

# PUBLIC HEALTH GRAND ROUNDS

Office of the Director

**February 18, 2010**



Office of The Director



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PUBLIC HEALTH GRAND ROUNDS



Grand Rounds

The Public Health Grand Rounds is a monthly series created to further strengthen CDC's common scientific culture and foster discussion and debate on major public health issues. Each session of the Public Health Grand Rounds will focus on key issues and challenges related to a specific health topic, including cutting-edge scientific evidence and potential impact of different interventions. The sessions will also highlight how CDC is already addressing these challenges and discuss the recommendations for future research and practice.

Grand Rounds sessions are typically held on the third Thursday of every month at Roybal's Global Communications Center, Auditorium A, between 9-10 a.m. For those unable to attend, the sessions will be available on [CDC IPTV](#).

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A-Z Index A B C D E F G H I J K L M N O P Q R S T U V W X Y Z #

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PUBLIC HEALTH GRAND ROUNDS

Grand Rounds

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CIGARETTES

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IPTV link also available on Grand Rounds [intranet](#) site:

<http://intranet.cdc.gov/od/odweb/about/directorGrandRounds.htm>

For those outside of CDC, a broadband link is available at:

<http://www.cdc.gov/about/grand-rounds> (Grand Rounds [internet](#) site)



# PHGR January 21: 4,404 External Viewers!



# Continuing Education Credits



As of January 2010

Credit Hours are available for:

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- ❑ Nurses (CNE)
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# Knowledge to Action Science Clips

Wednesday, February 17, 2010  
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**Public Health Library  
& Information Center**

**CDC Knowledge to Action Science Clips: February 8 - February 12, 2010**  
Vol. 2, Issue: 7

Previous Issues:  
Volume 1: [Issue 1](#), [Issue 2](#), [Issue 3](#), [Issue 4](#), [Issue 5](#), [Issue 6](#), [Issue 7](#), [Issue 8](#), [Issue 9](#), [Issue 10](#), [Issue 11](#), [Issue 12](#), [Issue 13](#), [Issue 14](#), [Issue 15](#), [Issue 16](#), [Issue 17](#), [Issue 18](#), [Issue 19](#)

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Welcome to Knowledge to Action Science Clips, CDC's new weekly digest!

**Selection of  
NTD and  
folic acid-related articles:  
RJ Berry (NCBDDD)**

## Maternal and Child Health - Folic Acid

70. Central nervous system congenital malformations in a developing country: issues and challenges against their prevention  
Adeleye AO, Dairo MD, Olowookere KG.  
Childs Nerv Syst. 2010 Jan 21.  
[+]Show Abstract
71. [Protective effect of periconceptional folic acid supplements on the risk of congenital heart defects: a registry-based case-control study in the northern Netherlands](#)  
van Beynum IM, Kapusta L, Bakker MK, den Heijer M, Blom HJ, de Walle HE.  
Eur Heart J. 2009 Dec 1.  
[+]Show Abstract
72. [Prevalence and predictors of periconceptional folic acid uptake—prospective cohort study in an Irish urban obstetric population](#)  
McGuire M, Cleary B, Sahm L, Murphy DJ.  
Hum Reprod. 2010 Feb;25(2):535-43.  
[+]Show Abstract
73. [Multivitamin use among non-pregnant females of childbearing age in the Western North Carolina multivitamin distribution program](#)  
Morgan LM, Major JL, Meyer RE, Mullenix A.  
N C Med J. 2009 Sep-Oct;70(5):386-90.  
[+]Show Abstract
74. [Cost-effectiveness of mandatory folate fortification v. other options for the prevention of neural tube defects: results from Australia and New Zealand](#)  
Dalziel K, Segal L, Katz R.  
Public Health Nutr. 2009 Sep 17:1-13.  
[+]Show Abstract

# Stay Tuned



- Mar 18** Radiological and Nuclear Preparedness
- Apr 15** Preventing Health Effects from Nanotechnology
- May 20** Chlamydia Prevention and Control
- June 17** Obesity



The Public Health Grand Rounds email address:  
[grandrounds@cdc.gov](mailto:grandrounds@cdc.gov)



# Factors that Affect Health

*Smallest  
Impact*

**Counseling  
& Education**

**Examples**

Eat healthy, be physically active

**Clinical  
Interventions**

Rx for high blood pressure, high cholesterol, diabetes

**Long-lasting  
Protective Interventions**

Immunizations, brief intervention, cessation treatment, colonoscopy

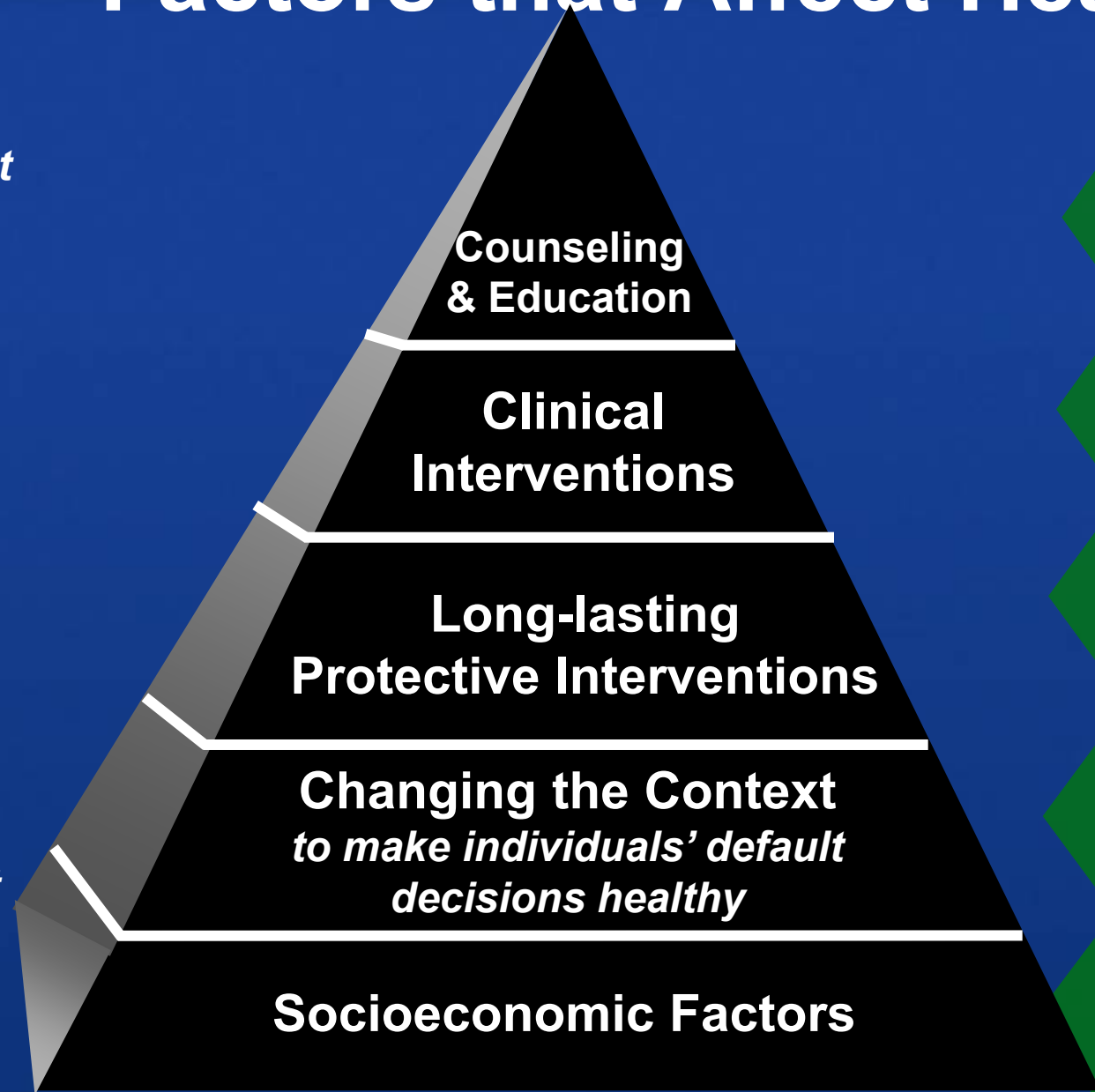
**Changing the Context  
to make individuals' default  
decisions healthy**

Fluoridation, 0g trans fat, folic acid fortification, iodization, smoke-free laws, tobacco tax

**Socioeconomic Factors**

Poverty, education, housing, inequality

*Largest  
Impact*



# The Prevention of Neural Tube Defects and Folic Acid Fortification



**National Center on Birth Defects and Developmental Disabilities  
NCBDDD**



# Outline

- ❑ Joe Mulinare, MD, MSPH
  - ***Prevention of Neural Tube Defects – the Scope of the Problem***
- ❑ William Dietz, MD, PhD
  - ***Global Strategies and Efforts to Reduce the Burden of Neural Tube Defects Worldwide***
- ❑ Richard B. Johnston, Jr., MD
  - ***Can Intake of Folic Acid Cause Harm? What Does the Evidence Show?***
- ❑ Jessica Leighton, PhD, MPH
  - ***Folic Acid Fortification. Next Steps: Fortification of Corn Masa Flour?***

# PREVENTION OF NEURAL TUBE DEFECTS - THE SCOPE OF THE PROBLEM



**Joe Mulinare MD, MSPH**  
*Prevention Research Team Lead*  
**National Center on Birth Defects and Developmental Disabilities**  
**NCBDDD**

# PREVENTION OF NEURAL TUBE DEFECTS - THE SCOPE OF THE PROBLEM

- ❑ **Neural tube defects (NTDs)**
- ❑ **Evidence-base for folic acid use and prevention of NTDs**
- ❑ **Strategies to achieve effective folic acid levels**
- ❑ **Impact of folic acid use to reduce the prevalence of NTDs**
- ❑ **Existing challenges**
  - Targeting higher risk populations
  - Achieving global efforts of fortification

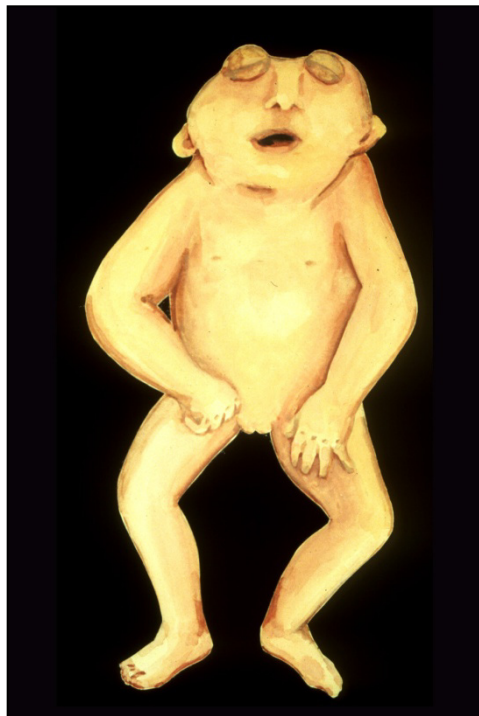
# PREVENTION OF NEURAL TUBE DEFECTS - THE SCOPE OF THE PROBLEM

## □ Neural tube defects (NTDs)

- Evidence-base for folic acid use and prevention of NTDs
- Strategies to achieve effective folic acid levels
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# Anencephaly and Spina bifida

## Embryo Development 22 - 28 Days of Gestation



Anencephaly



Spina bifida



# Neural Tube Defect Facts

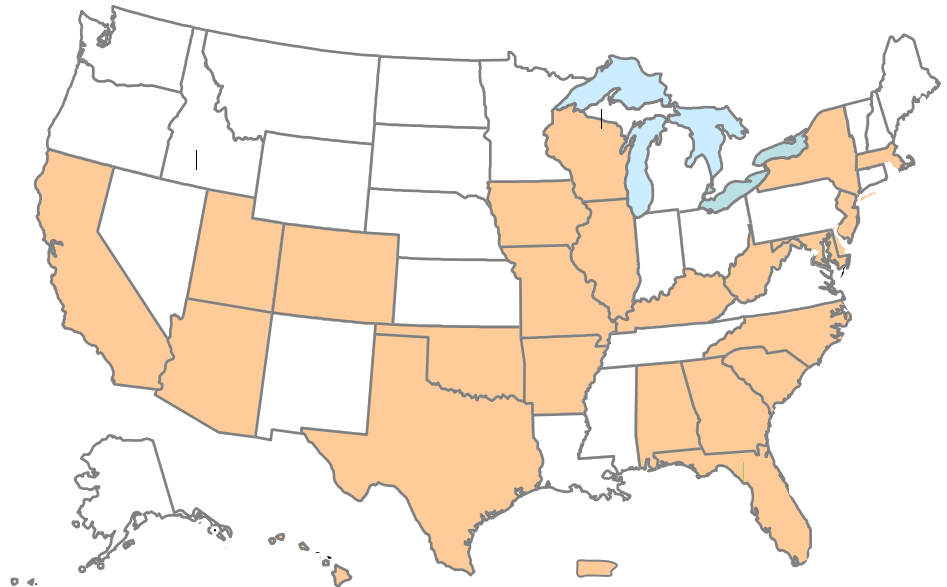
- ❑ **NTDs develop in 1<sup>st</sup> month after conception**
- ❑ **>50% of all pregnancies in the United States are unplanned**
- ❑ **Research studies on folic acid have shown that 50% to 70% of NTDs are preventable**
- ❑ **To prevent NTDs, it is recommended that all women capable of becoming pregnant consume at least 400 µg folic acid daily**

# Impact of Folic Acid Fortification

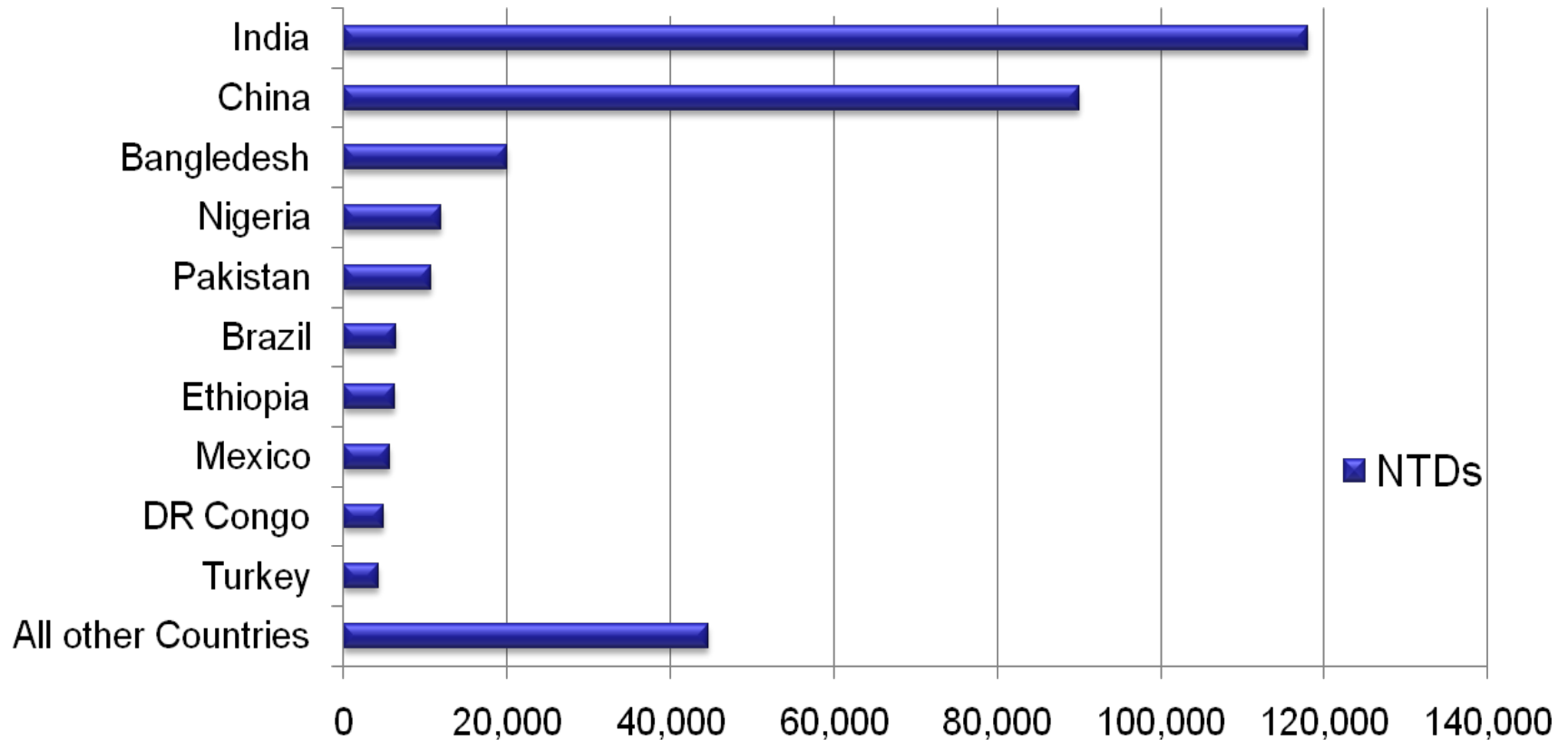
## 25 States, National Birth Defects Prevention Network

- ❑ Before folic acid fortification of cereal grain products, there were about 4,000 pregnancies with NTDs/year
- ❑ Since fortification began in January 1998, that number has decreased to about 3,000 affected pregnancies
- ❑ Since fortification began, NTDs have been prevented in more than 12,000 babies

States with NTD surveillance programs



# Neural Tube Defect Surveillance Worldwide 2006





# PREVENTION OF NEURAL TUBE DEFECTS - THE SCOPE OF THE PROBLEM

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# What Is Folate or Folic Acid?

- ❑ **Folate is generic term for 2 different forms of vitamin B9**
  - **Naturally occurring food folate** - polyglutamate form
    - Legumes, beef liver, green leafy vegetables, some fruits, whole grains
  - **Synthetic folic acid** - monoglutamate form
    - Enriched cereal grain products - breads, pasta, rice, etc.
    - Ready-to-eat cereals
    - Supplements
- ❑ **Folic acid is about 2x more bioavailable than food folate**

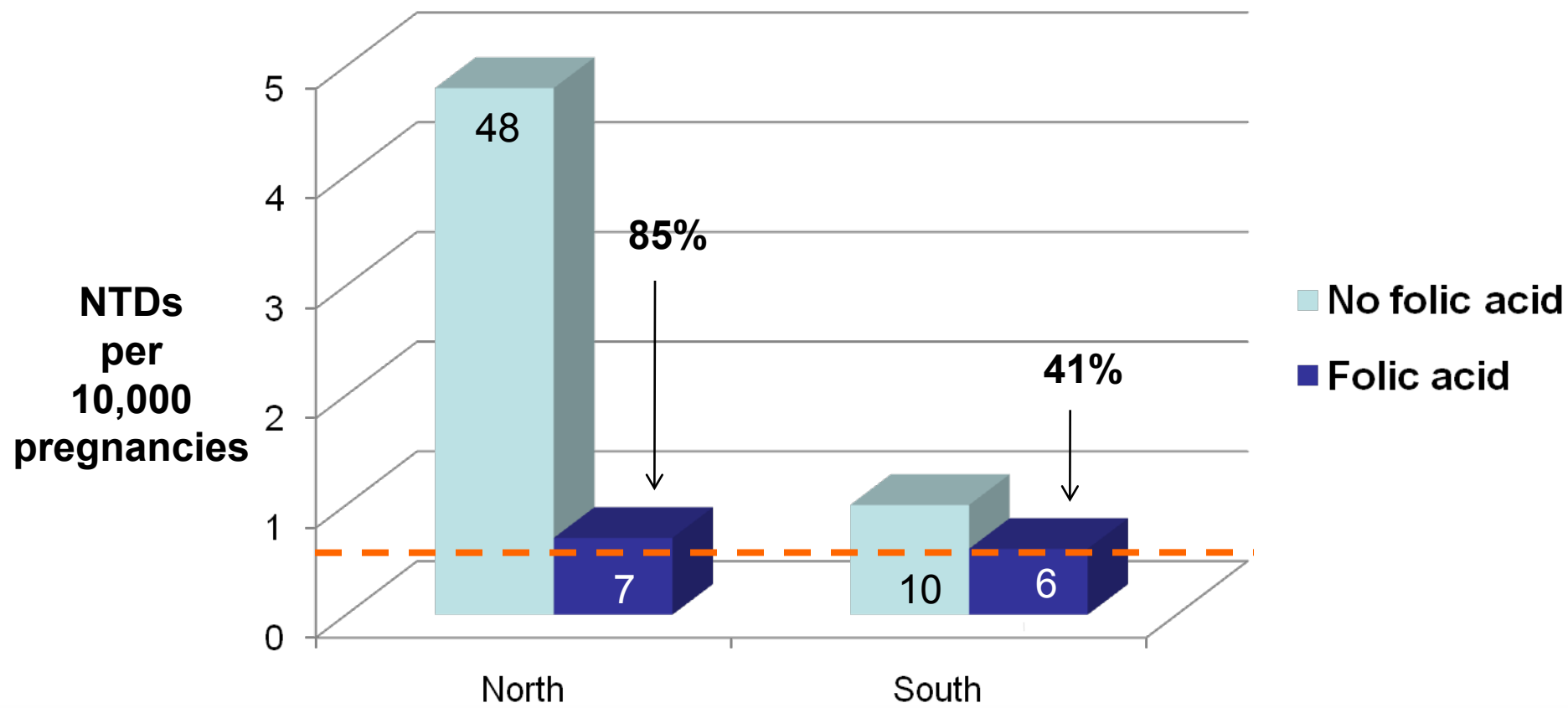
# Scientific Evidence for Prevention of NTDs

## NTD Studies, 1980-1999

Studies	Percentage NTD Reduction
1980 – England	86%
1981 – S. Wales	59%
1988 – Atlanta	60%
1989 – W. Australia	70%
1989 – California / Illinois	7%
1989 – Boston	65%
1990 – Cuba	100%
1991 – UK and Other Countries	71%
1992 – Hungary	100%
1993 – New England	60%
1995 – Ireland	80%
1999 – China	79%

# Periconceptional Folic Acid Community Trial to Prevent NTDs, China, 1993 – 1996

**Intervention = 400 µg Daily Folic Acid Supplement Alone**



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# Approaches to Increase Folate/Folic Acid Intake



**Diet...natural foods,  
vegetables, fruits, beans,  
yeast, liver**



**Pills... folic acid-containing  
dietary supplements**



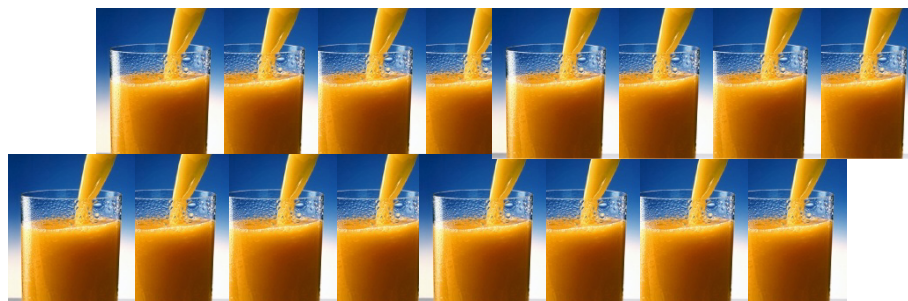
**Fortification ... folic  
acid added to foods -  
flour, rice, pasta,  
breakfast cereals**



# Are You Hungry?

## Daily Intake Equivalent of 400 µg of Folic Acid

- ❑ 4 slices of fried beef liver
- ❑ 44½ medium ripe tomatoes
- ❑ 14½ cups of raw broccoli
- ❑ 17½ cups of orange juice
- ❑ 19½ cups of raw green beans
- ❑ 5½ cups of black beans
- ❑ 200 medium red apples



# Folic Acid and Dietary Folate Consumption Study

## Mean Red Cell Folate Results, Ireland 1996

Intervention Approach	Mean Red Blood Cell Folate Percent Change
Controls	+ 5%
Dietary Advice	+16%
Dietary Food Folates 400 µg Folate	+11%
Supplements 400 µg Folic Acid	+40%
Fortified Foods 400 µg Folic Acid	+52%

Cuskelly et al., Lancet; 1996.





# Science-based Policy-making: USPHS, IOM, and FDA

## Folic Acid and Neural Tube Prevention

- ❑ **1992 - US Public Health Service recommendation:** improve dietary habits, take a daily folic acid supplement, consume folic acid-fortified foods
- ❑ **1996 - FDA regulation:** all enriched cereal grain flour and products must be fortified with folic acid (140  $\mu\text{g}/100\text{g}$ )
- ❑ **1998 - Institute of Medicine recommendation:** 400  $\mu\text{g}$  folic acid from fortified foods, supplements, or both in addition to consuming food folate from a varied diet

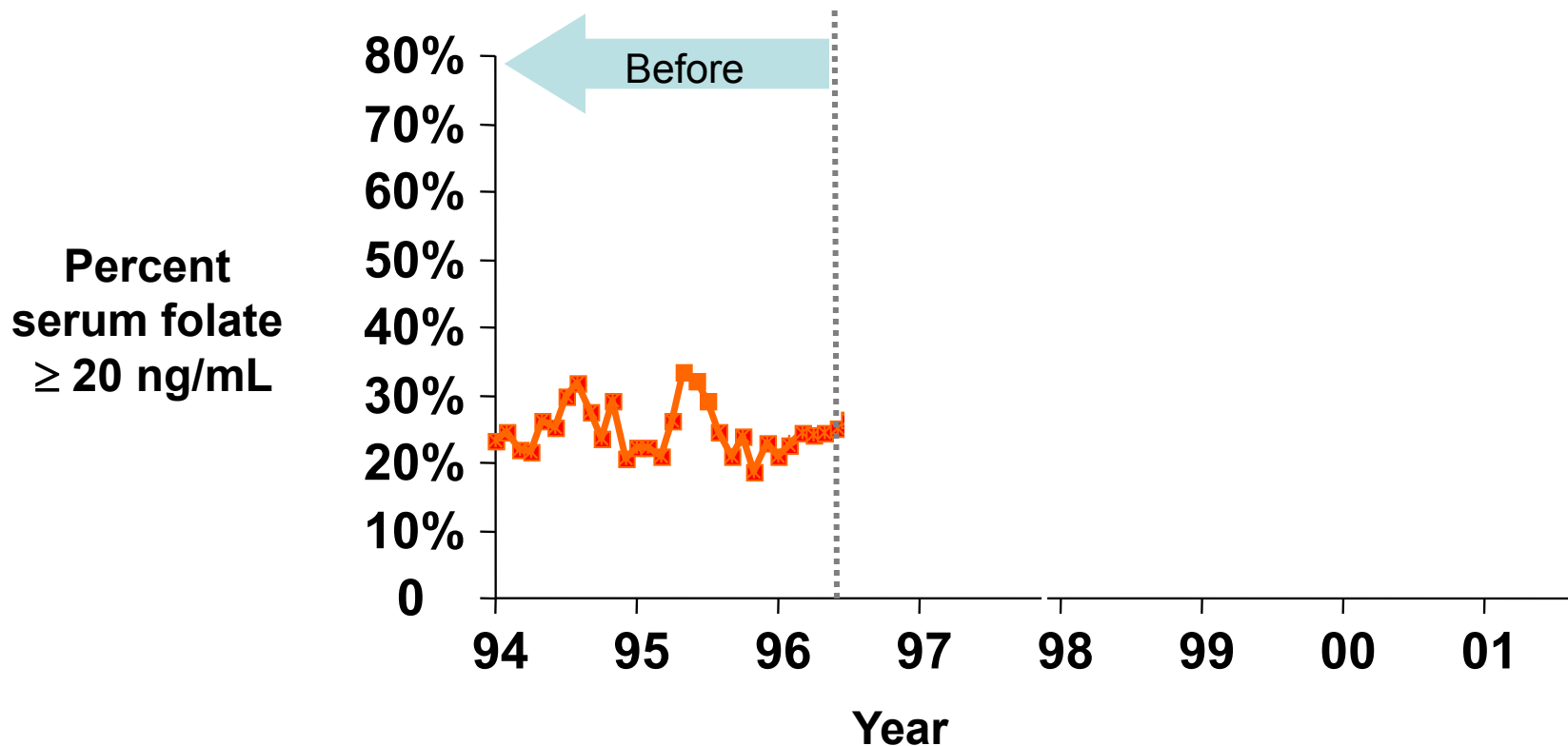
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# Serum Folate Concentrations ( $\geq 20$ ng/mL) Before and After Fortification

Kaiser Permanente Southern California, 1994-2001



Lawrence JM, Petitti DB, Watkins M, Umekubo MA. Lancet 1999;354:915-6.

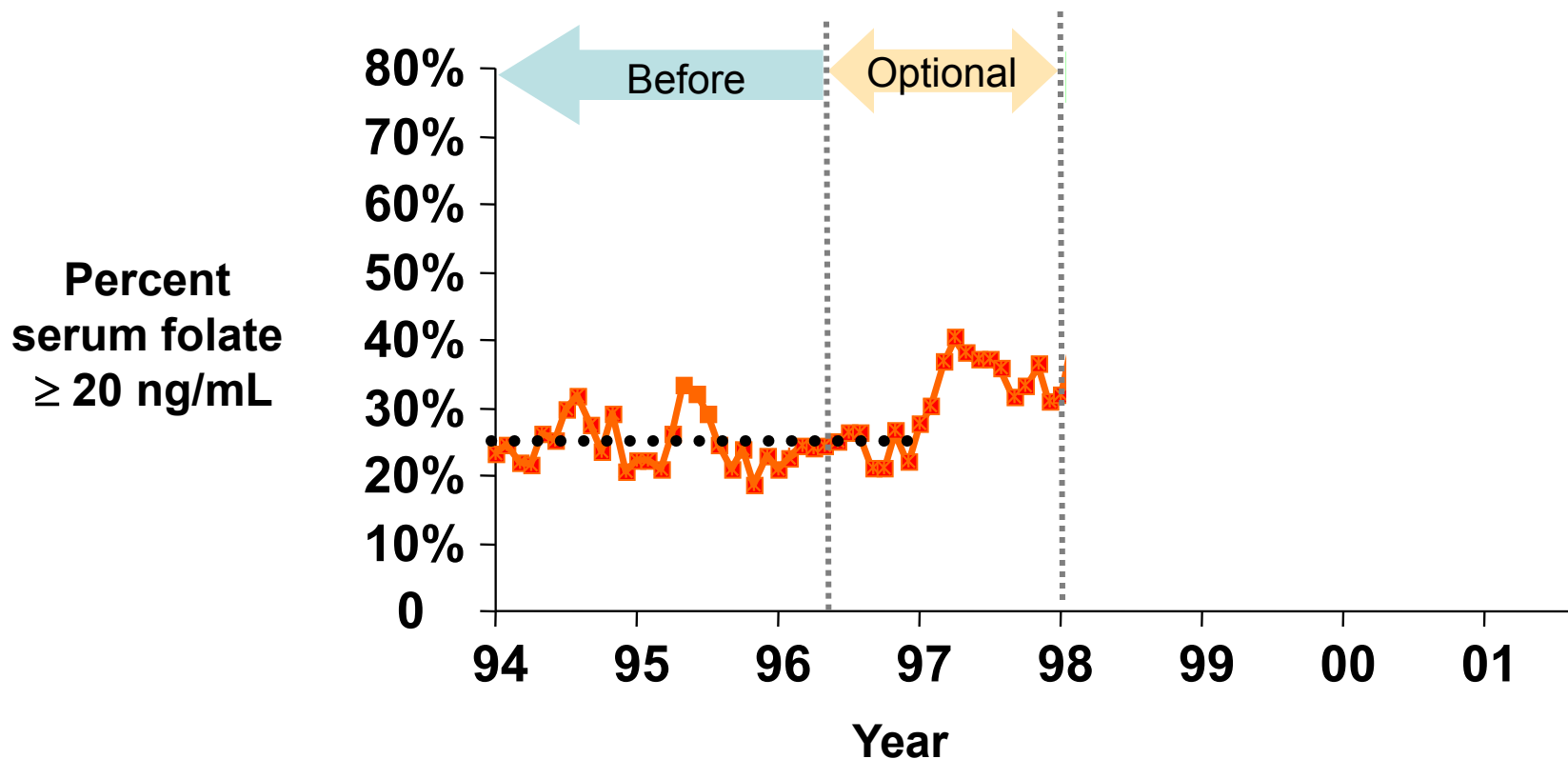
Lawrence JM, Chiu V, Petitti DB. NEJM 2000; 343: 970.

Data for 2000 and 2001 added since publication Data for 2001 is Jan-Sep, 2001. (12/4/01)



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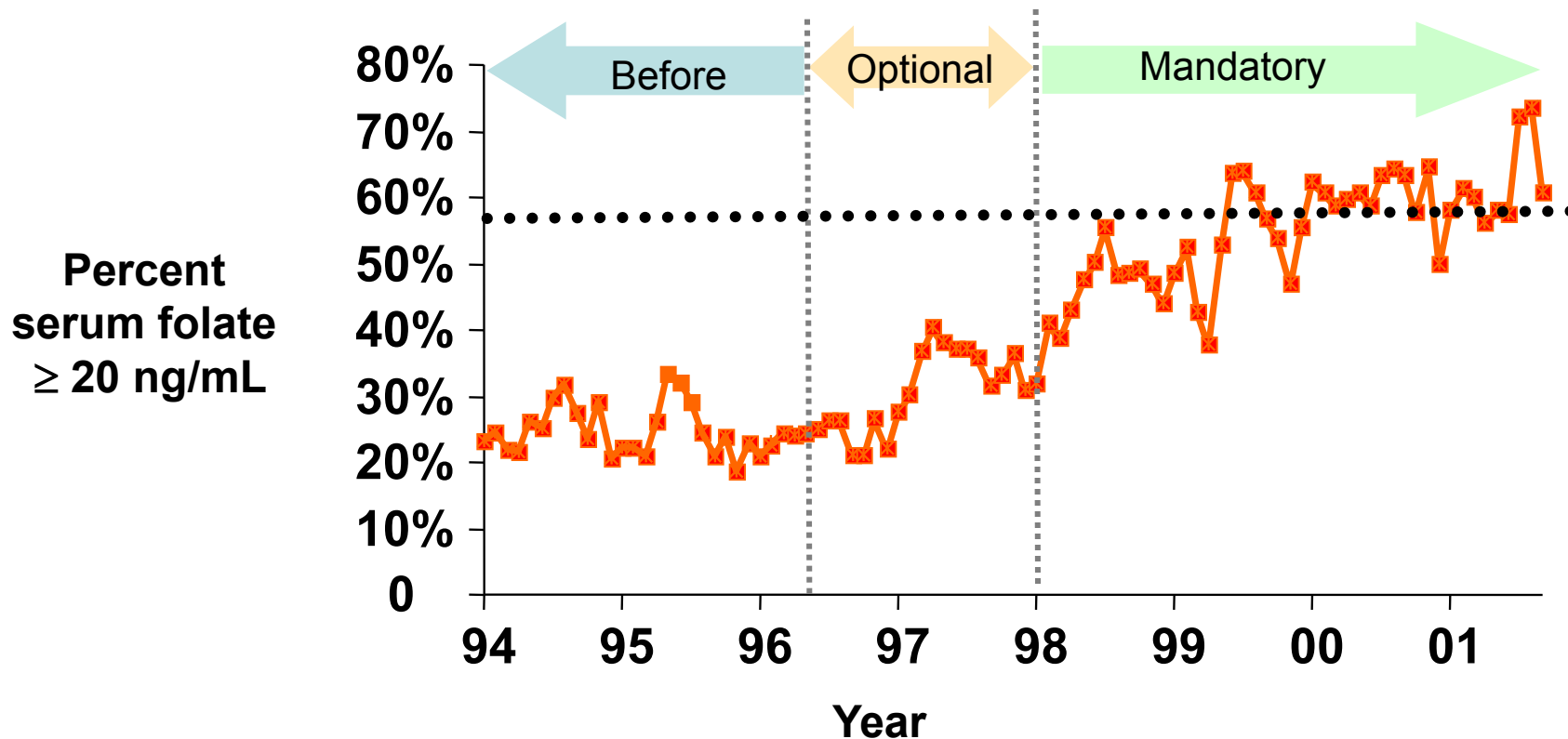
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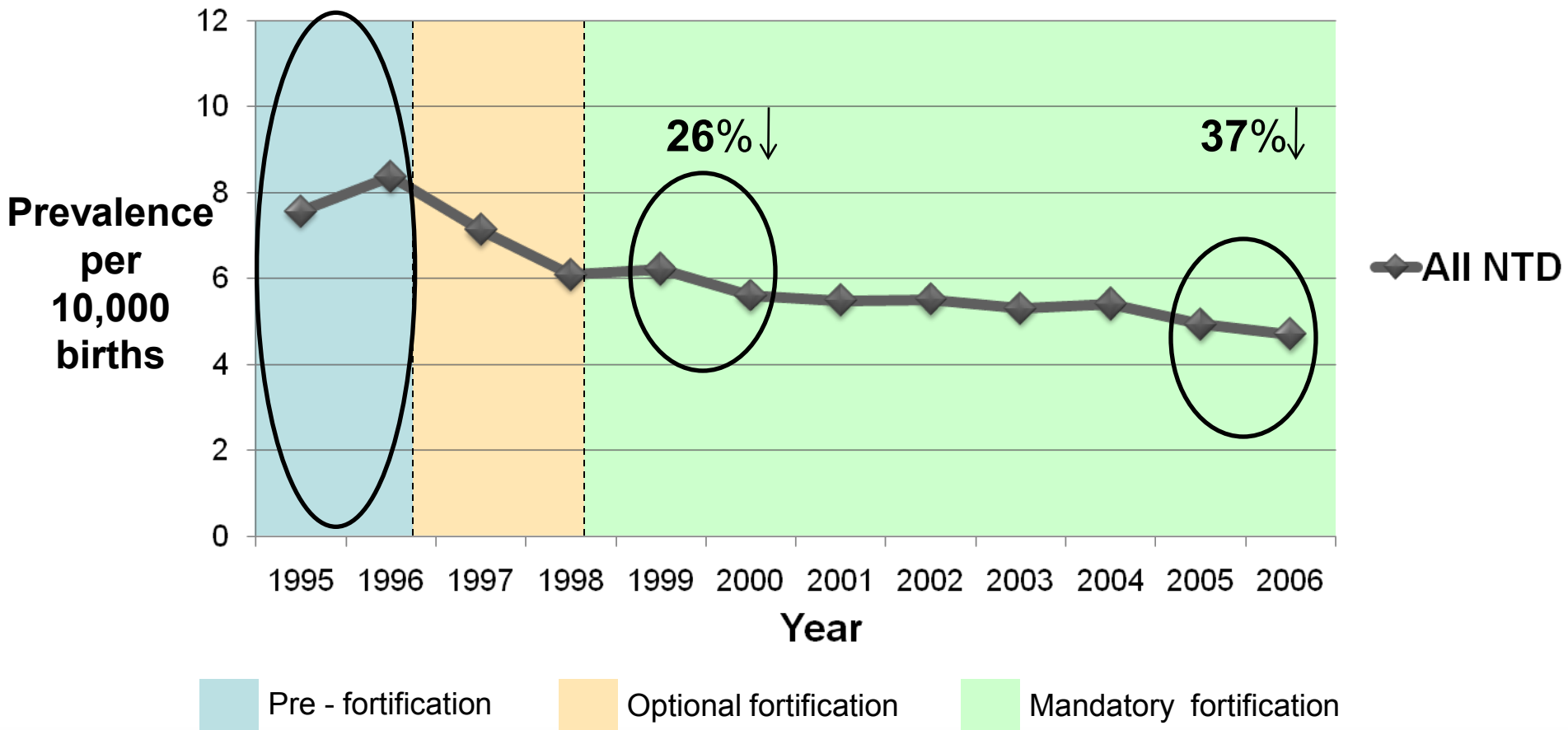




# NTD Prevalence by Fortification Status

## 25 States, National Birth Defects Prevention Network

### 1995-2006



# Economic Evaluation of Folic Acid Fortification in the United States

- ❑ Through 2006, 37% reduction in NTDs
- ❑ Program costs
  - Fortification of flour: \$3 million/year
  - Direct cost averted: \$145 million/year
  - For every \$1 invested there are >\$45 in medical costs averted/year
- ❑ Lifetime medical costs per child with spina bifida are \$461,000

# PREVENTION OF NEURAL TUBE DEFECTS - THE SCOPE OF THE PROBLEM

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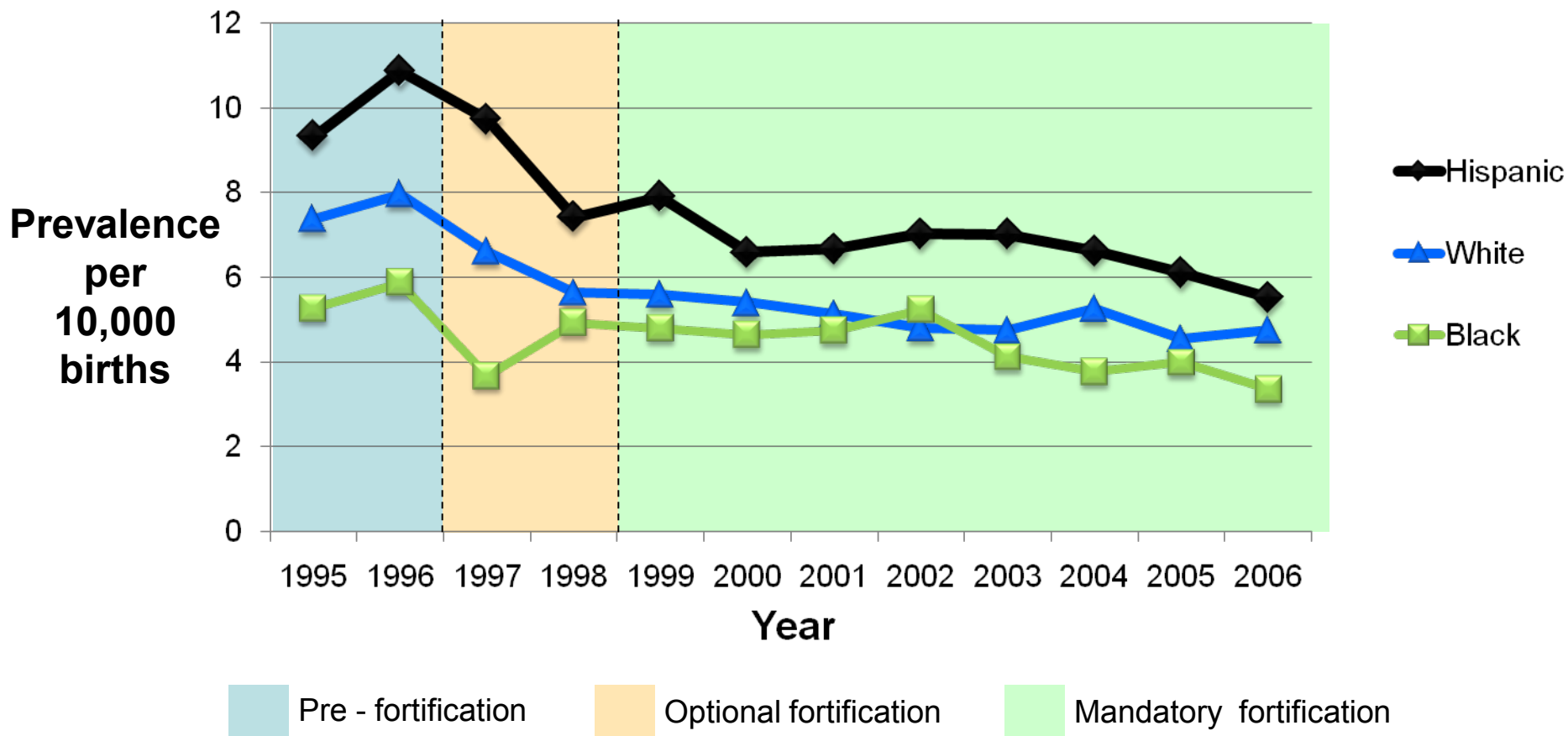


# Neural Tube Defects

## Other Risk Factors: 5%-10%

- ❑ Previous NTD-affected pregnancy
- ❑ Genetic variants
- ❑ Maternal diabetes
- ❑ Obesity
- ❑ Hyperthermia, fever
- ❑ Antiepileptic medications
- ❑ Lower socioeconomic status
- ❑ Race/ethnicity: Hispanic > white > black

# NTD Prevalence by Race, 25 States National Birth Defects Prevention Network 1995 - 2006



# Corn Masa Flour Fortification

## 2006 Annual Meeting National Council La Raza

- ❑ **Support for concept of fortified corn masa flour**
- ❑ **Partners**
  - National Council of La Raza
  - Wal-Mart Stores
  - Spina Bifida Association
  - Local and state partners
- ❑ **Gruma**, largest producer of corn masa flour in the United States expressed interest in fortification

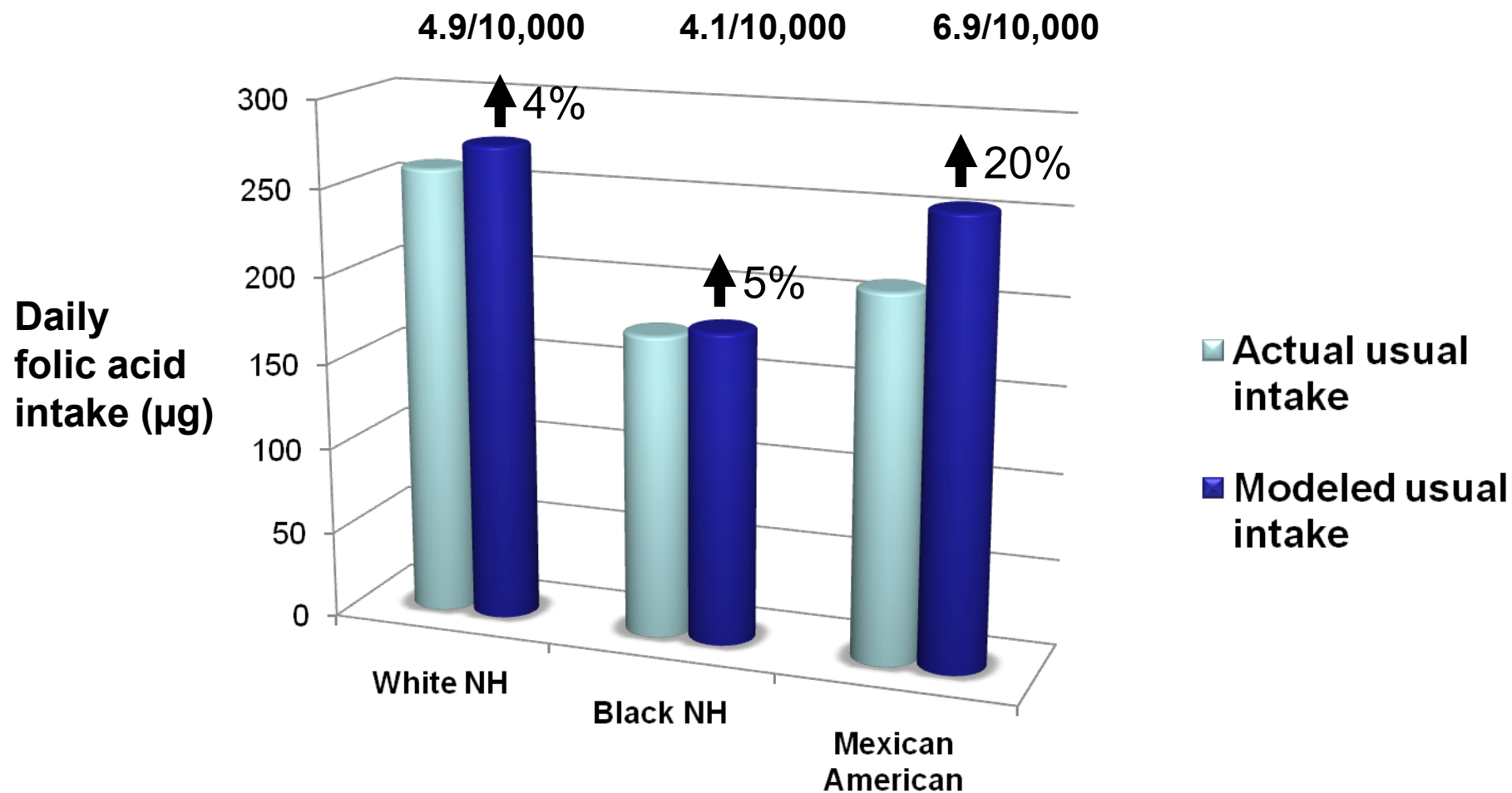


# Folic Acid Intake from Supplements and Corn Masa Flour

Women 15-44 yrs, NHANES 2001-2004

	Supplements	Corn Masa Flour
White Non-Hispanic	37%	23%
Black Non-Hispanic	15%	27%
Mexican-American	21%	60%

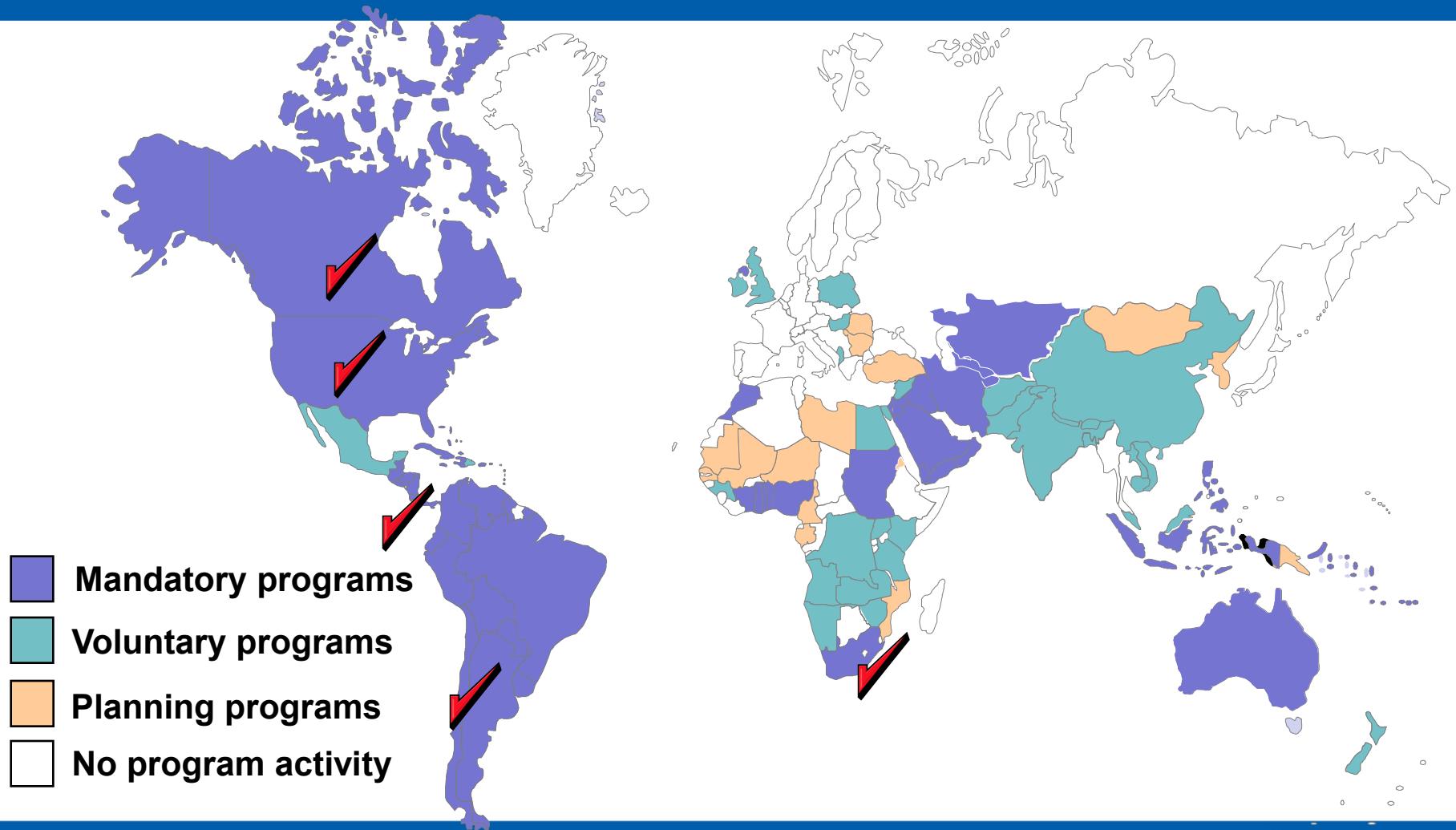
# Total Usual Daily Folic Acid Intakes Without (Actual) and With (Modeled) Folic Acid Fortification of Corn Masa Flour Women 15- 44 yrs, by Race/Ethnicity



Hamner H, AJCN 2009, Table 2  
NH, non-Hispanic



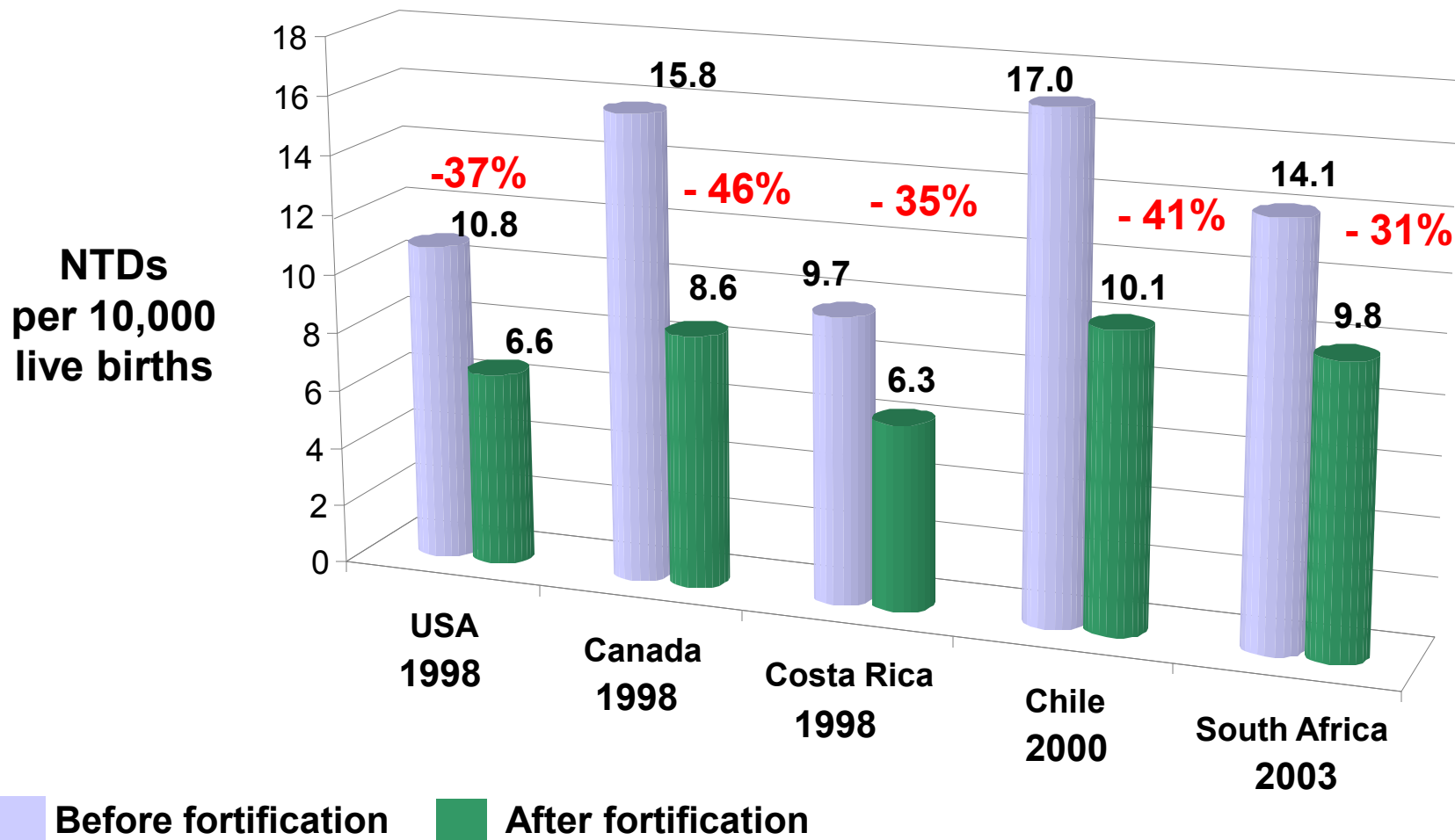
# Worldwide Wheat Flour Fortification Programs



Flour Fortification Initiative website, July 2009



# Global NTD Rate Changes Before and After Folic Acid Fortification



# Summary/Conclusions

- ❑ **NTDs are life-threatening and cause life-long disabilities**
- ❑ **50%-70% of NTDs can be prevented with 400 µg folic acid daily**
- ❑ **Fortification of foods with folic acid is a feasible, economical, safe, and effective public health policy to prevent neural tube defects worldwide**



# Remaining Challenges and Questions

**How will we know when we have eliminated all folic acid-preventable NTDs?**

- When all women reach a specified consumption or blood level?**
- When NTD rates stabilize at some specified level?**
- When we understand the underlying biology of NTD prevention?**

# Proposed Future Activities

## Global Focus

- ❑ **Partnerships**: Strengthen global partnerships to support mandatory folic acid fortification policies and programs
- ❑ **Monitoring and Evaluation**: Develop and improve surveillance and evaluation systems to assess program effectiveness
- ❑ **Communication**: Promote and sustain mandatory fortification programs
- ❑ **Research**: Expand science base for global mandatory folic acid fortification, include evaluation of studies related to adverse effects

# GLOBAL STRATEGIES AND EFFORTS TO REDUCE THE BURDEN OF NEURAL TUBE DEFECTS WORLDWIDE



**William Dietz, MD, PhD**  
*Director*

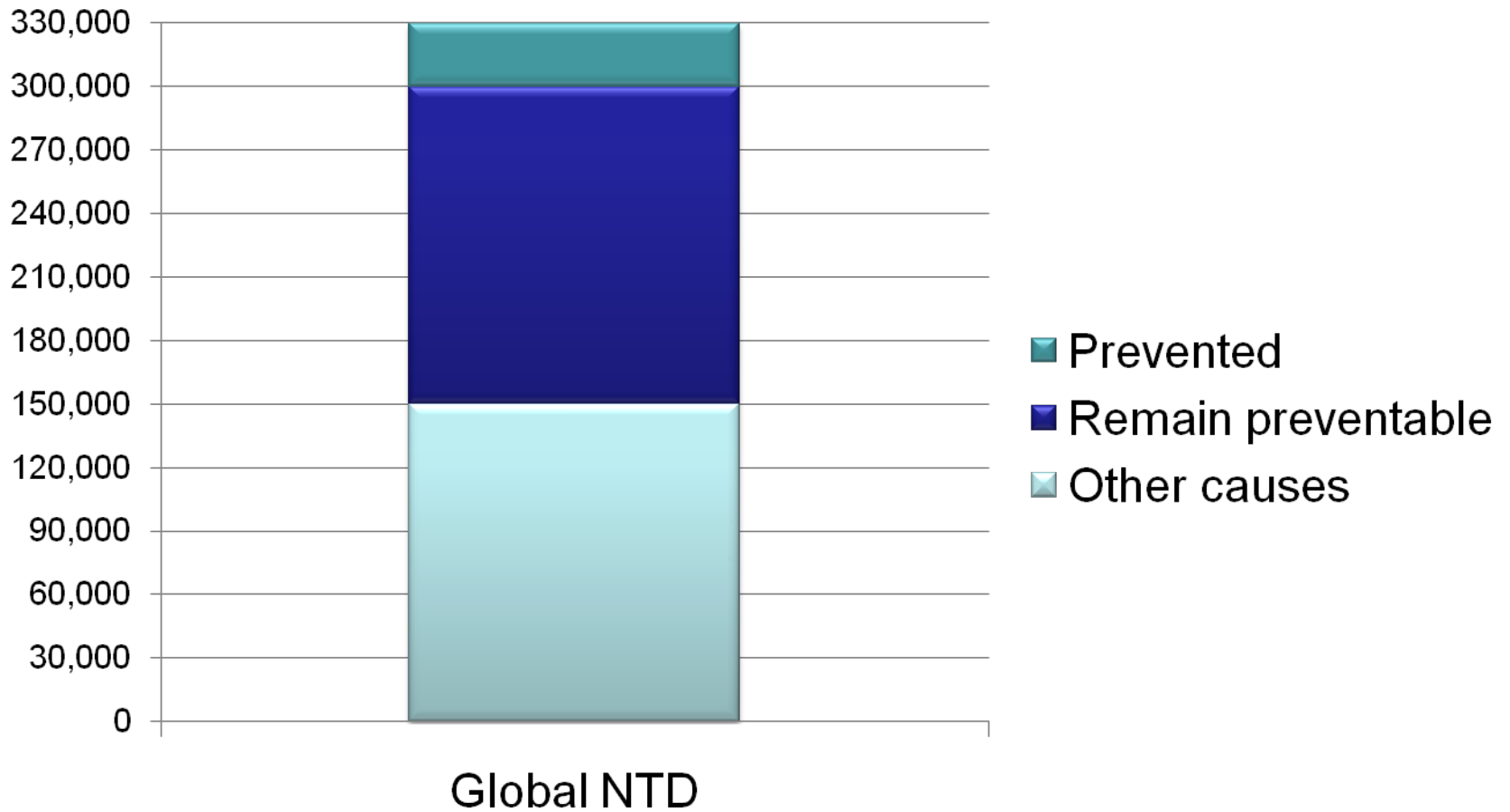
**Division of Nutrition, Physical Activity, and Obesity  
National Center for Chronic Disease Prevention  
and Health Promotion**



# Annual Burden Worldwide from Micronutrient Deficiencies

- ❑ 18,000,000 babies are born with impaired mental development due to iodine deficiency
- ❑ 1,100,000 children <5 years old die due to Vitamin A and Zn deficiency
- ❑ 350,000 children become blind due to Vitamin A deficiency
- ❑ 300,000 children are born with NTDs due to folic acid insufficiency
- ❑ 115,000 maternal deaths (20%) are associated with iron deficiency

# Folic Acid Preventable Neural Tube Defects in 2008



# Potential Impact

- ❑ **The 2008 Copenhagen Consensus concluded that nutrition interventions are 5 of the top 10 most cost-effective means to address global morbidity and mortality challenges**
- ❑ **More than 400 million tons of wheat is milled for human consumption every year.**

(Food and Agriculture Organization of the United Nations)



# Feasibility of Flour Fortification

- ❑ **Technology: simple and well established**
- ❑ **Economical: premix cost of adding iron and folic acid to flour**
  - Ferrous sulfate and folic acid: \$0.85-\$1.10/metric ton of flour



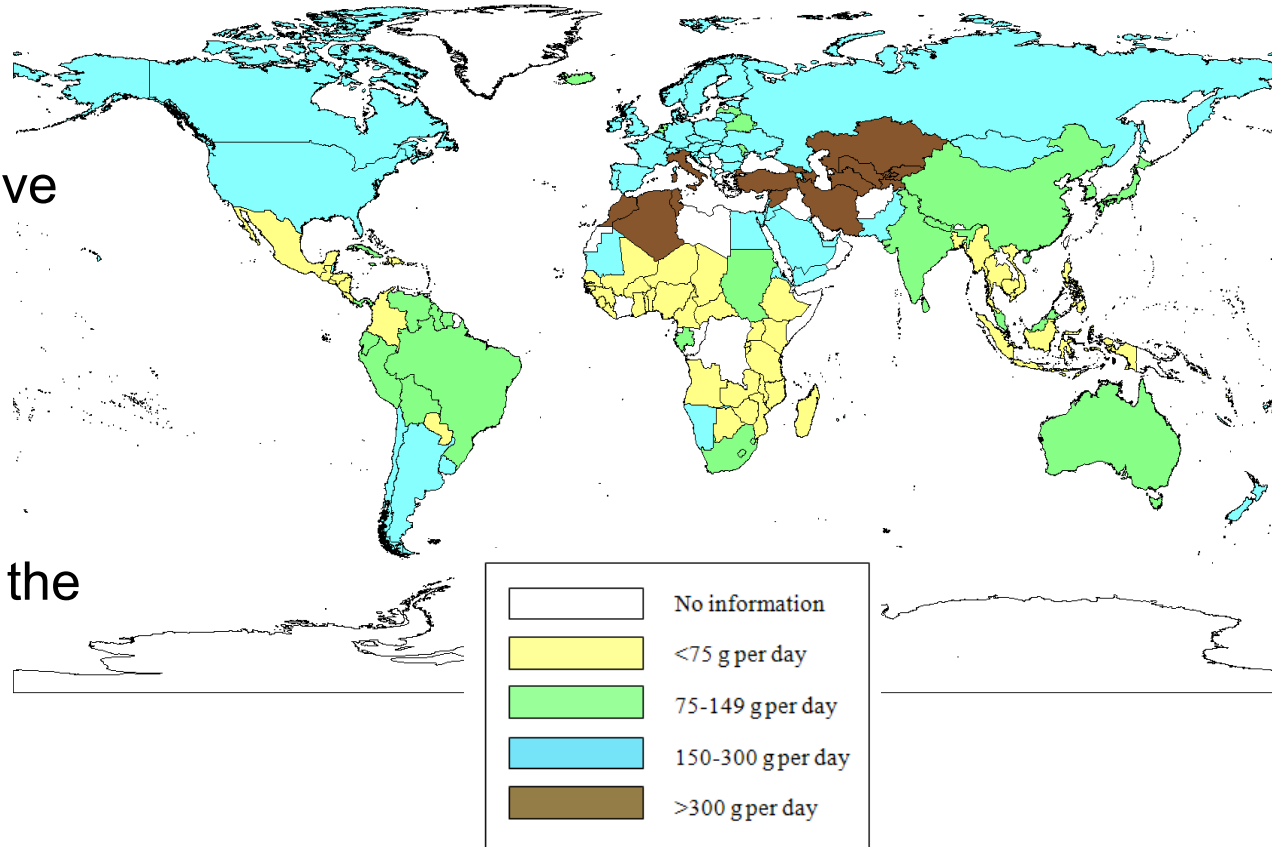
Modern high-through put milling facility

# Recommendations and Wheat Flour Consumption

## WHO recommendations on wheat and maize flour fortification:

Fortification likely to have an impact in countries where average flour consumption is  $\geq 75\text{g/person/day}$

## Wheat flour consumption: 80% of the world's population consumes on average $\geq 75\text{g/person/day}$







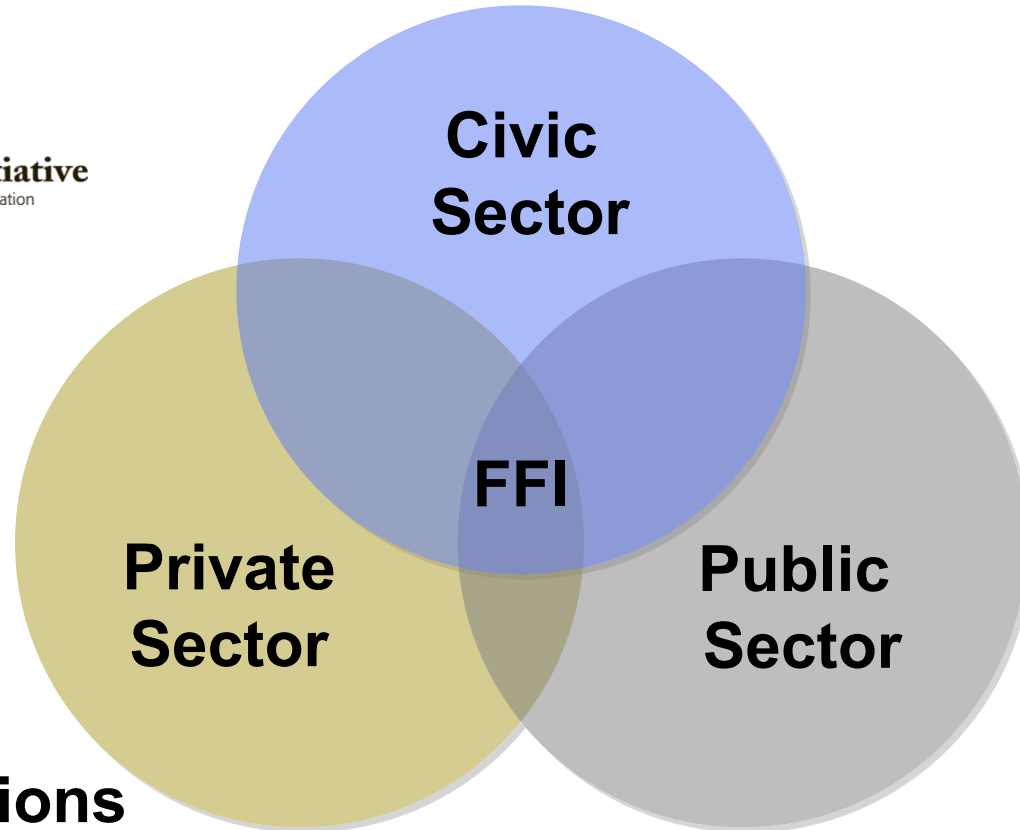
# Economic Evaluation of Folic Acid Fortification in Chile

- ❑ In 1998 Chile fortified wheat flour at 220  $\mu\text{g}$  /100g flour
- ❑ Reduction in NTDs (thru 2001): 41%
- ❑ Cost of fortification: \$0.2 million/ year (\$1)
- ❑ Direct cost averted: \$2.2 million/ year (\$11)

# Flour Fortification Initiative (FFI)



**Flour Fortification Initiative**  
A Public-Private-Civic Investment in Each Nation



- ❑ Cargill
- ❑ Buhler
- ❑ Millers' organizations

- ❑ WHO
- ❑ UNICEF
- ❑ GAIN

# Flour Fortification Progress Since 2004

- ❑ Growth in fortified flour from mills increased from 18% to 30%
- ❑ Nearly 2 billion people now have potential access to fortified flour - 858 million more than in 2004
- ❑ The number of countries with documented national regulations for mandatory wheat flour fortification increased from 33 to 58 (51 fortify with folic acid)
- ❑ Regulation does not imply compliance



# Challenges to Mandatory Flour Fortification

- ❑ Need for regulatory framework
- ❑ Large mills vs small mills
- ❑ Acceptance
- ❑ How to reach large population countries (China, India)
- ❑ Impact of fortification on NTDs in developing countries

# CAN INTAKE OF FOLIC ACID CAUSE HARM? WHAT DOES THE EVIDENCE SHOW?



**Richard B. Johnston, Jr., MD**

***Professor of Pediatrics, Associate Dean for Research Development  
University of Colorado School of Medicine***

# Potential Adverse Effects of Folic Acid: Concerns and Evidence

- ❑ **Progression of nerve damage in B12-deficient patients**
- ❑ **Excess intake in children**
- ❑ **Unmetabolized folic acid**
- ❑ **Blunting of antifolate therapy**
  - Methotrexate and phenytoin
- ❑ **Twinning and miscarriages**
- ❑ **Cognitive decline**
- ❑ **Epigenetic hypermethylation**
- ❑ **Cancer promotion**

# Progression of Nerve Damage in B12-Deficient Patients

- ❑ Case reports, 1940s-50s: Folic acid doses of  $\geq 5000$   $\mu\text{g}$  could eliminate the anemia of pernicious anemia while allowing neurologic damage to proceed
- ❑ IOM adopted 5000  $\mu\text{g}$  as lowest observed adverse effect level to derive tolerable upper intake level of 1000  $\mu\text{g}/\text{day}$
- ❑ NHANES data 2003-06: 2.7% of U.S. adult population exceeded 1000  $\mu\text{g}/\text{day}$  intake; only those who consumed  $>400$   $\mu\text{g}/\text{day}$  as supplement exceeded the upper level
- ❑ Conclusion: No known evidence that folic acid at current intake levels has masked B12 deficiency or harmed individuals with B12-deficiency or pernicious anemia



# Excess Intake in Children

- ❑ In absence of evidence of direct toxic effects of folic acid at any dose, any identified risk to children, and data on utilization and turnover in children, the IOM adjusted down upper intake level from 1000 µg/day on basis of relative body weight
- ❑ Conclusion: No known evidence that folic acid intake above IOM-recommended levels has harmed children. Considering the rapid growth that characterizes childhood, it is possible that relatively higher doses of folic acid are beneficial

# Unmetabolized Folic Acid

- ❑ Folic acid is converted to active form in tissues; excess folic acid enters the circulation and is excreted
- ❑ Circulating unmetabolized folic acid has been reported after intake of as little as 300 µg in bolus
- ❑ Surveys since 1980: ~25% of U.S. adults take folic acid in supplement form; most pregnant women take 600-800 µg/day in prenatal supplement
- ❑ Conclusion: Adult and newborn Americans have been exposed to unmetabolized folic acid for decades; no harm has been detected

# Blunting of Anti-Folate Therapy: Methotrexate and Phenytoin

- ❑ Concern raised that more folic acid intake could interfere with methotrexate therapy (cancer, inflammation) or phenytoin treatment (seizures)
- ❑ According to standards of care, both agents are used over wide dose ranges, and dosage is tailored to each individual to optimize benefit and avoid toxicity; folate supplement (commonly 1000 µg/day) is given routinely with methotrexate
- ❑ Conclusion: No known evidence that folic acid intake has interfered with standard antifolate therapy

# Twinning and Miscarriages

- ❑ Early studies suggested periconceptional vitamin use was associated with more multiple births and miscarriages, but confounding variables were not excluded
- ❑ Low blood folate levels, but not high levels, have been associated with increased miscarriages
- ❑ Twinning rates not affected by
  - Folic acid fortification in United States
  - 400 µg/day folic acid supplement in China trial
  - Higher blood folate levels
- ❑ Conclusion: No known evidence to indicate that increased folic acid intake increases multiple births or miscarriages

# Cognitive Decline

- ❑ Elevated blood homocysteine levels, low blood folate levels, or low folate intake have been associated with increased rates of dementia in most studies, including randomized controlled trials, but not in all
- ❑ Patients with low blood B12 levels but relatively high blood folate levels scored more poorly on memory tests
  - Due to folic acid interference with B12 metabolism in some way?
  - Due to preclinical pernicious anemia in supplement takers who absorb folates but not B12?
- ❑ 97% of those with normal B12 and high blood folate levels had evidence of increased cognition
- ❑ Conclusion: There is no evidence of harm and some evidence of benefit, but data are conflicting

# Epigenetic Methylation

- ❑ Folates are potent source of methyl groups. Could higher folic acid intake increase methylation of DNA residues that influence development of tumors or other disease?
  - Pregnant mice fed high doses of 4 methyl donors delivered offspring with hypermethylation of coat-color gene and change in coat color of newborns
  - Humans given 5000-10,000  $\mu\text{g}/\text{day}$  folic acid for 3-12 months had increased DNA methylation in resected colorectal adenomas; but 2000  $\mu\text{g}/\text{day}$  for 6 months did not modify lymphocyte DNA
- ❑ Conclusion: No evidence of harm to date, but epigenetic methylation is biologically plausible; further research is needed

# Cancer Promotion

- ❑ Higher folate status has been associated with relative protection against several cancers
- ❑ Periconceptional folic acid supplement and fortification have been associated with reduced risk of 3 childhood cancers
- ❑ Mice bred to develop colorectal adenomas
  - High-dose folic acid decreased adenomas if given before adenoma formation
  - But increased adenomas if given after adenoma formation had begun
- ❑ Humans with prior adenoma given 1000 µg/day folic acid for 3-5 years had increased risk of recurrence of  $\geq 3$  adenomas
- ❑ Conclusion: No evidence of harm at intakes recommended to prevent NTDs; possible risk of cancer at high doses in supplement takers; more research is needed

# Summary and Recommendations

- ❑ No data exist to indicate that intake of folic acid causes harm
  - At levels in fortified foods
  - At levels recommended to prevent NTDs
  - But data not yet clear with intake of supplements of  $>400$   $\mu\text{g}/\text{day}$
- ❑ Folic acid doses at recommended levels probably prevent occurrence of cancer; but folic acid at higher doses could promote growth of existing malignancy
- ❑ Continued monitoring and research are clearly needed to avoid the potential of harm in any form
- ❑ Should be emphasized that prevention of NTDs by periconceptional folic acid is accepted as proven
- ❑ And an estimated 150,000 NTDs/year could be prevented worldwide by adequate fortification of foods with folic acid



# FOLIC ACID FORTIFICATION. NEXT STEPS: FORTIFICATION OF CORN MASA FLOUR?



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**Office of the Commissioner, Office of Foods, FDA**



**U.S. Food and Drug Administration**  
Protecting and Promoting Public Health



# Regulation of Folic Acid Fortification

- ❑ **Manufacturers cannot arbitrarily add folic acid to foods**
- ❑ **Regulations allow folic acid fortification by**
  - Food Standards (Standard of Identity): e.g., enriched cereal grain product
  - Food Additives (folic acid added to enriched cereal products)

# Folic Acid Fortification

- ❑ **1941 standard of identity established for “enriched” flour**
  - Flour is not required to be enriched, but if claimed to be enriched, had to contain thiamin, riboflavin, niacin, iron
- ❑ **Regulation Approved 1996; Effective January 1998**
  - Mandated folic acid in “enriched” cereal grain products that conformed to a standard of identity
  - Allowed the fortification of breakfast cereals and dietary supplements



# Fortification Considerations

- ❑ Documentation of public health need
- ❑ Implementation issues
- ❑ Safety issues
- ❑ Monitoring and enforcement issues



# Fortification Considerations

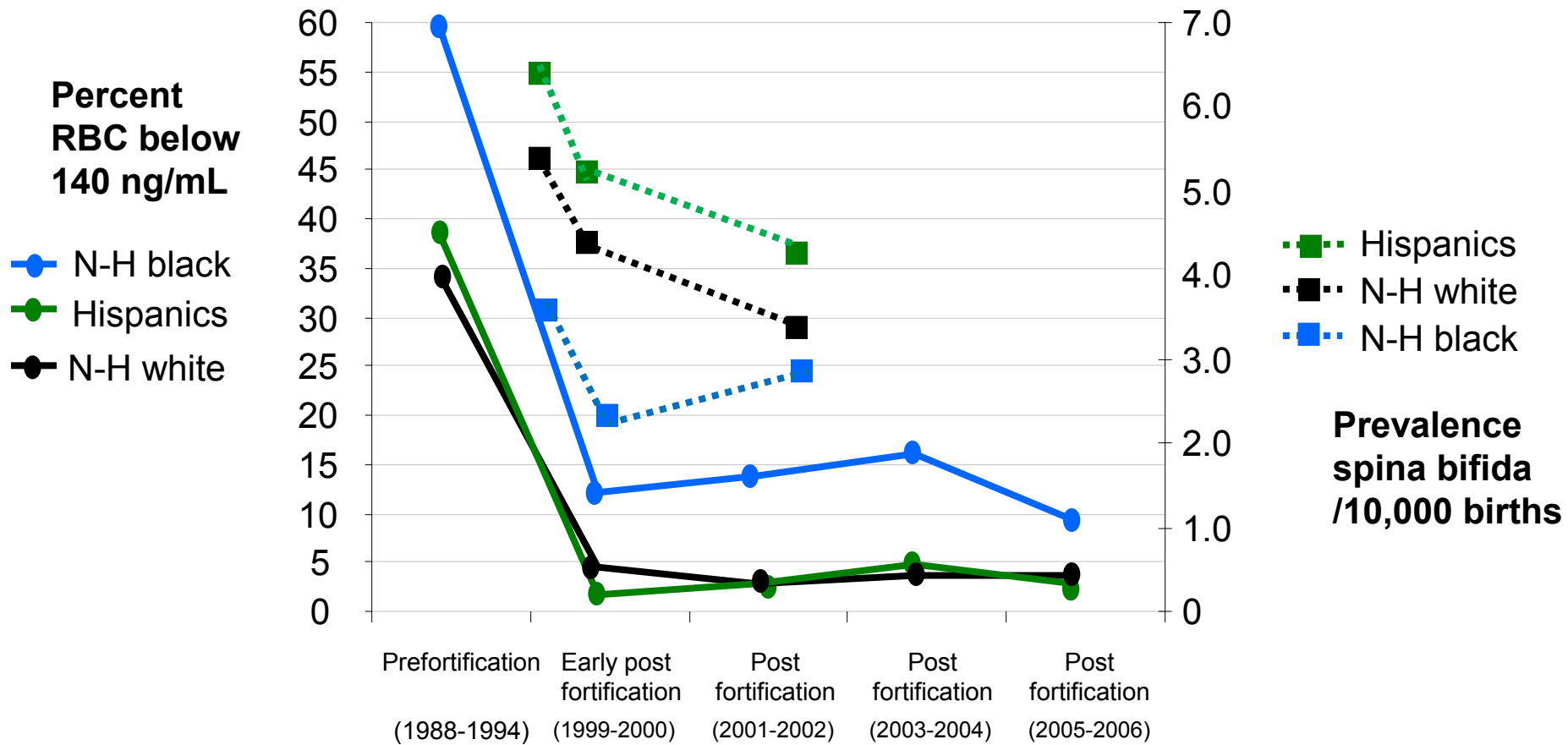
- ❑ **Documentation of public health need**
- ❑ Implementation issues
- ❑ Safety issues
- ❑ Monitoring and enforcement issues



# Public Health Need

- ❑ **Folic acid fortification of enriched cereal products has had a substantial impact in reducing NTDs**
- ❑ **Disparity: Hispanic women have 20% higher risk of a NTD-affected pregnancy**
- ❑ **How much more folic acid should be added**

# Dramatic Decline in Prevalence of Low Blood Folate Concentrations and Spina Bifida



# Fortification Considerations

- ❑ Documentation of public health need
- ❑ Implementation issues
- ❑ Safety issues
- ❑ Monitoring and enforcement issues







# Implementation Issue

## What Additional Foods Could be Fortified?

- ❑ **Proposal by industry, advocacy groups, CDC to fortify corn masa flour**
- ❑ **Products containing corn masa flour are more likely consumed by Mexican Americans than other U.S. populations**
- ❑ **Corn masa flour is prepared from corn boiled in an alkaline lime water solution**
- ❑ **Found in many types of food**
  - Corn tortillas, taco shell, corn and tortilla chips, tamales, enchiladas, chalupas
- ❑ **No existing federal regulations that permit folic acid fortification of corn masa flour**

# Implementation Issue

## How much?

- **How much should be added to achieve the final level desired considering natural levels in the corn masa flour and the potential stability issues?**



# Implementation Issue: Consumer Acceptance

- ❑ **How does fortification affect physical characteristics?**
  - Taste
  - Color
  - Texture
- ❑ **Cultural issues must also be considered**
- ❑ **Lessons learned from wheat flour can be informative but still need independent assessment for corn masa flour**

# Fortification Considerations

- ❑ Documentation of public health need
- ❑ Implementation issues
- ❑ Safety issues
- ❑ Monitoring and enforcement issues



# Safety Issues

- ❑ Safety is critical
- ❑ Food additive regulations do not consider risk benefit. They only consider safety issues.
  - Rather, there must be evidence of reasonable certainty of no harm



# Fortification Considerations

- ❑ Documentation of public health need
- ❑ Implementation issues
- ❑ Safety issues
- ❑ Monitoring and enforcement issues



# Monitoring

## ❑ Effectiveness

- Folic acid intake from all sources
- Blood folate concentrations
- Neural tube defects

## ❑ Safety

- Monitor potential for potential adverse effects

## ❑ Validated methods to analyze the manufactured and finished products

# Corn Masa Flour Fortification?

## The Regulatory Process

- ❑ **Safety assessments and food technology issues are key information needed**
  - First, need to demonstrate safety under requirements of reasonable certainty of no harm
  - Documentation of public health need
  - Amount of additive proposed for use
  - Description of methods to determine amount of food additive in raw, processed or finished food



# Corn Masa Fortification?

## Other Issues

### ❑ Implementation Issues

- Determine the stability and shelf life of folic acid added to corn masa flour
- Assess any acceptance issues

### ❑ Availability of validated methods for analysis of folic acid in fortified products and standards for

- Industry to ensure product content and labeling accuracy
- FDA in its enforcement role

# Summary

- ❑ Fortification of enriched flour with folic acid has been a public health success story in improving blood folate concentrations and reducing NTDs
- ❑ NTDs continue to affect thousands of Americans and disparities exist
- ❑ Fortification of additional foods with folic acid may reduce the disparities

# Next Steps

## ❑ Collaboration is essential and requires

- Defined roles of industry, academia, CDC, NIH, FDA, and others
- Public health consensus on solutions and safety
- Food technology research (stability, shelf life and analytic methodologies)
- Regulatory process



# PUBLIC HEALTH GRAND ROUNDS

Office of the Director

**February 18, 2010**

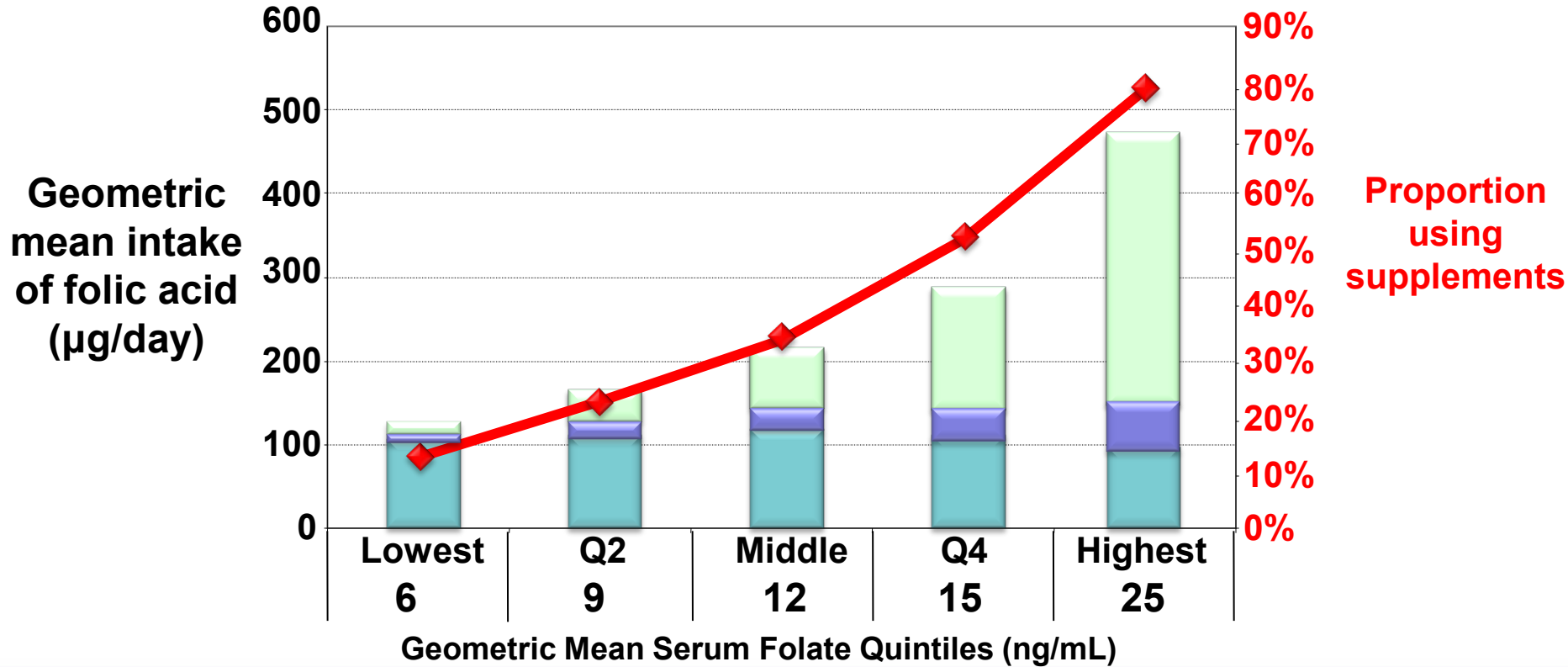


# Mean Folic Acid Intake, Enriched Cereal-Grain Products, RTE Cereals & Supplements by Serum Folate Quintiles

NHANES 2001-2004, ≥19 years, n=8,655

- Supplements containing folic acid
- Ready-to-eat cereals
- Enriched cereal grained products

**◆** Reported % folic acid supplement use



Adapted from Yeung, LY et al. JAMA 2008;300:2486-7

