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► Prevention of Birth Defects and Folic Acid Awareness

► Introduction

In the United States, approximately 1 in every 1000 pregnancies is affected by a neural tube defect¹ and during an average year birth defects have accounted for over 139,000 hospital stays resulting in \$2.5 billion in hospital costs alone.² Taking folic acid before pregnancy can prevent up to 70% of neural tube birth defects, birth defects of the brain and spine that result in a lifetime of physical, psychological, and educational challenges. Beyond the physical and emotional toll, the lifetime costs of care can easily exceed \$1 million dollars per individual.³ Families and the government share the burden of these costs. Prevention research has examined vitamin intake and reductions in other costly health care conditions,⁴ in particular to this report, the discovery that adequate levels of folate (folic acid)[‡] in the blood stream leads to

a significant reduction in the chances of a pregnancy being affected by a neural tube defect (NTD).^{5,6}

This report describes the burden and trends of neural tube defects, particularly spina bifida and anencephaly, among Montana births over the past decade. It also provides hospitalization rates for individuals with NTDs and the associated costs for Montanans. Finally, using BRFSS data, it describes trends in the knowledge and awareness of the benefits of folic acid and adherence to the recommended daily consumption of folic acid.

‡Folate is a B vitamin found in foods. Folic acid is a synthetic form of folate used in vitamin supplements and fortified foods.

► Background

The human nervous system develops from a small, specialized plate of cells along the back of an embryo.⁷ NTDs are birth defects of the central nervous system that occur early in development as the edges of the plate curl up toward each other and form a narrow sheath (neural tube) that closes to form the brain and spinal cord of the embryo. This typically occurs eighteen days after conception and as development continues the top of the tube becomes the brain and the remainder the spinal cord. This process usually is complete by the 28th day of pregnancy, typically before women even know that they are pregnant. If problems occur, neural tube defects result. The two most common disorders are spina bifida and anencephaly. Spina bifida is a condition where some portion of the spinal cord is not fully enclosed and which often leads to life-long disabilities with varying degrees of paralysis. Anencephaly is a much more severe defect where most of the brain is missing and typically results in fetal death. Every day in the United States about eight babies are born with spina bifida or a similar birth defect of the brain and spine.⁸

No one knows for sure what causes neural tube defects and it most likely results from a mix of genetic and environmental factors. Currently, identified risk factors for NTDs include a personal or family history of a pregnancy affected

by a neural tube defect, maternal diabetes, material obesity, the use of certain anti-seizure medications, genetic variants or mutations in enzymes related to folate metabolism, and poor nutrition, particularly folic acid insufficiency.⁹ However, controlled and randomized studies have shown that risks for NTDs are substantially reduced with the consumption of folic acid or folate, a water soluble B vitamin, taken *prior* to conception and during the first three months of pregnancy.^{10,11} Folic acid supports the rapid growth of the placenta and fetus and is needed to produce new DNA (genetic material) as cells multiply.

Prompted by the consistent scientific evidence, in 1992 the U.S. Public Health Service recommended that women of childbearing age consume 400 micrograms of folic acid per day to reduce the risk of having pregnancies affected by NTDs. Three approaches, which require changes at the individual and policy levels, have been used to increase intake of folate/folic acid: dietary improvements, supplementation, and food fortification. Everyone needs folic acid in their diet as it is essential to sustain human life and help the body make healthy new cells. Some foods are rich in folate, particularly dark green, leafy vegetables like spinach, as well as chicken or beef liver, beans (legumes), peas, and orange juice. Eating well gives an individual some of the daily requirements needed,

but most women cannot get enough daily folate from food alone. Folic acid is the synthetic form of folate and most multivitamins contain 400 mcg in each pill and some highly fortified cereals also contain the recommended daily value in a single serving. It has been estimated that 50% to 70% percent of births with NTDs could be prevented if women consumed 400 micrograms (mcg) of folic acid daily, before and during pregnancy.¹²

Since 50% of all pregnancies are unplanned and folic acid from vitamin supplements or nutritious foods works to prevent birth defects only if **consumed before conception** and during early pregnancy, improved diet and supplementation have not been effective alone.¹³ At the policy level, fortifying foods with folic acid was designed to be a more uniform intervention, because fortification makes folic acid accessible to all who eat "enriched" food products. In 1996, the U.S. Food and Drug Administration (FDA) made it optional to fortify enriched grain products with folic acid and by 1998 mandated that all fortified grain products also include folic acid. Fortification of staple foods has worked well in the past for iodine (in salt), vitamin D (in milk), and thiamin (in flour and bread).¹⁴ The current level of folic acid in fortified grain products (140 mcg per 100 g cereal grain product) is intended to increase a woman's intake by ap-

proximately 100 mcg per day, but may not be sufficient to provide the recommended intake of folic acid for women of reproductive age.¹⁵ In addition, some minimally processed whole grains which have been promoted for heart healthy, low-carb diets and some foods such as corn masa flour, used in many traditional Latin American cuisines that include corn tortillas, enchiladas and tamales, are generally not fortified and contain less folic acid than enriched grains.¹⁶ However, any grain product made in the US and labeled "enriched" does contain folic acid. The label on products reflects these additions and the percent of daily recommended value for those products that have been enriched.

The body does not use folate as easily as folic acid. Folic acid from vitamin supplements and fortified foods is more readily absorbed (100% and 85%, respectively) and made available for use by the body than natural folate from food (about 50% absorption).¹⁷ Taking a vitamin with folic acid or eating a breakfast cereal fortified with 400 mcg of folic acid per serving every day are important components of birth defect prevention efforts for women. Substantial research in the United States has shown that a *multivitamin is the best and easiest way to get the folic acid needed* and the costs are typically less than 3 cents per day.¹⁸

Incidence and Prevalence Data of NTDs

Incidence estimates for neural tube defects of spina bifida and anencephaly were provided by the Montana Department of Public Health and Human Services (DPHHS) Office of Vital Statistics (OVS) and the Maternal and Child Health (MCH) program.¹⁹ The estimates represent the numbers of each condition per 10,000 live births to Montana residents based on birth certificate data. Because Montana does not have a birth defects registry for monitoring birth defects or performing surveillance by case ascertainment to determine the number of pregnancies affected by neural tube defects each year, detailed case ascertainment was not possible and the data may underreport these defects based

solely on vital records information. In particular, spontaneous fetal loss or elective terminations associated with NTDs are under ascertained. Comparisons are made to U.S. rates where possible. Because of concerns about the completeness of fetal death reporting and variation from state to state in definition, only Montana infant and fetal death rates are provided in this report. Hospitalization rates for NTDs and the associated costs are provided by the Montana Hospital Discharge Data System of DPHHS based on data sets supplied by the Montana Hospital Association.

Results

Despite less than ideal population intake of folic acid, the overall incidence of *all* NTDs reported on birth certificates in the United States decreased from 3.8 per 10,000 live births before fortification (1995–96) to 3.1 per 10,000 live births after mandatory folic acid fortification (1999–2007), representing a 19% decline.²⁰ More recently, the CDC reported that 23 state population-based birth defect surveillance systems showed a 26% decline in NTD rates in these states before and after mandated fortification.²¹ For spina bifida alone, in the period of no folic acid fortification (1995–1996) in the U.S. the incidence based on birth records data was 2.8 per 10,000 births and in 2005–2007 after an eight year period of mandatory fortification the prevalence of spina bifida decreased 36% to 1.8 per 10,000 births (Figure 1a). In Montana, between 1995–1996 and 2005–2007 the rates of spina bifida decreased 50%, from 2.8 per 10,000 births to 1.4 per 10,000 births. These rates are based on small number of cases in any given year, leading to wide fluctuations in rates and unstable trends.

The U.S. rate of anencephaly showed no consistent trend from the pre-fortification to post-fortification periods (Figure 1b). While rates of anencephaly in Montana have been lower than the U.S. in general, in recent years the rates have increased slightly based on birth certificate records from 0.5 per 10,000 births to 0.8 per 10,000 births.^{22,23} It is unclear if this is the result of random fluctuation, better case ascertainment or will prove to be a stable trend.

Previous work done at the national level and in Montana show that rates of birth defects based on birth certificates alone are an underestimate of the true rates, even for those conditions (such as anencephaly and spina bifida) that are generally easily identifiable at birth.^{24,25} Birth defect registries or surveillance systems provide a much more complete perspective on the incidence of birth defects, but Montana currently does not have a data source comparable to the surveillance data found with the National Birth Defect Prevention Network.²⁶ Therefore, using birth certificate data alone provides Montanans with rates of anencephaly and spina bifida based on *live births* that are lower than what would be found through prenatal case ascertainment processes in birth defect registry systems, which would include total number of pregnancies, including live births, stillbirths, prenatally diagnosed cases, and elective terminations.

An examination of infant and fetal death records for Montanans during the time period of 1990–2009 revealed that the rate of infant deaths from spina bifida decreased from 0.38 to 0.08 per 10,000 births, a 79% change in the twenty year time period. Infant deaths records of Montanans also indicated that the rates of anencephaly showed a general decrease of 25% from 0.63 to 0.47 per 10,000 births in the pre-fortification to post-fortification time periods, though small numbers make for large fluctuations in yearly rates. (Figure 1c)

Fetal deaths in Montana from anencephaly also showed a dramatic decrease of 81% from pre-fortification rates of 1.26 per 10,000 births to post-fortification time period rates of 0.23 per 10,000 births. (Figure 1d) Fetal deaths from spina bifida were not ascertained due to incomplete data.²⁷

During the period 2000 through 2009 in Montana, there were 156 hospitalizations with primary diagnosis of NTDs (ICD-9-CM: 740-743) and 1582 hospitalizations with secondary diagnosis of NTDs. In 2008 and 2009, the 340 hospitalizations with primary or secondary diagnoses of NTDs were associated with an average cost of \$26,000 and \$21,000 per hospitalization, respectively. The total cost of for NTD related hospitalizations was approximately \$3.5 million per year.²⁸ Children with spina bifida or other survivable neural tube defects often face a lifetime of surgeries and medical costs. In 2009, the lifetime medical costs for a person with spina bifida in the United States was estimated to be \$460,923 and the lifetime non-medical costs for a child with spina bifida, which includes education and developmental services such as early intervention services and counseling, was estimated to be \$56,511 in 2009.²⁹

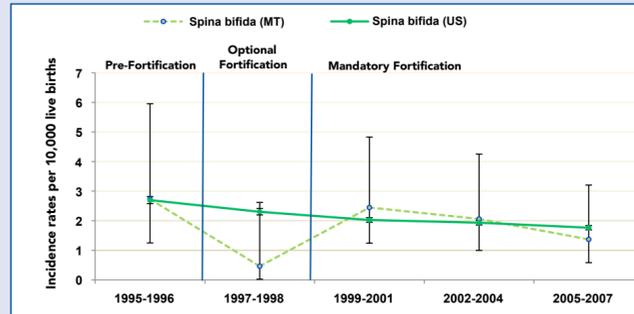


Figure 1A. Spina Bifida Incidence Trends: Montana & US Residents, 1995–2007

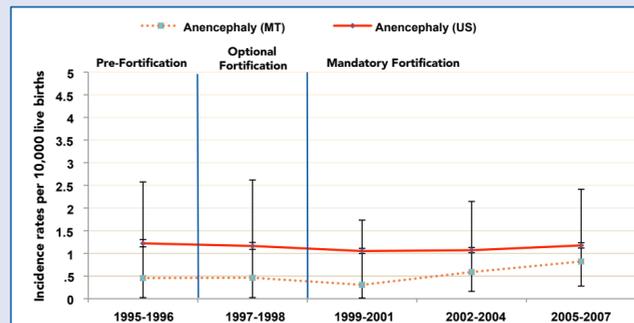


Figure 1B. Anencephaly Incidence Trends: Montana & US Residents, 1995–2007

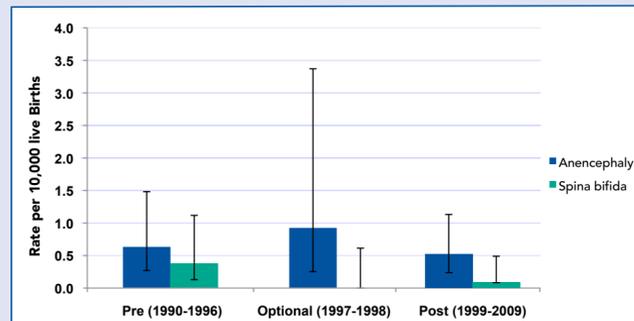


Figure 1C. Montana Infant Deaths Attributed to Neural Tube Defects by Folic Acid Fortification Periods, 1990–2009

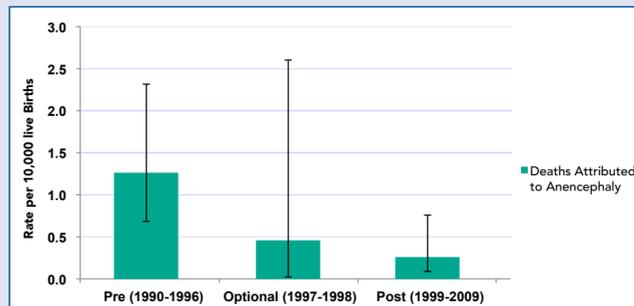


Figure 1D. Montana Fetal Deaths Attributed to Anencephaly by Folic Acid Fortification Periods, 1990–2009

BRFSS Prevalence Estimates of Folic Acid Use and Knowledge

Women's knowledge of folic acid in preventing birth defects and consumption of the recommended daily amount has been monitored by the Montana Behavioral Risk Factor Surveillance System (BRFSS), an ongoing telephone survey sponsored by the Centers for Disease Control and Prevention (CDC) and the Montana BRFSS Office at DPHHS. BRFSS data also has been used to monitor behaviors related to the leading causes of morbidity and mortality in the state and collected data have been statistically weighted to be representative of the Montana adult population.

In even years from 2002 to 2006, Montana women ages 18–44 years were surveyed regarding their intake of vitamins or supplements, in-

cluding multivitamins and supplements with folic acid, using a five question optional module.³⁰ Respondents were also questioned on their knowledge about folic acid and its role in birth defect prevention. Characteristics of the study population, daily folic acid use, and knowledge regarding folic acid and birth defects were examined. Data were weighted to be representative of the Montana adult population of women aged 18–44 in each time period. Women who were pregnant at the time of the interview were excluded from all analyses. The race/ethnicity composition of women surveyed was mostly white/non-Hispanic (about 86% each year), followed by American Indian/Alaska Native (7%).

Folic Acid Use

Despite the recommendations and efforts in the United States to increase folic acid intake, the desired levels in women of child-bearing age still have not been achieved. From 2002 to 2006, less than one-half of Montana women between the ages of 18 and 44 years did not take any vitamin or supplement (~38 to 45 percent, Table 1). However, the percent of women who did *not* take a *daily* multivitamin that contained folic acid in 2002 was about 50% and increased slightly in 2006 to 52% (Table 2).

The proportion of women who failed to take folic acid daily ranged from 37% to 62% depending on age, education, income and race/ethnicity. Women who were least likely to report taking folic acid daily were younger, non-white, those with less than a high school degree, and those with lower incomes. In 2004, the difference in daily folic acid use among women in the lowest and highest income categories was statistically significant. In 2006, the difference in daily folic acid use among women in the lowest and highest educational categories was statistically significant. Differences in daily folic acid use by race/ethnicity, e.g. between white/non-Hispanic and AI/AN women, had too few minority respondents to report within each survey period.

Knowledge of Folic Acid

Knowledge that folic acid can prevent birth defects varied in Montana women across a host of demographic characteristics. Overall from 2002 to 2006, 45% to 55% of Montana women were aware of the benefits of folic acid in the prevention of birth defects, Figure 2. Knowledge of the benefits of folic acid ranged from 27% to 73% depending on age, education, income and race/ethnicity, Table 3. Women who were white/non-Hispanic, had more than a high school education or incomes over \$25,000 were more likely to know that folic acid use can prevent some birth defects. In all years, significant differences were found between those with a high school education or less (43% to 27%) and those who had a college education (61% to 73%). In 2004 and 2006, there were also significant differences between those women with some college education (49% to 54%) and those women with a college degree or more education. For all years, there were significant differences between the lowest and highest income categories with more than 52% of women in households earning more than \$25,000 being aware of the association between folic acid intake and prevention of birth defects. In 2006, American Indian/Alaska Native and other minority women (29%) were significantly less likely to be aware of the benefits of folic acid in birth defect prevention than were White, non-Hispanic women (49%).

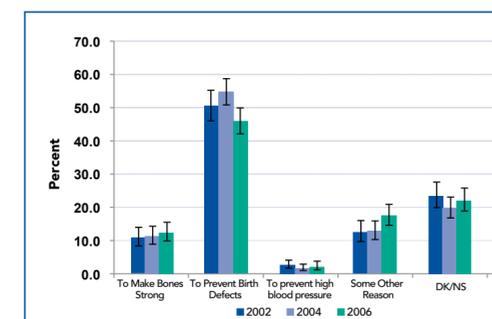


Figure 2. Reasons Given to Take Folic Acid by Year, Montana Women Aged 18–44

Table 1. Does Not Take a Vitamin or Multi-Vitamin Containing Folic Acid, Montana Women Aged 18–44, 2002–2006 BRFSS*

	2002				2004				2006			
	Wt.%	95% CI		UnWt. N	Wt.%	95% CI		UnWt. N	Wt.%	95% CI		UnWt. N
Sex:												
Female	43.4	38.9	48.0	374	38.4	34.4	42.6	354	44.8	40.9	48.8	442
Age:												
18 - 34	47.1	40.8	53.5	205	41.8	35.9	47.9	182	45.5	39.9	51.2	214
35 - 44	38.6	32.5	45.1	169	34.0	29.2	39.1	172	43.8	39.0	48.7	228
Education:												
High School or Less	48.9	41.2	56.6	147	45.5	38.5	52.7	149	58.2	51.4	64.7	186
Some College	44.0	36.2	52.1	126	38.6	31.3	46.4	115	44.9	37.7	52.3	141
College Degree	35.9	28.7	43.8	101	30.5	24.6	37.0	90	30.2	24.8	36.2	114
Income:												
Less than \$25,000	44.7	37.2	52.3	141	48.5	40.5	56.5	146	47.7	40.5	55.0	164
\$25,000 - \$49,999	40.5	33.4	48.0	119	37.0	30.7	43.9	111	41.5	34.9	48.4	123
\$50,000 or more	41.3	32.0	51.3	73	26.0	20.0	33.1	65	39.2	32.5	46.4	111
Race/Ethnicity:												
White, non-Hispanic	43.3	38.5	48.2	299	36.6	32.3	41.0	275	43.2	38.9	47.5	346
AI/AN or other minorities	NSD				NSD				NSD			

* Bolded estimates are statistically significantly different from estimates in other demographic subgroups

Table 2. Does NOT Take Folic Acid Daily, Montana Women Aged 18–44, 2002–2006 BRFSS*

	2002				2004				2006			
	Wt.%	95% CI		UnWt. N	Wt.%	95% CI		UnWt. N	Wt.%	95% CI		UnWt. N
Sex:												
Female	49.8	45.1	54.4	416	46.9	42.7	51.1	421	51.6	47.6	55.7	495
Age:												
18 - 34	52.2	45.8	58.7	217	51.0	44.9	57.0	216	52.6	46.8	58.3	248
35 - 44	46.6	40.1	53.3	199	41.5	36.4	46.7	205	50.0	45.1	55.0	247
Education:												
High School or less	54.6	46.7	62.4	164	50.3	43.2	57.4	158	62.4	55.4	68.8	195
Some College	49.4	41.3	57.6	139	45.7	38.1	53.5	133	51.7	44.2	59.1	154
College Degree	44.2	36.4	52.4	113	44.2	37.6	51.0	130	40.4	34.3	46.8	145
Income:												
Less than \$25,000	51.1	43.3	58.8	159	53.8	45.6	61.8	153	56.6	49.1	63.9	184
\$25,000 - \$49,999	47.8	40.2	55.5	136	46.8	40.1	53.7	140	47.3	40.4	54.3	138
\$50,000 or more	44.8	35.3	54.8	78	37.1	30.1	44.7	90	46.2	39.3	53.4	128
Race/Ethnicity:												
White, non-Hispanic	49.9	44.9	54.9	334	45.6	41.1	50.1	333	50.0	45.6	54.4	385
AI/AN and other minorities	NSD				NSD				NSD			

* Bolded estimates are statistically significantly different from estimates in other demographic subgroups

Table 3. Reason Takes Folic Acid to: Prevent Birth Defects, Montana Women Aged 18–44, 2002–2006 BRFSS*

	2002				2004				2006			
	Wt.%	95% CI		UnWt. N	Wt.%	95% CI		UnWt. N	Wt.%	95% CI		UnWt. N
Sex:												
Female	50.5	45.9	55.1	403	54.6	50.5	58.6	514	45.8	42.0	49.8	479
Age:												
18 - 34	48.1	41.8	54.5	207	57.8	51.7	63.6	263	42.3	36.9	47.9	227
35 - 44	53.5	47.0	60.0	196	50.4	45.2	55.6	251	51.6	46.7	56.4	252
Education:												
High School or less	42.6	35.1	50.5	109	39.1	32.2	46.5	121	26.5	21.1	32.6	100
Some College	49.8	41.8	57.8	136	53.4	45.8	60.9	165	48.7	41.4	56.0	156
College Degree	60.9	52.8	68.4	158	72.5	66.3	78.0	228	64.3	58.1	70.1	223
Income:												
Less than \$25,000	45.0	37.5	52.7	129	45.8	37.7	54.0	140	33.3	27.0	40.1	123
\$25,000 - \$49,999	55.0	47.5	62.3	153	57.5	50.7	64.0	185	52.0	45.2	58.8	152
\$50,000 or more	62.8	52.9	71.7	104	69.3	62.2	75.5	164	56.8	49.6	63.7	175
Race/Ethnicity:												
White, non-Hispanic	52.3	47.4	57.2	359	56.6	52.1	60.9	459	48.5	44.2	52.8	427
AI/AN and other minorities	NSD				NSD				NSD			

* Bolded estimates are statistically significantly different from estimates in other demographic subgroups

Discussion

The importance of folic acid in the reduction of birth defects has led to public health efforts to increase women's awareness and to increase the daily consumption of folic acid by women of childbearing age. The first step in behavioral change is awareness: if more women were aware of the potential benefits of taking folic acid daily in preventing birth defects the odds are greater that behavior will eventually change.

Efforts to change women's dietary habits so that they consume more foods rich in folate or take daily vitamin supplements containing folic acid has not been as successful as was anticipated, but there certainly has been improvement. Fortification of food alone has not assured the consumption of the recommended amount of folic acid, but it has increased the amount consumed by most people. Studies measuring blood folate levels of the U.S. population indicate dramatic increases between the 1988–1994 (pre-fortification) and 1999–2000 (post-fortification) periods.³¹ Red blood cell (RBC) folate measures long-term folate intake and low levels are associated with adverse health effects. In 2005–2006, for women aged 15–44, the prevalence of low RBC folate (less than 140 ng/mL) was 4.5%, down from 37.6% in 1988–1994.

Low socioeconomic status remains a marker for low folic acid knowledge and low multivitamin use. Because of low educational levels, a continued educational effort from nutritional and medical professionals is needed to increase knowledge and support behavioral change. In addition, a growing body of research also has shown that the recommendations made by health-care providers to their patients have a substantial impact on whether or not individuals follow preventive health measures.^{32,33} Health care providers can have a positive impact on increased use of folic acid containing supplements if they recommend to all women of childbearing age, regardless of pregnancy intentions, to take a daily multivitamin containing 400 mcg of folic acid. Research on health care providers has shown that they are more likely to recommend the use of folic acid supplementation if they, themselves, took a multivitamin.³⁴ However, research also indicates that knowing the correct dosage of folic acid for prevention of birth defects, the importance in taking folic acid at least one month before pregnancy and during the first trimester, and also the increased awareness that 50% of all pregnancies are unplanned in the United States, can help health care pro-

viders get the message out to all women of potential childbearing age. Health care providers must translate their knowledge into action, i.e., counseling patients.³⁵

The public health challenge now is to get the "folic acid" message to the people who need it most: women aged 15–49 years old. As Godfrey Oakley, former director of CDC's Division of Birth Defects and Developmental Disabilities, said repeatedly in his tenure as an epidemiologist and agency head in the 1990s, "the opportunities for primary prevention that are as simple as this are rare. The time has come to create the political will for the resources needed to provide the best quality of care for persons with birth defects....and to maximize the prevention of new cases."³⁶ A major education campaign by the Centers for Disease Control and Prevention and the March of Dimes was initiated in 1999. Future educational efforts should be directed to all women, but special efforts should be made to target those found to be least likely to be taking a vitamin or supplement with folic acid. This group includes younger, less-educated, and non-white women.

While public health continues to strive for NTD prevention through folic acid consumption for women of childbearing age, it is also important to provide services to those currently living with NTDs. Individuals with spina bifida and other neural tube defects often have special medical, educational, and financial needs throughout their lifetimes. Montana DPHHS responds to children and families with special needs through the Children with Special Health Services (CSHS), the public health program for developing support services for the care of these children and their families, including helping to support regional pediatric clinics, financial assistance and resources/referral services. For more information regarding [Children's Special Health Services](http://www.cshs.mt.gov), call 406-444-3620 or visit the website at: <http://www.cshs.mt.gov>. For further information about the Montana Behavioral Risk Factor Surveillance System (BRFSS), call 406-444-2973 or visit the website at: www.brfss.mt.gov. For more general information about folic acid and birth defects contact or visit: 1-800-232-4636 (CDC-INFO) or visit the website at: www.cdc.gov/folicacid.

Survey Limitations:

The BRFSS relies on self-reported data. This type of survey has certain limitations: many times, respondents have the tendency to underreport some behaviors that may be considered socially unacceptable (e.g., smoking, heavy alcohol use); conversely, respondents may over report behaviors that are desirable (e.g., physical activity, nutrition). Cross-sectional design makes causal conclusions impossible. BRFSS data through 2008 excludes households without land-line telephones.

Background:

The Montana Behavioral Risk Factor Surveillance System (BRFSS) has been collecting and reporting state-specific, population-based estimates of health-related data since 1984. The purpose of this statewide telephone survey of Montana residents aged 18 and older is to gather information regarding personal health risk behaviors, selected medical conditions, and the prevalence of preventive health care practices among Montana adults. These BRFSS results have been used by public health agencies, academic institutions, non-profit organizations, and others to develop programs that promote the health of Montana adults and reduce risks that contribute to the leading causes of death in the state. A full set of Montana yearly questionnaires and health indicators can be found on the Department of Public Health and Human Services (DPHHS) BRFSS database query system website at www.brfss.mt.gov. The CDC website (www.cdc.gov/brfss) also provides national, state, and some local area prevalence estimates of health indicators, as well as access to downloadable datasets for further analyses.

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Endnotes:

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