

MCH/CCS-03-05

MATERNAL BIRTHWEIGHT AND REPRODUCTIVE OUTCOMES

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Published March, 2002

Final Report  
Grant 4 R40 MC 00133-03  
Project Period: 09/01/95 – 12/31/01

Prepared for:

THE MATERNAL AND CHILD HEALTH RESEARCH PROGRAM  
MATERNAL AND CHILD HEALTH BUREAU, HRSA, PHS, DHHS  
PARKLAWN BUILDING  
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### **MATERNAL BIRTHWEIGHT AND REPRODUCTIVE OUTCOMES**

#### **Statement of the Problem:**

Known biological and sociodemographic factors relating to the time of pregnancy do not adequately explain the risk for many pregnancy problems and many abnormal infant outcomes. Particularly, the reasons why poor mothers and Black mothers are at excess risk for these problems remain poorly understood. And these risks remain even in the face of decades of socioeconomic improvement and broadly applied public health and clinical interventions. At the same time substantial evidence has accumulated over the past five decades documenting that intergenerational factors are related to a number of adverse pregnancy outcomes, including low birthweight, preterm birth, intrauterine growth retardation, and fetal, perinatal, and infant mortality. The intergenerational factors which have been most studied are maternal stature (height) and maternal birthweight. Intergenerational factors have been defined by the PI as “.. those factors, conditions, exposures and environments experienced by one generation that relate to the health, growth and development of the next generation.”. Also of interest and relevance was the documentation dating back at least to 1954. that coronary disease was also related inversely to adult stature, More recently, there has been increasing evidence that not only stature, but also birthweight is related to several chronic diseases of adults, including coronary disease, hypertension, stroke, type 2 diabetes mellitus, and the metabolic syndrome. Further, an intergenerational connection has been shown by the finding that women who die of coronary disease produced an excess of low birthweight infants previously. Therefore, the study of intergenerational associations of prenatal and postnatal growth can provide insights into adult reproductive and non-reproductive health problems. The availability of a unique statewide computerized database in Washington State with extensive clinical and sociodemographic data served as the basis for our further intergenerational investigations. Most intergenerational studies have been in Whites, with a small number in Blacks. The population of births in Washington State allowed us to study birth outcomes to mothers in four ethnic groups: non-Hispanic Whites, African Americans, Native Americans, and Hispanics (mostly of Mexican background). The availability of obstetric data also allowed us to seek more intergenerational connections between mothers’ birthweight and pregnancy problems.

#### **Research Objectives**

- I. This study tested the following hypotheses related to associations between mothers birthweight and the suboptimal birth outcomes and reproductive problems listed below, comparing four ethnic groups, non-Hispanic Whites, African Americans, Native Americans, Hispanics:
  1. Infant low birthweight
  2. Infant preterm birth
  3. Infant respiratory distress syndrome
  4. Need for a cesarean section
  5. Gestational diabetes mellitus
  6. Pre-eclampsia
  
- II. To describe the intergenerational changes in distributions of female birthweight and female stature in the same four ethnic groups.

## **Study Design and Methods**

We used a retrospective cohort study design, using information from vital records and pre-existing statewide computerized databases. Mothers born in Washington State since 1949, and their births in the State from 1987-1995 formed our intergenerational cohort. The state live birth/infant death/fetal death file, had been linked by the State Department of Health to a unique statewide database, consisting of detailed discharge summaries of all obstetric and neonatal admissions which existed at the time of our study. This linked file is the Birth Events Record Database (BERD). We further linked the BERD file for those years to the birth certificates of mothers born in the State since 1949, when birthweight was first added to the birth certificate. We took a 10% random sample of Births to White mothers, by year of infants' birth. We included all births to mothers in the other three ethnic groups in order to obtain enough births for analysis. We later also linked our cohort to the state drivers' license datafile in order to obtain self-reported statures of the parents and grandparents, which we ascertained were reliable enough for our epidemiological study.

We used a variety of statistical methodologies, including Poisson regression, linear regression, chi-squared statistics, t-tests, and correlation analysis. Samples of mother and infant pairs were as follows: Whites, 23,150; African Americans, 7,109; Native Americans, 7,869; Hispanics, 6,780

## **Findings**

We found that mothers birthweight was inversely related to infants' total low birthweight (<2500 gm), and to a lesser extent to infants' very low birthweight (<1500 gm). We found that mothers' birthweight was inversely related to infants' total preterm birth (<37 weeks), and to infants very preterm birth (<34 weeks). Findings were similar in all four ethnic groups. We also documented that the maternal birthweight distribution of African Americans was displaced downward compared to the other three groups, whose distributions were similar. We concluded that this downward displacement of African Americans was a partial reason why African American mothers continue to be at greater risk for having low birthweight infants than the Native Americans and the Hispanics, groups who are of similar socioeconomic circumstances.

There was a decreasing trend of risk for gestational diabetes mellitus as mothers birthweight increased from <2000 gm to the reference weight, 3000-3999 gm for Whites, Native Americans and Hispanics. The highest relative risk was for maternal birthweight <2000gm, in all four groups. African Americans also had a two-fold increased risk of gestational diabetes mellitus for maternal birthweights > 3999 gm.

Among White mothers maternal birthweight of 2500 –3999 gm was associated with a 20.9% risk of cesarean delivery, the lowest, compared with 24.5% for a maternal birthweight of <2500 gm, and a 24.0% for maternal birthweight >3999 gm. Similar risk patterns were seen for Native Americans and Hispanics, although they did not reach statistical significance. Among White mothers the risk of c-section was 3.23 times greater with maternal birthweight <2500 gm and an infant birthweight >3999 gm compared with both maternal and infant birthweights between 2500-3999 gm. Risk for cesarean section was not associated with maternal birthweight among the African Americans.

Rates for respiratory distress syndrome (RDS) were: Whites 1.2%, African Americans 1.9%, Native Americans 1.3%, Hispanics 1.0%. Maternal low birthweight <2500 gm was associated with increased relative risk in Whites and African Americans for infants born vaginally. Compared with mothers of normal infants, birthweights of mothers of infants with RDS and delivered vaginally were significantly lower in Whites, African Americans and Native Americans. The association of maternal low birthweight with RDS persisted in African Americans even after multiple risk factors were added to the model.

When our first results were challenged on a spurious statistical basis-using too few categories of maternal birthweight, we responded by showing that there is a dose/response association between mothers' birthweight and both infant low birthweight and infant preterm birth using 500 gm categories from <2000gm to >3999 Gm.

There is much unfinished work to be done on this cohort. While our funding has ended and the PI is now emeritus, we are attempting to associate various maternal prenatal and postnatal growth measure to infant birthweight, and to describe how socioeconomic factors relate to infant birthweight intergenerationally as well as in the current generation.

## **Discussion of the Findings**

Our results further demonstrate that maternal birthweight, an important measure of prenatal growth and infant health, has long term consequences for reproductive health of mothers. While most previous studies were among White populations, and only a few of Blacks, our studies show similar associations between maternal birthweight and infant low birthweight and preterm birth in four major American ethnic groups. The similar results in four groups can be interpreted as a confirmation of the associations, and an indication that similar results will be found in other ethnic groups.

We documented that the maternal birthweight distribution of African Americans is displaced downward compared to the other three groups, which are quite similar. We offered this as a partial explanation for the persistent high rate of low birthweight among African American infants., compared to Native Americans and Hispanics, two minority groups who are of similar socioeconomic circumstances.

The associations of maternal birthweight with the risk for some other outcomes is not as consistent among the four ethnic groups as are the associations with infant birthweight and gestational duration. For instance, while maternal birthweight < 2000 gm was associated with an elevated risk for gestational diabetes mellitus, only African American mothers of high birthweight, >3999 gm, were at elevated risk for this problem. Only the Whites had a statistically significant association between maternal birthweight and the risk for cesarean section, although Native Americans and Hispanics had similar relationships. Small sample sizes may be an explanation for some of these different findings among the four ethnic groups.. But African Americans had no association of maternal birthweight and cesarean section, and were the only group whose association between maternal birthweight and the risk for infant respiratory distress syndrome persisted after adjustment for multiple factors. Thus, while there seem to be similar associations in three of the ethnic groups, African Americans may have more postnatal environmental stresses, including during pregnancy and delivery, which attenuates or accentuates some associations.

Our finding of the association of maternal birthweight and gestational diabetes mellitus has also been shown by a small number of other workers. Since others have shown associations between birthweight and type 2 diabetes mellitus in men and women, the documentation of our association with gestational diabetes further supports an intergenerational link, since women who experience gestational diabetes are at increased risk for type 2 diabetes mellitus later in life.

## **Policy Implications**

An underlying importance of studies of birthweight and later reproductive and non-reproductive health problems is that some of the strongest associations are with low birthweight, some of which is undoubtedly modifiable and preventable. However, it must be realized that some of the current burden of infant low birthweight is related to the suboptimal birthweight distributions of the mothers of today. National data show only a slow rate of changes in birthweight distributions since 1950 when they were first reported, and some of them not favorable. This highlights the need to persist in our efforts to enhance maternal and child health. It is not just a question of preventing today's low birthweight, but to improve the birthweight distributions of female infants now being born. Most associations seen of birthweight and future reproductive and non-reproductive health problems are of a dose/response pattern. This indicates that a goal should not simply be the reduction of low birthweight, but the improvement of the entire distribution of birthweight from one generation to the next. All the evidence points to the slowness with which positive change occurs, which highlights the need for long-term commitments to improve maternal and child health. There are reasons to conclude that one reason the Western European countries have healthier infants and better vital statistics than the US, is that their efforts have been to improve both maternal and child health,

as well as the health of the total population through universal health care and other social and health services. These efforts have a history of many decades, whereas our efforts have been more recent, do not pertain to the entire population, and in some respects have gone in the wrong direction. For instance, the increasing survival of low birthweight infants suggests that this may have consequences for the future health of our population., although this remains to be demonstrated.

### **Suggestions for Future Research**

Intergenerational studies of reproductive problems have a long history of miserly funding, compared to, perhaps, studies of prenatal care and of other interventions. At the same time, there is little objective evidence that the increase in early prenatal care and other interventions after millions of dollars invested in these programs have had much effect. That is not to say that early prenatal care and other interventions are not important; it is important to the individual mothers and probably also to outcomes. Perhaps studies of prenatal care are looking at the wrong outcomes.

One reason for the sparsity of intergenerational studies is finding or developing adequate intergenerational databases. Computer technology is now highly developed so that linkage between individuals in different databases is now quite possible and accurate. We have demonstrated that! Another problem is the difficulty for researchers to think intergenerationally. The public health ethos concentrates on attacking current problems with current interventions. One thing that intergenerational studies strongly suggests is that current interventions may be necessary for future improvement. More and more imaginative intergenerational studies should be attempted. And one cannot always predict what will be found or what will be the best statistical analysis. Before prohibitively expensive longterm followup studies are instituted, as is currently being proposed, maximum utility should be made of possibilities of linking datafiles in a fashion that this study and others have been very successful in doing.

The age of imaginative growth studies has long passed. Tanner's books and articles are decades old. Physical growth as a subject for research has been replaced by obsession with biochemical and immunological approaches, often unrelated to the growth process. Modern studies of physical growth- both prenatal and postnatal- combined with associated biochemical and immunological correlates are needed. Such studies should also include histological and even electron microscopic approaches, since what is going on in cells must determine what chemicals are being produced or modified. And experimental teratological studies will probably also be of value. And the relative importance of socioeconomic factors in morphological, physical and physiological growth needs to be included.

Lastly, the intergenerational studies have shown that there are connections between prenatal and postnatal growth and reproductive and non-reproductive problems. The Western European investigators are aware of the connections, but few American investigators are, particularly absent are MCH investigators. Most of the investigators in the US and elsewhere have been interested in adult chronic diseases, and know little about obstetric and pediatric issues. There is a real role for MCH investigators to contribute to this emerging field, and research funding should become available.

Lastly, we must get beyond an obsessive concern about what is happening in the current generation, and recognize that there is now ample evidence that life goes on from one generation to the next, ad infinitum. What is occurring now will have long term consequences.

### **Presentations**

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**Final Report****Abstract****Grant 4 R40 MC 00133-03****Project Period: 09/01/95-12/31/01****Maternal Birthweight and Reproductive Outcomes****Irvin Emanuel, MD****Department of Epidemiology****School of Public Health and Community Medicine****University of Washington****Seattle, Washington 98195-7236**

This was an investigation of the relationship of mothers' birthweight to future pregnancy problems and birth outcomes. We linked several computerized statewide databases, including: live birth/infant death/fetal death, discharge summaries of obstetric and neonatal hospital admissions, and drivers licenses, to the birth certificate data of the mothers' own birth. Mothers and infants in four ethnic groups were studied: non-Hispanic Whites (23,150), African Americans (7,109), Native Americans (7,869), and Hispanics (6,780; mostly of Mexican background). We used a retrospective cohort study design with a variety of statistical analyses, including Poisson regression, linear regression, chi-squared statistics, t-tests, and correlation analysis. We found that mothers' birthweight was inversely related to infants' very low birthweight (<1500 g) and total low birthweight (<2500 g), and to very preterm birth (<34 weeks) and total preterm birth (<37 weeks). We documented that the maternal birthweight distributions of African Americans was displaced downward compared to that of the other three ethnic groups, whose distributions were similar. We concluded that this downward displacement of African Americans was a partial reason why African American mothers continue to be at high risk for having low birthweight infants compared to the Native Americans and Hispanics, who are of similar socioeconomic circumstances. There was a decreasing trend of risk for gestational diabetes mellitus as mothers' birthweight increased from <2000 gm., and the African American mothers whose own birthweights were >3999 gm also had a two-fold increased risk for this pregnancy complication. White maternal birthweight <2500 gm was associated with an increased risk for cesarean delivery; similar risks were seen for Native Americans and Hispanics, but these were not statistically significant. Among White mothers the risk for c-section was 3.23 times greater for maternal birthweight <2500 gm and an infant birthweight >3999 gm, compared with both mother and infant birthweight between 2500-3999 gm. Risk for cesarean section was not associated with mothers' birthweight in African Americans. Maternal birthweight <2500 gm was associated with increased risk in Whites and African Americans for infants delivered vaginally. This risk for African Americans persisted even after adjustment for multiple factors. Our study further documented the importance of mothers' birthweight in pregnancy problems and infant outcomes. This is the first study of such relationships in Native Americans and Hispanics. The downward displacement of the African American maternal birthweight distribution provides a partial reason why these mothers continue to be at high risk for suboptimal birth outcomes. The associations of mothers' birthweight to such problems leads to the conclusion that there probably will not be a dramatic and rapid reduction or elimination of such problems, but highlights the need for a longterm commitment to improve the health and wellbeing of each generation of mothers and infants.

**Key Words**

birth weight      low birth weight      gestational duration      preterm birth      prematurity  
preterm delivery      mothers      infants      prenatal growth      intrauterine growth      cesarean section  
respiratory distress syndrome      gestational diabetes mellitus