Prevention of Spina Bifida & Anencephaly: The Importance of Folic Acid Fortification of Flour
Assessing Effects Worldwide

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1st Central & Eastern Summit on Preconception Health and Prevention of Birth Defects
Budapest, Hungary, August 29, 2008

National Center on Birth Defects and Developmental Disabilities

Centers for Disease Control and Prevention

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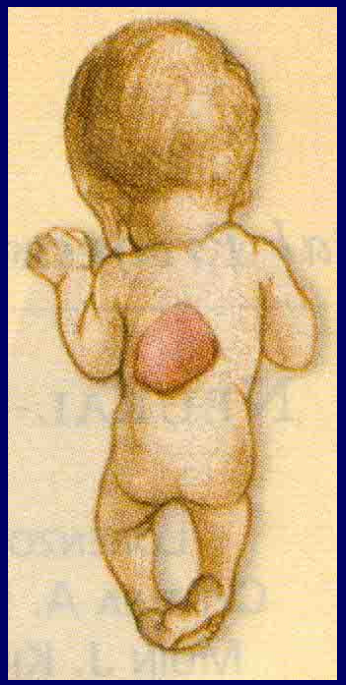
Outline

- Epidemiology of spina bifida and anencephaly (SBA) and folic acid
- Prevention of SBA through the use of folic acid
- Impact of folic acid fortification in reducing SBA in the U.S. and around the world

Spina bifida & Anencephaly

- Serious birth defects
  - spina bifida and anencephaly
- >1 of 1000 pregnancies
- > 300,000 yearly worldwide
- Increased consumption of folic acid can prevent 50 -70%
- Maternal folic acid levels need to be raised very early in pregnancy
- 50% of US pregnancies are unplanned



Lifelong disabilities of spina bifida

Loss of sensation

Paralysis of muscle groups

Loss of bladder, and
bowel control

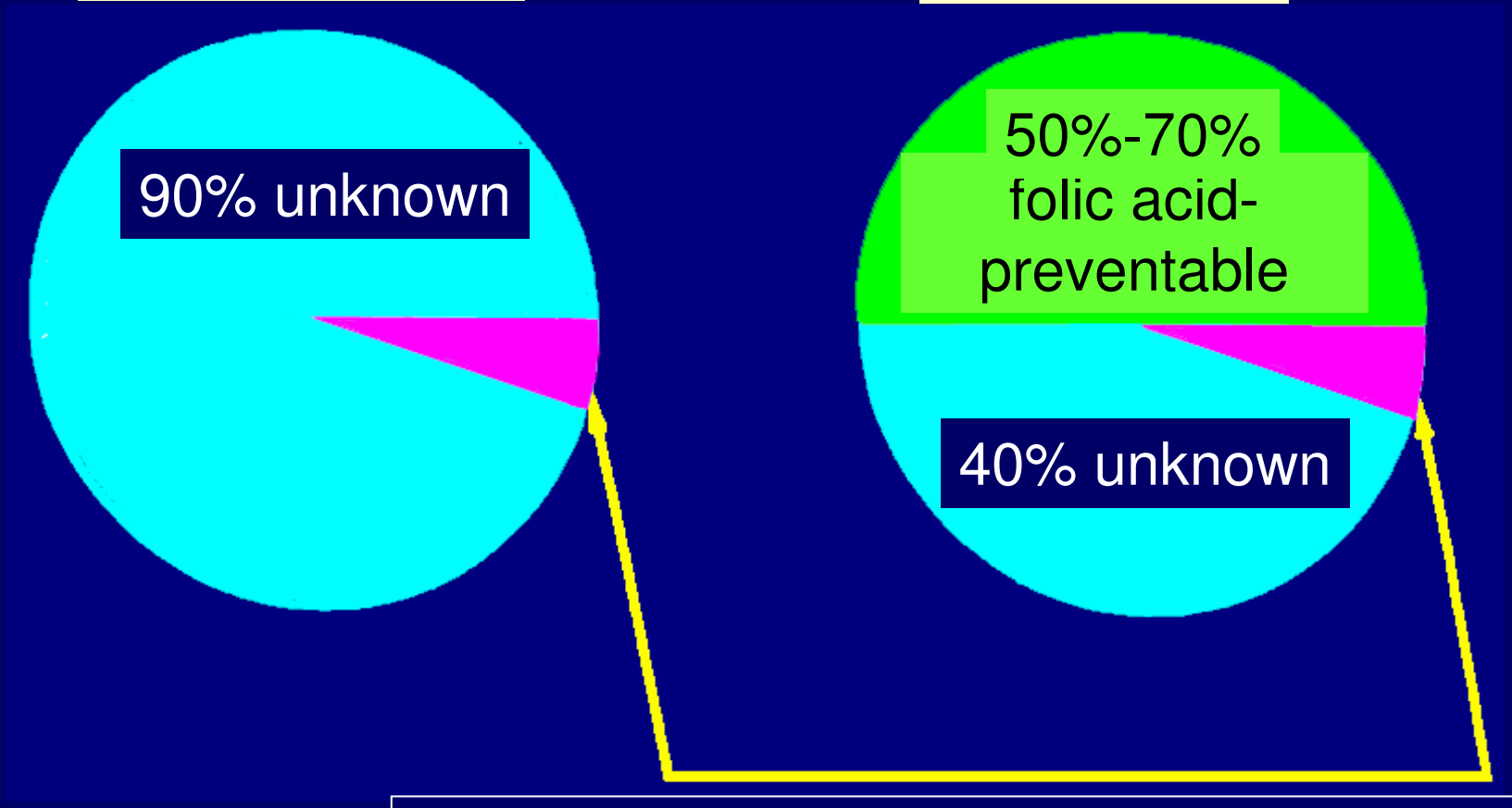
Learning and developmental
issues

Orthopedic problems

Causes of Spina Bifida and Anencephaly

Before 1980's

After 1980's



5% - 10% due to family history, maternal diabetes, antiepileptic medications, genetic conditions, etc.

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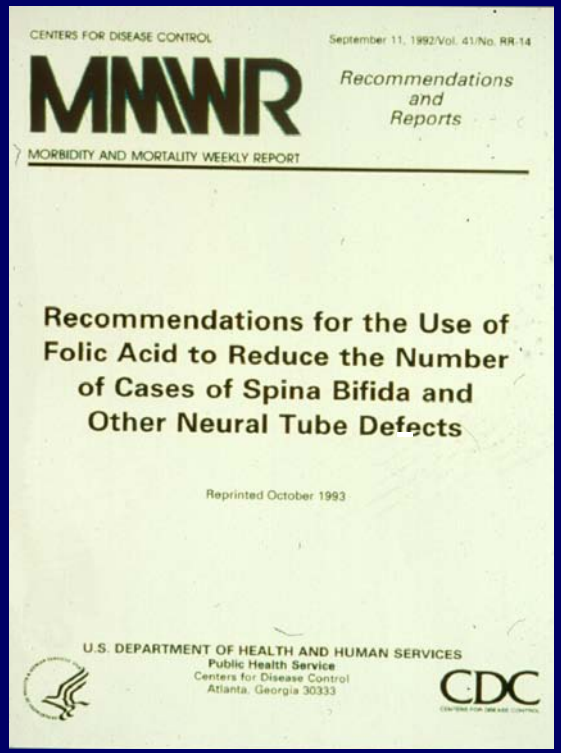
Folic Acid +/- Multivitamins
Neural Tube Defect Studies, 1980-1999

Studies	% reduction
'80-Smithells	86%
'81-S. Wales	59%
'88-Atlanta	60%
'89-W. Australia	70%
'89-CA/Illinois	7%
'89-Boston	65%
'90-Cuba	100%
'91-UK-MRC	71%
'92-Hungary	100%
'93-New England	60%
'95-California	52%
'99-P.R. China	80%

1992 U.S. Public Health Service Folic Acid Recommendation to Prevent SBA


CENTERS FOR DISEASE CONTROL

September 11, 1992/Vol. 41/No. RR-14

MMWR

Recommendations and Reports

MORBIDITY AND MORTALITY WEEKLY REPORT

Recommendations for the Use of Folic Acid to Reduce the Number of Cases of Spina Bifida and Other Neural Tube Defects

Reprinted October 1993

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service
Centers for Disease Control
Atlanta, Georgia 30333

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-400 micrograms (0.4mg) folic acid daily,

-for all women capable of becoming pregnant,

-to prevent spina bifida and other NTDs.

-Increase consumption of folic acid/folate:

- **Improve dietary habits**
- **Take a daily folic acid supplement**
- **Consume fortified foods**

Food vs. supplements

- Vitamin supplements

- "Natural" food folates

- Fortified foods

“Folate” is not equal to “Folic Acid”

Folate (food)

- Occurs naturally in many foods
- Not as bioavailable as folic acid

Folic acid (pills, foods)

- Synthetic form of ‘folate’
- Found in vitamin supplements. breakfast cereals, enriched flour, and enriched cereal-grain products

Dietary approach: to deliver folate to populations

Advantages

- Multiple benefits of healthy diet

Disadvantages

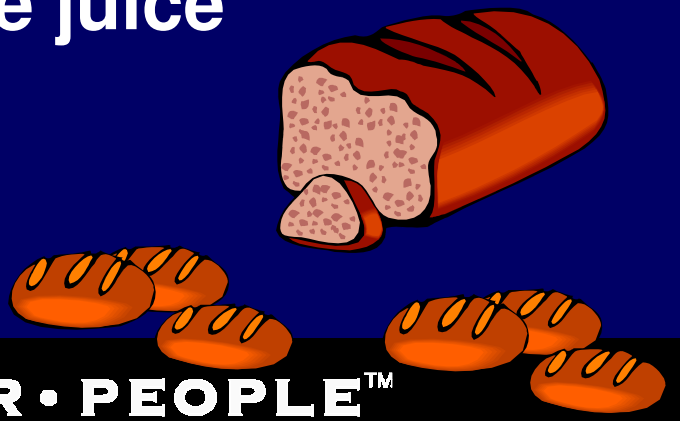
- Requires continuous public education
- Requires behavior change
- High cost of folate-rich foods
- Quantity, absorption and bioavailability

- U.S. women consume on average 200 mcg folate per day

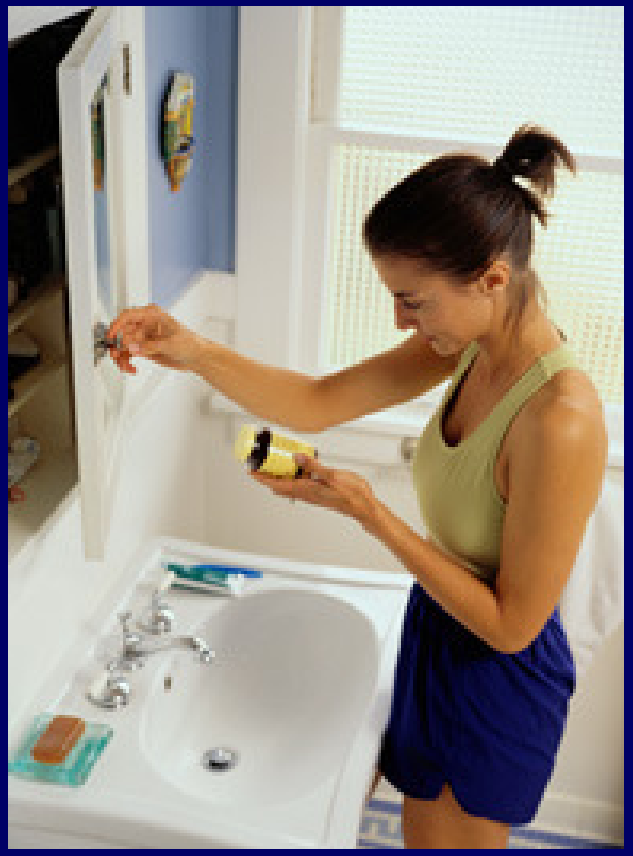
For Example…

To get enough folate from food that equals 400 mcg of folic acid **each day**, a person would have to eat one of the following:

4 slices of fried beef liver
5½ cups of black beans
14½ cups of raw broccoli
44½ medium ripe tomatoes
17½ cups of orange juice



Vitamin Supplement approach:



Advantages

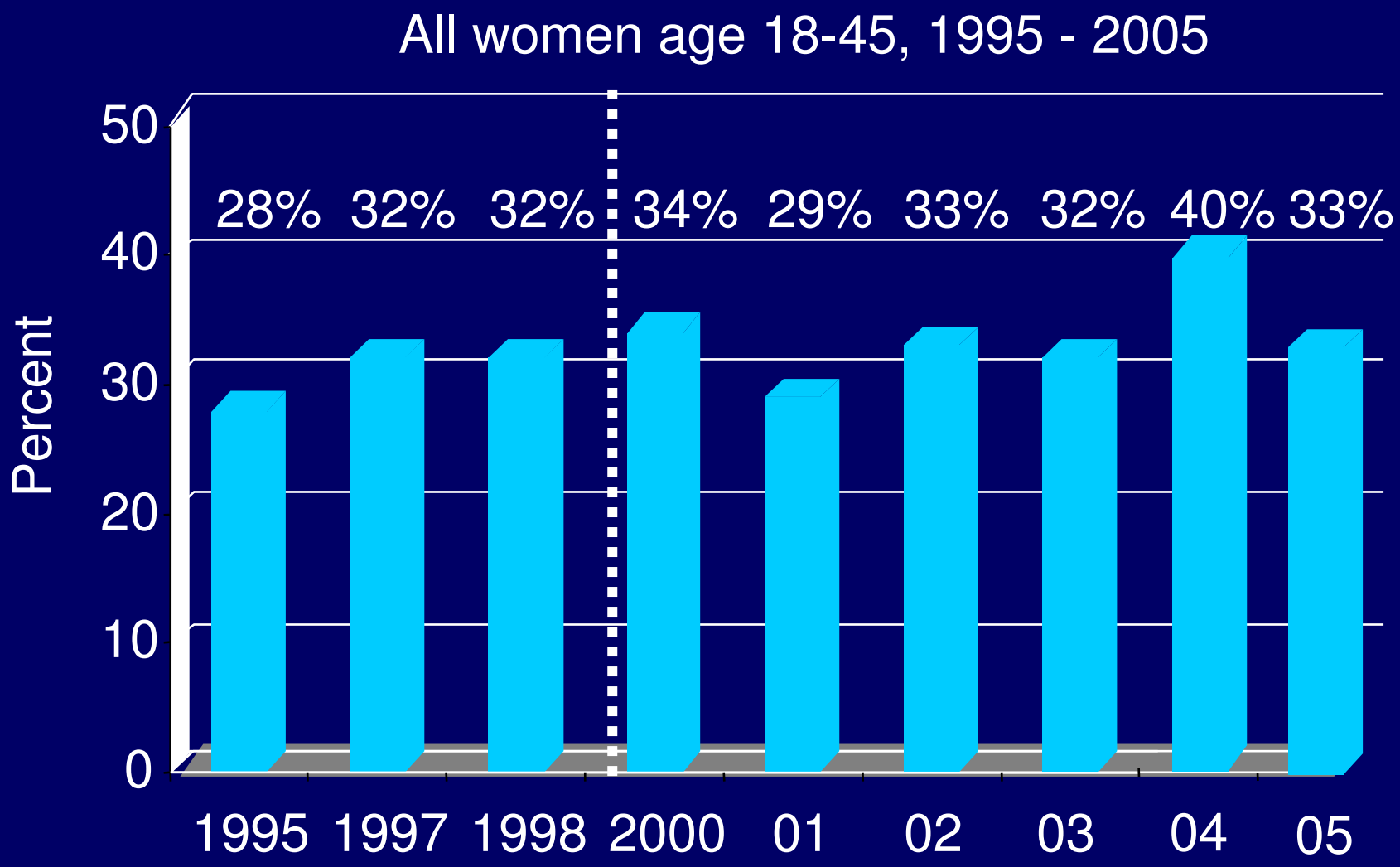
- Excellent bioavailability

Disadvantages

- Continuous public education
- Behavior change
- Relative high cost of tablets

- Most U.S. MV supplements contain 400 mcg FA
- ONLY 25% - 30% U.S. women consume 400 mcg FA/day

Percent women taking vitamins with folic acid daily



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Food fortification approach:

Advantages

- Good bioavailability
- Cost low
- Almost 100% coverage
- Convenient; minimal behavior change

Disadvantages

- Amount added to foods limits effectiveness.

- U.S. women consume on average 130 mcg folic acid per day

What Approaches Work? What is the best way to get Folate / Folic Acid?

- Diet….natural foods, vegetables, fruits, beans, yeast, liver
- Pills…..” folic fcid supplements,” “dietary supplements”
- Fortification…FA added to foods: flour, rice, pasta breakfast cereals

Consumption of Folic Acid & Dietary Folate:
Effect on Red Cell Folate, Ireland 1996.

Intervention method	Red Blood Cell Folate, % change
Dietary advice	+ 16%, NS
Diet natural folate 400 mcg folate	+ 11%, NS
Supplement 400 mcg Folic Acid	+ 40%, $p<0.05$
Fortified food 400 mcg Folic Acid	+ 52%, $p<0.05$

Cuskelly et al., Lancet; 1996.

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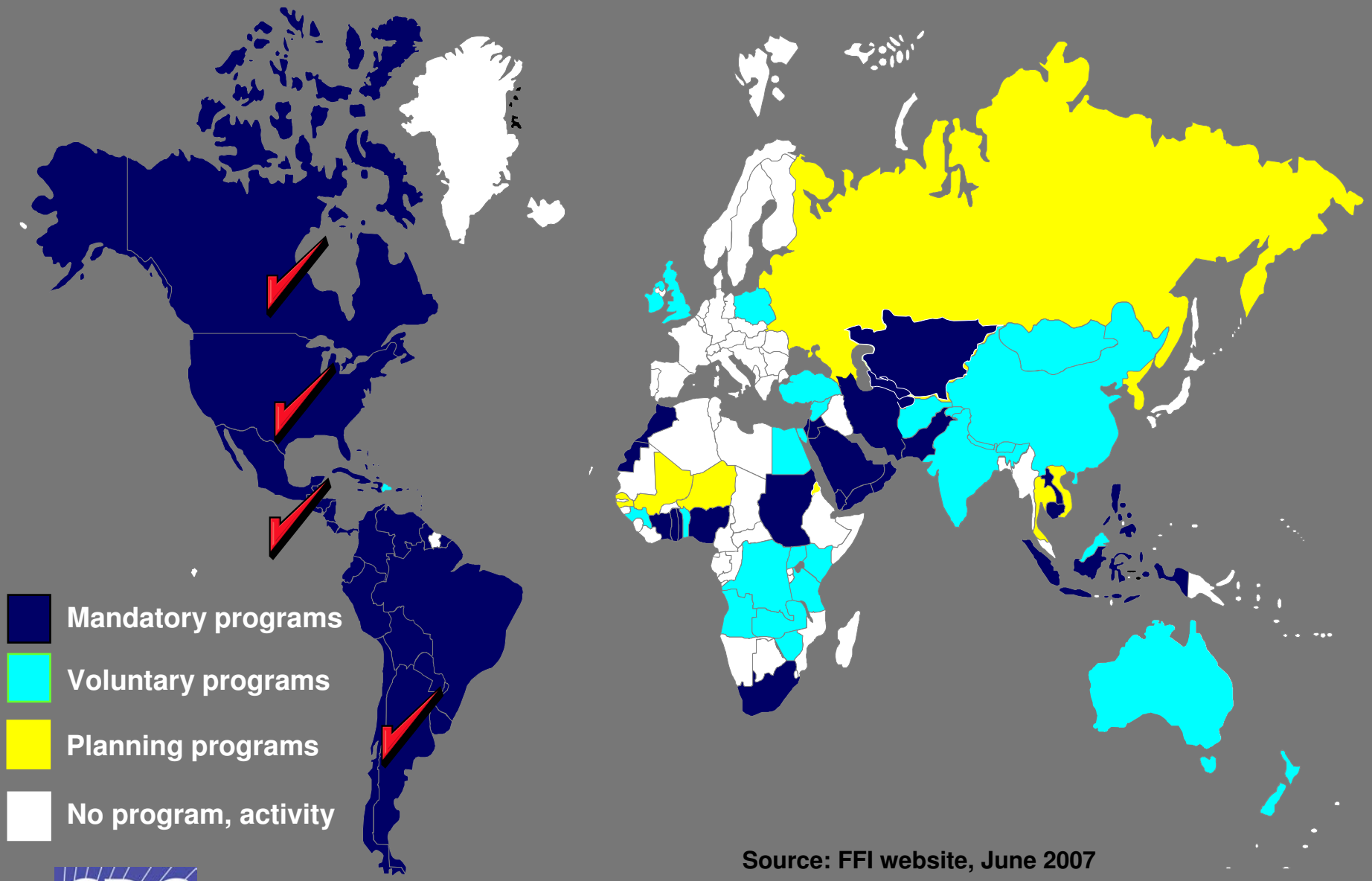
Folate Folic Acid Delivery Methods

- Diet….natural foods, vegetables, fruits, beans, yeast, liver
- Pills…..” FA supplements,” “dietary supplements”
- Fortification…FA added to foods: flour, rice, pasta breakfast cereals

Worldwide flour fortification programs



Source: FFI website, June 2007

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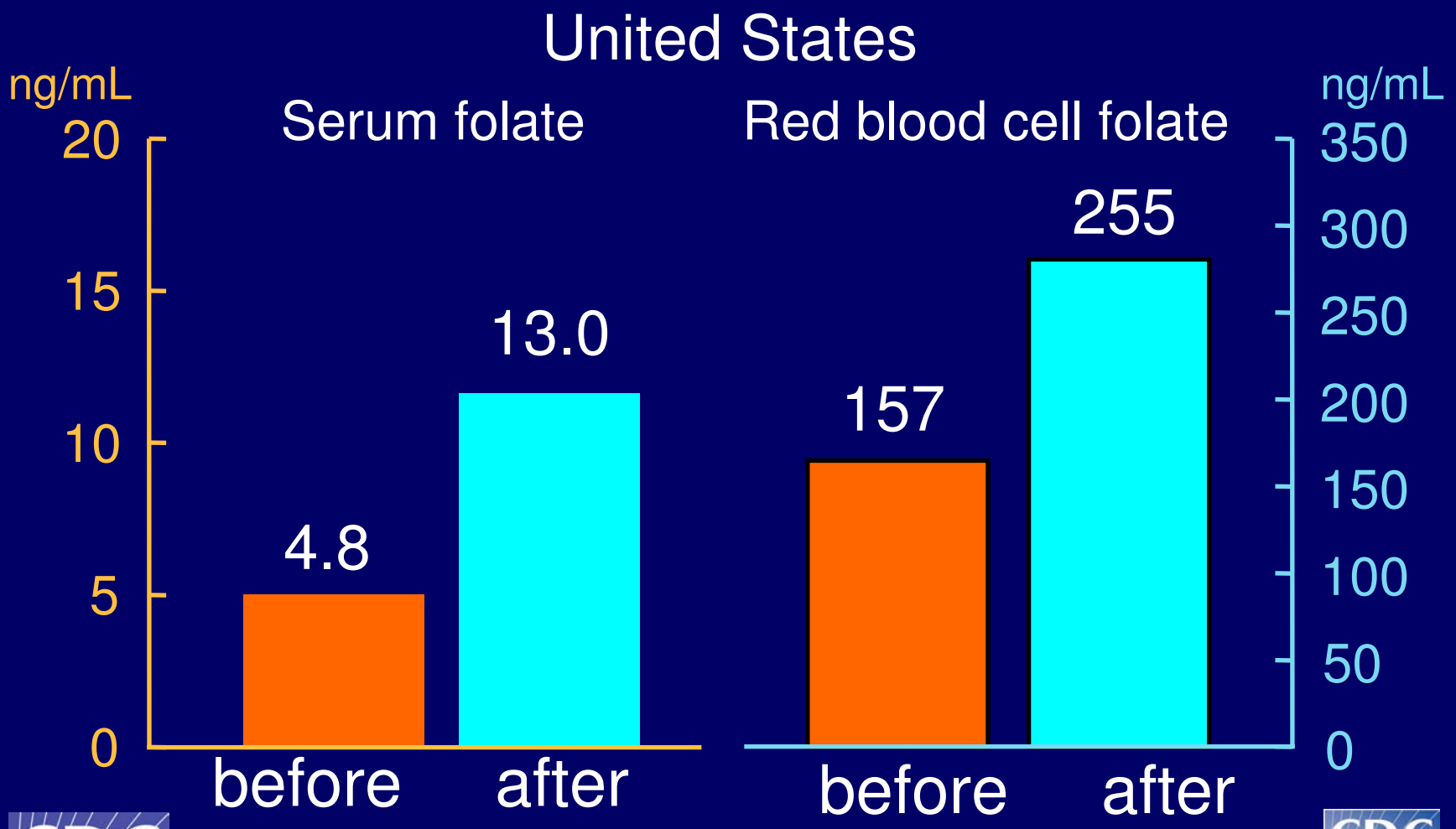
Folic acid fortification levels

Country	Food types	Folic acid ppm	mcg folic acid (design)
USA, 1998	Wheat, corn flours, rice, pasta	1.4 ppm	100 mcg
Canada, 1998	Wheat, corn flours, rice, pasta	1.5 ppm	100 mcg
Costa Rica, 1998	Wheat, corn flours, rice, milk	1.8 ppm	100 mcg
Chile, 2000	Wheat flour for bread	2.2 ppm	400 mcg

Evaluation and monitoring of flour fortification with folic acid to prevent spina bifida and anencephaly

- Blood folates
- SBA prevalence rates
- Cost benefit analyses

Median serum and red blood cell folate levels, before and after folic acid fortification, NHANES, non-pregnant women,15-44 years



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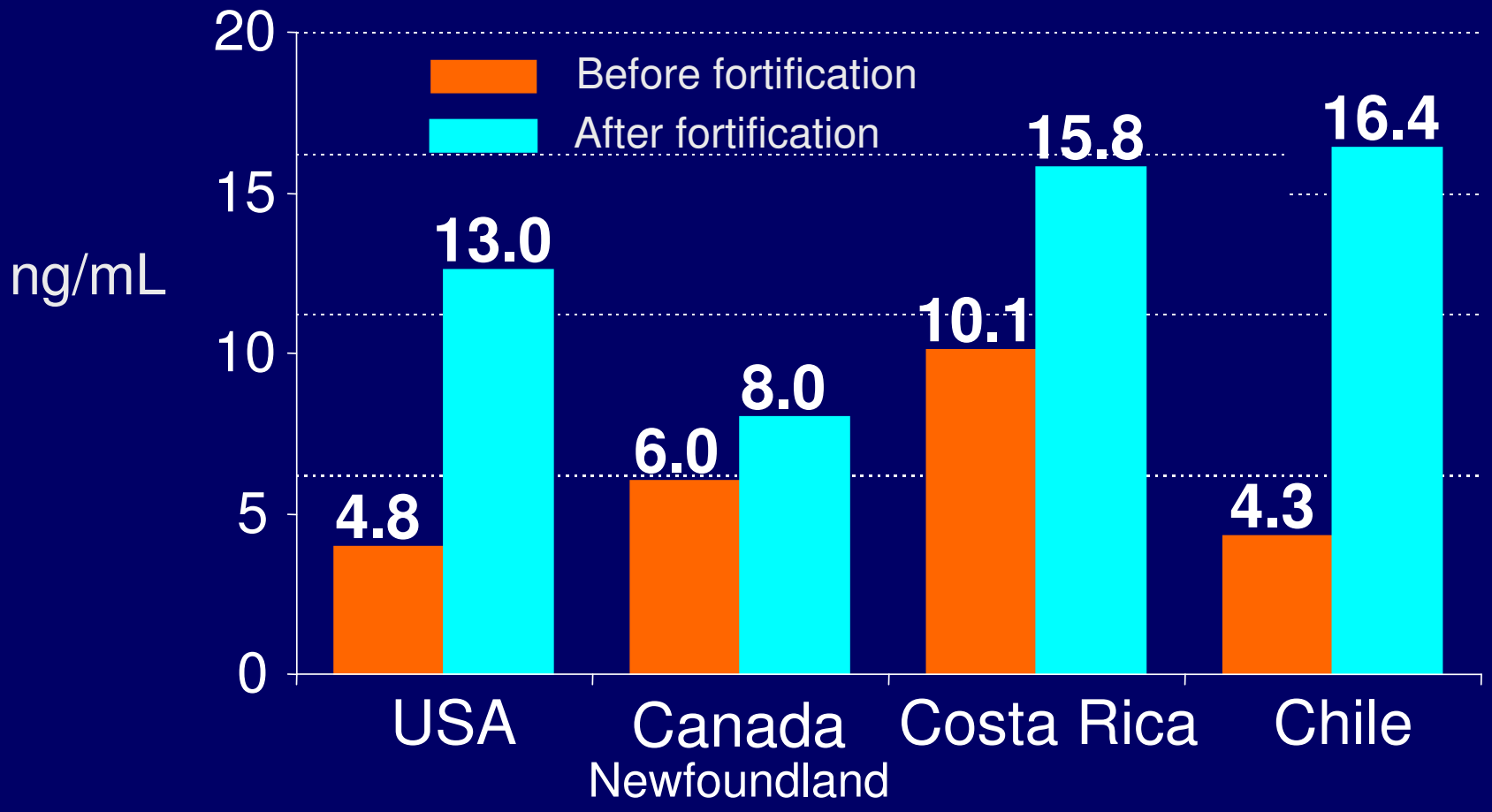
Serum folate changes in the Americas before and after folic acid fortification



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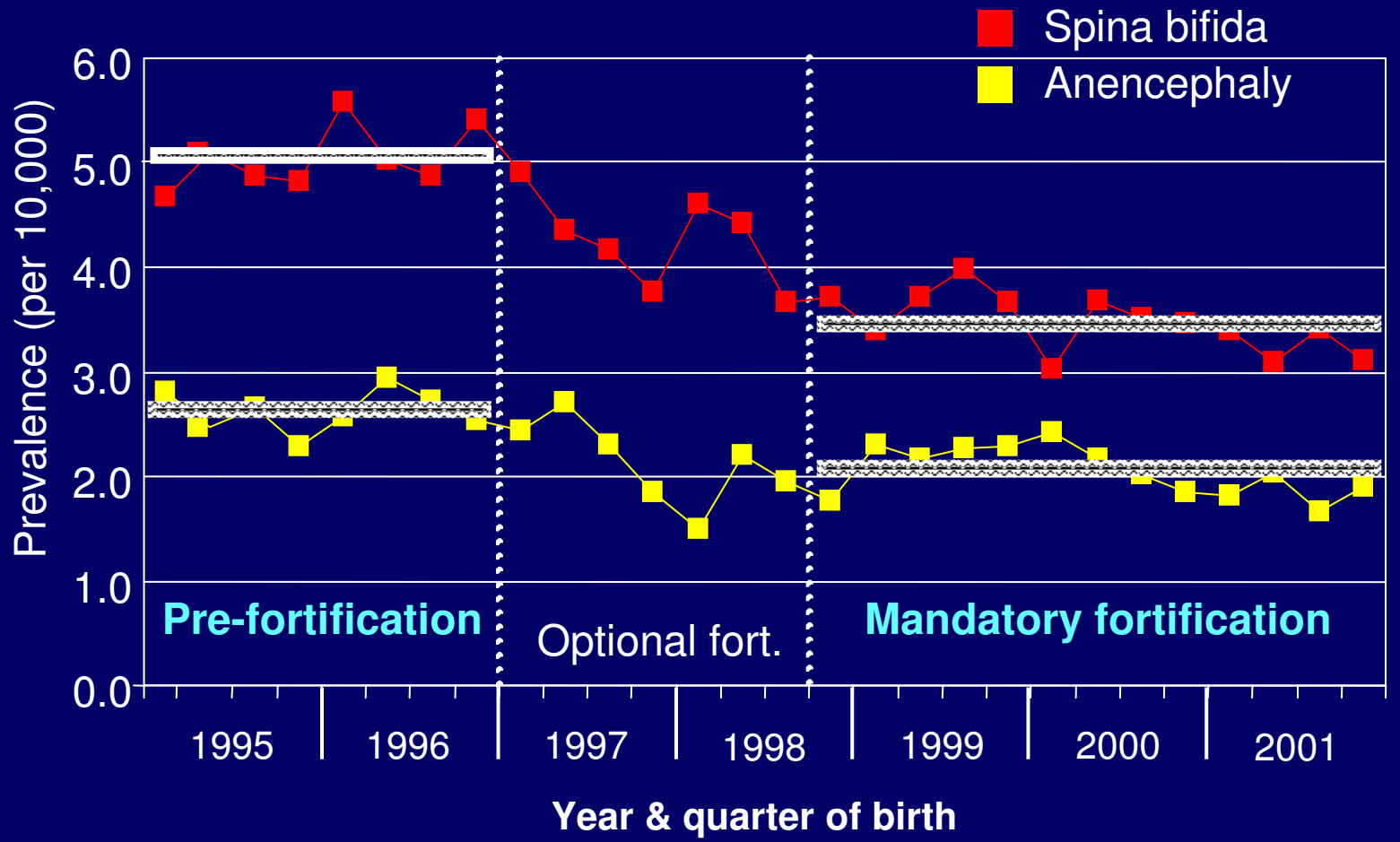
Change in U.S. NTD prevalence by fortification status, per 10,000, NBDPN, 24 surveillance programs



26% ↓

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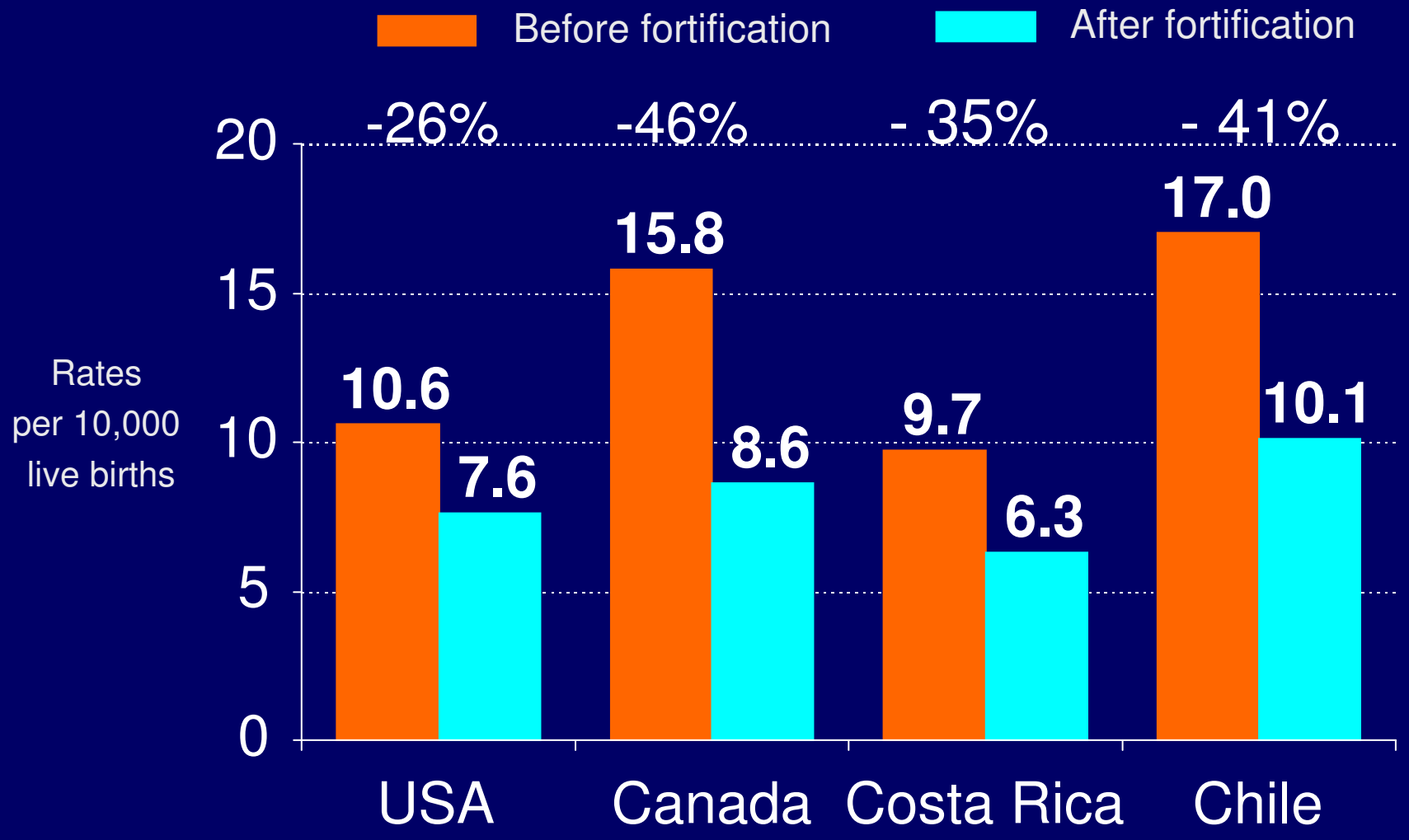
NTD Prevalence changes in the Americas before and after folic acid fortification



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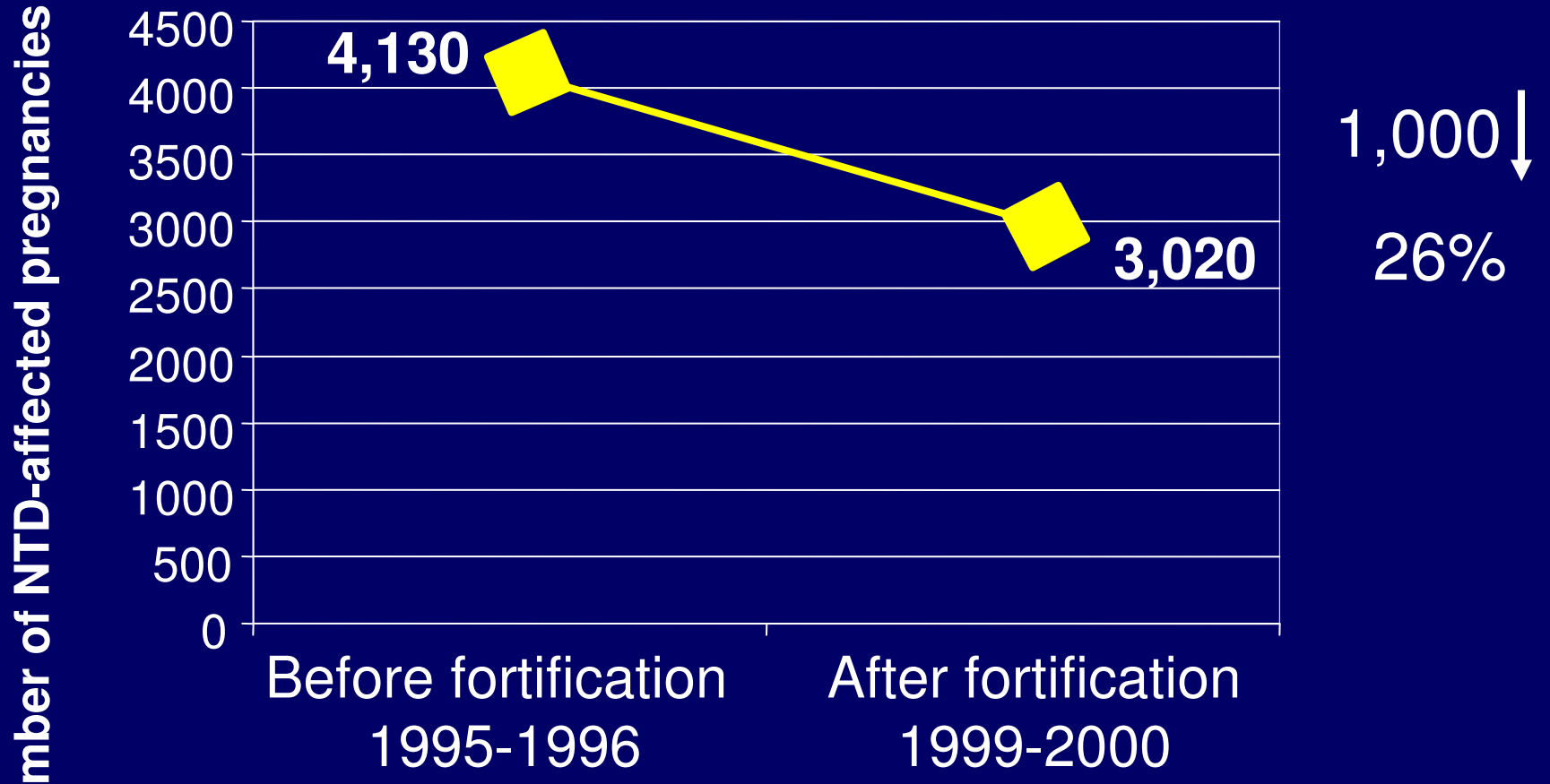
Decrease in the number of SBA-affected pregnancies in the United States per year, NBDPN



Source: National Birth Defects Prevention Network, includes prenatal ascertainment of cases

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United States
Economic Evaluation of Folic Acid Fortification

In 1998 U.S. fortified wheat flour at 140 mcg/ 100g flour

- Reduction in NTDs -- 26%

Cost of fortification	$3 million per year	($1)
Direct cost averted	$125 million per year	($40)

Grosse, Waitzman, Romano, Mulinare (*Am J Public Health,* 2005)

Chile
Economic Evaluation of Folic Acid Fortification

In 1998 Chile fortified wheat flour at 220 mcg/ 100g flour

- Reduction in NTDs -- 41%

Cost of fortification	$ 0.2 million per year	($1)
Direct cost averted	$2.2 million per year	($11)

Llanos, Hertrampf, Pardo, Grosse, and Uauy (Health Policy, 2007)

Evaluation and monitoring of flour fortification with folic acid to prevent spina bifida and anencephaly

Blood folates 

SBA prevalence rates 

Cost benefit analyses +

cost savings

Evaluation of the change in SBA prevalence, U.S.

Actual - SBA	Goal - SBA
% decline	% decline
26%	50%-70%
1,000	2,000

Evaluation of the change in SBA prevalence, U.S.

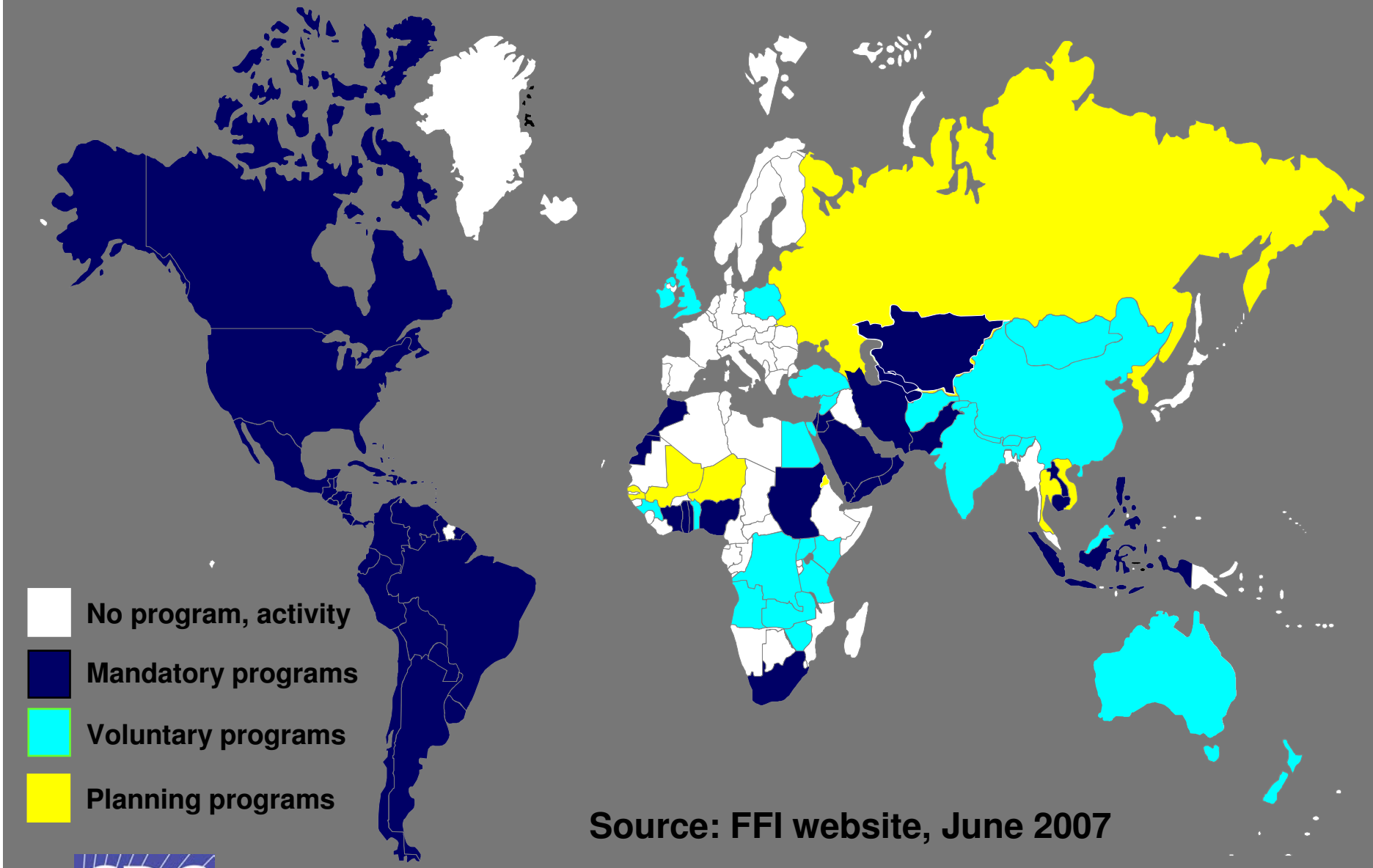
Actual - SBA

26% decline

1,000

Since 1998, more than 11,000 babies have been born healthy, who would have either died or had serious disabilities.

Worldwide flour fortification programs



Source: FFI website, June 2007

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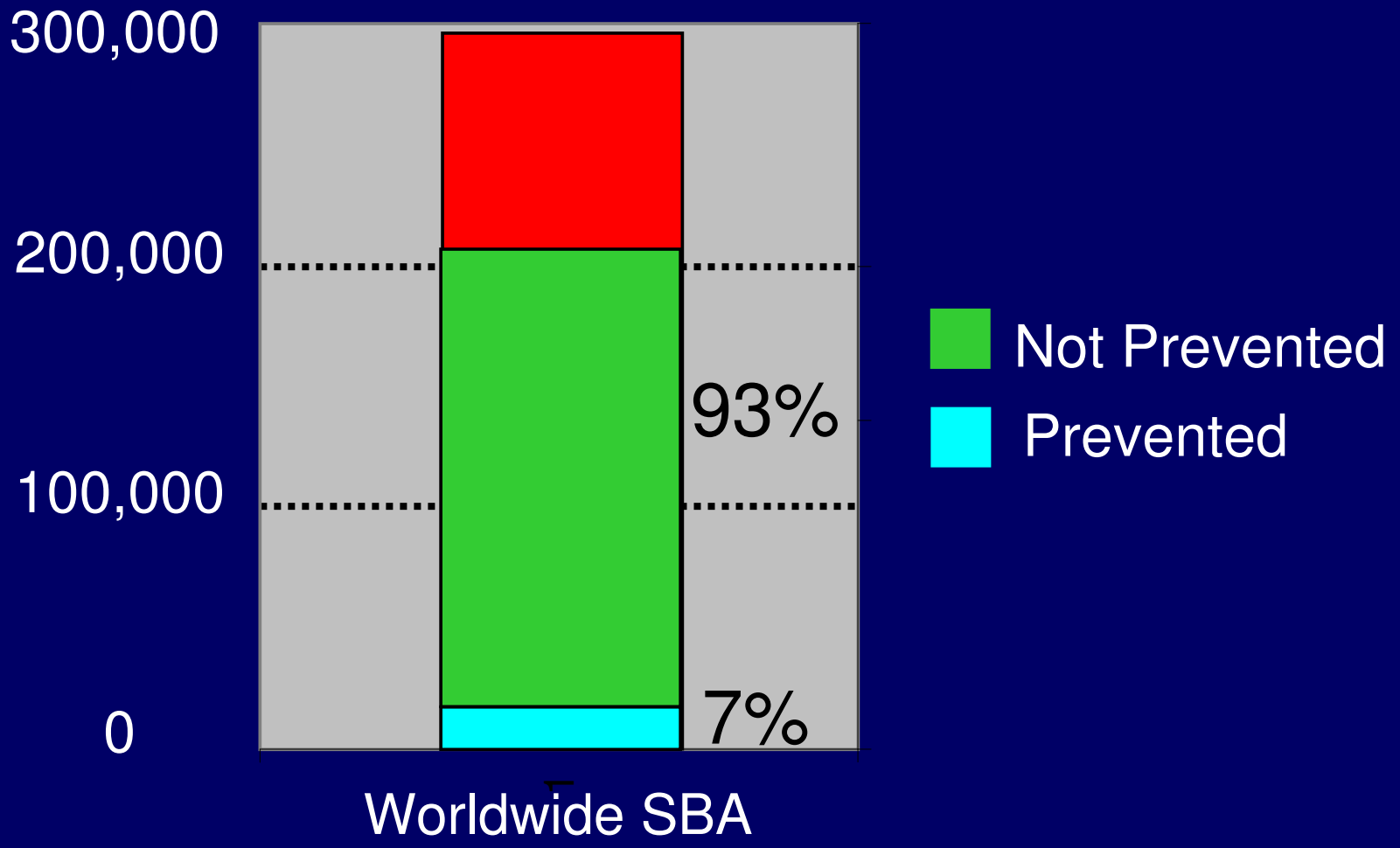
Folic Acid-Preventable SBA in 2006
300,000 affected babies worldwide



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Conclusions:
Current Knowledge and Practical Applications:
Flour Fortification

Adding folic acid to flour and bread:

- Blood folate levels have increased substantially
- Countries now report declines of SBA from 25% to 46%.
- Decreasing numbers of spina bifida and anencephaly are consistent with an increase in folic acid in fortified flour and foods

Conclusions (cont'd)

Adding folic acid to flour and bread:

- Fortification of foods with folic acid is feasible, effective and safe. It is excellent public health policy.
- At the present time, there are no proven adverse effects of folic acid fortification.
- The economic benefit in preventing SBA exceeds the costs of implementing food fortification efforts with folic acid.

U.S. National Folic Acid Campaign to Prevent Birth Defects

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