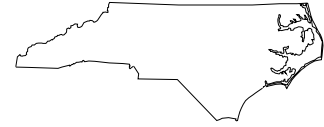


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# Statistical Brief



State Center for Health Statistics

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## Folic Acid Fortification: Initial Effects on Neural Tube Defect Prevalence in North Carolina

### A Report from the North Carolina Birth Defects Monitoring Program

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#### Introduction

Neural tube defects (NTDs), which include spina bifida, anencephaly, and encephalocele, are severe and sometimes lethal congenital malformations of the spine and central nervous system. Affecting an estimated 1 in 500 to 1 in 750 pregnancies in North Carolina, NTDs are among the most commonly occurring preventable birth defects in the state.<sup>1</sup>

Several observational studies have found that women who, prior to pregnancy, had supplemented their normal diets with the synthetic form of the B vitamin folic acid had a substantially reduced risk of having an infant with a neural tube defect.<sup>2-4</sup> These findings were confirmed in 1991 in a randomized controlled trial conducted by the Medical Research Council (MRC).<sup>5</sup> The MRC study demonstrated that preconceptional consumption of synthetic folic acid, in addition to the usual diet, will prevent approximately 70 percent of spina bifida and anencephaly – the two most commonly occurring NTDs. Based on these findings, in 1992 the U.S. Public Health Service published a recommendation that all women of childbearing age consume at least 400 µg of folic acid daily to reduce their risk of having a pregnancy

affected by an NTD.<sup>6</sup> In March 1996, the Food and Drug Administration issued a rule requiring all enriched grain products to be fortified by 1 January 1998 with 140 µg of folic acid per 100 g of cereal grain.<sup>7</sup> Anecdotal information suggests that most millers in the United States were in compliance with the rule by mid-1997.

In a study to determine the effect of fortification on blood folate levels, Jacques and colleagues reported that folate levels increased substantially in the Framingham, Massachusetts population soon after fortification was initiated.<sup>8</sup> The results from a similar study in California were consistent with the findings of Jacques et al.<sup>9</sup>

While these results suggest that fortification has increased blood folate levels in the population, some concern remains that the level of fortification adopted by the FDA is insufficient for full prevention of folic acid-preventable birth defects.<sup>10</sup> At the current level of fortification, the average woman's consumption of folic acid is projected to increase by only 100 µg per day, or one-fourth the amount recommended by CDC for birth defects prevention.<sup>11</sup> The purpose of this study is to provide an early assessment of the trends in neural tube defects in North Carolina after fortification was initiated.



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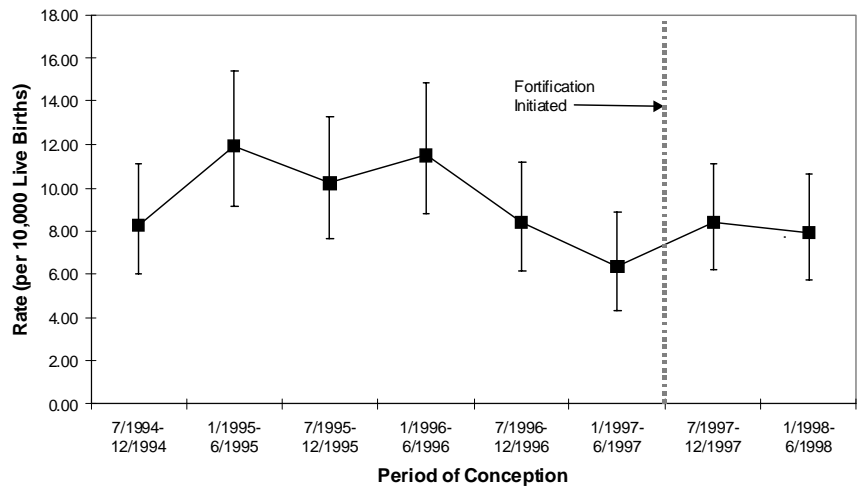
## Methods

Data from the North Carolina Birth Defects Monitoring Program (NCBDMP) were used for this study. Mandated in 1995 by the North Carolina General Assembly, the NCBDMP monitors and collects data statewide on infants born with major birth defects in order to help improve programs aimed at preventing and treating birth defects. From the NCBDMP registry database, 389 live-born and stillborn infants with NTDs who were delivered between 1 January 1995 and 31 March 1999 were identified. Case reports from the database were matched with vital statistics files, and the reported date of last menses was used to estimate the date of conception for each infant with an NTD. Rates of NTDs were determined based on the date of conception by dividing the number of cases conceived during a given period by the total number of live births whose conception occurred during that time. Ninety-five percent confidence intervals for the rates were based on the exact binomial limits. For this study, 1 July 1997 was selected as the point at which fortification was essentially complete in North Carolina, as suggested by anecdotal information from several major bakeries in the state and from national suppliers of food fortification products. The rate of NTDs following fortification is based on over 113,000 conceptions occurring between 1 July 1997 and 30 June 1998.

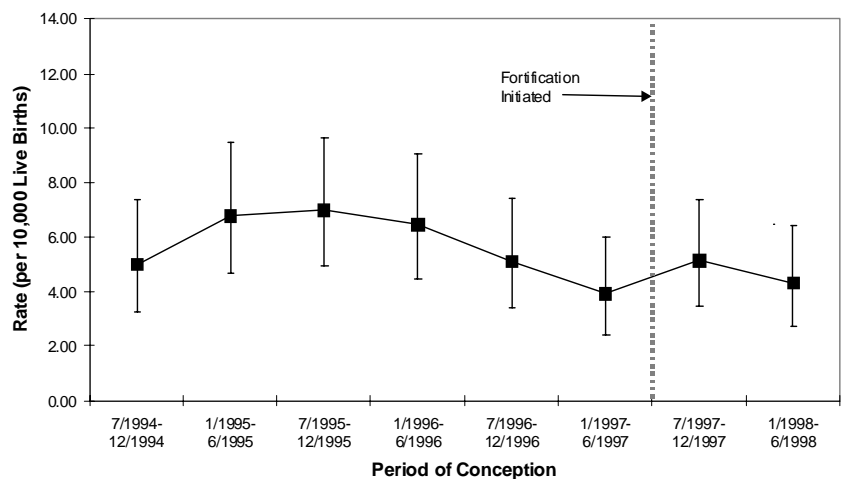
## Results

During the first 24 months of observation (July 1994-June 1996), the rate of total NTDs and spina bifida increased slightly (Figures 1 and 2). Between July 1996 and June 1997, these rates declined by about 20

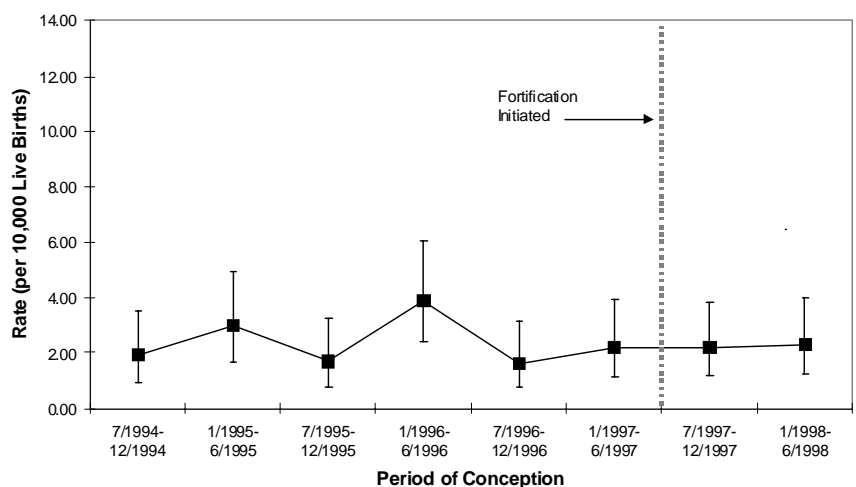
**Figure 1. Rate of Neural Tube Defects with 95% Confidence Limits by Period of Conception, N.C. Birth Defects Monitoring Program**



**Figure 2. Rate of Spina Bifida with 95% Confidence Limits by Period of Conception, N.C. Birth Defects Monitoring Program**



**Figure 3. Rate of Anencephaly with 95% Confidence Limits by Period of Conception, N.C. Birth Defects Monitoring Program**



percent. As seen in Figures 1 and 2, this decline occurred during the 12 months just prior to fortification. In the twelve-month period immediately after fortification (July 1997-June 1998), the downward trend for total NTDs and spina bifida leveled off and, in fact, the rates actually increased slightly compared to the six-month period prior to fortification. The rate for anencephaly remained relatively constant throughout the entire period of study, except for a transitory increase during the first half of 1996 (Figure 3).

Figures 1-3 also show the 95 percent confidence limits for each of the rates shown in the graphs. As seen in Figure 1, the lower bound of the confidence limits for total NTDs in the most recent time period (January-June 1998) is approximately 5.8, which is about 8 percent below the point estimate of 6.3 for the six-month period just prior to fortification (January-June 1997). Based on a comparison of these two rates, this study effectively rules out a decline in NTDs of 8 percent or more after fortification.

### Comment

The studies by Jacques et al.<sup>8</sup> and Lawrence et al.<sup>9</sup> demonstrated an increase in blood folate levels in the population shortly after fortification. In contrast, the results from this report show no evidence of a concomitant decline in the rate of neural tube defects among infants conceived following fortification, although a modest 8 percent reduction or less cannot be excluded. Given that sufficient fortification has been projected to reduce neural tube defects by 50 percent, these findings in North Carolina support the assertion that the current fortification concentration in the United States is too low for full prevention of birth defects.

The results of this report should be considered as preliminary and interpreted with caution until additional data are available. The Birth Defects Monitoring Program is closely tracking NTD rates in the state, and subsequent updates will follow. This report reaffirms the need to increase efforts to educate all women of childbearing age on the need to consume a balanced, varied diet that is supplemented with daily vitamins containing 400 µg of synthetic folic acid. Doing so will substantially reduce the incidence of folic acid-preventable birth defects such as anencephaly and spina bifida, and improve the health of children in North Carolina.

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