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Signature of Student, Monica E. Youngblood Date

GLOBAL UPDATE ON THE PREVENTION OF
FOLIC ACID-PREVENTABLE SPINA BIFIDA
AND ANENCEPHALY CASES

BY

Monica E. Youngblood
Degree to be awarded: M.P.H.
Career MPH

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GLOBAL UPDATE ON THE PREVENTION OF FOLIC ACID-PREVENTABLE SPINA BIFIDA AND ANENCEPHALY CASES

BY

Monica E. Youngblood
M.P.H., Emory University, 2011
B.S., California State Polytechnic University, Pomona, 2002

Thesis Committee Chair: Godfrey P. Oakley, Jr. MD, MSPM

An abstract of
A Thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
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2011

Abstract

GLOBAL UPDATE ON THE PREVENTION OF
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AND ANENCEPHALY CASES

BY
Monica E. Youngblood

BACKGROUND: Folic acid has been proven to prevent most cases of spina bifida and anencephaly. It is recommended that women of child-bearing age consume folic acid fortified grain products and/or supplements prior to pregnancy. Since 2006, there has been an increase in the number of countries that fortify their flour with folic acid. **METHODS:** Country specific data on fortification of flour with folic acid has been tracked along with amounts of fortified flour consumed per person. Estimates of spina bifida and anencephaly affected pregnancies and country-specific birth estimates were also utilized to estimate the amount of folic acid preventable spina bifida and anencephaly cases. **RESULTS:** Utilizing a predetermined prevention factor model, it is estimated that 13.81% of spina bifida and anencephaly cases are currently being prevented with folic acid flour fortification. Since the average US population consumes between 100 and 200 mcg folic acid from fortified flour, and this is associated with a significant decrease in the number of cases of spina bifida and anencephaly, an updated prevention factor model was created. Under these circumstances, it is estimated that 22.38% of spina bifida and anencephaly cases are globally prevented with folic acid flour fortification. **CONCLUSIONS:** Although these values show an increase in cases prevented since 2006, there is still a significant amount of work required in order to increase consumption of folic acid in women of child-bearing age and for countries to regulate and require flour fortification with folic acid.

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Table of Contents:

Introduction:

Folate is a water-soluble B-vitamin found in dark green vegetables, nuts, fruits and berries (Cooperman 1970). The synthetic form of folate is folic acid. Although the exact mechanism is unknown, folic acid is associated with decreasing the risk for having a pregnancy affected by a neural tube defect (NTD). In order to reduce neural tube defects, folic acid was added to cereal and grain products in 1998 under the United States folic acid fortification program (Lewis, Crane et al. 1999). Since then, many other countries have implemented similar mandates (CDC 1992).

A British study convincingly demonstrated that folic acid alone could prevent 72% of birth defects (MRC Vitamin Study Research Group 1991). In the United States, the current US Public Health Service recommendation is that all women capable of becoming pregnant should consume 400 micrograms (mcg) of folic acid, daily, to prevent spina bifida and other NTDs (CDC 1992). Since not all countries fortify their flour with folic acid and not all people have access to fortified flour, there is still a large amount of folic acid preventable spina bifida and anencephaly (FAPSBA) that could be avoided with fortification.

The fortification of grains does not require any additional equipment that cereal-grain companies don't already have. Millers would only have to pay a one-time fee to change product label settings. The cost per unit of folic acid fortification is insignificant; especially in comparison to the benefits that will result from fortification. The estimated unit cost of folic acid fortification would be approximately $0.0237 (US$) per 100 pounds of grain at 350 mcg per 100 grams produced (Romano, Waitzman et al. 1995). Grain fortification does not affect the taste, shelf-life, or appearance of cereal-grain products (Bentley, Ferrini et al. 1999). The

intervention of grain fortification is an approach that can help combat important health issues without modifying behaviors or increasing education in target populations. It is apparent, though, that collaborative efforts are necessary to help accomplish the goal of implementing grain fortification policies around the world.

The leading cause of death among babies less than one year of age is birth defects (Bentley, Ferrini et al. 1999). Expectant mothers who consume folic acid decrease the chance for a birth outcome with a NTD. Mothers with previous pregnancies affected by a NTD have a greater risk of another pregnancy to have a NTD (CDC 1992). Common NTDs include spina bifida and anencephaly in which there is incomplete closure of the neural tube; this occurs early in the developmental stage of a human embryo (Detrait, George et al.). Folic acid also has positive effects on birth weight and premature births (Vollset, Refsum et al. 2000). Globally, NTDs occur at an incidence rate of approximately 2.5 per 1000 live births (Christianson 2006). This amount is actually a lower count than total pregnancies affected by NTDs because many pregnancies are terminated and do not result in a live birth to be counted in such statistics.

Although there has been a decrease in the prevalence of NTDs since fortification of flour has been implemented, there are still a significant number of births affected by NTDs. In 2003-2004, the total US prevalence of spina bifida and anencephaly per 10,000 live births was 5.37 among all races and ethnicities (Boulet, Yang et al. 2008). The 2003-2004 prevalence was 4.86, 4.05, and 6.91 per 10,000 live births among non-Hispanic whites, non-Hispanic blacks, and Hispanics respectively [7]. In addition to living a life with an incurable condition, there is a high cost of care associated with a life affected by a NTD. The US estimates that in 2002, a child born with spina bifida would be associated with a cost of $636,000; a child born with anencephaly

would be associated with a cost of $1,020,000; these costs do not include the cost of time for receiving care (Grosse, Waitzman et al. 2005). It is assumed that much of the world's cases of spina bifida and anencephaly could be prevented with the proper amounts of folic acid (CDC 1992; Czeizel and Dudas 1992).

In 2006, Karen N. Bell and Godfrey P. Oakley Jr. published a paper that described a way to track the global prevention of spina bifida and anencephaly through folic acid flour fortification (Bell and Oakley 2006). The result of this paper described that approximately 6.8% of the world's births were prevented from having an outcome of a baby born with spina bifida or anencephaly in countries that fortify their flour with folic acid. At this time, 39 countries were fortifying their flour with folic acid (Bell and Oakley 2006). In 2008, Bell and Oakley published an update to the 2006 paper; this update stated that annually, 9.08% of NTDs were prevented in countries where folic acid fortified flour is consumed. At this time 68 countries were fortifying flour with folic acid (Bell and Oakley 2009).

This paper will attempt to answer the following questions: What countries currently, in 2010, fortify flour with folic acid? How much fortified flour is consumed on a daily basis in each country? At what level is each country fortifying flour with folic acid? And, what amount of neural tube defects are currently being prevented with folic acid fortification of flour? It is important to determine an updated value for the amount of folic acid each country is fortifying flour with in order to understand the global progress of preventing NTDs with folic acid fortified flour. It is believed that with continued and increasing country-specific mandates for flour fortification with folic acid, one day there will be no cases of FAPSBA affecting pregnancies. Although many countries do not have sufficient or advanced surveillance programs in place,

much work will be required in many portals of this public health concern in order to fully combat the issue at hand. Additionally, information about flour consumption and/or country-specific programs may have some deficiencies; however, this should not affect the results of this paper, but rather give these countries a stimulus to improve surveillance and increase folic acid flour fortification practices.

The journal article portion of this paper will be submitted to Birth Defects Research (Part A): Clinical and Molecular Teratology. This journal is interested in birth defects and in describing adverse pregnancy outcomes as a result of certain factors. The journal accepts manuscripts in English organized with a title page, abstract, key words, introduction, materials, methods, results, discussion, acknowledgements, literature cited and figure legends. Specifically, the title page should include a title, the full name of the authors, affiliations for the authors, any grant information with associated grant numbers, a running title not to exceed 45 characters and spaces, and the name, address, phone and fax number, and e-mail address of the corresponding author. The abstract should not be longer than 250 words and should be designed to serve in place of the summary. They abstract should state the significant findings without reference to the rest of the paper and structured as follows: Background, Methods, Results, and Conclusions. Three to eight key words should be appended at the end of the abstract. The article should be original work; manuscripts in this category should describe the results of the original research conducted in the broad area of congenital defects. The manuscript should be presented in the format of Abstract, Introduction, Methods, Results, and Discussion. Another requirement is to submit the manuscript, tables, and figures as separate files. Illustrations should be in TIFF format. Wiley's journal literature cited prefers utilizing

EndNote and is to be arranged alphabetically as: Author, year of publication, complete title, volume, and inclusive pages (Society 2010).

Previous research on country specific FAPSBA was conducted by Bell and Oakley in 2006 and 2008. Their work was submitted to Birth Defects Research (Part A): Clinical and Molecular Teratology. Updating the country specific data would be most valuable in this same journal as it would provide more current data for global numbers of FAPSBA, thus showing the progress of the world's fortification programs. Submitting to Birth Defects Research (Part A): Clinical and Molecular Teratology will also provide information about the benefits of fortification which countries could use to help decrease the amount of children born with neural tube defects and adverse pregnancy outcomes.

Literature Review:

In 1992, the U.S. Department of Health and Human Services Public Health Service Centers for Disease Control determined that women of childbearing age should consume 0.4 milligrams of folic acid on a daily basis. This recommendation was given in order to reduce the number of pregnancies affected by NTDs (CDC 1992). This publication cited randomized controlled trials as evidence supporting this recommendation. The first trial was by the British Medical Research Council (MRC) which showed a 72% protective effect for pregnant women taking high dose folic acid supplements (4.0 milligrams/day) who were at higher risk for having a pregnancy affected by a NTD because of a previous pregnancy with a NTD (MRC Vitamin Study Research Group 1991). The second trial that the published recommendation cited was the Hungarian Family Planning Program trial which showed a decrease in the incidence of neural tube defects for

pregnancies in which the mother consumed 0.8 milligrams of folic acid supplements (Czeizel and Dudas 1992).

In an attempt to reduce the number of birth outcomes with a NTD, the US Public Health Service wanted to make sure all women who were able to become pregnant consumed 400 mcg of folic acid daily (CDC 1992). In 1996, the US Food and Drug Administration created a standard to enrich grain products with folic acid. It was determined that by 1998, folic acid fortification of cereal-grain products would be fortified with 140 mcg folic acid per 100 grams of grains and that ready-to-eat breakfast cereals would be fortified with up to 100 mcg of folic acid per serving and dietary supplements fortified with up to 400 mcg per unit or serving (Food and Drug Administration 1996). Currently, ready-to-eat cereals and supplements are available with a higher amount of folic acid.

Similarly, a study conducted in NTD high incidence areas and in NTD low incidence areas of China asked participants to take a 0.4 mg pill of folic acid on a daily basis. For the women who took the pills at least 80 percent of the time, there was a decrease in the risk of a pregnancy affected by a NTD. This study concluded that women consuming 0.4 mg of folic acid reduced the rate of the first incident of a pregnancy affected by NTD (Berry, Li et al. 1999). Another study conducted in four Chinese provinces demonstrated on average an 80% preventive ratio against births affected by NTDs when folic acid supplementation is implemented (Chen, Song et al. 2008).

Another study conducted by Honein et al. looked at birth certificate records of babies born with spina bifida and anencephaly prior to fortification, from October 1995 to December 1996 and compared this data with data after fortification was implemented, from October 1998

to December 1999. This study found that 37.8 per 100,000 live births were affected by NTDs before fortification and after fortification, births affected by NTDs decreased to 30.5 per 100,000 live births. This was a 19% decrease in NTDs as a direct result of fortification (Honein, Paulozzi et al. 2001).

A similar study in Saudi Arabia by Safdar et al. investigated medical records of babies born before fortification, from 1997 to 2000, and after fortification, from 2001 to 2005. This study concluded that prior to fortification 1.9 per 1,000 live births had an outcome with NTDs and after fortification 0.76 per 1,000 live births were affected by NTDs. This study showed a 60% decrease in NTD rates after folic acid fortification (Safdar 2007).

Mosley et al. demonstrated in a case-control study that the use of folic acid supplements while pregnant had no effect on the risk of having a pregnancy affected by a NTD. The reasoning for this outcome is that fortification with folic acid provided enough of a protective effect to reduce the amount of folic acid sensitive NTDs (Mosley, Cleves et al. 2009). Similarly, an article by Berry described that people were receiving at least 100 mcg of folic acid daily from fortified foods (Berry, Carter et al. 2007).

The foundation of this paper is based upon previous research conducted specifically on the global prevention of spina bifida and anencephaly through flour fortification with folic acid. The 2006 Bell and Oakley paper tracked the prevention of spina bifida and anencephaly with folic acid flour fortification (Bell and Oakley 2006). The result of this paper described a total of 15,464 neural tube defects prevented in countries that fortify flour with folic acid. The paper also reported 228,975 to be a global estimate of total annual folic acid preventable NTDs. These values tell us that approximately 6.8% of the world's births in countries that fortify their flour

with folic acid did not have an outcome of a baby born with spina bifida or anencephaly (Bell and Oakley 2006). In 2008, Bell and Oakley published an update to the 2006 paper; this update stated that annually, 9.08% of NTDs were prevented in countries where folic acid fortified flour is consumed. At this time, 22,134 NTDs were prevented in folic acid fortifying countries and it was estimated that 243,691 NTDs could be prevented with complete fortification of flour with folic acid (Bell and Oakley 2009). Although there is an increase in the number of countries fortifying their flour and it appears that an increase in the percentage of NTDs that are being prevented with folic acid fortified flour, it is still necessary to track the global progress of FAPSBA. Many more pregnancies and live births could avoid being affected by an NTD.

Data Collection:

A table of data was designed to merge the global data into one location. The prevalence of NTDs in each country was obtained from the March of Dimes 2006 global report of birth defects (Christianson 2006). For countries that were not included in global report, NTD prevalence values were adapted from neighboring countries. The annual number of births for each country was obtained from the most current (2010) US Census data estimates for each country (Bureau 2011). For countries that were not included in the Census data, number of births per country was found from an alternate reputable source. The estimated annual prevalence of births affected by NTDs was calculated from the product of NTD prevalence and the specific country's births.

As in the previous Bell and Oakley paper, the amount of folic acid preventable NTDs per country is estimated to be 75% of the prevalence of NTD-affected births. Grams of fortified

flour consumed on a daily basis for each country was obtained from the Food and Agriculture Organization of the United Nations (FAO); Food Balance Sheets from 2002 were utilized, as FAO does not have more recent data (Nations 2011). For countries that were not included in Food Balance Sheets, values were adapted from neighboring countries. This information from Food Balance Sheets was converted to grams and included a 10% wastage based on the supply available per capita. The daily amount of folic acid consumed from either wheat or maize flour was then calculated as a product of the fortification level and the daily amount of fortified flour that is consumed in the country.

Table 1 estimates the percentage of FAPSBA that fortification will prevent based on a "prevention factor" model described in Bell and Oakley's 2006 and 2008 papers (Bell and Oakley 2006; Bell and Oakley 2009). Whereas the proportion of FAPSBA that have been prevented is 25% for people consuming 100mcg (20-150 mcg) folic acid fortified flour; 50% if 200 mcg (151-250 mcg); 75% if 300 mcg (251-350 mcg); and 100% if 400 mcg (greater than 350 mcg). This model assumes that 400 mcg creates total prevention, based on recommendations by the US. Program coverage was determined by previously reported data and from more recent country specific data through a personal correspondence with Quentin Johnson on March 13, 2011. The level of fortification for each country was obtained from the Flour Fortification Initiative (FFI 2010). The total amount of NTDs prevented, per country, with fortification was calculated as a product of FAPSBA cases, the percentage of NTDs that complete fortification will prevent, and the amount of coverage that the country specific fortification program reaches. The total amount of NTDs prevented was then calculated from

the quotient of total spina bifida and anencephaly cases prevented with fortification and all cases of FAPSBA.

Table 2 was created with all of the same calculations as Table 1; however, a new prevention factor model was used. This model assumes that 200 mcg is needed for total prevention, based on an elevated amount of folic acid consumed by people in the US that have proven to decrease the number of NTDs. In this table, the proportion of FAPSBA that have been prevented is 50% for people consuming 100 mcg (20-150 mcg) folic acid fortified flour; and 100% if they consume 200 mcg (151-250 mcg or greater). An assumption that folic acid from fortified flour is a sufficient amount to prevent NTDs was the premise of this new prevention factor (Mosley, Cleves et al. 2009). The model assumes that 200 mcg, rather than 400 mcg, of folic acid is required for full protection of a NTD. The updated method also reflects a clearer picture of reality in which most people consume their daily folic acid from fortified flour and the average person in the US consumes about 100 mcg of folic acid on a daily basis.

Analysis:

Table 1 estimates that 13.81% of FAPSBA cases are prevented under current conditions. On the other hand, under the new prevention factor, Table 2 reports 22.38% of NTDs are currently prevented with folic acid fortification. Therefore, the most real percentage of NTDs prevented with folic acid fortification lies somewhere between 13.81% and 22.38%. Although these values are greater than values reported in 2006 and 2008, they still demonstrate the need for an increase in country specific folic acid fortification programs. The reality that only

approximately one fifth of FAPSBA cases are being prevented globally is a reminder that much work needs to be done in order to eliminate all cases of FAPSBA.

Results:

See Table 1 and Table 2.

TABLE 1

Country	*NTD prevalence/1000 live births (α)*	*Births (β)*	Estimated annual prevalence of NTD births (γ)	Folic acid preventable NTDs (FAPSBA) (δ)	Daily grams fortified flour consumed (λ)	Daily mcg folic acid consumption from wheat and/or maize flour (π)	% of FAPSBA that complete fortification will prevent (σ)	Program coverage (ψ)	Folic acid fortification level for wheat/ maize, ppm (ϕ)	FAPSBA prevented (τ)
Afghanistan	2	1110000	2220	1665	225	337.5	75%	30%	1.50	374.625
Angola	2	566000	1132	849	43	0	0%	0%	0.00	0
Argentina	2.1	734000	1541.4	1156.05	198	435.6000094	100%	100%	2.20	1156.05
Australia	0.6	267000	160.2	120.15	142	284	75%	100%	2.00	90.1125
Azerbaijan	3.1	147000	455.7	341.775	362	543	100%	10%	1.50	34.1775
Bahrain	1.2	18000	21.6	16.2	225	337.5	75%	100%	1.50	12.15
Bangladesh	4.7	3658000	17192.6	12894.45	45	67.5	25%	0%	1.50	0
Barbados	1.8	4000	7.2	5.4	141	211.5	50%	100%	1.50	2.7
Belize	2.5	8000	20	15	138	207	50%	100%	1.50	7.5
Benin	2.7	350000	945	708.75	15	38.99999857	25%	100%	2.60	177.1875
Bolivia	2	250000	500	375	89	133.5	25%	100%	1.50	93.75
Brazil	1.9	3642000	6919.8	5189.85	88	132	25%	100%	1.50	1297.4625
Burkina Faso	2.7	714000	1927.8	1445.85	8	20.79999924	25%	100%	2.60	361.4625
Cambodia	1.9	370000	703	527.25	4	0	0%	0%	0.00	0
Cameroon	2	648000	1296	972	33	85.79999685	25%	0%	2.60	0
Canada	1.6	347000	555.2	416.4	163	244.5	50%	100%	1.50	208.2
Chile	1.9	242000	459.8	344.85	225	495.0000107	100%	100%	2.20	344.85
China	1.3	16188000	21044.4	15783.3	118	177	50%	1%	1.50	78.9165
Colombia	2	785000	1570	1177.5	52	80.07999802	25%	100%	1.54	294.375
Congo, Democratic Republic of the	2	2684000	5368	4026	40	60	25%	70%	1.50	704.55
Costa Rica	0.5	75000	37.5	28.125	83	149.399996	25%	100%	1.80	7.03125
Côte d'Ivoire	2.7	663000	1790.1	1342.575	40	103.9999962	25%	100%	2.60	335.64375
Cuba	1.8	111000	199.8	149.85	106	265	75%	100%	2.50	112.3875
Cyprus	1.2	13000	15.6	11.7	170	425	100%	40%	2.50	4.68
Dominica	1.8	1000	1.8	1.35	141	211.5	50%	100%	1.50	0.675

Dominican Republic	1.8	195000	351	263.25	50	89.99999762	25%	100%	1.80	65.8125
Ecuador	2	301000	602	451.5	58	34.80000138	25%	100%	0.60	112.875
Egypt	2.2	2013000	4428.6	3321.45	270	405	100%	70%	1.50	2325.015
El Salvador	2.5	109000	272.5	204.375	57	102.5999973	25%	100%	1.80	51.09375
Fiji	1.5	19000	28.5	21.375	182	273	75%	100%	1.50	16.03125
Gaza Strip ^	3.1	58000	179.8	134.85	242	242	50%	100%	1.00	67.425
Georgia	2	49000	98	73.5	242	363	100%	100%	1.50	73.5
Ghana	2.7	684000	1846.8	1385.1	20	40	25%	50%	2.00	173.1375
Grenada	1.8	2000	3.6	2.7	99	148.5	25%	100%	1.50	0.675
Guadeloupe * ^ ~	2	6814	13.628	10.221	50	0	0%	0%	0.00	0
Guatemala	2.5	371000	927.5	695.625	57	61.56000245	25%	100%	1.08	173.90625
Guinea	2.7	384000	1036.8	777.6	21	54.599998	25%	100%	2.60	194.4
Guinea-Bissau	2.7	56000	151.2	113.4	27	70.19999743	25%	0%	2.60	0
Guyana	2	13000	26	19.5	104	156	50%	100%	1.50	9.75
Haiti	1.8	240000	432	324	77	115.5	25%	100%	1.50	81
Honduras	2.5	205000	512.5	384.375	58	104.3999972	25%	100%	1.80	96.09375
Hungary	2.8	97000	271.6	203.7	198	0	0%	0%	0.00	0
India	4.7	25034000	117659.8	88244.85	123	184.5	50%	2%	1.50	882.4485
Indonesia	0.7	4483000	3138.1	2353.575	38	76	25%	100%	2.00	588.39375
Iran	2	1425000	2850	2137.5	364	546	100%	100%	1.50	2137.5
Iraq ^	1.8	873000	1571.4	1178.55	364	0	0%	0%	0.00	0
Ireland "	2	76000	152	114	177	265.5	75%	30%	1.50	25.65
Israel	1.4	143000	200.2	150.15	242	363	100%	100%	1.50	150.15
Jamaica	1.8	55000	99	74.25	140	210	50%	100%	1.50	37.125
Jordan	3.3	173000	570.9	428.175	142	213	50%	70%	1.50	149.86125
Kazakhstan	2	258000	516	387	261	391.5	100%	50%	1.50	193.5
Kenya	1.3	1407000	1829.1	1371.825	47	0	25%	0%	0.00	0
Kuwait	1.2	55000	66	49.5	169	253.5	75%	100%	1.50	37.125
Kyrgyzstan	2	130000	260	195	433	649.5	100%	40%	1.50	78
Laos * ^	2	169000	338	253.5	18	0	0%	0%	0.00	0
Lesotho	2.3	52000	119.6	89.7	87	124.4099954	25%	100%	1.43	22.425
Malawi	1.3	638000	829.4	622.05	25	51.49999857	25%	10%	2.06	15.55125
Malaysia	1.9	605000	1149.5	862.125	86	129	25%	20%	1.50	43.10625

Mali	2.7	636000	1717.2	1287.9	16	41.59999847	25%	100%	2.60	321.975
Mauritania	2.7	108000	291.6	218.7	247	642.1999764	100%	0%	2.60	0
Mexico	2.5	2181000	5452.5	4089.375	67	134	25%	100%	2.00	1022.3438
Mongolia	1.3	65000	84.5	63.375	223	334.5	75%	11%	1.50	5.2284375
Morocco	2.2	614000	1350.8	1013.1	332	498	100%	50%	1.50	506.55
Nepal	4.7	649000	3050.3	2287.725	87	130.5	25%	20%	1.50	114.38625
New Zealand "	1.7	59000	100.3	75.225	144	288	75%	0%	2.00	0
Nicaragua	2.5	111000	277.5	208.125	47	84.59999776	25%	100%	1.80	52.03125
Niger	2.7	811000	2189.7	1642.275	13	33.79999876	25%	0%	2.60	0
Oman	1.2	71000	85.2	63.9	180	270	75%	100%	1.50	47.925
Pakistan	2	4665000	9330	6997.5	247	370.5	100%	25%	1.50	1749.375
Palestine, Occupied Territory ~	5.5	63084	346.962	260.2215	207	207	50%	70%	1.00	91.077525
Panama	2.5	67000	167.5	125.625	73	131.3999965	25%	100%	1.80	31.40625
Paraguay	2	113000	226	169.5	35	105	25%	100%	3.00	42.375
Peru	2	570000	1140	855	92	110.4000044	25%	100%	1.20	213.75
Poland	2.7	386000	1042.2	781.65	220	0	0%	0%	0.00	0
Puerto Rico * ^	2	45000	90	67.5	150	225	50%	0%	1.50	0
Qatar	1.2	13000	15.6	11.7	180	270	75%	100%	1.50	8.775
Romania	2.5	210000	525	393.75	270	405	100%	0%	1.50	0
Russian Federation	2.5	1549000	3872.5	2904.375	257	102.8000015	25%	0%	0.40	0
Saint Vincent	1.8	2000	3.6	2.7	148	222	50%	100%	1.50	1.35
Saudi Arabia	1.2	500000	600	450	165	247.5	50%	100%	1.50	225
Senegal	2.7	459000	1239.3	929.475	52	135.199995	25%	100%	2.60	232.36875
South Africa	2.3	963000	2214.9	1661.175	121	181.5	50%	100%	1.50	830.5875
Sudan	2.2	1607000	3535.4	2651.55	90	135	25%	35%	1.50	232.01063
Swaziland "	2.3	37000	85.1	63.825	65	0	0%	0%	0.00	0
Syria	1.8	543000	977.4	733.05	308	462	100%	0%	1.50	0
Taiwan * ^	1	207000	207	155.25	118	177	50%	0%	1.50	0
Tajikistan	2	198000	396	297	258	387	100%	71%	1.50	210.87
Tanzania ^	1.3	1401000	1821.3	1365.975	47	0	0%	0%	0.00	0
Togo	2.7	236000	637.2	477.9	35	90.99999666	25%	100%	2.60	119.475
Turkey	3	1422000	4266	3199.5	371	0	0%	0%	0.00	0

Turkmenistan	2	97000	194	145.5	412	618	100%	60%	1.50	87.3
Uganda	1.3	1588000	2064.4	1548.3	11	27.71999979	25%	50%	2.52	193.5375
Ukraine	2.1	437000	917.7	688.275	253	556.6000121	100%	20%	2.20	137.655
United Arab Emirates	1.2	80000	96	72	188	282	75%	100%	1.50	54
United States	1.4	4291000	6007.4	4505.55	150	209.9999964	50%	100%	1.40	2252.775
Uruguay	1	45000	45	33.75	182	436.8000174	100%	100%	2.40	33.75
Uzbekistan	2	488000	976	732	298	298	75%	40%	1.00	219.6
Vietnam	1.9	1549000	2943.1	2207.325	18	36	25%	15%	2.00	82.774688
Yemen	1.2	808000	969.6	727.2	225	360.0000054	100%	100%	1.60	727.2
Brazil (maize flour)	1.9	3642000	6919.8	5189.85	46	69	25%	100%	1.50	1297.4625
Costa Rica (maize flour)	0.5	75000	37.5	28.125	9	11.7	25%	100%	1.30	7.03125
Dominican Republic (maize flour)	1.8	195000	351	263.25	23	35.42	25%	100%	1.54	65.8125
Mexico (maize flour)	2.5	2181000	5452.5	4089.375	268	107.2	25%	100%	0.40	1022.3438
South Africa (maize flour)	2.3	963000	2214.9	1661.175	237	474	50%	100%	2.00	830.5875
Uganda (maize flour)	1.3	1588000	2064.4	1548.3	66	66	25%	50%	1.00	193.5375
United States (maize flour)	1.4	4291000	6007.4	4505.55	25	38.5	25%	100%	1.54	1126.3875
Zambia (maize flour)	1.3	601000	781.3	585.975	276	110.4	25%	60%	0.40	87.89625

Total births	Total NTDs	Total prevented
103917898	270167.29	27978.549
	FAPSBA	**% FAPSBA prevented**
	202625.468	**13.81%**

TABLE 2

Country	*NTD prevalence/1000 live births (α)*	*Births (β)*	Estimated annual prevalence of NTD births (γ)	Folic acid preventable NTDs (FAPSBA) (δ)	Daily grams fortified flour consumed (λ)	Daily mcg folic acid consumption from wheat and/or maize flour (π)	% of FAPSBA that complete fortification will prevent (σ)	Program coverage (ψ)	Folic acid fortification level for wheat/ maize, ppm (ϕ)	FAPSBA prevented (τ)
Afghanistan	2	1110000	2220	1665	225	337.5	100%	30%	1.50	499.5
Angola	2	566000	1132	849	43	0	0%	0%	0.00	0
Argentina	2.1	734000	1541.4	1156.05	198	435.6000094	100%	100%	2.20	1156.05
Australia	0.6	267000	160.2	120.15	142	284	100%	100%	2.00	120.15
Azerbaijan	3.1	147000	455.7	341.775	362	543	100%	10%	1.50	34.1775
Bahrain	1.2	18000	21.6	16.2	225	337.5	100%	100%	1.50	16.2
Bangladesh	4.7	3658000	17192.6	12894.45	45	67.5	50%	0%	1.50	0
Barbados	1.8	4000	7.2	5.4	141	211.5	100%	100%	1.50	5.4
Belize	2.5	8000	20	15	138	207	100%	100%	1.50	15
Benin	2.7	350000	945	708.75	15	38.99999857	50%	100%	2.60	354.375
Bolivia	2	250000	500	375	89	133.5	50%	100%	1.50	187.5
Brazil	1.9	3642000	6919.8	5189.85	88	132	50%	100%	1.50	2594.925
Burkina Faso	2.7	714000	1927.8	1445.85	8	20.79999924	50%	100%	2.60	722.925
Cambodia	1.9	370000	703	527.25	4	0	0%	0%	0.00	0
Cameroon	2	648000	1296	972	33	85.79999685	50%	0%	2.60	0
Canada	1.6	347000	555.2	416.4	163	244.5	100%	100%	1.50	416.4
Chile	1.9	242000	459.8	344.85	225	495.0000107	100%	100%	2.20	344.85
China	1.3	16188000	21044.4	15783.3	118	177	100%	1%	1.50	157.833
Colombia	2	785000	1570	1177.5	52	80.07999802	50%	100%	1.54	588.75
Congo, Democratic Republic of the	2	2684000	5368	4026	40	60	50%	70%	1.50	1409.1
Costa Rica	0.5	75000	37.5	28.125	83	149.399996	50%	100%	1.80	14.0625
Côte d'Ivoire	2.7	663000	1790.1	1342.575	40	103.9999962	50%	100%	2.60	671.2875
Cuba	1.8	111000	199.8	149.85	106	265	100%	100%	2.50	149.85
Cyprus	1.2	13000	15.6	11.7	170	425	100%	40%	2.50	4.68
Dominica	1.8	1000	1.8	1.35	141	211.5	100%	100%	1.50	1.35

Dominican Republic	1.8	195000	351	263.25	50	89.99999762	50%	100%	1.80	131.625
Ecuador	2	301000	602	451.5	58	34.80000138	50%	100%	0.60	225.75
Egypt	2.2	2013000	4428.6	3321.45	270	405	100%	70%	1.50	2325.015
El Salvador	2.5	109000	272.5	204.375	57	102.5999973	50%	100%	1.80	102.1875
Fiji	1.5	19000	28.5	21.375	182	273	100%	100%	1.50	21.375
Gaza Strip ^	3.1	58000	179.8	134.85	242	242	100%	100%	1.00	134.85
Georgia	2	49000	98	73.5	242	363	100%	100%	1.50	73.5
Ghana	2.7	684000	1846.8	1385.1	20	40	50%	50%	2.00	346.275
Grenada	1.8	2000	3.6	2.7	99	148.5	50%	100%	1.50	1.35
Guadeloupe * ^ ˜	2	6814	13.628	10.221	50	0	0%	0%	0.00	0
Guatemala	2.5	371000	927.5	695.625	57	61.56000245	50%	100%	1.08	347.8125
Guinea	2.7	384000	1036.8	777.6	21	54.599998	50%	100%	2.60	388.8
Guinea-Bissau	2.7	56000	151.2	113.4	27	70.19999743	50%	0%	2.60	0
Guyana	2	13000	26	19.5	104	156	100%	100%	1.50	19.5
Haiti	1.8	240000	432	324	77	115.5	50%	100%	1.50	162
Honduras	2.5	205000	512.5	384.375	58	104.3999972	50%	100%	1.80	192.1875
Hungary	2.8	97000	271.6	203.7	198	0	0%	0%	0.00	0
India	4.7	25034000	117659.8	88244.85	123	184.5	100%	2%	1.50	1764.897
Indonesia	0.7	4483000	3138.1	2353.575	38	76	50%	100%	2.00	1176.7875
Iran	2	1425000	2850	2137.5	364	546	100%	100%	1.50	2137.5
Iraq ^	1.8	873000	1571.4	1178.55	364	0	0%	0%	0.00	0
Ireland "	2	76000	152	114	177	265.5	100%	30%	1.50	34.2
Israel	1.4	143000	200.2	150.15	242	363	100%	100%	1.50	150.15
Jamaica	1.8	55000	99	74.25	140	210	100%	100%	1.50	74.25
Jordan	3.3	173000	570.9	428.175	142	213	100%	70%	1.50	299.7225
Kazakhstan	2	258000	516	387	261	391.5	100%	50%	1.50	193.5
Kenya	1.3	1407000	1829.1	1371.825	47	0	50%	0%	0.00	0
Kuwait	1.2	55000	66	49.5	169	253.5	100%	100%	1.50	49.5
Kyrgyzstan	2	130000	260	195	433	649.5	100%	40%	1.50	78
Laos * ^	2	169000	338	253.5	18	0	0%	0%	0.00	0
Lesotho	2.3	52000	119.6	89.7	87	124.4099954	50%	100%	1.43	44.85
Malawi	1.3	638000	829.4	622.05	25	51.49999857	50%	10%	2.06	31.1025
Malaysia	1.9	605000	1149.5	862.125	86	129	50%	20%	1.50	86.2125

Mali	2.7	636000	1717.2	1287.9	16	41.59999847	50%	100%	2.60	643.95
Mauritania	2.7	108000	291.6	218.7	247	642.1999764	100%	0%	2.60	0
Mexico	2.5	2181000	5452.5	4089.375	67	134	50%	100%	2.00	2044.6875
Mongolia	1.3	65000	84.5	63.375	223	334.5	100%	11%	1.50	6.97125
Morocco	2.2	614000	1350.8	1013.1	332	498	100%	50%	1.50	506.55
Nepal	4.7	649000	3050.3	2287.725	87	130.5	50%	20%	1.50	228.7725
New Zealand "	1.7	59000	100.3	75.225	144	288	100%	0%	2.00	0
Nicaragua	2.5	111000	277.5	208.125	47	84.59999776	50%	100%	1.80	104.0625
Niger	2.7	811000	2189.7	1642.275	13	33.79999876	50%	0%	2.60	0
Oman	1.2	71000	85.2	63.9	180	270	100%	100%	1.50	63.9
Pakistan	2	4665000	9330	6997.5	247	370.5	100%	25%	1.50	1749.375
Palestine, Occupied Territory ~	5.5	63084	346.962	260.2215	207	207	100%	70%	1.00	182.15505
Panama	2.5	67000	167.5	125.625	73	131.3999965	50%	100%	1.80	62.8125
Paraguay	2	113000	226	169.5	35	105	50%	100%	3.00	84.75
Peru	2	570000	1140	855	92	110.4000044	50%	100%	1.20	427.5
Poland	2.7	386000	1042.2	781.65	220	0	0%	0%	0.00	0
Puerto Rico * ^	2	45000	90	67.5	150	225	100%	0%	1.50	0
Qatar	1.2	13000	15.6	11.7	180	270	100%	100%	1.50	11.7
Romania	2.5	210000	525	393.75	270	405	100%	0%	1.50	0
Russian Federation	2.5	1549000	3872.5	2904.375	257	102.8000015	50%	0%	0.40	0
Saint Vincent	1.8	2000	3.6	2.7	148	222	100%	100%	1.50	2.7
Saudi Arabia	1.2	500000	600	450	165	247.5	100%	100%	1.50	450
Senegal	2.7	459000	1239.3	929.475	52	135.199995	50%	100%	2.60	464.7375
South Africa	2.3	963000	2214.9	1661.175	121	181.5	100%	100%	1.50	1661.175
Sudan	2.2	1607000	3535.4	2651.55	90	135	50%	35%	1.50	464.02125
Swaziland "	2.3	37000	85.1	63.825	65	0	0%	0%	0.00	0
Syria	1.8	543000	977.4	733.05	308	462	100%	0%	1.50	0
Taiwan * ^	1	207000	207	155.25	118	177	100%	0%	1.50	0
Tajikistan	2	198000	396	297	258	387	100%	71%	1.50	210.87
Tanzania ^	1.3	1401000	1821.3	1365.975	47	0	0%	0%	0.00	0
Togo	2.7	236000	637.2	477.9	35	90.99999666	50%	100%	2.60	238.95
Turkey [f]	3	1422000	4266	3199.5	371	0	0%	0%	0.00	0

Turkmenistan	2	97000	194	145.5	412	618	100%	60%	1.50	87.3
Uganda	1.3	1588000	2064.4	1548.3	11	27.71999979	50%	50%	2.52	387.075
Ukraine	2.1	437000	917.7	688.275	253	556.6000121	100%	20%	2.20	137.655
United Arab Emirates	1.2	80000	96	72	188	282	100%	100%	1.50	72
United States	1.4	4291000	6007.4	4505.55	150	209.9999964	100%	100%	1.40	4505.55
Uruguay	1	45000	45	33.75	182	436.8000174	100%	100%	2.40	33.75
Uzbekistan	2	488000	976	732	298	298	100%	40%	1.00	292.8
Vietnam	1.9	1549000	2943.1	2207.325	18	36	50%	15%	2.00	165.54938
Yemen	1.2	808000	969.6	727.2	225	360.0000054	100%	100%	1.60	727.2
Brazil (maize flour)	1.9	3642000	6919.8	5189.85	46	69	50%	100%	1.50	2594.925
Costa Rica (maize flour)	0.5	75000	37.5	28.125	9	11.7	50%	100%	1.30	14.0625
Dominican Republic (maize flour)	1.8	195000	351	263.25	23	35.42	50%	100%	1.54	131.625
Mexico (maize flour)	2.5	2181000	5452.5	4089.375	268	107.2	50%	100%	0.40	2044.6875
South Africa (maize flour)	2.3	963000	2214.9	1661.175	237	474	100%	100%	2.00	1661.175
Uganda (maize flour)	1.3	1588000	2064.4	1548.3	66	66	50%	50%	1.00	387.075
United States (maize flour)	1.4	4291000	6007.4	4505.55	25	38.5	50%	100%	1.54	2252.775
Zambia (maize flour)	1.3	601000	781.3	585.975	276	110.4	50%	60%	0.40	175.7925

Total births	Total NTDs	Total prevented
103917898	270167.29	45337.902

FAPSBA	**% FAPSBA prevented**
202625.468	**22.38%**

Table 1 and Table 2 Key:

α: 2006 March of Dimes report.

β: US Census estimates, 2010.

γ: Calculated from NTD prevalences in 2006 March of Dimes report and US Census estimates of births in 2010.

δ: Assumed to be 75% of annual NTD prevalence in population that does not consume folic acid.

λ: From Food Balance Sheets, 2002-FAO does not have more recent estimates.

π: Calculated from grams of wheat x fortification levels for wheat flour and grams of maize flour x fortification level for maize.

σ: Prevention percentage: % annual NTDs prevented through flour fortificaiton, as function of folic acid consumption and prefortification annual estimate of NTDs, using model in this article.

ψ: FFI estimates and personal communication with Quentin Johnson, 03/13/2011

ϕ: FFI estimates.

τ: # of NTDs prevented by wheat/maize flour fortification, calculated as product of folic acid-preventable NTD estimate x prevention percentage x program coverage.

*: NTD prevalence not in MOD 2006 report, values based on neighboring country data.

^: Daily grams fortified flour consumed not in2002 Food Balance Sheets; values adapted from neighboring country.

~: Birth estimates not in US census data, estimated from another source.

": Program coverage from alternate source.

Figure 1:

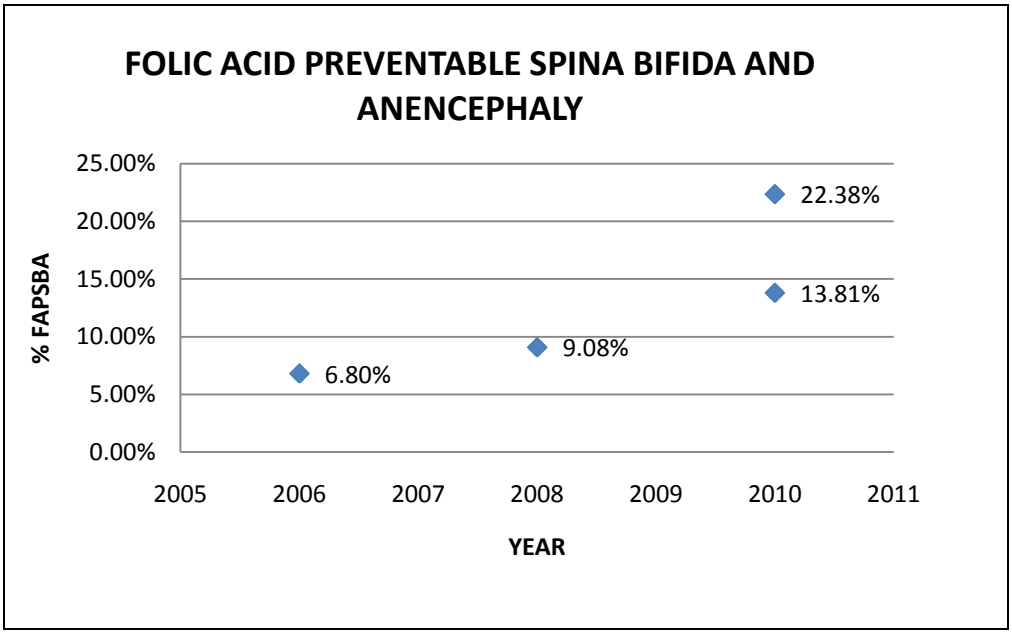
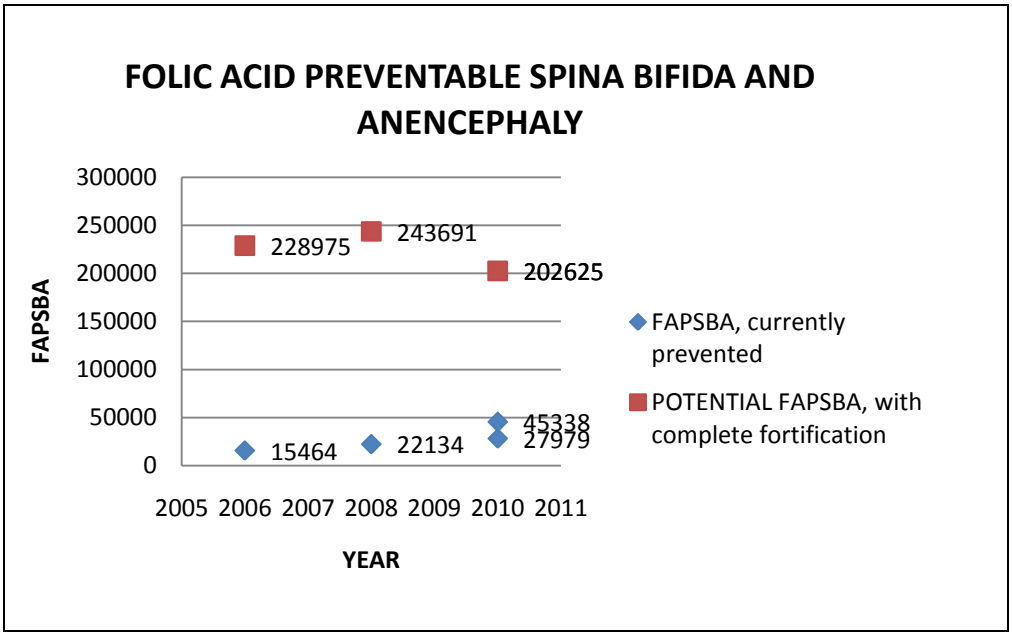


Figure 2:



Discussion:

These estimated values of FAPSBA depend on each country's reporting values and surveillance systems in place. As not all surveillance and reporting systems may be sophisticated, data acquired from sources that rely on surveillance may contain some errors. Similarly, data from FAO Food Balance Sheets was based on 2002 data because FAO has modified some of its methodologies and it is more consistent to report utilizing data from the same time-frame that is the most current available. 2002 FAO data was also utilized in this paper to maintain a common baseline of wheat and maize flour consumption.

Program coverage is another area that could contain errors. Country specific data is limited in describing how much of the country has access to folic acid fortified flour and/or how much of a country's flour is fortified with folic acid. Another reason why coverage is subject to errors is because of imported flour which is not required to follow country specific mandated on fortification. Information for program coverage is quite limited because the availability of fortified flour does not always equate to access to and consumption of fortified flour.

Also, values of NTD rates may be lesser than actuality since many pregnancies are terminated prior to the NTD-affected birth being counted in statistics. Currently there are 78 countries that have some program coverage with folic acid fortified flour. This is an increase from 2006 and 2008, in which there were 39 and 68 countries that fortified flour with folic acid, respectively.

The results show that although there has been an increase in the amount of spina bifida and anencephaly currently being globally prevented, there is much needed work in order to prevent all cases FAPSBA with regard to increasing flour fortification in countries currently

fortifying and those that are not. As visualized in Figure 1 and Figure 2, it is currently estimated that between 27,979 of 202,625, or 13.81% and 45,338 of 202,625, or 22.38% of FAPSBA cases are being prevented. It is anticipated that since not all folic acid sensitive cases of spina bifida and anencephaly are being prevented, this will be a stimulus for non-fortifying countries to begin fortification mandates and for countries that currently fortify to increase fortification levels so 100% of NTDs could be prevented. In an ideal future setting, risk of pregnancies affected by FAPSBA could be assessed by determining serum folate levels in women of child-bearing age.

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Journal Article:

Global Update on the Prevention of Folic Acid-Preventable Spina Bifida and Anencephaly Cases

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ABSTRACT:

BACKGROUND: Folic acid has been proven to prevent most cases of spina bifida and anencephaly. It is recommended that women of child-bearing age consume folic acid fortified grain products and/or supplements prior to pregnancy. Since 2006, there has been an increase in the number of countries that fortify their flour with folic acid. **METHODS:** Country specific data on fortification of flour with folic acid has been tracked along with amounts of fortified flour consumed per person. Estimates of spina bifida and anencephaly affected pregnancies and country-specific birth estimates were also utilized to estimate the amount of folic acid preventable spina bifida and anencephaly cases. **RESULTS:** Utilizing a predetermined prevention factor model, it is estimated that 13.81% of spina bifida and anencephaly cases are currently being prevented with folic acid flour fortification. Since the average US population consumes between 100 and 200 mcg folic acid from fortified flour, and this is associated with a significant decrease in the number of cases of spina bifida and anencephaly, an updated prevention factor model was created. Under these circumstances, it is estimated that 22.38% of spina bifida and anencephaly cases are globally prevented with folic acid flour fortification. **CONCLUSIONS:** Although these values show an increase in cases prevented since 2006, there is still a significant amount of work required in order to increase consumption of folic acid in women of child-bearing age and for countries to regulate and require flour fortification with folic acid.

Key words: spina bifida, anencephaly, prevention, folic acid, flour fortification

INTRODUCTION:

Folate is a water-soluble B-vitamin found in dark green vegetables, nuts, fruits and berries (Cooperman 1970). The synthetic form of folate is folic acid. Although the exact mechanism is unknown, folic acid is associated with decreasing the risk for having a pregnancy affected by a neural tube defect (NTD). In order to reduce neural tube defects, folic acid was added to cereal and grain products in 1998 under the United States folic acid fortification program (Lewis, Crane et al. 1999). Since then, many other countries have implemented similar mandates (CDC 1992).

A British study convincingly demonstrated that folic acid alone could prevent 72% of birth defects (MRC Vitamin Study Research Group 1991). In the United States, the current US Public Health Service recommendation is that all women capable of becoming pregnant should consume 400 micrograms (mcg) of folic acid, daily, to prevent spina bifida and other NTDs (CDC 1992). Since not all countries fortify their flour with folic acid and not all people have access to fortified flour, there is still a large amount of folic acid-preventable spina bifida and anencephaly (FAPSBA) that could be avoided with fortification.

The fortification of grains does not require any additional equipment that cereal-grain companies don't already have. Millers would only have to pay a one-time fee to change product label settings. The cost per unit of folic acid fortification is insignificant; especially in comparison to the benefits that will result from fortification. The estimated unit cost of folic acid fortification would be approximately $0.0237 (US$) per 100 pounds of grain at 350 mcg per 100 grams produced (Romano, Waitzman et al. 1995). Grain fortification does not affect the

taste, shelf-life, or appearance of cereal-grain products (Bentley, Ferrini et al. 1999). The intervention of grain fortification is an approach that can help combat important health issues without modifying behaviors or increasing education in target populations. It is apparent, though, that collaborative efforts are necessary to help accomplish the goal of implementing grain fortification policies around the world.

The leading cause of death among babies less than one year of age is birth defects (Bentley, Ferrini et al. 1999). Expectant mothers who consume folic acid decrease the chance for a birth outcome with a NTD. Mothers with previous pregnancies affected by a NTD have a greater risk of another pregnancy to have a NTD (CDC 1992). Common NTDs include spina bifida and anencephaly in which there is incomplete closure of the neural tube; this occurs early in the developmental stage of a human embryo (Detrait, George et al.). Folic acid also has positive effects on birth weight and premature births (Vollset, Refsum et al. 2000). Globally, NTDs occur at an incidence rate of approximately 2.5 per 1000 live births (Christianson 2006). This amount is actually a lower count than total pregnancies affected by NTDs because many pregnancies are terminated and do not result in a live birth to be counted in such statistics.

Although there has been a decrease in the prevalence of NTDs since fortification of flour has been implemented, there are still a significant number of births affected by NTDs. In 2003-2004, the total US prevalence of spina bifida and anencephaly per 10,000 live births was 5.37 among all races and ethnicities (Boulet, Yang et al. 2008). The 2003-2004 prevalence was 4.86, 4.05, and 6.91 per 10,000 live births among non-Hispanic whites, non-Hispanic blacks, and Hispanics respectively [7]. In addition to living a life with an incurable condition, there is a high cost of care associated with a life affected by a NTD. The US estimated that in 2002, a child born with spina bifida would be associated to a cost of $636,000; a child born with anencephaly would be associated with a cost of $1,020,000; these costs do not include the cost of time for receiving care (Grosse, Waitzman et al. 2005). It is assumed that much of the world's cases of spina bifida and anencephaly could be prevented with the proper amounts of folic acid (CDC 1992; Czeizel and Dudas 1992).

In 2006, Karen N. Bell and Godfrey P. Oakley Jr. published a paper that described a way to track the global prevention of spina bifida and anencephaly through folic acid flour fortification (Bell and Oakley 2006). The result of this paper described that approximately 6.8% of the world's births were prevented from having an outcome of a baby born with spina bifida or anencephaly in countries that fortify their flour with folic acid. At this time, 39 countries were fortifying their flour with folic acid (Bell and Oakley 2006). In 2008, Bell and Oakley published an update to the 2006 paper; this update stated that annually, 9.08% of NTDs were prevented in countries where folic acid fortified flour is consumed. At this time 68 countries were fortifying flour with folic acid (Bell and Oakley 2009).

It is important to determine an updated value for the amount of folic acid each country is fortifying flour with in order to understand the global progress of preventing NTDs with folic acid fortified flour showing the progress of the world's fortification programs. It is believed that with continued and increasing country-specific mandates for flour fortification with folic acid, one day there will be no cases of FAPSBA affecting pregnancies. Although many countries do not have sufficient or advanced surveillance programs in place, much work will be required in many portals of this public health concern in order to fully combat the issue at hand. Additionally, information about flour consumption and/or country-specific programs may have

some deficiencies; however, this should not affect the results of this paper, but rather give these countries a stimulus to improve surveillance and increase folic acid flour fortification practices. We will also provide information about the benefits of fortification which countries could use to help decrease the amount of children born with neural tube defects and adverse pregnancy outcomes.

METHODS:

A table of data was designed to merge the global data into one location. The prevalence of NTDs in each country was obtained from the March of Dimes 2006 global report of birth defects (Christianson 2006). For countries that were not included in global report, NTD prevalence values were adapted from neighboring countries. The annual number of births for each country was obtained from the most current (2010) US Census data estimates for each country (Bureau 2011). For countries that were not included in the Census data, number of births per country was found from an alternate reputable source. The estimated annual prevalence of births affected by NTDs was calculated from the product of NTD prevalence and the specific country's births.

As in the previous Bell and Oakley paper, the amount of folic acid preventable NTDs per country is estimated to be 75% of the prevalence of NTD-affected births. Grams of fortified flour consumed on a daily basis for each country was obtained from the Food and Agriculture Organization of the United Nations (FAO); Food Balance Sheets from 2002 were utilized, as FAO does not have more recent data (Nations 2011). For countries that were not included in Food Balance Sheets, values were adapted from neighboring countries. This information from Food Balance Sheets was converted to grams and included a 10% wastage based on the supply available per capita. The daily amount of folic acid consumed from either wheat or maize flour was then calculated as a product of the fortification level and the daily amount of fortified flour that is consumed in the country.

Table 1 estimates the percentage of FAPSBA that fortification will prevent based on a "prevention factor" model described in Bell and Oakley's 2006 and 2008 papers (Bell and Oakley 2006; Bell and Oakley 2009). Whereas the proportion of FAPSBA that have been prevented is 25% for people consuming 100mcg (20-150 mcg) folic acid fortified flour; 50% if 200 mcg (151-250 mcg); 75% if 300 mcg (251-350 mcg); and 100% if 400 mcg (greater than 350 mcg). This model assumes that 400 mcg creates total prevention, based on recommendations by the US. Program coverage was determined by previously reported data and from more recent country specific data through a personal correspondence with Quentin Johnson on March 13, 2011. The level of fortification for each country was obtained from the Flour Fortification Initiative (FFI 2010). The total amount of NTDs prevented, per country, with fortification was calculated as a product of FAPSBA cases, the percentage of NTDs that complete fortification will prevent, and the amount of coverage that the country specific fortification program reaches. The total amount of NTDs prevented was then calculated from the quotient of total spina bifida and anencephaly cases prevented with fortification and all cases of FAPSBA.

Table 2 was created with all of the same calculations as Table 1; however, a new prevention factor model was used. This model assumes that 200 mcg is needed for total

prevention, based on an elevated amount of folic acid consumed by people in the US that have proven to decrease the number of NTDs. In this table, the proportion of FAPSBA that have been prevented is 50% for people consuming 100 mcg (20-150 mcg) folic acid fortified flour; and 100% if they consume 200 mcg (151-250 mcg or greater). An assumption that folic acid from fortified flour is a sufficient amount to prevent NTDs was the premise of this new prevention factor (Mosley, Cleves et al. 2009). The model assumes that 200 mcg, rather than 400 mcg, of folic acid is required for full protection of a NTD. The updated method also reflects a clearer picture of reality in which most people consume their daily folic acid from fortified flour and the average person in the US consumes about 100 mcg of folic acid on a daily basis.

RESULTS:

Table 1 estimates that 13.81% of FAPSBA cases are prevented under current conditions. On the other hand, under the new prevention factor, Table 2 reports 22.38% of NTDs are currently prevented with folic acid fortification. Therefore, the most real percentage of NTDs prevented with folic acid fortification lies somewhere between 13.81% and 22.38%. Although these values are greater than values reported in 2006 and 2008, they still demonstrate the need for an increase in country specific folic acid fortification programs. The reality that only approximately one fifth of FAPSBA cases are being prevented globally is a reminder that much work needs to be done in order to eliminate all cases of FAPSBA. See Table 1 and Table 2 and Figure 1 and Figure 2, attached.

DISCUSSION:

These estimated values of FAPSBA depend on each country's reporting values and surveillance systems in place. As not all surveillance and reporting systems may be sophisticated, data acquired from sources that rely on surveillance may contain some errors. Similarly, data from FAO Food Balance Sheets was based on 2002 data because FAO has modified some of its methodologies and it is more consistent to report utilizing data from the same time-frame that is the most current available. 2002 FAO data was also utilized in this paper to maintain a common baseline of wheat and maize flour consumption.

Program coverage is another area that could contain errors. Country specific data is limited in describing how much of the country has access to folic acid fortified flour and/or how much of a country's flour is fortified with folic acid. Another reason why coverage is subject to errors is because of imported flour which is not required to follow country specific mandated on fortification. Information for program coverage is quite limited because the availability of fortified flour does not always equate to access to and consumption of fortified flour.

Also, values of NTD rates may be lesser than actuality since many pregnancies are terminated prior to the NTD-affected birth being counted in statistics. Currently there are 78 countries that have some program coverage with folic acid fortified flour. This is an increase from 2006 and 2008, in which there were 39 and 68 countries that fortified flour with folic acid, respectively.

The results show that although there has been an increase in the amount of spina bifida and anencephaly currently being globally prevented, there is much needed work in order to

prevent all cases FAPSBA with regard to increasing flour fortification in countries currently fortifying and those that are not. As visualized in Figure 1 and Figure 2, it is currently estimated that between 27,979 of 202,625, or 13.81% and 45,338 of 202,625, or 22.38% of FAPSBA cases are being prevented. It is anticipated that since not all folic acid sensitive cases of spina bifida and anencephaly are being prevented, this will be a stimulus for non-fortifying countries to begin fortification mandates and for countries that currently fortify to increase fortification levels so 100% of NTDs could be prevented. In an ideal future setting, risk of pregnancies affected by FAPSBA could be assessed by determining serum folate levels in women of child-bearing age.

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TABLE 1

Country	*NTD prevalence/1000 live births (α)*	*Births (β)*	Estimated annual prevalence of NTD births (γ)	Folic acid preventable NTDs (FAPSBA) (δ)	Daily grams fortified flour consumed (λ)	Daily mcg folic acid consumption from wheat and/or maize flour (π)	% of FAPSBA that complete fortification will prevent (σ)	Program coverage (ψ)	Folic acid fortification level for wheat/ maize, ppm (ϕ)	FAPSBA prevented (τ)
Afghanistan	2	1110000	2220	1665	225	337.5	75%	30%	1.50	374.625
Angola	2	566000	1132	849	43	0	0%	0%	0.00	0
Argentina	2.1	734000	1541.4	1156.05	198	435.6000094	100%	100%	2.20	1156.05
Australia	0.6	267000	160.2	120.15	142	284	75%	100%	2.00	90.1125
Azerbaijan	3.1	147000	455.7	341.775	362	543	100%	10%	1.50	34.1775
Bahrain	1.2	18000	21.6	16.2	225	337.5	75%	100%	1.50	12.15
Bangladesh	4.7	3658000	17192.6	12894.45	45	67.5	25%	0%	1.50	0
Barbados	1.8	4000	7.2	5.4	141	211.5	50%	100%	1.50	2.7
Belize	2.5	8000	20	15	138	207	50%	100%	1.50	7.5
Benin	2.7	350000	945	708.75	15	38.99999857	25%	100%	2.60	177.1875
Bolivia	2	250000	500	375	89	133.5	25%	100%	1.50	93.75
Brazil	1.9	3642000	6919.8	5189.85	88	132	25%	100%	1.50	1297.4625
Burkina Faso	2.7	714000	1927.8	1445.85	8	20.79999924	25%	100%	2.60	361.4625
Cambodia	1.9	370000	703	527.25	4	0	0%	0%	0.00	0
Cameroon	2	648000	1296	972	33	85.79999685	25%	0%	2.60	0
Canada	1.6	347000	555.2	416.4	163	244.5	50%	100%	1.50	208.2
Chile	1.9	242000	459.8	344.85	225	495.0000107	100%	100%	2.20	344.85
China	1.3	16188000	21044.4	15783.3	118	177	50%	1%	1.50	78.9165
Colombia	2	785000	1570	1177.5	52	80.07999802	25%	100%	1.54	294.375
Congo, Democratic Republic of the	2	2684000	5368	4026	40	60	25%	70%	1.50	704.55
Costa Rica	0.5	75000	37.5	28.125	83	149.399996	25%	100%	1.80	7.03125
Côte d'Ivoire	2.7	663000	1790.1	1342.575	40	103.9999962	25%	100%	2.60	335.64375
Cuba	1.8	111000	199.8	149.85	106	265	75%	100%	2.50	112.3875
Cyprus	1.2	13000	15.6	11.7	170	425	100%	40%	2.50	4.68
Dominica	1.8	1000	1.8	1.35	141	211.5	50%	100%	1.50	0.675

Dominican Republic	1.8	195000	351	263.25	50	89.99999762	25%	100%	1.80	65.8125
Ecuador	2	301000	602	451.5	58	34.80000138	25%	100%	0.60	112.875
Egypt	2.2	2013000	4428.6	3321.45	270	405	100%	70%	1.50	2325.015
El Salvador	2.5	109000	272.5	204.375	57	102.5999973	25%	100%	1.80	51.09375
Fiji	1.5	19000	28.5	21.375	182	273	75%	100%	1.50	16.03125
Gaza Strip ^	3.1	58000	179.8	134.85	242	242	50%	100%	1.00	67.425
Georgia	2	49000	98	73.5	242	363	100%	100%	1.50	73.5
Ghana	2.7	684000	1846.8	1385.1	20	40	25%	50%	2.00	173.1375
Grenada	1.8	2000	3.6	2.7	99	148.5	25%	100%	1.50	0.675
Guadeloupe * ^ ~	2	6814	13.628	10.221	50	0	0%	0%	0.00	0
Guatemala	2.5	371000	927.5	695.625	57	61.56000245	25%	100%	1.08	173.90625
Guinea	2.7	384000	1036.8	777.6	21	54.599998	25%	100%	2.60	194.4
Guinea-Bissau	2.7	56000	151.2	113.4	27	70.19999743	25%	0%	2.60	0
Guyana	2	13000	26	19.5	104	156	50%	100%	1.50	9.75
Haiti	1.8	240000	432	324	77	115.5	25%	100%	1.50	81
Honduras	2.5	205000	512.5	384.375	58	104.3999972	25%	100%	1.80	96.09375
Hungary	2.8	97000	271.6	203.7	198	0	0%	0%	0.00	0
India	4.7	25034000	117659.8	88244.85	123	184.5	50%	2%	1.50	882.4485
Indonesia	0.7	4483000	3138.1	2353.575	38	76	25%	100%	2.00	588.39375
Iran	2	1425000	2850	2137.5	364	546	100%	100%	1.50	2137.5
Iraq ^	1.8	873000	1571.4	1178.55	364	0	0%	0%	0.00	0
Ireland "	2	76000	152	114	177	265.5	75%	30%	1.50	25.65
Israel	1.4	143000	200.2	150.15	242	363	100%	100%	1.50	150.15
Jamaica	1.8	55000	99	74.25	140	210	50%	100%	1.50	37.125
Jordan	3.3	173000	570.9	428.175	142	213	50%	70%	1.50	149.86125
Kazakhstan	2	258000	516	387	261	391.5	100%	50%	1.50	193.5
Kenya	1.3	1407000	1829.1	1371.825	47	0	25%	0%	0.00	0
Kuwait	1.2	55000	66	49.5	169	253.5	75%	100%	1.50	37.125
Kyrgyzstan	2	130000	260	195	433	649.5	100%	40%	1.50	78
Laos * ^	2	169000	338	253.5	18	0	0%	0%	0.00	0
Lesotho	2.3	52000	119.6	89.7	87	124.4099954	25%	100%	1.43	22.425
Malawi	1.3	638000	829.4	622.05	25	51.49999857	25%	10%	2.06	15.55125

Malaysia	1.9	605000	1149.5	862.125	86	129	25%	20%	1.50	43.10625
Mali	2.7	636000	1717.2	1287.9	16	41.59999847	25%	100%	2.60	321.975
Mauritania	2.7	108000	291.6	218.7	247	642.1999764	100%	0%	2.60	0
Mexico	2.5	2181000	5452.5	4089.375	67	134	25%	100%	2.00	1022.3438
Mongolia	1.3	65000	84.5	63.375	223	334.5	75%	11%	1.50	5.2284375
Morocco	2.2	614000	1350.8	1013.1	332	498	100%	50%	1.50	506.55
Nepal	4.7	649000	3050.3	2287.725	87	130.5	25%	20%	1.50	114.38625
New Zealand "	1.7	59000	100.3	75.225	144	288	75%	0%	2.00	0
Nicaragua	2.5	111000	277.5	208.125	47	84.59999776	25%	100%	1.80	52.03125
Niger	2.7	811000	2189.7	1642.275	13	33.79999876	25%	0%	2.60	0
Oman	1.2	71000	85.2	63.9	180	270	75%	100%	1.50	47.925
Pakistan	2	4665000	9330	6997.5	247	370.5	100%	25%	1.50	1749.375
Palestine, Occupied Territory ~	5.5	63084	346.962	260.2215	207	207	50%	70%	1.00	91.077525
Panama	2.5	67000	167.5	125.625	73	131.3999965	25%	100%	1.80	31.40625
Paraguay	2	113000	226	169.5	35	105	25%	100%	3.00	42.375
Peru	2	570000	1140	855	92	110.4000044	25%	100%	1.20	213.75
Poland	2.7	386000	1042.2	781.65	220	0	0%	0%	0.00	0
Puerto Rico * ^	2	45000	90	67.5	150	225	50%	0%	1.50	0
Qatar	1.2	13000	15.6	11.7	180	270	75%	100%	1.50	8.775
Romania	2.5	210000	525	393.75	270	405	100%	0%	1.50	0
Russian Federation	2.5	1549000	3872.5	2904.375	257	102.8000015	25%	0%	0.40	0
Saint Vincent	1.8	2000	3.6	2.7	148	222	50%	100%	1.50	1.35
Saudi Arabia	1.2	500000	600	450	165	247.5	50%	100%	1.50	225
Senegal	2.7	459000	1239.3	929.475	52	135.199995	25%	100%	2.60	232.36875
South Africa	2.3	963000	2214.9	1661.175	121	181.5	50%	100%	1.50	830.5875
Sudan	2.2	1607000	3535.4	2651.55	90	135	25%	35%	1.50	232.01063
Swaziland "	2.3	37000	85.1	63.825	65	0	0%	0%	0.00	0
Syria	1.8	543000	977.4	733.05	308	462	100%	0%	1.50	0
Taiwan * ^	1	207000	207	155.25	118	177	50%	0%	1.50	0
Tajikistan	2	198000	396	297	258	387	100%	71%	1.50	210.87
Tanzania ^	1.3	1401000	1821.3	1365.975	47	0	0%	0%	0.00	0

Togo	2.7	236000	637.2	477.9	35	90.99999666	25%	100%	2.60	119.475
Turkey	3	1422000	4266	3199.5	371	0	0%	0%	0.00	0
Turkmenistan	2	97000	194	145.5	412	618	100%	60%	1.50	87.3
Uganda	1.3	1588000	2064.4	1548.3	11	27.71999979	25%	50%	2.52	193.5375
Ukraine	2.1	437000	917.7	688.275	253	556.6000121	100%	20%	2.20	137.655
United Arab Emirates	1.2	80000	96	72	188	282	75%	100%	1.50	54
United States	1.4	4291000	6007.4	4505.55	150	209.9999964	50%	100%	1.40	2252.775
Uruguay	1	45000	45	33.75	182	436.8000174	100%	100%	2.40	33.75
Uzbekistan	2	488000	976	732	298	298	75%	40%	1.00	219.6
Vietnam	1.9	1549000	2943.1	2207.325	18	36	25%	15%	2.00	82.774688
Yemen	1.2	808000	969.6	727.2	225	360.0000054	100%	100%	1.60	727.2
Brazil (maize flour)	1.9	3642000	6919.8	5189.85	46	69	25%	100%	1.50	1297.4625
Costa Rica (maize flour)	0.5	75000	37.5	28.125	9	11.7	25%	100%	1.30	7.03125
Dominican Republic (maize flour)	1.8	195000	351	263.25	23	35.42	25%	100%	1.54	65.8125
Mexico (maize flour)	2.5	2181000	5452.5	4089.375	268	107.2	25%	100%	0.40	1022.3438
South Africa (maize flour)	2.3	963000	2214.9	1661.175	237	474	50%	100%	2.00	830.5875
Uganda (maize flour)	1.3	1588000	2064.4	1548.3	66	66	25%	50%	1.00	193.5375
United States (maize flour)	1.4	4291000	6007.4	4505.55	25	38.5	25%	100%	1.54	1126.3875
Zambia (maize flour)	1.3	601000	781.3	585.975	276	110.4	25%	60%	0.40	87.89625

Total births	Total NTDs	Total prevented
103917898	270167.29	27978.549
	FAPSBA	**% FAPSBA prevented**
	202625.468	**13.81%**

TABLE 2

Country	*NTD prevalence/1000 live births (α)*	*Births (β)*	Estimated annual prevalence of NTD births (γ)	Folic acid preventable NTDs (FAPSBA) (δ)	Daily grams fortified flour consumed (λ)	Daily mcg folic acid consumption from wheat and/or maize flour (π)	% of FAPSBA that complete fortification will prevent (σ)	Program coverage (ψ)	Folic acid fortification level for wheat/ maize, ppm (ϕ)	FAPSBA prevented (τ)
Afghanistan	2	1110000	2220	1665	225	337.5	100%	30%	1.50	499.5
Angola	2	566000	1132	849	43	0	0%	0%	0.00	0
Argentina	2.1	734000	1541.4	1156.05	198	435.6000094	100%	100%	2.20	1156.05
Australia	0.6	267000	160.2	120.15	142	284	100%	100%	2.00	120.15
Azerbaijan	3.1	147000	455.7	341.775	362	543	100%	10%	1.50	34.1775
Bahrain	1.2	18000	21.6	16.2	225	337.5	100%	100%	1.50	16.2
Bangladesh	4.7	3658000	17192.6	12894.45	45	67.5	50%	0%	1.50	0
Barbados	1.8	4000	7.2	5.4	141	211.5	100%	100%	1.50	5.4
Belize	2.5	8000	20	15	138	207	100%	100%	1.50	15
Benin	2.7	350000	945	708.75	15	38.99999857	50%	100%	2.60	354.375
Bolivia	2	250000	500	375	89	133.5	50%	100%	1.50	187.5
Brazil	1.9	3642000	6919.8	5189.85	88	132	50%	100%	1.50	2594.925
Burkina Faso	2.7	714000	1927.8	1445.85	8	20.79999924	50%	100%	2.60	722.925
Cambodia	1.9	370000	703	527.25	4	0	0%	0%	0.00	0
Cameroon	2	648000	1296	972	33	85.79999685	50%	0%	2.60	0
Canada	1.6	347000	555.2	416.4	163	244.5	100%	100%	1.50	416.4
Chile	1.9	242000	459.8	344.85	225	495.0000107	100%	100%	2.20	344.85
China	1.3	16188000	21044.4	15783.3	118	177	100%	1%	1.50	157.833
Colombia	2	785000	1570	1177.5	52	80.07999802	50%	100%	1.54	588.75
Congo, Democratic Republic of the	2	2684000	5368	4026	40	60	50%	70%	1.50	1409.1
Costa Rica	0.5	75000	37.5	28.125	83	149.399996	50%	100%	1.80	14.0625
Côte d'Ivoire	2.7	663000	1790.1	1342.575	40	103.9999962	50%	100%	2.60	671.2875
Cuba	1.8	111000	199.8	149.85	106	265	100%	100%	2.50	149.85
Cyprus	1.2	13000	15.6	11.7	170	425	100%	40%	2.50	4.68
Dominica	1.8	1000	1.8	1.35	141	211.5	100%	100%	1.50	1.35

Dominican Republic	1.8	195000	351	263.25	50	89.99999762	50%	100%	1.80	131.625
Ecuador	2	301000	602	451.5	58	34.80000138	50%	100%	0.60	225.75
Egypt	2.2	2013000	4428.6	3321.45	270	405	100%	70%	1.50	2325.015
El Salvador	2.5	109000	272.5	204.375	57	102.5999973	50%	100%	1.80	102.1875
Fiji	1.5	19000	28.5	21.375	182	273	100%	100%	1.50	21.375
Gaza Strip ^	3.1	58000	179.8	134.85	242	242	100%	100%	1.00	134.85
Georgia	2	49000	98	73.5	242	363	100%	100%	1.50	73.5
Ghana	2.7	684000	1846.8	1385.1	20	40	50%	50%	2.00	346.275
Grenada	1.8	2000	3.6	2.7	99	148.5	50%	100%	1.50	1.35
Guadeloupe * ^ ˜	2	6814	13.628	10.221	50	0	0%	0%	0.00	0
Guatemala	2.5	371000	927.5	695.625	57	61.56000245	50%	100%	1.08	347.8125
Guinea	2.7	384000	1036.8	777.6	21	54.599998	50%	100%	2.60	388.8
Guinea-Bissau	2.7	56000	151.2	113.4	27	70.19999743	50%	0%	2.60	0
Guyana	2	13000	26	19.5	104	156	100%	100%	1.50	19.5
Haiti	1.8	240000	432	324	77	115.5	50%	100%	1.50	162
Honduras	2.5	205000	512.5	384.375	58	104.3999972	50%	100%	1.80	192.1875
Hungary	2.8	97000	271.6	203.7	198	0	0%	0%	0.00	0
India	4.7	25034000	117659.8	88244.85	123	184.5	100%	2%	1.50	1764.897
Indonesia	0.7	4483000	3138.1	2353.575	38	76	50%	100%	2.00	1176.7875
Iran	2	1425000	2850	2137.5	364	546	100%	100%	1.50	2137.5
Iraq ^	1.8	873000	1571.4	1178.55	364	0	0%	0%	0.00	0
Ireland "	2	76000	152	114	177	265.5	100%	30%	1.50	34.2
Israel	1.4	143000	200.2	150.15	242	363	100%	100%	1.50	150.15
Jamaica	1.8	55000	99	74.25	140	210	100%	100%	1.50	74.25
Jordan	3.3	173000	570.9	428.175	142	213	100%	70%	1.50	299.7225
Kazakhstan	2	258000	516	387	261	391.5	100%	50%	1.50	193.5
Kenya	1.3	1407000	1829.1	1371.825	47	0	50%	0%	0.00	0
Kuwait	1.2	55000	66	49.5	169	253.5	100%	100%	1.50	49.5
Kyrgyzstan	2	130000	260	195	433	649.5	100%	40%	1.50	78
Laos * ^	2	169000	338	253.5	18	0	0%	0%	0.00	0
Lesotho	2.3	52000	119.6	89.7	87	124.4099954	50%	100%	1.43	44.85
Malawi	1.3	638000	829.4	622.05	25	51.49999857	50%	10%	2.06	31.1025

Malaysia	1.9	605000	1149.5	862.125	86	129	50%	20%	1.50	86.2125
Mali	2.7	636000	1717.2	1287.9	16	41.59999847	50%	100%	2.60	643.95
Mauritania	2.7	108000	291.6	218.7	247	642.1999764	100%	0%	2.60	0
Mexico	2.5	2181000	5452.5	4089.375	67	134	50%	100%	2.00	2044.6875
Mongolia	1.3	65000	84.5	63.375	223	334.5	100%	11%	1.50	6.97125
Morocco	2.2	614000	1350.8	1013.1	332	498	100%	50%	1.50	506.55
Nepal	4.7	649000	3050.3	2287.725	87	130.5	50%	20%	1.50	228.7725
New Zealand "	1.7	59000	100.3	75.225	144	288	100%	0%	2.00	0
Nicaragua	2.5	111000	277.5	208.125	47	84.59999776	50%	100%	1.80	104.0625
Niger	2.7	811000	2189.7	1642.275	13	33.79999876	50%	0%	2.60	0
Oman	1.2	71000	85.2	63.9	180	270	100%	100%	1.50	63.9
Pakistan	2	4665000	9330	6997.5	247	370.5	100%	25%	1.50	1749.375
Palestine, Occupied Territory ~	5.5	63084	346.962	260.2215	207	207	100%	70%	1.00	182.15505
Panama	2.5	67000	167.5	125.625	73	131.3999965	50%	100%	1.80	62.8125
Paraguay	2	113000	226	169.5	35	105	50%	100%	3.00	84.75
Peru	2	570000	1140	855	92	110.4000044	50%	100%	1.20	427.5
Poland	2.7	386000	1042.2	781.65	220	0	0%	0%	0.00	0
Puerto Rico * ^	2	45000	90	67.5	150	225	100%	0%	1.50	0
Qatar	1.2	13000	15.6	11.7	180	270	100%	100%	1.50	11.7
Romania	2.5	210000	525	393.75	270	405	100%	0%	1.50	0
Russian Federation	2.5	1549000	3872.5	2904.375	257	102.8000015	50%	0%	0.40	0
Saint Vincent	1.8	2000	3.6	2.7	148	222	100%	100%	1.50	2.7
Saudi Arabia	1.2	500000	600	450	165	247.5	100%	100%	1.50	450
Senegal	2.7	459000	1239.3	929.475	52	135.199995	50%	100%	2.60	464.7375
South Africa	2.3	963000	2214.9	1661.175	121	181.5	100%	100%	1.50	1661.175
Sudan	2.2	1607000	3535.4	2651.55	90	135	50%	35%	1.50	464.02125
Swaziland "	2.3	37000	85.1	63.825	65	0	0%	0%	0.00	0
Syria	1.8	543000	977.4	733.05	308	462	100%	0%	1.50	0
Taiwan * ^	1	207000	207	155.25	118	177	100%	0%	1.50	0
Tajikistan	2	198000	396	297	258	387	100%	71%	1.50	210.87
Tanzania ^	1.3	1401000	1821.3	1365.975	47	0	0%	0%	0.00	0

Togo	2.7	236000	637.2	477.9	35	90.99999666	50%	100%	2.60	238.95
Turkey [f]	3	1422000	4266	3199.5	371	0	0%	0%	0.00	0
Turkmenistan	2	97000	194	145.5	412	618	100%	60%	1.50	87.3
Uganda	1.3	1588000	2064.4	1548.3	11	27.71999979	50%	50%	2.52	387.075
Ukraine	2.1	437000	917.7	688.275	253	556.6000121	100%	20%	2.20	137.655
United Arab Emirates	1.2	80000	96	72	188	282	100%	100%	1.50	72
United States	1.4	4291000	6007.4	4505.55	150	209.9999964	100%	100%	1.40	4505.55
Uruguay	1	45000	45	33.75	182	436.8000174	100%	100%	2.40	33.75
Uzbekistan	2	488000	976	732	298	298	100%	40%	1.00	292.8
Vietnam	1.9	1549000	2943.1	2207.325	18	36	50%	15%	2.00	165.54938
Yemen	1.2	808000	969.6	727.2	225	360.0000054	100%	100%	1.60	727.2
Brazil (maize flour)	1.9	3642000	6919.8	5189.85	46	69	50%	100%	1.50	2594.925
Costa Rica (maize flour)	0.5	75000	37.5	28.125	9	11.7	50%	100%	1.30	14.0625
Dominican Republic (maize flour)	1.8	195000	351	263.25	23	35.42	50%	100%	1.54	131.625
Mexico (maize flour)	2.5	2181000	5452.5	4089.375	268	107.2	50%	100%	0.40	2044.6875
South Africa (maize flour)	2.3	963000	2214.9	1661.175	237	474	100%	100%	2.00	1661.175
Uganda (maize flour)	1.3	1588000	2064.4	1548.3	66	66	50%	50%	1.00	387.075
United States (maize flour)	1.4	4291000	6007.4	4505.55	25	38.5	50%	100%	1.54	2252.775
Zambia (maize flour)	1.3	601000	781.3	585.975	276	110.4	50%	60%	0.40	175.7925

Total births	Total NTDs	Total prevented
103917898	270167.29	45337.902

FAPSBA	**% FAPSBA prevented**
202625.468	**22.38%**

Table 1 and Table 2 Key:

α: 2006 March of Dimes report.

β: US Census estimates, 2010.

γ: Calculated from NTD prevalences in 2006 March of Dimes report and US Census estimates of births in 2010.

δ: Assumed to be 75% of annual NTD prevalence in population that does not consume folic acid.

λ: From Food Balance Sheets, 2002-FAO does not have more recent estimates.

π: Calculated from grams of wheat x fortification levels for wheat flour and grams of maize flour x fortification level for maize.

σ: Prevention percentage: % annual NTDs prevented through flour fortificaiton, as function of folic acid consumption and prefortification annual estimate of NTDs, using model in this article.

ψ: FFI estimates and personal communication with Quentin Johnson, 03/13/2011

ϕ: FFI estimates.

τ: # of NTDs prevented by wheat/maize flour fortification, calculated as product of folic acid-preventable NTD estimate x prevention percentage x program coverage.

*: NTD prevalence not in MOD 2006 report, values based on neighboring country data.

^: Daily grams fortified flour consumed not in2002 Food Balance Sheets; values adapted from neighboring country.

~: Birth estimates not in US census data, estimated from another source.

": Program coverage from alternate source.

Figure 1:

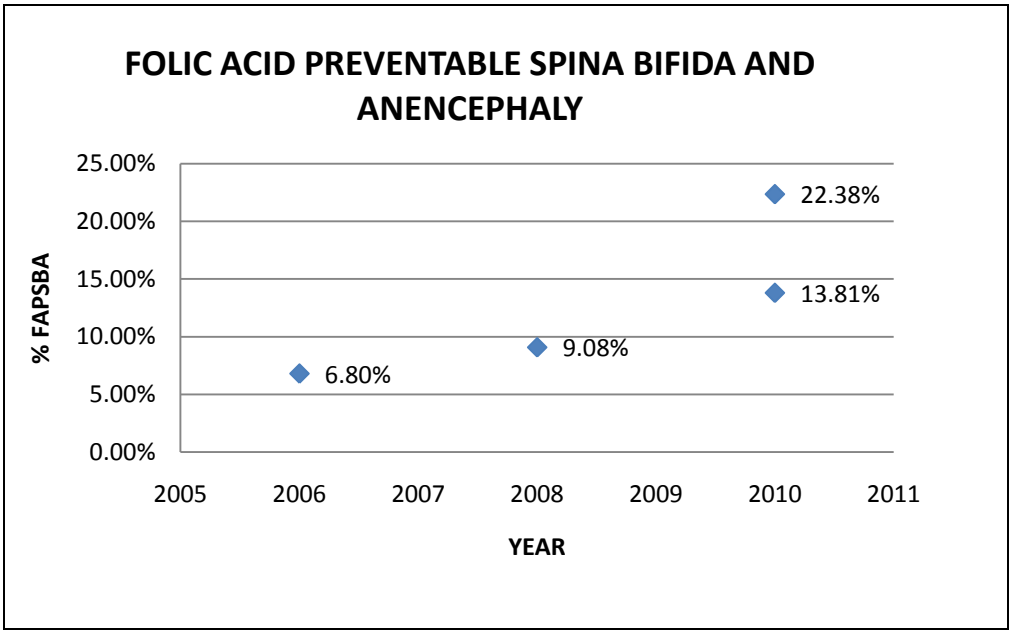

Figure 2: