Research Article

# Use of Family History Information for Neural Tube Defect Prevention: Integration into State-based Recurrence Prevention Programs

*Ridgely Fisk Green, Joan Ehrhardt, Margaret F. Ruttenber, and Richard S. Olney*

**ABSTRACT**

***Background:*** *A family history of neural tube defects (NTDs) can increase the risk of a pregnancy affected by an NTD. Periconceptional folic acid use decreases this risk.* ***Purpose:*** *Our objective was to determine whether second-degree relatives of NTD-affected children showed differences in folic acid use compared with the general population and to provide them with folic acid education.* ***Methods:*** *Michigan and Colorado health workers contacted families with a previous pregnancy or child affected by an NTD, identified through NTD recurrence prevention programs. Families were interviewed to identify the number of second-degree relatives of child-bearing age. Families mailed surveys to these relatives, who returned them to the state health departments. The survey assessed folic acid use, views on having an affected child, and reproductive planning. Folic acid education materials were sent to relatives who provided contact information.* ***Results:*** *Folic acid supplement use among relatives was similar to that of the general population, despite elevated risk perceptions.* ***Discussion:*** *Both state health departments plan to increase efforts to contact affected families and their relatives through partnerships with family support groups.* ***Translation to Health Education Practice:*** *Including outreach to second-degree relatives in NTD recurrence prevention programs could increase the impact of these programs.*

*Green RF, Ehrhardt J, Ruttenber MF, Olney RS. Use of family history information for neural tube defect prevention: integration into state-based recurrence prevention programs.* Am J Health Educ. *2011; 43(5):296-308. This paper was submitted to the* Journal *on February 9, 2011, revised and accepted for publication on June 25, 2011.*

## BACKGROUND

Spina bifida and other neural tube defects (NTDs) are serious birth defects, with spina bifida affecting approximately 3.5 per 10,000 live births in the U.S.[1] In the general population, folic acid supplementation has been shown to reduce the risk of NTDs.[2] The NTD risk is higher in certain individuals with a family history of NTDs, with a 2-5% recurrence risk in siblings with a single affected child and a risk in other close relatives that is increased above that of the general population.[3-7] For women with a previous affected pregnancy, 4 mg of folic acid supplementation daily, 10 times the dosage recommended for the general population, is recommended to reduce risk of recurrence in siblings,[8] and folic acid supplement use has been shown to

*Ridgely Fisk Green is a pediatric genetics researcher at Carter Consulting, Inc. and National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, GA 30333; E-mail: grf1@cdc.gov. Joan Ehrhardt is the Birth Defects program coordinator at the Michigan Department of Community Health, Bureau of Epidemiology, Lansing, MI 48913. Margaret F. Ruttenber is the program director at Colorado Responds to Children with Special Needs, Colorado Department of Public Health and Environment, Denver CO 80246. Richard S. Olney is a medical officer at the National Center on Birth Defects and Developmental Disabilities; Centers for Disease Control and Prevention, Atlanta, GA 30333.*

result in an 87% reduction in recurrence in siblings.[5]

Despite public health campaigns to increase folic acid supplement use in the general population, only about 40% of women of childbearing age report consuming the recommended daily level of supplemental folic acid.[9] Even among those women with an affected child, a sizeable fraction does not take folic acid supplements.[5, 10-13] Familial cases account for 3.7-18% of all NTD cases,[14] and recurrence prevention programs have been shown to be effective in increasing supplemental folic acid intake and reducing recurrence.[5, 15-18]

Only one group has examined use of folic acid supplements in close relatives of children with an NTD, in studies performed in Ireland and the U.S.[19-21] These studies focused on aunts and female first cousins of the affected child, who were interviewed before and after receiving a folic acid information pack. The information packs included: (1) a letter from the principal investigator; (2) folic acid education materials from the Centers for Disease Control and Prevention (CDC), March of Dimes, the local Department of Health and cereal manufacturers; (3) vouchers from cereal manufacturers; and (4) a package of folic acid tablets (Ireland only). These studies found that these brief interventions increased both knowledge and use of folic acid supplements among relatives in the short-term, consistent with previous studies that have shown that brief interventions can increase folic acid awareness.[22-25] In the Irish study, although 73% of relatives had knowledge of the benefits of folic acid, only 8.8% took folic acid supplements prior to receiving the information pack, with an increase to 19% afterward, compared with 2.7% in the general population.[20] In a retrospective cross-sectional study from 1998 to 2000, aunts reported preconceptional use of folic acid supplements for 57.9% of pregnancies and use of folic acid supplements during pregnancy for 89.5% of pregnancies.[19] In a Washington, D.C. study, at baseline 80.2% of relatives reported knowing that folic acid prevented birth defects, compared with 20% of the general population, and following the intervention, relatives' folic acid supplement use increased from 41.9% to 48.5%.[21]

Our project used family history information to identify and enroll women who were at increased risk for having a pregnancy affected by an NTD and was integrated into existing state-based recurrence prevention programs in Colorado and Michigan. The project included a survey to determine folic acid supplement use, reproductive planning and views on having an affected child. Participants who provided contact information were sent standard folic acid education materials and a follow-up survey (Michigan only). Our project extended the work of Byrne and colleagues[19-21] to other populations in the U.S. and illustrated the challenges in incorporating such a program into the state health department setting.

## PURPOSE

The primary goals of the project were: (1) to assess whether women at increased risk of having a pregnancy affected by an NTD, due to their or their partner's family history, showed differences in folic acid supplement use compared with the general population; (2) to determine whether perceptions of risk and pregnancy-planning status affected folic acid supplement use; and (3) to provide these women with folic acid education materials.

## METHODS

### *Overview*

Our project took advantage of existing recurrence prevention programs in Colorado and Michigan by extending prevention education to second-degree relatives. Through these programs, probands (pregnancies or children affected by an NTD) had been identified, and contact information for their mothers was available. The project targeted second-degree female relatives and female partners of second-degree male relatives of an affected child: paternal and maternal grandmothers and aunts, as well as sisters and female partners of brothers, of childbearing age (ages 18-44). Families were considered ineligible if the affected child had been adopted, because relatives would not be at an increased risk due to a lack of a biological relationship to the child, or in certain other circumstances. We conducted a retrospective survey to determine whether these relatives were more likely to take folic acid supplements than the general population and planned to begin a prospective intervention project to promote folic acid supplement use among these relatives. We aimed to evaluate the effectiveness of the intervention, measured both by whether or not an increased number of relatives took folic acid supplements and by rates of NTD recurrence within the family (i.e., whether any relatives of the affected child had a pregnancy or child affected by an NTD after either the birth of the affected child or the intervention). However, this plan was limited by the small number of participants and the inability to contact relatives directly.

### *Survey Design and Distribution*

The first steps were protocol development and submission of project materials to the Institutional Review Board (IRB) of each state health department. A survey was developed to determine folic acid supplement use, reproductive planning and contraception use, previous pregnancies and outcomes, knowledge about folic acid and NTDs, and views on having an affected child (Appendix 1). Questions were based on those from field-tested surveys (e.g., Behavioral Risk Factor Surveillance System (BRFSS), Pregnancy Risk Assessment Monitoring System (PRAMS), and HealthStyles™) whenever possible.

The Michigan and Colorado state health departments identified probands with NTDs through their existing statewide birth defects surveillance programs. The NTDs captured were spina bifida, anencephaly and encephalocele. Pre-contact letters briefly describing the project were sent to probands' mothers, who were then contacted by telephone to obtain consent to participate in the project and to determine the number of eligible relatives (female second-degree relatives and female partners of male second-degree relatives of childbearing age). The IRBs determined that to protect the relatives' privacy, only the

probands' mothers could be contacted directly to solicit participation. Thus, surveys were sent to the probands' mothers for distribution to relatives. This method had the advantage of engaging the index family. A disadvantage was that state health workers were unable to re-contact nonparticipating relatives with reminders, which likely affected the quantity of surveys returned.

Surveys were returned directly to the state health departments. Contact information was requested from relatives, and those relatives who provided this information were sent folic acid education materials about the importance of folic acid for the prevention of NTDs. Standard folic acid education materials were used, rather than recurrence prevention information, since current data are not sufficient to provide a quantitative assessment of the relatives' risk and current folic acid supplement recommendations for those with a family history of neural tube defects in a second- or third-degree relative are the same as those for the general population. These materials, developed previously by CDC, were "Emma's Story," a narrative aimed at pregnancy contemplators and selected because it was designed for those with limited literacy skills, and the "Ready…Not" pamphlet, designed for non-contemplators. These folic acid education materials are available on the CDC website (http://www2.cdc.gov/ncbddd/faorder/orderform.htm). If the participating relative was discovered to be already pregnant, she was sent the "Congratulations, Mom, You Have a Beautiful Baby" pamphlet, produced by the National Birth Defects Prevention Network to support post-partum/interconception folic acid consumption. This pamphlet was thought to be more appropriate for pregnant women because it focuses on taking supplemental folic acid postpartum, prior to a future pregnancy, an action these women could take. By comparison, "Emma's Story" stresses the importance of supplemental folic acid use before pregnancy and might cause anxiety in pregnant women who had not taken supplements prior to conception. In Michigan, relatives who provided contact information were re-contacted and sent a second survey to assess differences in folic acid supplement use following the intervention. Respondents had the option to reply electronically or through the mail.

### *Differences in Protocols between States*

Protocols differed slightly between Colorado and Michigan, in part due to different IRB restrictions. The Colorado protocol was exempt from IRB review, while the Michigan protocol underwent expedited IRB review. The Colorado state health department birth defects data collection included data on fetal deaths, whereas Michigan program staff did not have access to this information. Colorado chose not to provide incentives, whereas Michigan provided an incentive (a gift card from a national retail store) to participants. The project coordinator for Colorado had direct access to the birth defects registry data, whereas the Michigan group did not. Surveys from Colorado were completely anonymous, while those from Michigan were coded by family. Colorado included infants with birth dates from 2006-2007, while Michigan included infants with 2005-2007 birth dates.

### *Statistical Analyses*

We calculated frequency distributions for each question stratified by state. For these analyses, responses to survey questions 5-10 were categorized as disagree (response of 1 or 2 on the Likert scale), neutral (response of 3 on the Likert scale), or agree (response of 4 or 5 on the Likert scale) (Table 1 and Appendix 1). Given that the demographics of the respondents from the two states were similar (Appendix 2) and the number of respondents was low, we combined the data from the two states for further analyses. In these analyses, survey questions 5-10 were dichotomized as disagree (response of 1 or 2 on the Likert scale) or agree (response of 4 or 5 on the Likert scale), excluding responses of 3 (neutral) (Table 2). Because all variables contained at least one category for which the cell count was less than 5, we used Fisher's exact tests to determine any statistically significant associations between responses and adequacy of folic acid supplement use and pregnancy planning status using SPSS v17.0 (Table 2 and data not shown). Respondents were coded as having adequate folic acid supplement use if they reported using a supplement or vitamin pill containing folic acid ("Yes" on Questions 1 and 2 (Appendix 1)) and taking the supplement 4-6 times a week or every day (Appendix 1, Question 3).

## RESULTS

Response rates for the two states are shown in Figure 1. In Colorado, 16/50 (32%) index families that were eligible and able to be contacted agreed to participate. Notably, of the families that did not participate, 10 families indicated that they did not want any further contact from the recurrence prevention program. 17/28 (61%) surveys were returned, with contact information provided by 13 (76% of those responding). In Michigan, 30/68 (44%) index families contacted were eligible and agreed to participate. 27/49 (55%) surveys were returned, with contact information included on 18 (67% of those responding). Upon completion of the survey, relatives who provided contact information were sent folic acid education materials and, in Michigan, a second follow-up survey. Two surveys were completed electronically, with folic acid education materials sent to those respondents by email. For the follow-up survey, 12/18 (67%) were completed. While surveys were intended only for the relatives, in some cases surveys were completed by the index mother as well.

Table 1 lists the frequency distributions by state for selected survey questions. Combining results from both states, 70.5% (31) of respondents reported taking a vitamin pill or supplement. Of those, 35.5% (11) reported "No" or "Don't know" when asked whether the vitamin pill or supplement contained folic acid. For women reporting use of folic acid-containing vitamin pills or supplements, 60.0% (12) reported daily use, 20.0% (4) reported taking multivitamins 4-6 times per week, 15.0% (3) 1-3 times per week, and 5.0% (1) less than once a week. Table 2 lists the frequency distributions for selected questions, stratified by whether or not the respondent had adequate folic acid

supplement use. Overall, 36.4% (16/44) women reported adequate folic acid supplement use, defined as taking a folic acid-containing supplement or vitamin 4 or more times per week. Of those women planning a pregnancy or currently pregnant, 80% (8/10) had adequate folic acid supplement use. (The two women who did not report adequate folic acid were planning a pregnancy.) Adequate folic acid supplement use was significantly associated with intention to take a folic acid-containing supplement and pregnancy plans (currently pregnant or planning pregnancy within next year or so), and marginally associated with maternal age 25 years and older. A higher percentage of maternal relatives, relatives with more than 12 years of education, and married relatives reported adequate folic acid intake, but these differences were not statistically significant (data not shown).

Responses to the open-ended question, "I take a folic acid containing vitamin because…" included: (1) being currently pregnant, planning a pregnancy, or in case of a pregnancy (6 respondents); (2) for other health reasons or for general health (5 respondents); (3) folic acid being already included in a multivitamin (4 respondents); (4) to prevent NTDs (2 respondents); (5) having an affected pregnancy or relative (2 respondents); and (6) following doctors' advice from a previous pregnancy (1 respondent).

The survey included two similar questions addressing intention to take a folic acid-containing multivitamin (Appendix 1, Questions 5 and 8), perceived likelihood of having an affected child (Appendix 1, Questions 6 and 9), and concern about having an affected child (Appendix 1, Questions 7 and 10). Agreement between responses to these questions was moderate for all three, with kappa scores of 0.680 ($P < 0.001$) for intention, 0.562 ($P < 0.001$) for likelihood, and 0.548 ($P < 0.001$) for concern.

## DISCUSSION

While the small number of survey participants limits interpretation of our findings, the percentage of female relatives who reported adequate folic acid supplement

**Figure 1. Survey Response Rates by State**

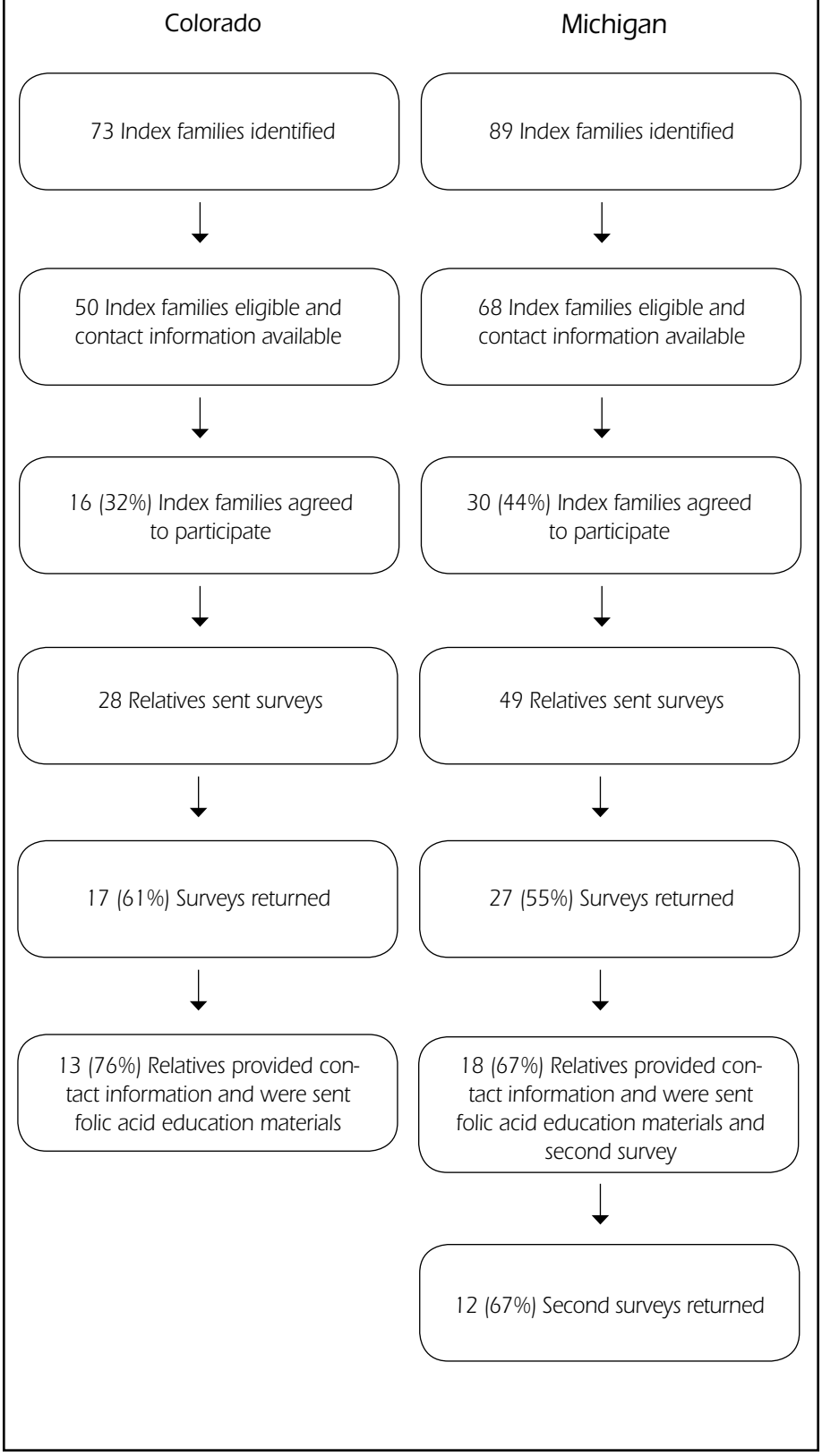

**Table 1. Frequency distributions by state for selected survey questions, Colorado, 2006-2007, and Michigan, 2005-2007**

| Survey question and response | Colorado (Survey 1) % respondents (number respondents) | Michigan (Survey 1) % respondents (number respondents) | Total (Survey 1) % respondents (number respondents) | Michigan (Survey 2) % respondents (number respondents) |
|---|---|---|---|---|
| Do you currently take any vitamin pills or supplements? (Question 1) | | | | |
| Yes | 82.4% (14) | 63.0% (17) | 70.5% (31) | 81.8% (9) |
| No | 17.6% (3) | 33.3% (9) | 27.3% (12) | 18.2% (2) |
| Don't Know | 0% (0) | 3.7% (1) | 2.3% (1) | 0% (0) |
| Do any of the vitamin pills or supplements you take contain folic acid? (Question 2)[a] | | | | |
| Yes | 57.1% (8) | 70.6% (12) | 64.5% (20) | 100% (9) |
| No | 14.3% (2) | 5.9% (1) | 9.7% (3) | 0% (0) |
| Don't Know | 28.6% (4) | 23.5% (4) | 25.8% (8) | 0% (0) |
| How often do you take this vitamin pill or supplement? (Question 3)[b] | | | | |
| <1x/week | 0% (0) | 8.3% (1) | 5.0% (1) | 11.1% (1) |
| 1-3x/week | 25.0% (2) | 8.3% (1) | 15.0% (3) | 22.2% (2) |
| 4-6x/week | 25.0% (2) | 16.7% (2) | 20.0% (4) | 11.1% (1) |
| Daily | 50.0% (4) | 66.7% (8) | 60.0% (12) | 55.6% (5) |
| I intend to take a multivitamin every day (Question 5) | | | | |
| Disagree (1-2[c]) | 5.9% (1) | 18.5% (5) | 13.6% (6) | 25.0% (3) |
| Neutral (3[c]) | 23.5% (4) | 18.5% (5) | 20.5% (9) | 8.3% (1) |
| Agree (4-5[c]) | 70.6% (12) | 63.0% (17) | 65.9% (29) | 66.7% (8) |
| I will take a multivitamin every day (Question 8) | | | | |
| Disagree (1-2) | 17.6% (3) | 22.2% (6) | 20.5% (9) | 0% (0) |
| Neutral (3) | 11.8% (2) | 18.5% (5) | 15.9% (7) | 8.3% (1) |
| Agree (4-5) | 70.6% (12) | 59.3% (16) | 63.6% (28) | 91.7% (11) |
| It is likely that I could have a pregnancy affected by a birth defect (Question 6) | | | | |
| Disagree (1-2) | 23.5% (4) | 44.4% (12) | 36.4% (16) | 33.3% (4) |
| Neutral (3) | 29.4% (5) | 33.3% (9) | 31.8% (14) | 41.7% (5) |
| Agree (4-5) | 47.1% (8) | 22.2%(6) | 31.8% (14) | 25.0% (3) |
| It is possible that I could have a pregnancy affected by a birth defect (Question 9) | | | | |
| Disagree (1-2) | 11.8% (2) | 29.6% (8) | 22.7% (10) | 25.0 (3) |
| Neutral (3) | 29.4% (5) | 22.2% (6) | 25.0% (11) | 25.0 (3) |
| Agree (4-5) | 58.8% (10) | 48.1% (13) | 52.3% (23) | 50.0 (6) |

*continued*

**Table 1. Frequency distributions by state for selected survey questions, Colorado, 2006-2007, and Michigan, 2005-2007 (con't)**

| Survey question and response | Colorado (Survey 1) % respondents (number respondents) | Michigan (Survey 1) % respondents (number respondents) | Total (Survey 1) % respondents (number respondents) | Michigan (Survey 2) % respondents (number respondents) |
|---|---|---|---|---|
| I am afraid of having a baby with serious birth defects (Question 7) | | | | |
| Disagree (1-2) | 17.6% (3) | 37.0% (10) | 29.5% (13) | 16.7% (2) |
| Neutral (3) | 23.5% (4) | 7.4% (2) | 13.6% (6) | 0% (0) |
| Agree (4-5) | 58.8% (10) | 55.6% (15) | 56.8% (25) | 83.3% (10) |
| The possibility of having a baby with serious birth defects scares me (Question 10) | | | | |
| Disagree (1-2) | 14.3% (2) | 18.5% (5) | 17.1% (7) | 8.3% (1) |
| Neutral (3) | 21.4% (3) | 7.4% (2) | 12.2% (5) | 8.3% (1) |
| Agree (4-5) | 64.3% (9) | 74.1% (20) | 70.7% (29) | 83.3% (10) |
| Which one of the following best describes your pregnancy plans? (Question 11) | | | | |
| Currently pregnant (a) | 0% (0) | 7.4% (2) | 4.5% (2) | 16.7% (2) |
| Planning pregnancy (b) | 23.5% (4) | 14.8% (4) | 18.2% (8) | 25.0% (3) |
| Future planning (c) | 29.4% (5) | 40.7% (11) | 36.4% (16) | 33.3% (4) |
| Not planning (d) | 23.5% (4) | 25.9% (7) | 25.0% (11) | 25.0% (3) |
| Cannot get pregnant (e) | 23.5% (4) | 11.1% (3) | 15.9% (7) | 0% (0) |

Notes:
[a] Of those reporting taking a vitamin or supplement
[b] Of those reporting taking a folic acid-containing vitamin
[c] Responses on the Likert scale

use, 36.4%, is similar to what is seen in the general population. For example, in the 2007 Gallup Organization survey, 40% of all women reported daily consumption of a folic-acid containing supplement.[9] In their U.S. study, Byrne et al.[21] observed slightly higher rates of intake of folic-acid containing vitamins in relatives in NTD-affected families compared with the general public (37% vs. 33%), but comparable to the rate seen in our project. In our project, folic acid supplement use for those relatives planning a pregnancy or currently pregnant, 80%, is similar to rates seen in women who are currently pregnant (76.8%) and pregnancy planners (71.6%) in the general population from the 2002 and 2004 BRFSS survey.[26]

Comparison with responses to surveys containing similar questions is helpful as well. We modeled our questions on intention to take a multivitamin (Appendix 1, Question 5) and likelihood of having a pregnancy affected by a birth defect (Appendix 1, Questions 6 and 9) after questions from the 2007 HealthStyles™ survey. HealthStyles,™ administered by the public relations firm Porter Novelli, is an annual mail survey of the U.S. population aged 18 years and older that examines health-related attitudes and behaviors. As shown in Table 3, a greater percentage of the respondents in our survey reported that they intended to take a multivitamin and that they were at risk of having a pregnancy affected by a birth defect than the national sample in the 2007 HealthStyles™ survey. However, whether this difference is statistically significant is difficult to determine, given the small number of respondents in our survey. Being pregnant or planning a pregnancy was associated with intention to take a multivitamin (chi square = 4.516, $P = 0.034$) and agreeing that it was possible that the respondent could have a pregnancy associated with a birth defect (chi square = 7.101, $P = 0.008$) in the HealthStyles™ survey. Demographics might explain some of the differences between the results of our survey and HealthStyles™.

The HealthStyles™ survey respondents had a greater diversity of race and ethnicity, age, and education than the respondents in our survey, with approximately 50% of HealthStyles™ respondents older than our cutoff of 44 years of age.

In their studies, Byrne et al.[21] observed an increase in folic acid supplement use following a brief intervention which included providing folic acid education materials. We found a higher percentage of women reporting folic acid supplement use (50%) in the follow-up survey from Michigan, but since not all relatives completed the follow-up survey, we cannot determine whether the increase is real or reflects increased interest in completing the survey by those already taking folic acid supplements.

Our study had some important limitations, including the low numbers of surveys completed, reliance on self-reported information, the retrospective design, and the differences between the states, for example in use of incentives. The low participation rates for index families (32% for Colorado and 44% for Michigan) could indicate a self-selection bias in families choosing to participate. For example, participation rates might be higher for those families more aware of the importance of folic acid or for families who have a closer relationship with their relatives. Such a bias might be reflected in the higher intention to take folic acid supplements and the elevated risk perception of the respondents. However, folic acid supplement intake rates in relatives were similar to those in the general population. The inability to contact relatives directly likely decreased the response rate and did not allow for any formative research on relatives' perceived risk and other issues. Furthermore, this hampered our ability to evaluate the program by determining changes in survey responses, since first and second surveys could not be linked. However, our project had some important strengths, including the unique method of outreach to relatives through the index family. The outreach and prevention effectiveness of these intervention programs might have been increased through contact with multiple family members for each proband. A recent study showed that NTD recurrence prevention programs are cost effective,[17,27] and extending these programs to second-degree relatives might improve cost effectiveness while not substantially raising the overall cost.

## TRANSLATION TO HEALTH EDUCATION PRACTICE

### *Lessons Learned*

This project offered lessons learned that could be applicable to similar programs in the future. In an effort to be transparent, the probands' families were sent the same education materials that would be distributed to relatives. Some index families had a negative reaction to some of the standard folic acid education materials, such as "Emma's Story." While we believed that the standard folic acid message was most appropriate for the relatives, separate folic acid education materials have been developed addressing recurrence, and sensitivity is required in addressing the needs of these different groups.

Probands' mothers who were unaware of folic acid prior to having a pregnancy or child affected by an NTD were encountered in both states. While most relatives were aware of their family history of an NTD, a few were not. Women whose NTD-affected pregnancies resulted in fetal loss might have been expected to have been less likely to participate in our project. However, the experience of the Colorado State Health Department, whose registry included information on fetal loss, was that these women were among the most willing to participate.

The Colorado State Health Department plans to reinstate the maternal interview with all mothers with a pregnancy or child affected by an NTD. This is in response to the finding that every affected family contacted for this project had been sent a letter within 3 months of having had an NTD-affected pregnancy, but not one had contacted the state health department. However, the state health worker found that many of the affected families had many questions and concerns and they greatly appreciated and benefited from active contact from the State Health Department.

The Michigan State Public Health Department also plans to modify its routine NTD follow-up protocol to include outreach to female relatives as in this project. This information will be added to the cover letter when index families are first contacted, and ~6 folic acid pamphlets will be included in the mailing, with different pamphlets to target pregnancy contemplators and non-contemplators, as well as postpartum mothers.

In both states, success rates in contacting families were higher when state health workers were able to call after regular work hours (e.g., 5-6 pm). Also, the Colorado state health worker found that the ability to access the entire birth defects registry file for each family was helpful, in terms of being able to gain a more complete understanding of the families' experiences and to relate to families better when contacting them. Contact information was more likely to be correct the closer the contact date was to the date that information was collected, reinforcing the importance of timely data collection. Use of web-based tools for locating addresses increased the number of families that could be contacted.

Expanding upon this method of outreach, involving clinicians or other trusted sources of information might help reach more at-risk relatives. For a pilot project in one county, the Colorado State Health Department has partnered with a family-based support group, who will be the first one to contact families about referral to services. This project could be expanded to include the NTD recurrence prevention program. Families may be more responsive to being contacted by family-based groups, and involving the broader support group community in the effort may also reinforce the program's message (e.g., the importance of folic acid supplementation). This approach might also be helpful in decreasing staff time and cost required for the state health departments. One important consideration is compliance with the Health Insurance Portability and Accountability Act (HIPAA), which restricts the ability to share information acquired in the public health setting

**Table 2. Supplemental folic acid adequacy and survey question responses by frequency distribution, Colorado, 2006-2007, and Michigan, 2005-2007**

| Survey question and response | % adequate folic acid supplement use (number of respondents) | % inadequate folic acid supplement use (number of respondents) | Fisher's exact test *P* value |
|---|---|---|---|
| Intention to take folic acid: I intend to take a multivitamin every day (Question 5) | | | |
| Disagree (1-2[a]) | 0% (0) | 100% (6) | |
| Agree (4-5[a]) | 51.7% (15) | 48.3% (14) | 0.03 |
| I will take a multivitamin every day (Question 8) | | | |
| Disagree (1-2) | 0% (0) | 100% (9) | |
| Agree (4-5) | 53.6% (15) | 46.4% (13) | 0.005 |
| Likely have affected pregnancy: It is likely that I could have a pregnancy affected by a birth defect (Question 6) | | | |
| Disagree (1-2) | 31.3% (5) | 68.8% (11) | |
| Agree (4-5) | 35.7% (5) | 64.3% (9) | N.S.[b] |
| It is possible that I could have a pregnancy affected by a birth defect (Question 9) | | | |
| Disagree (1-2) | 20.0% (2) | 80.0% (8) | |
| Agree (4-5) | 47.8% (11) | 52.2% (12) | N.S. |
| Afraid of having affected baby: I am afraid of having a baby with serious birth defects (Question 7) | | | |
| Disagree (1-2) | 30.8% (4) | 69.2% (9) | |
| Agree (4-5) | 40.0% (10) | 60.0% (15) | N.S. |
| The possibility of having a baby with serious birth defects scares me (Question 10) | | | |
| Disagree (1-2) | 14.3% (1) | 85.7% (6) | |
| Agree (4-5) | 34.5% (10) | 65.5% (19) | N.S. |
| Pregnancy plans (Questions 11-12): | | | |
| Not planning or unable | 23.5% (8) | 76.5% (26) | |
| Currently or planning | 80.0% (8) | 20.0% (2) | 0.002 |
| Age (Question 18) | | | |
| <25 years | 0% (0) | 100% (6) | |
| ≥25 years | 43.2% (16) | 56.8% (21) | 0.07 |
| Overall | 36.4% (16) | 63.6% (28) | |

Notes:
[a] Responses on the Likert scale
[b] N.S. = not significant.

**Table 3. Comparison of Responses from Our Survey and 2007 HealthStyles.™**

| Survey question and response | HealthStyles™ | Our survey |
|---|---|---|
| I intend to take a multivitamin every day (Question 5) | | |
| Disagree (1-2[a]) | 23.8% | 13.6% |
| Neutral (3[a]) | 55.1% | 20.5% |
| Agree (4-5[a]) | 21.1% | 65.9% |
| It is likely that I could have a pregnancy affected by a birth defect (Question 6) | | |
| Disagree (1-2) | 57.1% | 36.4% |
| Neutral (3) | 18.6% | 31.8% |
| Agree (4-5) | 31.8% | 24.4% |
| It is possible that I could have a pregnancy affected by a birth defect (Question 9) | | |
| Disagree (1-2) | 57.6% | 22.7% |
| Neutral (3) | 19.4% | 25.0% |
| Agree (4-5) | 22.9% | 52.3% |

Note:
[a] Responses on the Likert scale

with private entities. Another approach would be to work with spina bifida treatment centers to include outreach to relatives as part of their follow-up activities.

*Role of Health Educators*

Our project was carried out by state public health departments as part of their activities for families with children with special needs. Health educators are often the first contact for these families who are then referred to more specialized care if needed. Often, families do not receive information on their risk or know how to access it, so this program provides a way to arm them with this information. With half of pregnancies in the U.S. unplanned or mistimed, folic acid education of women, especially those in higher risk groups, should not be reserved for the prenatal setting. Pre-pregnancy messaging is often carried out by health educators. To maximize its benefits, folic acid should be taken prior to pregnancy, so that this information would be best embedded in a broader health education initiative.

Health education strategies for at-risk relatives might vary both from those aimed at women with previously affected pregnancies and those used for the general population. For example, relatives in our project reported a higher intention of taking a folic acid-containing vitamin and increased perceptions of risk of having an affected baby, compared with a national sample. However, these relatives' supplemental folic acid intake was similar to that seen for the general population. Thus, health education initiatives centered on relatives of affected families might focus on the step between behavioral intention and behavioral change, although further studies should be done to confirm our findings.

Our project, especially if done on a larger scale, offers one way of examining the utility of family history information as a motivator for behavioral change, a goal of many health education initiatives and an area of active research with challenges in finding behavior changes that are easily measured. The gap between relatives' intention to take a folic acid-containing vitamin and their actual folic acid supplement use means that this priority population has room for improvement, an important factor in effecting behavior change. Our project not only contributed to the state health departments' development of public health capacity by increasing awareness of the importance and practical applications of family history information, but also established a system for contacting close relatives of affected children. Family history is a potentially cost effective tool for disease prevention. Targeted, early interventions can be especially beneficial to those at high risk due to family history, allowing scarce resources to be directed to those most at risk.[28] The methods used in our project could inform methods for identifying at-risk relatives for other rare disorders.

## ACKNOWLEDGMENTS

The authors would like to thank Christine Prue, Alina Flores, Joe Mulinare, Cara Mai, Bethany Schierbeek and Coleen Boyle for helpful discussions on this project. J.E. thanks Janice Bach, Glenn Copeland, Darlene El Reda, Carrie Langbo and Jane Simmermon for their contributions to the project.

## Appendix 1. Survey Questions

1. Do you currently take any vitamin pills or supplements?
   a. Yes
   b. No (GO TO QUESTION 5)
   c. Don't know/Not sure (GO TO QUESTION 5)
2. Do any of the vitamin pills or supplements you take contain folic acid?
   a. Yes
   b. No (GO TO QUESTION 5)
   c. Don't know/Not sure (GO TO QUESTION 5)
3. How often do you take this vitamin pill or supplement?
   a. Less than once a week
   b. 1-3 times a week
   c. 4-6 times a week
   d. Every day of the week
4. I take a folic acid-containing vitamin because…
5. I intend to take a multivitamin every day:

   Strongly disagree — Strongly agree

   1 2 3 4 5
6. It is likely that I could have a pregnancy affected by a birth defect:

   Strongly disagree — Strongly agree

   1 2 3 4 5
7. I am afraid of having a baby with serious birth defects:

   Strongly disagree — Strongly agree

   1 2 3 4 5
8. I will take a multivitamin every day:

   Strongly disagree — Strongly agree

   1 2 3 4 5
9. It is possible that I could have a pregnancy affected by a birth defect:

   Strongly disagree — Strongly agree

   1 2 3 4 5
10. The possibility of having a baby with serious birth defects scares me:

    Strongly disagree — Strongly agree

    1 2 3 4 5
11. Which one of the following best describes your pregnancy plans?
    a. I am currently pregnant
    b. I am planning to get pregnant in the next year or so
    c. I am not planning a pregnancy in the next year or so, but I plan to at some time in the future
    d. I do not plan to get pregnant at any time in the future
    e. I cannot get pregnant (post-menopausal, tubal ligation, hysterectomy (GO TO QUESTION 13))
12. Of the following, which is the main method of birth control you used during the last 6 months?
    a. I didn't use any birth control regularly
    b. Surgical (partner's vasectomy, tubal ligation, hysterectomy, etc.)
    c. Hormone (birth control pill, Norplant, Depo-Provera)
    d. Barrier (condoms, diaphragm, cervical cap)
    e. Abstinence (not currently sexually active)
    f. Rhythm method (periodic abstinence), withdrawal
    g. Other (sponge, IUD, spermicide)
13. Did you have a neural tube defect (NTD) such as spina bifida or encephalocele at birth?
    a. Yes
    b. No
    c. Don't know/Not sure

*continued*

## Appendix 1. Survey Questions (con't)

14. Have you had a pregnancy affected by a neural tube defect (NTD) such as spina bifida, anencephaly, or encephalocele?
    a. Yes
    b. No
    c. Don't know/Not sure

    *You have been contacted because you have a relative with a pregnancy or child affected by a neural tube defect (NTD) such as spina bifida, anencephaly, or encephalocele.*

15. Did you know that you had a relative with a pregnancy or child affected by a neural tube defect (NTD) such as spina bifida, anencephaly, or encephalocele?
    a. Yes
    b. No (GO TO QUESTION 17)

16. How were you told about your relative with a pregnancy or child affected by a neural tube defect (NTD) such as spina bifida, anencephaly, or encephalocele?
    a. The parents of the infant told me
    b. Another relative told me
    c. Someone outside the family (such as a family friend or clergyperson) told me
    d. Other (please tell us):

17. What is your relationship to the relative with a pregnancy or child affected by a neural tube defect (NTD) such as spina bifida, anencephaly, or encephalocele?
    a. She is my sister
    b. She is the sister of my husband or partner
    c. She is my brother's wife or partner
    d. She is the wife or partner of my husband/partner's brother
    e. She is my aunt
    f. She is my daughter
    g. She is my son's wife or partner
    h. She is my mother
    i. She is the mother of my husband or partner

18. What is your current age? _____

19. Which of these groups would you say best represents your race?
    a. White
    b. Black or African American
    c. Asian
    d. Native Hawaiian or Other Pacific Islander
    e. American Indian or Alaska Native
    f. Multiracial (parents of different background, please indicate)

20. Are you Hispanic or Latino?
    a. Yes
    b. No
    c. Don't know/Not sure

21. Are you Arabic or Chaldean?
    a. Yes
    b. No
    c. Don't know/Not sure

22. What is the highest grade or year of school you completed?
    a. Never attended school or only attended kindergarten
    b. Grades 1 through 8 (Elementary)
    c. Grades 9 through 11 (Some high school)
    d. Grade 12 or GED (High school graduate)
    e. College 1 year to 3 years (Some college or technical school)
    f. College 4 years or more (College graduate)

*continued*

**Appendix 1. Survey Questions (con't)**

23. Are you…?
    a. Married
    b. Divorced
    c. Widowed
    d. Separated
    e. Never married
    f. A member of an unmarried couple
24. What state do live in?
    a. Colorado
    b. Michigan
    c. Other (please specify):

**Appendix 2. Demographic Responses by State, Colorado, 2006-2007, and Michigan, 2005-2007**

| Survey question and response | Colorado (Survey 1) % respondents (number respondents) | Michigan (Survey 1) % respondents (number respondents) | Total (Survey 1) % respondents (number respondents) |
|---|---|---|---|
| Age (Question 18) | | | |
| <25 years | 5.9% (1) | 19.2% (5) | 14.0% (6) |
| ≥25 years | 94.1% (16) | 80.8% (21) | 86.0% (37) |
| Race/ethnicity (Questions 19 and 20) | | | |
| Non-Hispanic White | 94.1% (16) | 92.6% (25) | 93.2% (41) |
| All other races and ethnicities | 5.9% (1) | 7.4% (2) | 6.8% (3) |
| Education (Question 22) | | | |
| 0-12 years | 0% (0) | 18.5% (5) | 11.4% (5) |
| >12 years | 100.0% (17) | 81.5% (22) | 88.6% (39) |
| Marital Status (Question 23) | | | |
| Not Married | 23.5% (4) | 29.6% (8) | 27.3% (12) |
| Married | 76.5% (13) | 70.4% (19) | 72.7% (32) |

## REFERENCES


1. Neural Tube Defect Ascertainment Project. Available at: http://nbdpn.org/current/2010pdf/NTD%20fact%20sheet%2001-10%20for%20website.pdf. Accessed February 9, 2011.

2. Botto LD, Olney RS, Erickson JD. Vitamin supplements and the risk for congenital anomalies other than neural tube defects. *Am J Med Genet C Semin Med Genet.* 2004;125(1):12-21.

3. Little J. Risk in siblings and other relatives. In: Elwood JM, Little J, Elwood JH, eds. *Epidemiology and control of neural tube defects*. Oxford: Oxford University Press; 1992:604-676.

4. Toriello HV, Higgins JV. Occurrence of neural tube defects among first-, second-, and third-degree relatives of probands: results of a United States study. *Am J Med Genet.* 1983;15(4):601-606.

5. Grosse SD, Collins JS. Folic acid supplementation and neural tube defect recurrence prevention. *Birth Defects Res A Clin Mol Teratol.* 2007;79(11):737-742.

6. Cowchock S, Ainbender E, Prescott G, et al. The recurrence risk for neural tube defects in the United States: a collaborative study. *Am J Med Genet.* 1980;5(3):309-314.

7. Khoury MJ, Erickson JD, James LM. Etiologic heterogeneity of neural tube defects. II. Clues from family studies. *Am J Hum Genet.* 1982;34(6):980-987.

8. Use of folic acid for prevention of spina bifida and other neural tube defects – 1983-1991. *MMWR Morb Mortal Wkly Rep.*

1991;40(30):513-516.

9. Use of supplements containing folic acid among women of childbearing age--United States, 2007. *MMWR Morb Mortal Wkly Rep.* 2008;57(1):5-8.

10. Callender ES, Rickard R, Miller L, Rinsky-Eng J. Knowledge and use of folic acid supplementation: a study of Colorado women whose pregnancies were affected by a fetal neural tube defect. *Clin Invest Med.* 2001;24(3):124-128.

11. Canfield MA, Anderson JL, Waller DK, Palmer SE, Kaye CI. Folic acid awareness and use among women with a history of a neural tube defect pregnancy--Texas, 2000-2001. *MMWR Recomm Rep.*13 2002;51(RR-13):16-19.

12. Pepe F, Pepe P, Grillo S, Insolia G. [Periconceptual folic acid intake by Sicilian couples at a risk of recurrence of NTD]. *Minerva Ginecol.* 1999;51(10):399-401.

13. Rinsky-Eng J, Miller L. Knowledge, use, and education regarding folic acid supplementation: continuation study of women in Colorado who had a pregnancy affected by a neural tube defect. *Teratology.* 2002;66 Suppl 1:S29-31.

14. Detrait ER, George TM, Etchevers HC, Gilbert JR, Vekemans M, Speer MC. Human neural tube defects: developmental biology, epidemiology, and genetics. *Neurotoxicol Teratol.* 2005;27(3):515-524.

15. Stevenson RE, Allen WP, Pai GS, et al. Decline in prevalence of neural tube defects in a high-risk region of the United States. *Pediatrics.* 2000;106(4):677-683.

16. Neural tube defect surveillance and folic acid intervention--Texas-Mexico border, 1993-1998. *MMWR Morb Mortal Wkly Rep.* 2000;49(1):1-4.

17. Grosse SD, Ouyang L, Collins JS, Green D, Dean JH, Stevenson RE. Economic evaluation of a neural tube defect recurrence-prevention program. *Am J Prev Med.* 2008;35(6):572-577.

18. Collins JS, Atkinson KK, Dean JH, Best RG, Stevenson RE. Long term maintenance of neural tube defects prevention in a high prevalence state. *J Pediatr.* 2011;159(1):143-149.

19. Byrne J, Byrne C, Collins D. Trends in periconceptional folic acid use by relatives in Irish families with neural tube defects. *Ir Med J.* 2001;94(10):302-305.

20. Byrne J. Folic acid knowledge and use among relatives in Irish families with neural tube defects: an intervention study. *Ir J Med Sci.* 2003;172(3):118-122.

21. Byrne J, Carolan S, Arcement R, et al. An intervention study to increase knowledge and use of folic acid among relatives in neural tube defect-affected families in Washington, D.C. *Birth Defects Res A Clin Mol Teratol. 2*005;73(6):424-429.

22. Robbins JM, Cleves MA, Collins HB, Andrews N, Smith LN, Hobbs CA. Randomized trial of a physician-based intervention to increase the use of folic acid supplements among women. *Am J Obstet Gynecol.* 2005;192(4):1126-1132.

23. Schwarz EB, Sobota M, Gonzales R, Gerbert B. Computerized counseling for folate knowledge and use: a randomized controlled trial. *Am J Prev Med.* 2008;35(6):568-571.

24. Watkins ML, Brustrom J, Schulman J. Effectiveness of a free folic acid supplement program in family planning clinics. *Birth Defects Res A Clin Mol Teratol.* 2004;70(6):403-407.

25. Watson M, Watson L, Bell R, Halliday J. The increasing knowledge of the role of periconceptional folate in Victorian women of child-bearing age: follow-up of a randomised community intervention trial. *Aust N Z J Public Health.* 2001;25(5):389-395.

26. Xaverius PK, Tenkku LE, Salas J, Morris D. Exploring health by reproductive status: an epidemiological analysis of preconception health. *J Womens Health (Larchmt).* 2009;18(1):49-56.

27. Collins JS, Canfield MA, Pearson K, et al. Public health projects for preventing the recurrence of neural tube defects in the United States. Birth Defects Res A Clin Mol Teratol. Nov 2009;85(11):935-938.

28. Yoon PW, Scheuner MT, Peterson-Oehlke KL, Gwinn M, Faucett A, Khoury MJ. Can family history be used as a tool for public health and preventive medicine? *Genet Med.* Jul-Aug 2002;4(4):304-310.

**AUTHOR NOTE:** The three co-authors contributed equally to the production of the paper.