213	0.5547	0.4564	2.141
phyper1	1	1.38034	0.46700	8.7367	0.0031	3.976

Table F.2. Results of parameter estimates using the Discrete method

Summary of the Number of Event and Censored Values

Total	Event	Censored	Percent Censored
39667	74	39593	99.81

Testing Global Null Hypothesis: BETA=0

Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	45.2207	12	<.0001
Score	76.3476	12	<.0001
Wald	62.5750	12	<.0001

Analysis of Maximum Likelihood Estimates

Variable	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio
mage1	1	-0.29417	0.40690	0.5227	0.4697	0.745
mage2	1	0.98075	0.32205	9.2738	0.0023	2.666
race	1	0.12043	0.28284	0.1813	0.6703	1.128
meduct	1	-0.58521	0.26381	4.9207	0.0265	0.557
mprev1	1	-0.68883	0.26629	6.6912	0.0097	0.502
marital	1	0.02363	0.30717	0.0059	0.9387	1.024
nullipar	1	-0.26362	0.25068	1.1059	0.2930	0.768
sex	1	-0.17783	0.23385	0.5783	0.4470	0.837
tobacc	1	0.26506	0.05726	21.4256	<.0001	1.304
diabetes1	1	1.03579	0.52537	3.8870	0.0487	2.817
chyper1	1	0.76738	1.02684	0.5585	0.4549	2.154
phyper1	1	1.37812	0.46857	8.6502	0.0033	3.967

Table F.3. Results of parameter estimates using the Efron method

Summary of the Number of Event and Censored Values

Total	Event	Censored	Percent Censored
39667	74	39593	99.81

Analysis of Maximum Likelihood Estimates

Variable	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio
mage1	1	-0.29269	0.40641	0.5187	0.4714	0.746
mage2	1	0.97600	0.32131	9.2265	0.0024	2.654
race	1	0.11847	0.28247	0.1759	0.6749	1.126
meduct	1	-0.58724	0.26353	4.9658	0.0259	0.556
mprev1	1	-0.68908	0.26574	6.7239	0.0095	0.502
marital	1	0.02358	0.30687	0.0059	0.9388	1.024
nullipar	1	-0.26010	0.25022	1.0806	0.2986	0.771
sex	1	-0.18012	0.23346	0.5952	0.4404	0.835
tobacc	1	0.26487	0.05663	21.8750	<.0001	1.303
diabetes1	1	1.04206	0.52139	3.9945	0.0456	2.835
chyper1	1	0.76138	1.02213	0.5549	0.4563	2.141
phyper1	1	1.38036	0.46698	8.7374	0.0031	3.976

Table F.4. Results of parameter estimates using the Breslow method

Summary of the Number of Event and Censored Values

Total	Event	Censored	Percent Censored
39667	74	39593	99.81

Analysis of Maximum Likelihood Estimates

Variable	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio
mage1	1	-0.29349	0.40641	0.5215	0.4702	0.746
mage2	1	0.97779	0.32122	9.2661	0.0023	2.659
race	1	0.12016	0.28241	0.1810	0.6705	1.128
meduct	1	-0.58268	0.26330	4.8973	0.0269	0.558
mprev1	1	-0.68577	0.26575	6.6590	0.0099	0.504
marital	1	0.02389	0.30671	0.0061	0.9379	1.024
nullipar	1	-0.26288	0.25018	1.1040	0.2934	0.769
sex	1	-0.17701	0.23344	0.5750	0.4483	0.838
tobacc	1	0.26256	0.05666	21.4763	<.0001	1.300
diabetes1	1	1.02488	0.52185	3.8569	0.0495	2.787
chyper1	1	0.76346	1.02193	0.5581	0.4550	2.146
phyper1	1	1.37329	0.46680	8.6548	0.0033	3.948

Appendix G. Results of Poisson regression model analyses of effect of induction of labor in Whites and Blacks, 1997 vs 1991

Table G.1. Results of Poisson regression model for period effect on fetal death at 40-43 weeks in all pregnancies in Whites, before and after adjustment for induction of labor, 49 states and D.C., 1997 vs 1991

The GENMOD Procedure

Model Information

Data Set	WORK.ST49
Distribution	Poisson
Link Function	Log
Response Variable (Events)	deaths
Response Variable (Trials)	den
Observations Used	200
Number Of Events	3775
Number Of Trials	2802645

Class Level Information

Class	Levels	Values
state	50	1 2 3 4 5 6 7 8 9 10 11 12 13 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51
birthyr	2	0 1

Criteria For Assessing Goodness Of Fit

Criterion	DF	Value	Value/DF
Deviance	149	225.9341	1.5163
Scaled Deviance	149	225.9341	1.5163
Pearson Chi-Square	149	220.2817	1.4784
Scaled Pearson X2	149	220.2817	1.4784
Log Likelihood		-2831233.039	

Analysis Of Parameter Estimates

Parameter		DF	Estimate	Standard Error	Wald 95% Confidence Limits		Chi-Square	Pr > ChiSq
Intercept		1	-6.3592	0.3538	-7.0526	-5.6657	323.05	<.0001
state	1	1	-0.3176	0.3865	-1.0752	0.4399	0.68	0.4112
state	2	1	-1.3167	0.6770	-2.6436	0.0102	3.78	0.0518
state	3	1	-0.4497	0.3793	-1.1931	0.2938	1.41	0.2358
state	4	1	0.2062	0.3825	-0.5434	0.9558	0.29	0.5897
state	5	1	0.1266	0.3553	-0.5699	0.8230	0.13	0.7217
state	6	1	-0.1737	0.3776	-0.9137	0.5663	0.21	0.6455
state	7	1	0.0313	0.3760	-0.7057	0.7683	0.01	0.9336
state	8	1	0.3102	0.4378	-0.5479	1.1682	0.50	0.4786
state	9	1	-0.2383	0.7906	-1.7878	1.3112	0.09	0.7631
state	10	1	-0.2210	0.3619	-0.9303	0.4884	0.37	0.5415
state	11	1	0.0125	0.3670	-0.7069	0.7318	0.00	0.9729
state	12	1	0.1048	0.4859	-0.8476	1.0572	0.05	0.8293
state	13	1	-0.6447	0.4494	-1.5255	0.2360	2.06	0.1514
state	15	1	-0.2951	0.3702	-1.0207	0.4304	0.64	0.4253
state	16	1	-0.1695	0.3831	-0.9203	0.5813	0.20	0.6581
state	17	1	-0.3227	0.3919	-1.0908	0.4453	0.68	0.4102
state	18	1	-0.0898	0.3750	-0.8248	0.6452	0.06	0.8108
state	19	1	-0.7378	0.4062	-1.5339	0.0584	3.30	0.0693
state	20	1	-0.7670	0.4647	-1.6778	0.1437	2.72	0.0988
state	21	1	-0.2225	0.3772	-0.9617	0.5167	0.35	0.5553
state	22	1	-0.2862	0.3704	-1.0121	0.4398	0.60	0.4397
state	23	1	-0.4959	0.3673	-1.2158	0.2239	1.82	0.1769
state	24	1	-0.3858	0.3764	-1.1235	0.3519	1.05	0.3053
state	25	1	-0.1623	0.4043	-0.9547	0.6301	0.16	0.6881
state	26	1	-0.1622	0.3717	-0.8907	0.5663	0.19	0.6626
state	27	1	-0.5721	0.5000	-1.5520	0.4079	1.31	0.2526
state	28	1	-0.3031	0.4105	-1.1076	0.5014	0.55	0.4603
state	29	1	-0.2582	0.4129	-1.0674	0.5510	0.39	0.5316
state	30	1	-0.7735	0.4647	-1.6842	0.1372	2.77	0.0960
state	31	1	-0.6089	0.3732	-1.3404	0.1226	2.66	0.1028
state	32	1	-0.5253	0.4215	-1.3513	0.3008	1.55	0.2127
state	33	1	-0.1382	0.3589	-0.8415	0.5651	0.15	0.7002
state	34	1	-0.1631	0.3688	-0.8859	0.5597	0.20	0.6583
state	35	1	0.0876	0.4564	-0.8070	0.9822	0.04	0.8477

state	36	1	-0.1736	0.3622	-0.8834	0.5363	0.23	0.6317
state	37	1	0.5304	0.3683	-0.1915	1.2522	2.07	0.1499
state	38	1	-0.4006	0.3865	-1.1582	0.3569	1.07	0.2999
state	39	1	-0.1783	0.3621	-0.8879	0.5314	0.24	0.6225
state	40	1	-0.8474	0.5000	-1.8274	0.1326	2.87	0.0901
state	41	1	-0.1302	0.3865	-0.8878	0.6273	0.11	0.7361
state	42	1	0.4728	0.4155	-0.3415	1.2871	1.29	0.2551
state	43	1	-0.0143	0.3727	-0.7448	0.7161	0.00	0.9693
state	44	1	-0.1307	0.3579	-0.8322	0.5708	0.13	0.7150
state	45	1	-0.0287	0.3858	-0.7848	0.7274	0.01	0.9407
state	46	1	-0.3652	0.5000	-1.3452	0.6148	0.53	0.4651
state	47	1	-0.3354	0.3732	-1.0669	0.3961	0.81	0.3688
state	48	1	-0.5320	0.3750	-1.2670	0.2030	2.01	0.1560
state	49	1	0.0669	0.3953	-0.7078	0.8417	0.03	0.8656
state	50	1	-0.2929	0.3741	-1.0261	0.4403	0.61	0.4336
state	51	0	0.0000	0.0000	0.0000	0.0000	.	.
birthyr	0	1	-0.2353	0.0333	-0.3006	-0.1701	50.01	<.0001
birthyr	1	0	0.0000	0.0000	0.0000	0.0000	.	.
Scale		0	1.0000	0.0000	1.0000	1.0000		

NOTE: The scale parameter was held fixed.

The GENMOD Procedure

Model Information

Data Set	WORK.ST49
Distribution	Poisson
Link Function	Log
Response Variable (Events)	deaths
Response Variable (Trials)	den
Observations Used	200
Number Of Events	3775
Number Of Trials	2802645

Class Level Information

Class	Levels	Values

state	50	1 2 3 4 5 6 7 8 9 10 11 12 13 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51
birthyr	2	0 1

Criteria For Assessing Goodness Of Fit

Criterion	DF	Value	Value/DF
Deviance	148	219.2828	1.4816
Scaled Deviance	148	219.2828	1.4816
Pearson Chi-Square	148	212.1380	1.4334
Scaled Pearson X2	148	212.1380	1.4334
Log Likelihood		-2831229.713	

Analysis Of Parameter Estimates

Parameter		DF	Estimate	Standard Error	Wald 95% Confidence Limits		Chi-Square	Pr > ChiSq
Intercept		1	-5.8989	0.3965	-6.6761	-5.1218	221.31	<.0001
state	1	1	-0.4340	0.3893	-1.1970	0.3290	1.24	0.2649
state	2	1	-1.3440	0.6771	-2.6711	-0.0169	3.94	0.0472
state	3	1	-0.5663	0.3821	-1.3151	0.1825	2.20	0.1383
state	4	1	0.1773	0.3826	-0.5726	0.9273	0.21	0.6430
state	5	1	-0.1820	0.3751	-0.9172	0.5532	0.24	0.6275
state	6	1	-0.2452	0.3787	-0.9874	0.4969	0.42	0.5172
state	7	1	-0.1938	0.3861	-0.9505	0.5629	0.25	0.6156
state	8	1	0.1605	0.4417	-0.7053	1.0262	0.13	0.7164
state	9	1	-0.4532	0.7950	-2.0114	1.1050	0.32	0.5686
state	10	1	-0.3935	0.3681	-1.1150	0.3280	1.14	0.2851
state	11	1	-0.1828	0.3748	-0.9174	0.5519	0.24	0.6259
state	12	1	-0.1465	0.4961	-1.1188	0.8257	0.09	0.7677
state	13	1	-0.7410	0.4509	-1.6248	0.1428	2.70	0.1003
state	15	1	-0.4144	0.3731	-1.1456	0.3169	1.23	0.2667
state	16	1	-0.2524	0.3844	-1.0058	0.5011	0.43	0.5115
state	17	1	-0.4387	0.3945	-1.2119	0.3345	1.24	0.2661
state	18	1	-0.1893	0.3770	-0.9282	0.5496	0.25	0.6157

state	19	1	-0.9848	0.4175	-1.8031	-0.1665	5.56	0.0183
state	20	1	-0.8318	0.4654	-1.7438	0.0803	3.19	0.0739
state	21	1	-0.4060	0.3840	-1.1586	0.3467	1.12	0.2904
state	22	1	-0.4813	0.3781	-1.2223	0.2597	1.62	0.2030
state	23	1	-0.6666	0.3732	-1.3981	0.0649	3.19	0.0741
state	24	1	-0.4654	0.3777	-1.2056	0.2748	1.52	0.2178
state	25	1	-0.3312	0.4096	-1.1340	0.4716	0.65	0.4188
state	26	1	-0.1570	0.3717	-0.8855	0.5715	0.18	0.6728
state	27	1	-0.6008	0.5001	-1.5811	0.3794	1.44	0.2296
state	28	1	-0.2902	0.4105	-1.0947	0.5144	0.50	0.4796
state	29	1	-0.3364	0.4140	-1.1478	0.4750	0.66	0.4164
state	30	1	-0.9033	0.4674	-1.8194	0.0128	3.73	0.0533
state	31	1	-0.7896	0.3798	-1.5339	-0.0453	4.32	0.0376
state	32	1	-0.6595	0.4247	-1.4920	0.1729	2.41	0.1205
state	33	1	-0.2816	0.3634	-0.9938	0.4306	0.60	0.4384
state	34	1	-0.3019	0.3727	-1.0323	0.4286	0.66	0.4180
state	35	1	0.0946	0.4564	-0.8000	0.9893	0.04	0.8357
state	36	1	-0.2602	0.3638	-0.9732	0.4529	0.51	0.4745
state	37	1	0.3648	0.3739	-0.3680	1.0977	0.95	0.3292
state	38	1	-0.3234	0.3877	-1.0832	0.4364	0.70	0.4041
state	39	1	-0.3508	0.3682	-1.0726	0.3710	0.91	0.3408
state	40	1	-1.0308	0.5051	-2.0207	-0.0409	4.17	0.0413
state	41	1	-0.1915	0.3872	-0.9505	0.5675	0.24	0.6210
state	42	1	0.3332	0.4190	-0.4880	1.1545	0.63	0.4265
state	43	1	0.0494	0.3735	-0.6827	0.7814	0.02	0.8948
state	44	1	-0.3005	0.3639	-1.0138	0.4128	0.68	0.4089
state	45	1	0.0067	0.3860	-0.7498	0.7633	0.00	0.9861
state	46	1	-0.4320	0.5007	-1.4133	0.5494	0.74	0.3883
state	47	1	-0.4683	0.3769	-1.2070	0.2703	1.54	0.2140
state	48	1	-0.6260	0.3768	-1.3646	0.1126	2.76	0.0967
state	49	1	0.0171	0.3958	-0.7586	0.7928	0.00	0.9655
state	50	1	0.0591	0.3983	-0.7216	0.8398	0.02	0.8821
state	51	0	0.0000	0.0000	0.0000	0.0000	.	.
birthyr	0	1	-0.0225	0.0889	-0.1969	0.1518	0.06	0.8001
birthyr	1	0	0.0000	0.0000	0.0000	0.0000	.	.
induct4043		1	-0.0239	0.0093	-0.0421	-0.0057	6.61	0.0101
Scale		0	1.0000	0.0000	1.0000	1.0000		

NOTE: The scale parameter was held fixed.

Table G.2. Results of Poisson regression model for period effect on fetal death at 40-43 weeks in low-risk Whites, before and after adjustment for induction of labor, 49 states and D.C., 1997 vs 1991

The GENMOD Procedure

Model Information

Data Set	WORK.ST49
Distribution	Poisson
Link Function	Log
Response Variable (Events)	deaths
Response Variable (Trials)	den
Observations Used	200
Number Of Events	2095
Number Of Trials	2046485

Class Level Information

Class	Levels	Values
state	50	1 2 3 4 5 6 7 8 9 10 11 12 13 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51
birthyr	2	0 1

Criteria For Assessing Goodness Of Fit

Criterion	DF	Value	Value/DF
Deviance	149	195.9932	1.3154
Scaled Deviance	149	195.9932	1.3154
Pearson Chi-Square	149	189.1559	1.2695
Scaled Pearson X2	149	189.1559	1.2695
Log Likelihood		-2062825.529	

Analysis Of Parameter Estimates

Parameter		DF	Estimate	Standard Error	Wald 95% Confidence Limits		Chi-Square	Pr > ChiSq
Intercept		1	-6.7784	0.5003	-7.7590	-5.7978	183.55	<.0001
state	1	1	-0.0455	0.5358	-1.0956	1.0046	0.01	0.9323
state	2	1	-1.0183	0.8660	-2.7156	0.6791	1.38	0.2397
state	3	1	-0.1153	0.5263	-1.1469	0.9163	0.05	0.8265
state	4	1	0.4040	0.5345	-0.6436	1.4517	0.57	0.4497
state	5	1	0.3116	0.5021	-0.6725	1.2956	0.39	0.5349
state	6	1	0.1952	0.5238	-0.8314	1.2219	0.14	0.7093
state	7	1	-0.1193	0.5455	-1.1885	0.9500	0.05	0.8269
state	8	1	0.6790	0.5839	-0.4654	1.8234	1.35	0.2449
state	9	1	-0.0925	1.1180	-2.2838	2.0989	0.01	0.9341
state	10	1	-0.0271	0.5097	-1.0261	0.9720	0.00	0.9577
state	11	1	0.1913	0.5159	-0.8198	1.2025	0.14	0.7107
state	12	1	-15.2642	1022.650	-2019.62	1989.094	0.00	0.9881
state	13	1	-0.0988	0.5839	-1.2432	1.0455	0.03	0.8656
state	15	1	-0.0285	0.5179	-1.0435	0.9865	0.00	0.9561
state	16	1	0.1573	0.5294	-0.8804	1.1950	0.09	0.7664
state	17	1	-0.1567	0.5455	-1.2259	0.9126	0.08	0.7740
state	18	1	0.0727	0.5286	-0.9633	1.1088	0.02	0.8905
state	19	1	-0.3814	0.5528	-1.4648	0.7021	0.48	0.4903
state	20	1	-1.0871	0.7071	-2.4730	0.2988	2.36	0.1242
state	21	1	-17.2622	1050.760	-2076.71	2042.189	0.00	0.9869
state	22	1	-4.0101	1.1180	-6.2014	-1.8188	12.86	0.0003
state	23	1	-0.2066	0.5147	-1.2154	0.8022	0.16	0.6882
state	24	1	-0.0580	0.5238	-1.0846	0.9687	0.01	0.9119
state	25	1	0.1641	0.5528	-0.9193	1.2475	0.09	0.7666
state	26	1	-0.0464	0.5227	-1.0710	0.9781	0.01	0.9292
state	27	1	-1.2635	0.8660	-2.9609	0.4338	2.13	0.1446
state	28	1	0.0395	0.5557	-1.0497	1.1287	0.01	0.9433
state	29	1	-0.2782	0.5839	-1.4226	0.8662	0.23	0.6337
state	30	1	-0.3260	0.6009	-1.5038	0.8518	0.29	0.5875
state	31	1	-0.5162	0.5250	-1.5452	0.5129	0.97	0.3256
state	32	1	-0.0024	0.5627	-1.1054	1.1005	0.00	0.9965
state	33	1	0.0306	0.5065	-0.9620	1.0233	0.00	0.9518
state	34	1	0.0272	0.5179	-0.9878	1.0422	0.00	0.9582
state	35	1	0.3027	0.6124	-0.8976	1.5029	0.24	0.6211

state	36	1	-0.0392	0.5105	-1.0398	0.9614	0.01	0.9388
state	37	1	-3.0145	1.1180	-5.2058	-0.8232	7.27	0.0070
state	38	1	0.0463	0.5313	-0.9950	1.0876	0.01	0.9306
state	39	1	-0.0264	0.5101	-1.0262	0.9733	0.00	0.9587
state	40	1	-2.1758	1.1180	-4.3671	0.0156	3.79	0.0516
state	41	1	0.2757	0.5313	-0.7656	1.3170	0.27	0.6038
state	42	1	0.7810	0.5627	-0.3219	1.8840	1.93	0.1652
state	43	1	0.3848	0.5189	-0.6322	1.4018	0.55	0.4584
state	44	1	-0.1926	0.5076	-1.1876	0.8024	0.14	0.7044
state	45	1	0.1908	0.5358	-0.8593	1.2408	0.13	0.7218
state	46	1	0.2037	0.6268	-1.0247	1.4322	0.11	0.7451
state	47	1	-0.3454	0.5278	-1.3799	0.6891	0.43	0.5128
state	48	1	-0.2495	0.5250	-1.2785	0.7795	0.23	0.6346
state	49	1	-0.0240	0.5669	-1.1352	1.0872	0.00	0.9662
state	50	1	-0.0404	0.5217	-1.0630	0.9822	0.01	0.9383
state	51	0	0.0000	0.0000	0.0000	0.0000	.	.
birthyr	0	1	-0.1916	0.0446	-0.2790	-0.1042	18.45	<.0001
birthyr	1	0	0.0000	0.0000	0.0000	0.0000	.	.
Scale		0	1.0000	0.0000	1.0000	1.0000		

NOTE: The scale parameter was held fixed.

The GENMOD Procedure

Model Information

Data Set	WORK.ST49
Distribution	Poisson
Link Function	Log
Response Variable (Events)	deaths
Response Variable (Trials)	den
Observations Used	200
Number Of Events	2095
Number Of Trials	2046485

Class Level Information

Class	Levels	Values

state	50	1 2 3 4 5 6 7 8 9 10 11 12 13 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51
birthyr	2	0 1

Criteria For Assessing Goodness Of Fit

Criterion	DF	Value	Value/DF
Deviance	148	184.1148	1.2440
Scaled Deviance	148	184.1148	1.2440
Pearson Chi-Square	148	174.4012	1.1784
Scaled Pearson X2	148	174.4012	1.1784
Log Likelihood		-2062819.590	

Analysis Of Parameter Estimates

Parameter		DF	Estimate	Standard Error	Wald 95% Confidence Limits		Chi-Square	Pr > ChiSq
Intercept		1	-6.0002	0.5494	-7.0771	-4.9233	119.26	<.0001
state	1	1	-0.2267	0.5386	-1.2823	0.8288	0.18	0.6737
state	2	1	-1.0740	0.8662	-2.7717	0.6238	1.54	0.2150
state	3	1	-0.2865	0.5287	-1.3229	0.7498	0.29	0.5879
state	4	1	0.3835	0.5346	-0.6642	1.4313	0.51	0.4731
state	5	1	-0.2148	0.5251	-1.2441	0.8144	0.17	0.6825
state	6	1	0.0786	0.5251	-0.9506	1.1077	0.02	0.8810
state	7	1	-0.4064	0.5519	-1.4881	0.6753	0.54	0.4615
state	8	1	0.4078	0.5893	-0.7472	1.5628	0.48	0.4889
state	9	1	-0.4159	1.1221	-2.6152	1.7835	0.14	0.7109
state	10	1	-0.3132	0.5165	-1.3256	0.6992	0.37	0.5443
state	11	1	-0.1391	0.5248	-1.1678	0.8895	0.07	0.7910
state	12	1	-15.7678	1046.008	-2065.91	2034.370	0.00	0.9880
state	13	1	-0.2613	0.5858	-1.4095	0.8868	0.20	0.6556
state	15	1	-0.2151	0.5207	-1.2357	0.8054	0.17	0.6795
state	16	1	0.0024	0.5313	-1.0390	1.0438	0.00	0.9965
state	17	1	-0.3551	0.5486	-1.4304	0.7202	0.42	0.5175
state	18	1	-0.0999	0.5310	-1.1406	0.9408	0.04	0.8508

state	19	1	-0.7924	0.5658	-1.9013	0.3165	1.96	0.1613
state	20	1	-1.2216	0.7082	-2.6096	0.1665	2.98	0.0845
state	21	1	-17.4658	1048.630	-2072.74	2037.810	0.00	0.9867
state	22	1	-4.3427	1.1222	-6.5422	-2.1432	14.98	0.0001
state	23	1	-0.5119	0.5223	-1.5356	0.5118	0.96	0.3270
state	24	1	-0.1767	0.5249	-1.2055	0.8522	0.11	0.7365
state	25	1	-0.1022	0.5582	-1.1963	0.9918	0.03	0.8547
state	26	1	-0.0194	0.5228	-1.0440	1.0053	0.00	0.9705
state	27	1	-1.3214	0.8662	-3.0192	0.3763	2.33	0.1271
state	28	1	0.0770	0.5558	-1.0124	1.1664	0.02	0.8899
state	29	1	-0.3777	0.5846	-1.5235	0.7681	0.42	0.5182
state	30	1	-0.5452	0.6043	-1.7297	0.6393	0.81	0.3670
state	31	1	-0.8279	0.5328	-1.8721	0.2164	2.41	0.1202
state	32	1	-0.2448	0.5673	-1.3566	0.8671	0.19	0.6661
state	33	1	-0.2140	0.5119	-1.2173	0.7893	0.17	0.6759
state	34	1	-0.2177	0.5227	-1.2422	0.8068	0.17	0.6771
state	35	1	0.3159	0.6124	-0.8843	1.5162	0.27	0.6059
state	36	1	-0.1832	0.5123	-1.1874	0.8209	0.13	0.7206
state	37	1	-3.1035	1.1183	-5.2954	-0.9116	7.70	0.0055
state	38	1	0.1894	0.5330	-0.8552	1.2340	0.13	0.7223
state	39	1	-0.3207	0.5172	-1.3345	0.6930	0.38	0.5352
state	40	1	-2.4710	1.1213	-4.6688	-0.2732	4.86	0.0275
state	41	1	0.1946	0.5318	-0.8477	1.2369	0.13	0.7144
state	42	1	0.5267	0.5676	-0.5859	1.6393	0.86	0.3535
state	43	1	0.5250	0.5205	-0.4952	1.5451	1.02	0.3132
state	44	1	-0.4397	0.5127	-1.4446	0.5652	0.74	0.3912
state	45	1	0.2799	0.5364	-0.7714	1.3311	0.27	0.6018
state	46	1	0.0669	0.6281	-1.1642	1.2981	0.01	0.9151
state	47	1	-0.5704	0.5320	-1.6131	0.4724	1.15	0.2837
state	48	1	-0.4166	0.5275	-1.4504	0.6173	0.62	0.4297
state	49	1	-0.1145	0.5676	-1.2270	0.9979	0.04	0.8401
state	50	1	0.5934	0.5537	-0.4918	1.6787	1.15	0.2838
state	51	0	0.0000	0.0000	0.0000	0.0000	.	.
birthyr	0	1	0.1783	0.1163	-0.0496	0.4061	2.35	0.1252
birthyr	1	0	0.0000	0.0000	0.0000	0.0000	.	.
induct4043		1	-0.0425	0.0124	-0.0668	-0.0182	11.72	0.0006
Scale		0	1.0000	0.0000	1.0000	1.0000		

NOTE: The scale parameter was held fixed.

Table G.3. Results of Poisson regression model for period effect on fetal death at 40-43 weeks in high-risk Whites, before and after adjustment for induction of labor, 49 states and D.C., 1997 vs 1991

The GENMOD Procedure

Model Information

Data Set	WORK.ST49
Distribution	Poisson
Link Function	Log
Response Variable (Events)	deaths
Response Variable (Trials)	den
Observations Used	200
Number Of Events	1209
Number Of Trials	695416

Class Level Information

Class	Levels	Values
state	50	1 2 3 4 5 6 7 8 9 10 11 12 13 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51
birthyr	2	0 1

Criteria For Assessing Goodness Of Fit

Criterion	DF	Value	Value/DF
Deviance	149	174.8512	1.1735
Scaled Deviance	149	174.8512	1.1735
Pearson Chi-Square	149	159.1018	1.0678
Scaled Pearson X2	149	159.1018	1.0678
Log Likelihood		-704242.0178	

Analysis Of Parameter Estimates

Parameter		DF	Estimate	Standard Error	Wald 95% Confidence Limits		Chi-Square	Pr > ChiSq
Intercept		1	-5.9550	0.5779	-7.0876	-4.8224	106.19	<.0001
state	1	1	-0.3994	0.6362	-1.6463	0.8476	0.39	0.5302
state	2	1	-1.4631	1.1547	-3.7263	0.8000	1.61	0.2051
state	3	1	-0.6756	0.6292	-1.9087	0.5575	1.15	0.2829
state	4	1	0.2188	0.6213	-0.9988	1.4365	0.12	0.7247
state	5	1	0.0010	0.5807	-1.1371	1.1391	0.00	0.9987
state	6	1	-0.6883	0.6405	-1.9437	0.5671	1.15	0.2825
state	7	1	-0.4710	0.6405	-1.7264	0.7844	0.54	0.4621
state	8	1	-0.6283	0.9129	-2.4175	1.1609	0.47	0.4913
state	9	1	-15.1171	1728.615	-3403.14	3372.907	0.00	0.9930
state	10	1	-0.2425	0.5916	-1.4020	0.9171	0.17	0.6819
state	11	1	0.0538	0.5991	-1.1205	1.2281	0.01	0.9285
state	12	1	-0.3167	0.9129	-2.1059	1.4725	0.12	0.7286
state	13	1	-1.5441	0.9129	-3.3333	0.2451	2.86	0.0907
state	15	1	-0.4070	0.6098	-1.6021	0.7881	0.45	0.5045
state	16	1	-0.3435	0.6405	-1.5989	0.9119	0.29	0.5917
state	17	1	-0.5344	0.6583	-1.8246	0.7558	0.66	0.4169
state	18	1	-0.3866	0.6191	-1.6001	0.8268	0.39	0.5323
state	19	1	-0.9997	0.6901	-2.3522	0.3528	2.10	0.1474
state	20	1	-0.2180	0.6901	-1.5705	1.1345	0.10	0.7521
state	21	1	-0.2083	0.6191	-1.4218	1.0052	0.11	0.7365
state	22	1	-0.2325	0.6046	-1.4175	0.9526	0.15	0.7006
state	23	1	-0.6379	0.6055	-1.8247	0.5489	1.11	0.2922
state	24	1	-0.5757	0.6292	-1.8088	0.6575	0.84	0.3602
state	25	1	-0.6528	0.7071	-2.0387	0.7331	0.85	0.3559
state	26	1	-0.0547	0.6046	-1.2398	1.1304	0.01	0.9279
state	27	1	-0.5786	0.8165	-2.1789	1.0217	0.50	0.4786
state	28	1	-0.6905	0.7303	-2.1219	0.7408	0.89	0.3444
state	29	1	-0.2101	0.6770	-1.5370	1.1169	0.10	0.7564
state	30	1	-1.3491	0.9129	-3.1383	0.4401	2.18	0.1394
state	31	1	-0.4528	0.6075	-1.6434	0.7379	0.56	0.4561
state	32	1	-1.5539	0.8165	-3.1542	0.0464	3.62	0.0570
state	33	1	-0.2481	0.5873	-1.3992	0.9031	0.18	0.6727
state	34	1	-0.1188	0.6009	-1.2966	1.0590	0.04	0.8433
state	35	1	-0.4506	0.9129	-2.2398	1.3385	0.24	0.6215

state	36	1	-0.0751	0.5907	-1.2329	1.0827	0.02	0.8989
state	37	1	0.1473	0.6110	-1.0503	1.3448	0.06	0.8096
state	38	1	-0.9147	0.6583	-2.2049	0.3755	1.93	0.1647
state	39	1	-0.2007	0.5929	-1.3627	0.9614	0.11	0.7350
state	40	1	-0.2850	0.7303	-1.7163	1.1464	0.15	0.6964
state	41	1	-0.5382	0.6583	-1.8284	0.7520	0.67	0.4136
state	42	1	0.3663	0.7071	-1.0196	1.7523	0.27	0.6044
state	43	1	-0.6919	0.6325	-1.9315	0.5477	1.20	0.2740
state	44	1	-0.4413	0.5865	-1.5908	0.7082	0.57	0.4518
state	45	1	-0.2858	0.6513	-1.5624	0.9908	0.19	0.6608
state	46	1	-16.3802	1717.311	-3382.25	3349.488	0.00	0.9924
state	47	1	-0.5183	0.6172	-1.7280	0.6914	0.71	0.4011
state	48	1	-0.7544	0.6191	-1.9679	0.4591	1.48	0.2230
state	49	1	0.3113	0.6262	-0.9161	1.5387	0.25	0.6191
state	50	1	-0.2863	0.6155	-1.4925	0.9200	0.22	0.6418
state	51	0	0.0000	0.0000	0.0000	0.0000	.	.
birthyr	0	1	-0.2497	0.0581	-0.3636	-0.1357	18.44	<.0001
birthyr	1	0	0.0000	0.0000	0.0000	0.0000	.	.
Scale		0	1.0000	0.0000	1.0000	1.0000		

NOTE: The scale parameter was held fixed.

The GENMOD Procedure

Model Information

Data Set	WORK.ST49
Distribution	Poisson
Link Function	Log
Response Variable (Events)	deaths
Response Variable (Trials)	den
Observations Used	200
Number Of Events	1209
Number Of Trials	695416

Class Level Information

Class	Levels	Values

state	50	1 2 3 4 5 6 7 8 9 10 11 12 13 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51
birthyr	2	0 1

Criteria For Assessing Goodness Of Fit

Criterion	DF	Value	Value/DF
Deviance	148	172.5593	1.1659
Scaled Deviance	148	172.5593	1.1659
Pearson Chi-Square	148	156.5014	1.0574
Scaled Pearson X2	148	156.5014	1.0574
Log Likelihood		-704240.8719	

Analysis Of Parameter Estimates

Parameter		DF	Estimate	Standard Error	Wald 95% Confidence Limits		Chi-Square	Pr > ChiSq
Intercept		1	-5.4360	0.6723	-6.7537	-4.1182	65.37	<.0001
state	1	1	-0.5569	0.6452	-1.8214	0.7076	0.75	0.3881
state	2	1	-1.4916	1.1549	-3.7551	0.7719	1.67	0.1965
state	3	1	-0.8512	0.6399	-2.1055	0.4030	1.77	0.1835
state	4	1	0.1349	0.6238	-1.0878	1.3575	0.05	0.8288
state	5	1	-0.3387	0.6228	-1.5594	0.8819	0.30	0.5865
state	6	1	-0.7857	0.6439	-2.0477	0.4763	1.49	0.2224
state	7	1	-0.7010	0.6583	-1.9913	0.5893	1.13	0.2870
state	8	1	-0.7421	0.9160	-2.5374	1.0533	0.66	0.4179
state	9	1	-15.3844	1721.734	-3389.92	3359.153	0.00	0.9929
state	10	1	-0.4414	0.6061	-1.6294	0.7466	0.53	0.4665
state	11	1	-0.1603	0.6158	-1.3673	1.0466	0.07	0.7946
state	12	1	-0.5403	0.9254	-2.3541	1.2735	0.34	0.5593
state	13	1	-1.6362	0.9149	-3.4293	0.1570	3.20	0.0737
state	15	1	-0.5604	0.6181	-1.7719	0.6512	0.82	0.3647
state	16	1	-0.3981	0.6415	-1.6554	0.8593	0.39	0.5349
state	17	1	-0.6556	0.6632	-1.9554	0.6443	0.98	0.3229
state	18	1	-0.4746	0.6219	-1.6935	0.7442	0.58	0.4453
state	19	1	-1.2909	0.7166	-2.6953	0.1135	3.25	0.0716

state	20	1	-0.2563	0.6905	-1.6097	1.0971	0.14	0.7105
state	21	1	-0.3746	0.6290	-1.6074	0.8583	0.35	0.5515
state	22	1	-0.4383	0.6198	-1.6531	0.7764	0.50	0.4794
state	23	1	-0.8060	0.6157	-2.0128	0.4007	1.71	0.1905
state	24	1	-0.6349	0.6304	-1.8705	0.6006	1.01	0.3139
state	25	1	-0.8736	0.7220	-2.2887	0.5415	1.46	0.2263
state	26	1	-0.0773	0.6048	-1.2627	1.1081	0.02	0.8983
state	27	1	-0.5978	0.8166	-2.1984	1.0027	0.54	0.4641
state	28	1	-0.6905	0.7303	-2.1219	0.7408	0.89	0.3444
state	29	1	-0.3444	0.6829	-1.6830	0.9941	0.25	0.6140
state	30	1	-1.4880	0.9175	-3.2863	0.3104	2.63	0.1049
state	31	1	-0.6347	0.6193	-1.8486	0.5791	1.05	0.3054
state	32	1	-1.6941	0.8218	-3.3048	-0.0834	4.25	0.0393
state	33	1	-0.4017	0.5964	-1.5706	0.7671	0.45	0.5005
state	34	1	-0.2575	0.6079	-1.4489	0.9340	0.18	0.6719
state	35	1	-0.4199	0.9131	-2.2095	1.3698	0.21	0.6456
state	36	1	-0.1730	0.5944	-1.3380	0.9919	0.08	0.7710
state	37	1	-0.0451	0.6241	-1.2684	1.1782	0.01	0.9424
state	38	1	-0.8510	0.6596	-2.1438	0.4418	1.66	0.1970
state	39	1	-0.3812	0.6048	-1.5667	0.8042	0.40	0.5285
state	40	1	-0.4723	0.7409	-1.9244	0.9799	0.41	0.5238
state	41	1	-0.6422	0.6619	-1.9394	0.6550	0.94	0.3319
state	42	1	0.2610	0.7105	-1.1316	1.6536	0.13	0.7134
state	43	1	-0.6769	0.6325	-1.9166	0.5629	1.15	0.2846
state	44	1	-0.6401	0.6010	-1.8181	0.5379	1.13	0.2869
state	45	1	-0.2898	0.6513	-1.5664	0.9868	0.20	0.6564
state	46	1	-16.4351	1727.707	-3402.68	3369.807	0.00	0.9924
state	47	1	-0.6635	0.6248	-1.8882	0.5612	1.13	0.2883
state	48	1	-0.8102	0.6203	-2.0260	0.4057	1.71	0.1916
state	49	1	0.2579	0.6273	-0.9715	1.4873	0.17	0.6809
state	50	1	0.0542	0.6555	-1.2304	1.3389	0.01	0.9341
state	51	0	0.0000	0.0000	0.0000	0.0000	.	.
birthyr	0	1	-0.0463	0.1464	-0.3332	0.2405	0.10	0.7516
birthyr	1	0	0.0000	0.0000	0.0000	0.0000	.	.
induct4043		1	-0.0231	0.0153	-0.0532	0.0069	2.28	0.1310
Scale		0	1.0000	0.0000	1.0000	1.0000		

NOTE: The scale parameter was held fixed.

Table G.4. Results of Poisson regression model for period effect on fetal death at 42-43 weeks in all pregnancies in Blacks, before and after adjustment for induction of labor, 49 states and D.C., 1997 vs 1991

The GENMOD Procedure

Model Information

Data Set	WORK.ST49
Distribution	Poisson
Link Function	Log
Response Variable (Events)	deaths
Response Variable (Trials)	den
Observations Used	164
Number Of Events	455
Number Of Trials	114467

Class Level Information

Class	Levels	Values
state	41	1 2 3 4 5 6 7 8 9 10 11 12 15 16 17 18 19 21 22 23 24 25 26 28 29 31 32 33 34 36 37 38 39 40 41 43 44 47 48 49 50
birthyr	2	0 1

Criteria For Assessing Goodness Of Fit

Criterion	DF	Value	Value/DF
Deviance	122	147.9350	1.2126
Scaled Deviance	122	147.9350	1.2126
Pearson Chi-Square	122	138.7688	1.1374
Scaled Pearson X2	122	138.7688	1.1374
Log Likelihood		-117342.7403	

Analysis Of Parameter Estimates

Parameter		DF	Standard Estimate	Error	Wald 95% Confidence Limits		Chi-Square	Pr > ChiSq
Intercept		1	-5.6832	0.5016	-6.6664	-4.7001	128.37	<.0001
state	1	1	-0.3006	0.6009	-1.4785	0.8772	0.25	0.6169
state	2	1	-16.4410	7473.823	-14664.9	14631.98	0.00	0.9982
state	3	1	0.4455	0.8660	-1.2519	2.1429	0.26	0.6069
state	4	1	-19.4199	7660.223	-15033.2	14994.34	0.00	0.9980
state	5	1	1.0393	0.5099	0.0398	2.0387	4.15	0.0415
state	6	1	-0.1898	1.1181	-2.3812	2.0016	0.03	0.8652
state	7	1	1.2555	0.5593	0.1593	2.3518	5.04	0.0248
state	8	1	-0.2624	1.1181	-2.4539	1.9291	0.06	0.8145
state	9	1	0.4321	0.6270	-0.7968	1.6609	0.47	0.4907
state	10	1	0.4840	0.5250	-0.5451	1.5131	0.85	0.3566
state	11	1	0.6288	0.5297	-0.4094	1.6671	1.41	0.2352
state	12	1	-16.8019	7759.768	-15225.7	15192.06	0.00	0.9983
state	15	1	0.1436	0.6455	-1.1216	1.4088	0.05	0.8240
state	16	1	0.3873	1.1180	-1.8040	2.5786	0.12	0.7290
state	17	1	-0.4478	1.1181	-2.6392	1.7435	0.16	0.6888
state	18	1	-0.2478	0.8660	-1.9452	1.4497	0.08	0.7748
state	19	1	-0.7497	0.6268	-1.9782	0.4788	1.43	0.2317
state	21	1	0.8704	0.5219	-0.1526	1.8933	2.78	0.0954
state	22	1	0.1017	0.7071	-1.2842	1.4876	0.02	0.8856
state	23	1	-1.0667	0.6456	-2.3320	0.1987	2.73	0.0985
state	24	1	-18.5449	7758.232	-15224.4	15187.31	0.00	0.9981
state	25	1	-0.0364	0.5839	-1.1809	1.1080	0.00	0.9503
state	26	1	0.1212	0.6269	-1.1074	1.3498	0.04	0.8466
state	28	1	-17.5417	7538.209	-14792.2	14757.08	0.00	0.9981
state	29	1	0.5203	0.8661	-1.1771	2.2177	0.36	0.5480
state	31	1	-0.2987	0.6124	-1.4990	0.9016	0.24	0.6257
state	32	1	1.2052	1.1180	-0.9861	3.3965	1.16	0.2811
state	33	1	0.3314	0.5228	-0.6933	1.3560	0.40	0.5262
state	34	1	-0.1265	0.5628	-1.2295	0.9765	0.05	0.8221
state	36	1	-0.5115	0.6124	-1.7118	0.6887	0.70	0.4036
state	37	1	0.9075	0.5917	-0.2522	2.0672	2.35	0.1251
state	38	1	-17.3253	7513.456	-14743.4	14708.78	0.00	0.9982
state	39	1	0.3601	0.5529	-0.7235	1.4437	0.42	0.5149
state	40	1	-17.5209	7701.093	-15111.4	15076.34	0.00	0.9982
state	41	1	0.1613	0.5917	-0.9985	1.3210	0.07	0.7852
state	43	1	0.0661	0.6010	-1.1118	1.2440	0.01	0.9124

state	44	1	0.0296	0.5418	-1.0323	1.0914	0.00	0.9565
state	47	1	-0.8476	0.6709	-2.1624	0.4672	1.60	0.2064
state	48	1	-18.4846	7657.087	-15026.1	14989.13	0.00	0.9981
state	49	1	1.0150	1.1180	-1.1763	3.2063	0.82	0.3640
state	50	0	0.0000	0.0000	0.0000	0.0000	.	.
birthyr	0	1	-0.3728	0.1018	-0.5723	-0.1733	13.41	0.0002
birthyr	1	0	0.0000	0.0000	0.0000	0.0000	.	.
Scale		0	1.0000	0.0000	1.0000	1.0000		

NOTE: The scale parameter was held fixed.

The GENMOD Procedure

Model Information

Data Set	WORK.ST49
Distribution	Poisson
Link Function	Log
Response Variable (Events)	deaths
Response Variable (Trials)	den
Observations Used	164
Number Of Events	455
Number Of Trials	114467

Class Level Information

Class	Levels	Values
state	41	1 2 3 4 5 6 7 8 9 10 11 12 15 16 17 18 19 21 22 23 24 25 26 28 29 31 32 33 34 36 37 38 39 40 41 43 44 47 48 49 50
birthyr	2	0 1

Criteria For Assessing Goodness Of Fit

Criterion	DF	Value	Value/DF

Deviance	121	147.9350	1.2226
Scaled Deviance	121	147.9350	1.2226
Pearson Chi-Square	121	138.7707	1.1469
Scaled Pearson X2	121	138.7707	1.1469
Log Likelihood		-117342.7403	

Analysis Of Parameter Estimates

Parameter		DF	Estimate	Standard Error	Wald 95% Confidence Limits		Chi-Square	Pr > ChiSq
Intercept		1	-5.6788	0.8492	-7.3432	-4.0144	44.72	<.0001
state	1	1	-0.3042	0.8169	-1.9053	1.2969	0.14	0.7096
state	2	1	-16.4375	7452.944	-14623.9	14591.06	0.00	0.9982
state	3	1	0.4430	0.9516	-1.4221	2.3081	0.22	0.6416
state	4	1	-19.4242	7665.668	-15043.9	15005.01	0.00	0.9980
state	5	1	1.0356	0.7673	-0.4683	2.5395	1.82	0.1771
state	6	1	-0.1923	1.1845	-2.5138	2.1292	0.03	0.8710
state	7	1	1.2524	0.7445	-0.2068	2.7115	2.83	0.0925
state	8	1	-0.2647	1.1765	-2.5707	2.0413	0.05	0.8220
state	9	1	0.4286	0.8237	-1.1858	2.0430	0.27	0.6028
state	10	1	0.4806	0.7394	-0.9685	1.9297	0.42	0.5157
state	11	1	0.6255	0.7383	-0.8214	2.0725	0.72	0.3968
state	12	1	-16.8022	7747.730	-15202.1	15168.47	0.00	0.9983
state	15	1	0.1405	0.8029	-1.4331	1.7142	0.03	0.8611
state	16	1	0.3847	1.1862	-1.9402	2.7097	0.11	0.7457
state	17	1	-0.4504	1.1847	-2.7724	1.8717	0.14	0.7038
state	18	1	-0.2493	0.8972	-2.0077	1.5092	0.08	0.7811
state	19	1	-0.7534	0.8524	-2.4241	0.9173	0.78	0.3768
state	21	1	0.8668	0.7567	-0.6162	2.3499	1.31	0.2520
state	22	1	0.0991	0.8166	-1.5014	1.6995	0.01	0.9034
state	23	1	-1.0702	0.8463	-2.7288	0.5884	1.60	0.2060
state	24	1	-18.5470	7756.736	-15221.5	15184.38	0.00	0.9981
state	25	1	-0.0400	0.8053	-1.6184	1.5384	0.00	0.9604
state	26	1	0.1184	0.7619	-1.3748	1.6117	0.02	0.8765
state	28	1	-17.5450	7542.420	-14800.4	14765.33	0.00	0.9981
state	29	1	0.5184	0.9160	-1.2769	2.3136	0.32	0.5714
state	31	1	-0.3011	0.7202	-1.7127	1.1104	0.17	0.6758
state	32	1	1.2018	1.2303	-1.2094	3.6131	0.95	0.3286
state	33	1	0.3284	0.6929	-1.0296	1.6865	0.22	0.6355

state	34	1	-0.1295	0.7247	-1.5499	1.2910	0.03	0.8582
state	36	1	-0.5145	0.7663	-2.0165	0.9875	0.45	0.5020
state	37	1	0.9037	0.8346	-0.7321	2.5395	1.17	0.2789
state	38	1	-17.3270	7517.825	-14752.0	14717.34	0.00	0.9982
state	39	1	0.3572	0.7110	-1.0363	1.7506	0.25	0.6154
state	40	1	-17.5244	7705.020	-15119.1	15084.04	0.00	0.9982
state	41	1	0.1584	0.7383	-1.2887	1.6056	0.05	0.8301
state	43	1	0.0631	0.7547	-1.4160	1.5423	0.01	0.9333
state	44	1	0.0265	0.7228	-1.3902	1.4432	0.00	0.9708
state	47	1	-0.8505	0.8108	-2.4396	0.7385	1.10	0.2942
state	48	1	-18.4823	7639.683	-14992.0	14955.02	0.00	0.9981
state	49	1	1.0126	1.1777	-1.2956	3.3209	0.74	0.3899
state	50	0	0.0000	0.0000	0.0000	0.0000	.	.
birthyr	0	1	-0.3720	0.1589	-0.6834	-0.0606	5.48	0.0192
birthyr	1	0	0.0000	0.0000	0.0000	0.0000	.	.
induct		1	-0.0001	0.0192	-0.0377	0.0374	0.00	0.9949
Scale		0	1.0000	0.0000	1.0000	1.0000		

NOTE: The scale parameter was held fixed.

Table G.5. Results of Poisson regression model for period effect on fetal death at 42-43 weeks in low-risk Blacks, before and after adjustment for induction of labor, 49 states and D.C., 1997 vs 1991

The GENMOD Procedure

Model Information

Data Set	WORK.ST49
Distribution	Poisson
Link Function	Log
Response Variable (Events)	deaths
Response Variable (Trials)	den
Observations Used	164
Number Of Events	217
Number Of Trials	72524

Class Level Information

Class	Levels	Values
state	41	1 2 3 4 5 6 7 8 9 10 11 12 15 16 17 18 19 21 22 23 24 25 26 28 29 31 32 33 34 36 37 38 39 40 41 43 44 47 48 49 50
birthyr	2	0 1

Criteria For Assessing Goodness Of Fit

Criterion	DF	Value	Value/DF
Deviance	122	92.5588	0.7587
Scaled Deviance	122	92.5588	0.7587
Pearson Chi-Square	122	87.8871	0.7204
Scaled Pearson X2	122	87.8871	0.7204
Log Likelihood		-73929.9996	

Analysis Of Parameter Estimates

Parameter		DF	Standard Estimate	Error	Wald 95% Confidence Limits		Chi-Square	Pr > ChiSq
Intercept		1	-5.4024	0.5798	-6.5388	-4.2659	86.80	<.0001
state	1	1	-0.5038	0.7071	-1.8898	0.8822	0.51	0.4762
state	2	1	-17.3754	12198.74	-23926.5	23891.71	0.00	0.9989
state	3	1	0.6719	0.9129	-1.1173	2.4611	0.54	0.4617
state	4	1	-20.1498	12480.34	-24481.2	24440.87	0.00	0.9987
state	5	1	0.6869	0.5912	-0.4719	1.8457	1.35	0.2453
state	6	1	-0.0450	1.1549	-2.3085	2.2185	0.00	0.9689
state	7	1	1.0776	0.6904	-0.2754	2.4307	2.44	0.1185
state	8	1	-18.8096	11835.96	-23216.9	23179.25	0.00	0.9987
state	9	1	-0.6361	0.9131	-2.4258	1.1537	0.49	0.4861
state	10	1	0.0143	0.6192	-1.1993	1.2279	0.00	0.9816
state	11	1	0.4380	0.6143	-0.7660	1.6421	0.51	0.4758
state	12	1	-17.8316	12691.12	-24892.0	24856.31	0.00	0.9989
state	15	1	-0.0244	0.7638	-1.5213	1.4726	0.00	0.9746
state	16	1	0.6916	1.1547	-1.5715	2.9548	0.36	0.5492
state	17	1	-0.2990	1.1548	-2.5623	1.9644	0.07	0.7957
state	18	1	-19.4505	12481.09	-24481.9	24443.04	0.00	0.9988
state	19	1	-0.9079	0.7303	-2.3393	0.5235	1.55	0.2138
state	21	1	-2.2417	1.1547	-4.5049	0.0215	3.77	0.0522
state	22	1	-20.0621	12569.70	-24656.2	24616.11	0.00	0.9987
state	23	1	-1.2725	0.7639	-2.7697	0.2247	2.77	0.0958
state	24	1	-19.1651	12717.43	-24944.9	24906.55	0.00	0.9988
state	25	1	-0.8423	0.7639	-2.3394	0.6549	1.22	0.2702
state	26	1	-0.9253	0.9130	-2.7147	0.8640	1.03	0.3108
state	28	1	-18.3628	12527.36	-24571.5	24534.82	0.00	0.9988
state	29	1	-18.8502	12317.98	-24161.6	24123.95	0.00	0.9988
state	31	1	-0.5788	0.7304	-2.0103	0.8527	0.63	0.4281
state	32	1	-17.4379	12676.74	-24863.4	24828.51	0.00	0.9989
state	33	1	-0.1206	0.6139	-1.3239	1.0827	0.04	0.8443
state	34	1	-0.3484	0.6584	-1.6387	0.9420	0.28	0.5967
state	36	1	-1.0130	0.7638	-2.5101	0.4840	1.76	0.1848
state	37	1	-19.4763	12389.51	-24302.5	24263.52	0.00	0.9987
state	38	1	-18.1466	12257.70	-24042.8	24006.50	0.00	0.9988
state	39	1	-0.2552	0.6772	-1.5825	1.0720	0.14	0.7063
state	40	1	-18.2120	12463.22	-24445.7	24409.24	0.00	0.9988
state	41	1	-0.1959	0.7073	-1.5823	1.1905	0.08	0.7818

state	43	1	-0.3306	0.7304	-1.7621	1.1010	0.20	0.6508
state	44	1	-1.1439	0.7303	-2.5753	0.2875	2.45	0.1173
state	47	1	-1.6099	0.9129	-3.3992	0.1794	3.11	0.0778
state	48	1	-19.1678	12616.95	-24747.9	24709.60	0.00	0.9988
state	49	1	1.3401	1.1547	-0.9231	3.6033	1.35	0.2458
state	50	0	0.0000	0.0000	0.0000	0.0000	.	.
birthyr	0	1	-0.5378	0.1523	-0.8364	-0.2392	12.46	0.0004
birthyr	1	0	0.0000	0.0000	0.0000	0.0000	.	.
Scale		0	1.0000	0.0000	1.0000	1.0000		

NOTE: The scale parameter was held fixed.

The GENMOD Procedure

Model Information

Data Set	WORK.ST49
Distribution	Poisson
Link Function	Log
Response Variable (Events)	deaths
Response Variable (Trials)	den
Observations Used	164
Number Of Events	217
Number Of Trials	72524

Class Level Information

Class	Levels	Values
state	41	1 2 3 4 5 6 7 8 9 10 11 12 15 16 17 18 19 21 22 23 24 25 26 28 29 31 32 33 34 36 37 38 39 40 41 43 44 47 48 49 50
birthyr	2	0 1

Criteria For Assessing Goodness Of Fit

Criterion	DF	Value	Value/DF

Deviance	121	92.5588	0.7649
Scaled Deviance	121	92.5588	0.7649
Pearson Chi-Square	121	87.8972	0.7264
Scaled Pearson X2	121	87.8972	0.7264
Log Likelihood		-73929.9996	

Analysis Of Parameter Estimates

Parameter		DF	Estimate	Standard Error	Wald 95% Confidence Limits		Chi-Square	Pr > ChiSq
Intercept		1	-5.3951	1.1803	-7.7084	-3.0818	20.89	<.0001
state	1	1	-0.5095	1.0769	-2.6202	1.6011	0.22	0.6361
state	2	1	-17.3867	12245.69	-24018.5	23983.72	0.00	0.9989
state	3	1	0.6678	1.0863	-1.4613	2.7969	0.38	0.5387
state	4	1	-20.1572	12495.74	-24511.4	24471.05	0.00	0.9987
state	5	1	0.6808	1.0448	-1.3669	2.7286	0.42	0.5146
state	6	1	-0.0491	1.2896	-2.5767	2.4786	0.00	0.9697
state	7	1	1.0736	0.8962	-0.6829	2.8301	1.44	0.2309
state	8	1	-18.8276	11918.15	-23378.0	23340.31	0.00	0.9987
state	9	1	-0.6416	1.2088	-3.0109	1.7276	0.28	0.5956
state	10	1	0.0087	1.0059	-1.9629	1.9803	0.00	0.9931
state	11	1	0.4326	0.9869	-1.5017	2.3669	0.19	0.6611
state	12	1	-17.8347	12674.91	-24860.2	24824.53	0.00	0.9989
state	15	1	-0.0295	1.0589	-2.1049	2.0459	0.00	0.9778
state	16	1	0.6868	1.3421	-1.9436	3.3172	0.26	0.6088
state	17	1	-0.3031	1.2986	-2.8484	2.2421	0.05	0.8154
state	18	1	-19.4474	12447.43	-24416.0	24377.06	0.00	0.9988
state	19	1	-0.9139	1.1262	-3.1213	1.2935	0.66	0.4171
state	21	1	-2.2467	1.3529	-4.8983	0.4049	2.76	0.0968
state	22	1	-20.0677	12577.72	-24672.0	24631.82	0.00	0.9987
state	23	1	-1.2783	1.1202	-3.4739	0.9174	1.30	0.2538
state	24	1	-19.1686	12716.24	-24942.5	24904.21	0.00	0.9988
state	25	1	-0.8482	1.1390	-3.0806	1.3842	0.55	0.4565
state	26	1	-0.9301	1.1376	-3.1598	1.2996	0.67	0.4136
state	28	1	-18.3665	12527.55	-24571.9	24535.17	0.00	0.9988
state	29	1	-18.8514	12304.57	-24135.4	24097.67	0.00	0.9988
state	31	1	-0.5829	0.9382	-2.4218	1.2559	0.39	0.5344

state	32	1	-17.4403	12657.41	-24825.5	24790.62	0.00	0.9989
state	33	1	-0.1255	0.9354	-1.9589	1.7078	0.02	0.8932
state	34	1	-0.3532	0.9560	-2.2269	1.5205	0.14	0.7118
state	36	1	-1.0181	1.0498	-3.0756	1.0394	0.94	0.3321
state	37	1	-19.4824	12393.59	-24310.5	24271.52	0.00	0.9987
state	38	1	-18.1500	12271.33	-24069.5	24033.22	0.00	0.9988
state	39	1	-0.2602	0.9756	-2.1724	1.6520	0.07	0.7897
state	40	1	-18.2194	12488.78	-24495.8	24459.34	0.00	0.9988
state	41	1	-0.2008	0.9956	-2.1521	1.7505	0.04	0.8401
state	43	1	-0.3355	1.0108	-2.3166	1.6456	0.11	0.7400
state	44	1	-1.1489	1.0188	-3.1458	0.8480	1.27	0.2595
state	47	1	-1.6149	1.1571	-3.8828	0.6530	1.95	0.1628
state	48	1	-19.1696	12607.38	-24729.2	24690.84	0.00	0.9988
state	49	1	1.3357	1.3111	-1.2341	3.9055	1.04	0.3083
state	50	0	0.0000	0.0000	0.0000	0.0000	.	.
birthyr	0	1	-0.5368	0.2059	-0.9403	-0.1332	6.80	0.0091
birthyr	1	0	0.0000	0.0000	0.0000	0.0000	.	.
induct		1	-0.0002	0.0280	-0.0550	0.0546	0.00	0.9944
Scale		0	1.0000	0.0000	1.0000	1.0000		

NOTE: The scale parameter was held fixed.

Table G.6. Results of Poisson regression model for period effect on fetal death at 42-43 weeks in high-risk Blacks, before and after adjustment for induction of labor, 49 states and D.C., 1997 vs 1991

The GENMOD Procedure

Model Information

Data Set	WORK.ST49
Distribution	Poisson
Link Function	Log
Response Variable (Events)	deaths
Response Variable (Trials)	den
Observations Used	156
Number Of Events	154
Number Of Trials	37923

Class Level Information

Class	Levels	Values
state	39	1 3 4 5 6 7 8 9 10 11 15 16 17 18 19 21 22 23 24 25 26 28 29 31 32 33 34 36 37 38 39 40 41 43 44 47 48 49 50
birthyr	2	0 1

Criteria For Assessing Goodness Of Fit

Criterion	DF	Value	Value/DF
Deviance	116	115.4269	0.9951
Scaled Deviance	116	115.4269	0.9951
Pearson Chi-Square	116	103.8699	0.8954
Scaled Pearson X2	116	103.8699	0.8954
Log Likelihood		-38893.8288	

Analysis Of Parameter Estimates

Parameter		DF	Estimate	Standard Error	Wald 95% Confidence Limits		Chi-Square	Pr > ChiSq
Intercept		1	-6.2156	1.0027	-8.1809	-4.2504	38.43	<.0001
state	1	1	0.1324	1.1547	-2.1308	2.3956	0.01	0.9087
state	3	1	-17.6506	12715.53	-24939.6	24904.32	0.00	0.9989
state	4	1	-18.9995	12775.45	-25058.4	25020.41	0.00	0.9988
state	5	1	1.4821	1.0171	-0.5114	3.4756	2.12	0.1451
state	6	1	-17.4816	12728.03	-24964.0	24929.00	0.00	0.9989
state	7	1	1.3270	1.1551	-0.9369	3.5909	1.32	0.2506
state	8	1	1.2322	1.4143	-1.5399	4.0042	0.76	0.3837
state	9	1	0.1145	1.4144	-2.6576	2.8866	0.01	0.9355
state	10	1	1.0632	1.0328	-0.9612	3.0875	1.06	0.3033
state	11	1	1.0637	1.0492	-0.9927	3.1200	1.03	0.3107
state	15	1	0.5389	1.2248	-1.8616	2.9393	0.19	0.6599
state	16	1	-17.1615	12774.27	-25054.3	25019.96	0.00	0.9989
state	17	1	-17.7461	12764.65	-25036.0	25000.51	0.00	0.9989
state	18	1	-18.3224	12557.67	-24630.9	24594.27	0.00	0.9988
state	19	1	-0.4208	1.2248	-2.8213	1.9797	0.12	0.7312
state	21	1	1.1380	1.0446	-0.9094	3.1853	1.19	0.2760
state	22	1	0.4867	1.4142	-2.2851	3.2585	0.12	0.7308
state	23	1	-0.6120	1.2249	-3.0128	1.7889	0.25	0.6174
state	24	1	-18.0045	12761.21	-25029.5	24993.52	0.00	0.9989
state	25	1	0.8694	1.0802	-1.2477	2.9864	0.65	0.4209
state	26	1	1.3000	1.0956	-0.8473	3.4474	1.41	0.2354
state	28	1	-16.8996	11945.34	-23429.3	23395.53	0.00	0.9989
state	29	1	1.4383	1.4142	-1.3336	4.2101	1.03	0.3092
state	31	1	0.3426	1.1547	-1.9206	2.6058	0.09	0.7667
state	32	1	2.6614	1.4143	-0.1105	5.4333	3.54	0.0599
state	33	1	1.0118	1.0308	-1.0086	3.0321	0.96	0.3263
state	34	1	0.1065	1.1181	-2.0850	2.2979	0.01	0.9241
state	36	1	0.3379	1.1181	-1.8535	2.5292	0.09	0.7625
state	37	1	1.5219	1.1183	-0.6698	3.7137	1.85	0.1735
state	38	1	-16.7170	12465.06	-24447.8	24414.36	0.00	0.9989
state	39	1	1.1996	1.0543	-0.8667	3.2659	1.29	0.2552
state	40	1	-16.9306	12783.26	-25071.7	25037.80	0.00	0.9989
state	41	1	0.8498	1.1181	-1.3416	3.0413	0.58	0.4472
state	43	1	0.7935	1.1181	-1.3979	2.9849	0.50	0.4779

state	44	1	0.6224	1.0541	-1.4436	2.6885	0.35	0.5549
state	47	1	0.2634	1.1547	-1.9998	2.5266	0.05	0.8196
state	48	1	-17.9306	12783.11	-25072.4	25036.50	0.00	0.9989
state	49	1	-16.5176	12492.85	-24502.1	24469.02	0.00	0.9989
state	50	0	0.0000	0.0000	0.0000	0.0000	.	.
birthyr	0	1	-0.2107	0.1675	-0.5391	0.1176	1.58	0.2084
birthyr	1	0	0.0000	0.0000	0.0000	0.0000	.	.
Scale		0	1.0000	0.0000	1.0000	1.0000		

NOTE: The scale parameter was held fixed.

The GENMOD Procedure

Model Information

Data Set	WORK.ST49
Distribution	Poisson
Link Function	Log
Response Variable (Events)	deaths
Response Variable (Trials)	den
Observations Used	156
Number Of Events	154
Number Of Trials	37923

Class Level Information

Class	Levels	Values
state	39	1 3 4 5 6 7 8 9 10 11 15 16 17 18 19 21 22 23 24 25 26 28 29 31 32 33 34 36 37 38 39 40 41 43 44 47 48 49 50
birthyr	2	0 1

Criteria For Assessing Goodness Of Fit

Criterion	DF	Value	Value/DF

Deviance	115	113.3996	0.9861
Scaled Deviance	115	113.3996	0.9861
Pearson Chi-Square	115	99.7523	0.8674
Scaled Pearson X2	115	99.7523	0.8674
Log Likelihood		-38892.8151	

Analysis Of Parameter Estimates

Parameter		DF	Estimate	Standard Error	Wald 95% Confidence Limits		Chi-Square	Pr > ChiSq
Intercept		1	-5.0465	1.2373	-7.4716	-2.6214	16.64	<.0001
state	1	1	-0.8076	1.2815	-3.3193	1.7041	0.40	0.5286
state	3	1	-18.2547	12704.22	-24918.1	24881.56	0.00	0.9989
state	4	1	-19.6356	12777.95	-25063.9	25024.68	0.00	0.9988
state	5	1	0.5641	1.1520	-1.6939	2.8220	0.24	0.6244
state	6	1	-18.1003	12696.08	-24902.0	24865.76	0.00	0.9989
state	7	1	0.6123	1.2246	-1.7879	3.0125	0.25	0.6171
state	8	1	0.7576	1.4335	-2.0520	3.5672	0.28	0.5972
state	9	1	-0.7735	1.5074	-3.7280	2.1810	0.26	0.6078
state	10	1	0.2629	1.1292	-1.9504	2.4761	0.05	0.8159
state	11	1	0.2453	1.1506	-2.0097	2.5004	0.05	0.8312
state	15	1	-0.1603	1.2837	-2.6762	2.3557	0.02	0.9006
state	16	1	-17.5979	12720.13	-24948.6	24913.39	0.00	0.9989
state	17	1	-18.2925	12687.70	-24885.7	24849.15	0.00	0.9988
state	18	1	-18.5435	12527.37	-24571.7	24534.65	0.00	0.9988
state	19	1	-1.3911	1.3549	-4.0466	1.2644	1.05	0.3045
state	21	1	0.2863	1.1576	-1.9827	2.5552	0.06	0.8047
state	22	1	-0.0637	1.4414	-2.8888	2.7613	0.00	0.9647
state	23	1	-1.5012	1.3313	-4.1104	1.1081	1.27	0.2595
state	24	1	-18.5344	12636.98	-24786.6	24749.48	0.00	0.9988
state	25	1	0.0034	1.1913	-2.3316	2.3384	0.00	0.9977
state	26	1	0.7011	1.1403	-1.5338	2.9359	0.38	0.5386
state	28	1	-17.2883	11133.62	-21838.8	21804.21	0.00	0.9988
state	29	1	1.0952	1.4247	-1.6971	3.8876	0.59	0.4420
state	31	1	-0.1304	1.1763	-2.4359	2.1751	0.01	0.9118
state	32	1	1.7210	1.5503	-1.3177	4.7596	1.23	0.2670
state	33	1	0.3857	1.0845	-1.7399	2.5114	0.13	0.7221
state	34	1	-0.5804	1.1799	-2.8930	1.7322	0.24	0.6228
state	36	1	-0.3096	1.1710	-2.6046	1.9855	0.07	0.7915

state	37	1	0.5715	1.2534	-1.8850	3.0281	0.21	0.6484
state	38	1	-16.5849	12520.63	-24556.6	24523.39	0.00	0.9989
state	39	1	0.5781	1.1046	-1.5868	2.7430	0.27	0.6007
state	40	1	-17.6026	12785.91	-25077.5	25042.33	0.00	0.9989
state	41	1	0.2789	1.1565	-1.9878	2.5455	0.06	0.8094
state	43	1	0.0998	1.1866	-2.2258	2.4254	0.01	0.9330
state	44	1	-0.0647	1.1196	-2.2591	2.1298	0.00	0.9539
state	47	1	-0.3716	1.2046	-2.7326	1.9895	0.10	0.7577
state	48	1	-18.3982	12780.43	-25067.6	25030.78	0.00	0.9989
state	49	1	-16.9312	11897.22	-23335.0	23301.19	0.00	0.9989
state	50	0	0.0000	0.0000	0.0000	0.0000	.	.
birthyr	0	1	0.0542	0.2529	-0.4414	0.5499	0.05	0.8302
birthyr	1	0	0.0000	0.0000	0.0000	0.0000	.	.
induct		1	-0.0385	0.0277	-0.0929	0.0159	1.93	0.1652
Scale		0	1.0000	0.0000	1.0000	1.0000		

NOTE: The scale parameter was held fixed.