Title: "Birth Outcomes and Neural Tube Defects in the United States before and After Folic Acid Fortification."
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INTRODUCTION

The diets of pre-conceptional women have deteriorated in the United States over the past thirty years (Putnam and Gerior 1999), which has had serious implications for infant and maternal health. In addition to poorer overall health and well-being (Ward et al 1997), it has been established that women with poor diets have more adverse pregnancy outcomes and complications including preterm births, low birth weight births, pre-eclampsia, spontaneous abortions, placental abruptions and fetal growth restriction (Hibbard 1967, Watkins 1998, Scholl and Johnson 2000). Maternal diets and nutrition have also been shown to have a strong influence on the occurrence of a relatively rare but serious birth defect of the central nervous system. Inadequate levels of dietary maternal folate have been associated with an increased risk of having a neural tube defect affected pregnancy (Milunsky 1989). Research shows that nearly 70 percent of neural tube defect cases are preventable with adequate maternal folate levels (CDC 1992). Thus, there has been greater emphasis in public health on increasing maternal dietary folate as part of an overall plan to improve the health of women before they conceive (Atrash 2006). It has been suggested that improving pre-conceptional health will result in improved reproductive outcomes and a reduction of societal medical care costs (US Department of Health and Human Services 1989, Jack and Culpepper 1991, Cefalo and Moos 1995).

We have two primary aims with this research. First, we are interested in assessing the influence of social and demographic characteristics on the incidence of neural tube defect births

using otherwise very detailed and unique vital statistics. Second, we are also interested in the usefulness of vital registration data for analyzing birth outcomes that are undesirable, but also subject to medical intervention.

BACKGROUND

Fetuses exposed to low levels of maternal folate are at increased risk for neural tube defects such as anencephaly and spina bifida (Smithells, Sheppard and Schorah 1976, Botto et al 1999, Oakley 2004). Anencephaly and spina bifida are part of a larger class of rare malformations of the central nervous system and originate in the earliest phases of pregnancy. Hence, the period during which maternal folate levels may prevent neural tube defects is small (the first 12 weeks), which is often before the woman is even aware that she is pregnant (Buttriss 2004). Since half of all pregnancies in the United States are unplanned (Williams et al 2006), it is vital that all women of reproductive ages have adequate folate levels to ensure positive birth outcomes, and not just for those women who have been planning pregnancy (Atrash et al 2006).

Neural tube defects have been associated with a variety of behavioral, socioeconomic, and demographic characteristics. Maternal behavioral risk factors include: poor nutrition (Green 2002, Caudill et al 2001), smoking (Blatter et al 1994), obesity (Shaw et al 1996), and maternal emotional stress (Suarez et al 2003). Various indicators of low socioeconomic status have been associated with neural tube defects including, parental occupation (Blatter et al 1994), parental education (Eichholzer et al 2006), and neighborhood social conditions (Wasserman et al 1998). Broader demographic characteristics also seem to be associated with occurrence of neural tube defects such that younger women aged 14-19 years (Reefhuis and Honein 2004) and Hispanic women have greater risk than older and non-Hispanic women (Czeizel et al 1992). Specifically, among Hispanic women, Mexican women have the greatest risk of NTD affected pregnancies than any other Hispanic ethnic group (Suarez et al 2000, Blatter et al 1994). It has been suggested that this relationship is due to the higher consumption of unfortified corn products by Mexican women that may limit access to adequate levels of dietary folate by their embryos (Green 2002). Additionally, Correia and Hauser (2007) find a relationship between nativity and risk of NTD affected pregnancies, such that foreign-born Hispanics exhibited higher risk than native-born Hispanics.

METHODS

DATA

In order to assess the research questions, we will use the U.S. Natality files for 1990 and 2002, made available by the National Center for Health Statistics. This data includes birth information collected on U.S. birth certificates for all births in the U.S. in 1990 and 2002. The natality files for 1990 and 2002 are assumed to be complete, as the registration of births in the United States is near universal.

There are some shortcomings in using this data to assess the effects of social and demographic characteristics associated with neural tube defects before and after the folate fortification mandate by the Federal Drug Administration. While underreporting of neural tube defects is not likely, (as the major symptoms of spina bifida and anencephaly are apparent at birth) it is likely that there is a selection effect occurring with neural tube defect births. It has been suggested that the increased ability to detect, diagnose, and terminate neural tube defect pregnancies in utero has altered its occurrence in the population. Previous estimates hold that in some areas of the United States, the ability to detect and terminate neural tube defects has

reduced the prevalence of spina bifida at birth by 20-30 percent and anencephaly by 60-70 percent (Cragan et al 1995). This suggests that women who do give birth to infants diagnosed with a neural tube defect are "selected" by virtue of the availability of NTD screening and prenatal care as well as abortion services utilization. Despite these methodological concerns, this vital statistics data has substantial informative potential regarding births complicated by neural tube defects.

MEASURES AND ANALYSES

We examine the occurrence of neural tube defects and maternal and infant characteristics surrounding the birth that are reported on the U.S. birth certificate in 1990 and 2002. These data allow for the examination of maternal and infant characteristics and their effects on neural tube defects. These characteristics include demographic variables such as age of mother, maternal race and ethnicity. Additional independent variables of interest include: maternal education, nativity, state of residence, marital status and behavioral risk factors (such as adequacy of prenatal care, maternal smoking and alcohol use), which are also included on the birth certificate. Characteristics of the infant are considered, including infant sex, birth weight, and gestational age.

We use multivariate analyses use logistic regression models to estimate the effects of socio-economic status, demographic variables, and birth characteristics on the occurrence of neural tube defects in the United States. We use data from before and after the mandatory fortification do determine the influence that maternal and infant characteristics surrounding births have had on the occurrence of neural tube defects. This may allow us to investigate the

policy implications of federal guidelines whose purpose was to improve health outcomes and also the usefulness in using vital registration data to examine birth defects.

PROGRESS TO DATE: Data for this project are in hand, and analysis has begun.

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