



Micronutrients, Health, and Development: Evidence-based Programs

**Flour Fortification Recommendations
Micronutrient Forum Satellite Session
Folic Acid Work Group Report
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Disclaimer: The findings and conclusions in this presentation have not been formally disseminated by the Centers for Disease Control and Prevention and should not be construed to represent any agency determination or policy.



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What is Folate?

- **Folate is a generic term for different forms of the vitamin**
 - naturally occurring “food folate”
 - synthetic folic acid

Food Folate

Occurs naturally
Concentrated in selected foods



Folic Acid

Folic acid:
- supplements



- fortified foods
(“enriched” products,
RTE cereals)



Fortification of food with folic acid in the United States

- **Before 1996 only a few products were voluntarily fortified with folic acid**
- **Since 1996, the number of voluntarily fortified products has increased**
- **After 1998, mandatory fortification “enriched” cereal grain products**

Most positive outcome attributable to folic acid fortification

Prevention of NTDs

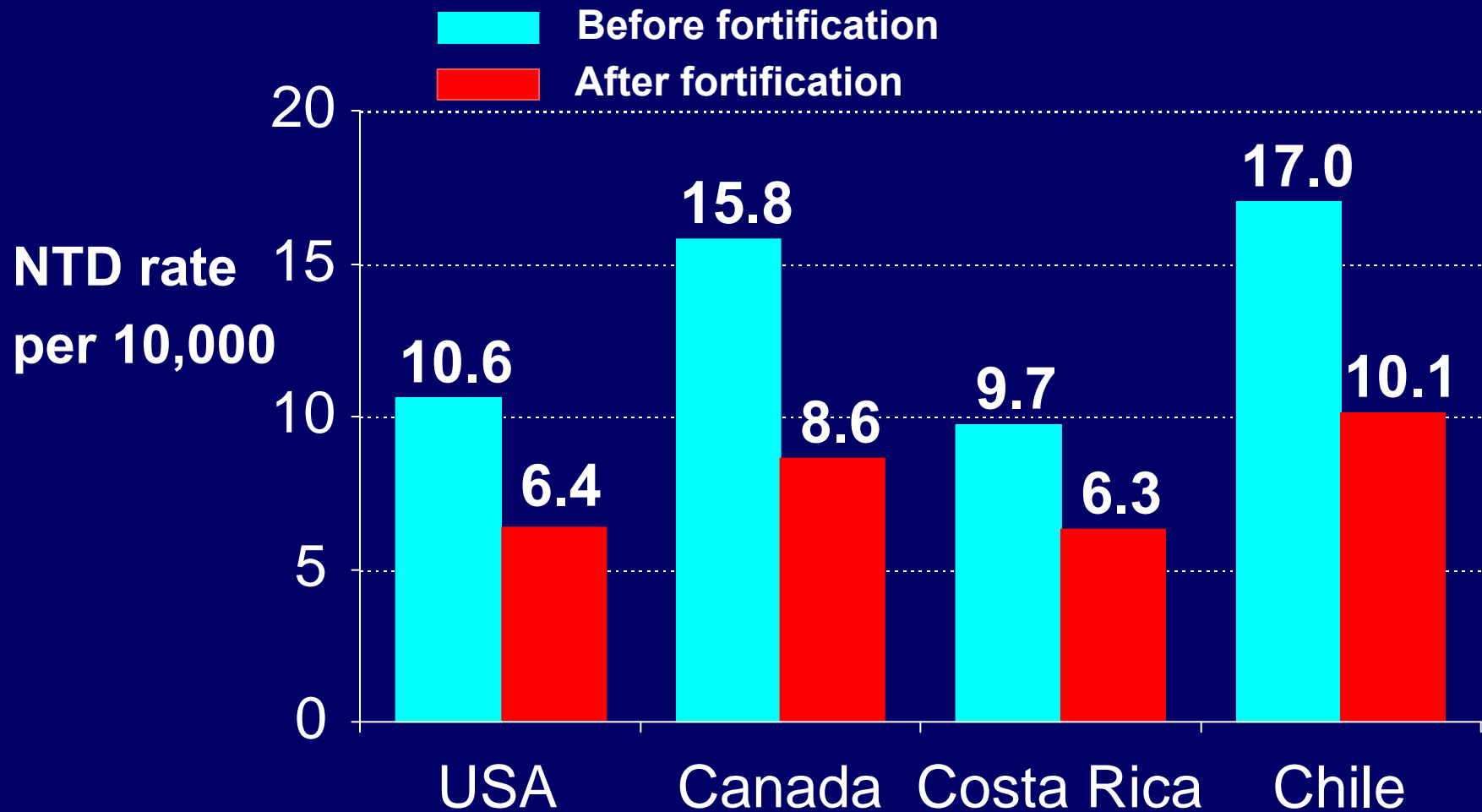


Spina bifida

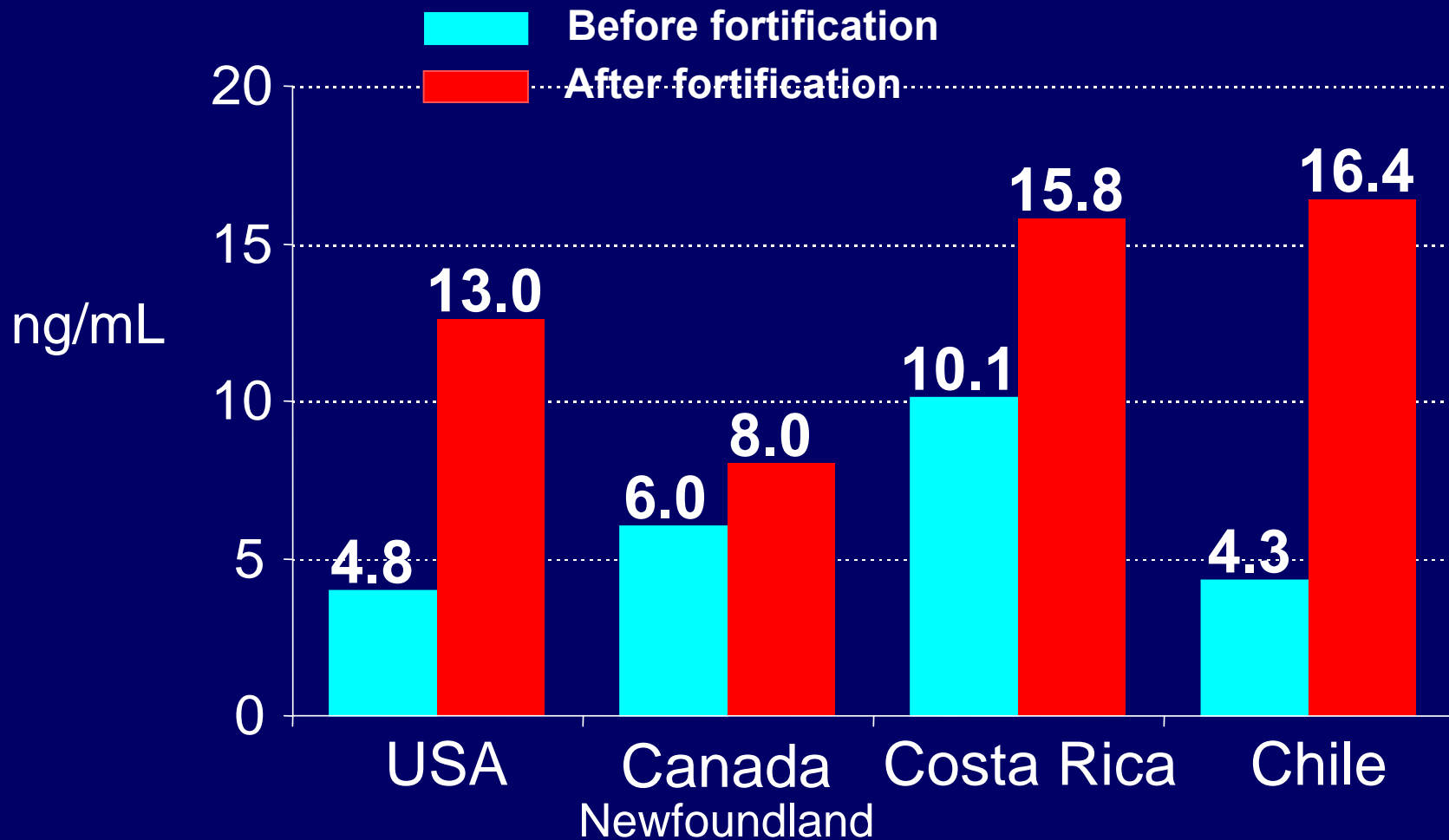


Anencephaly

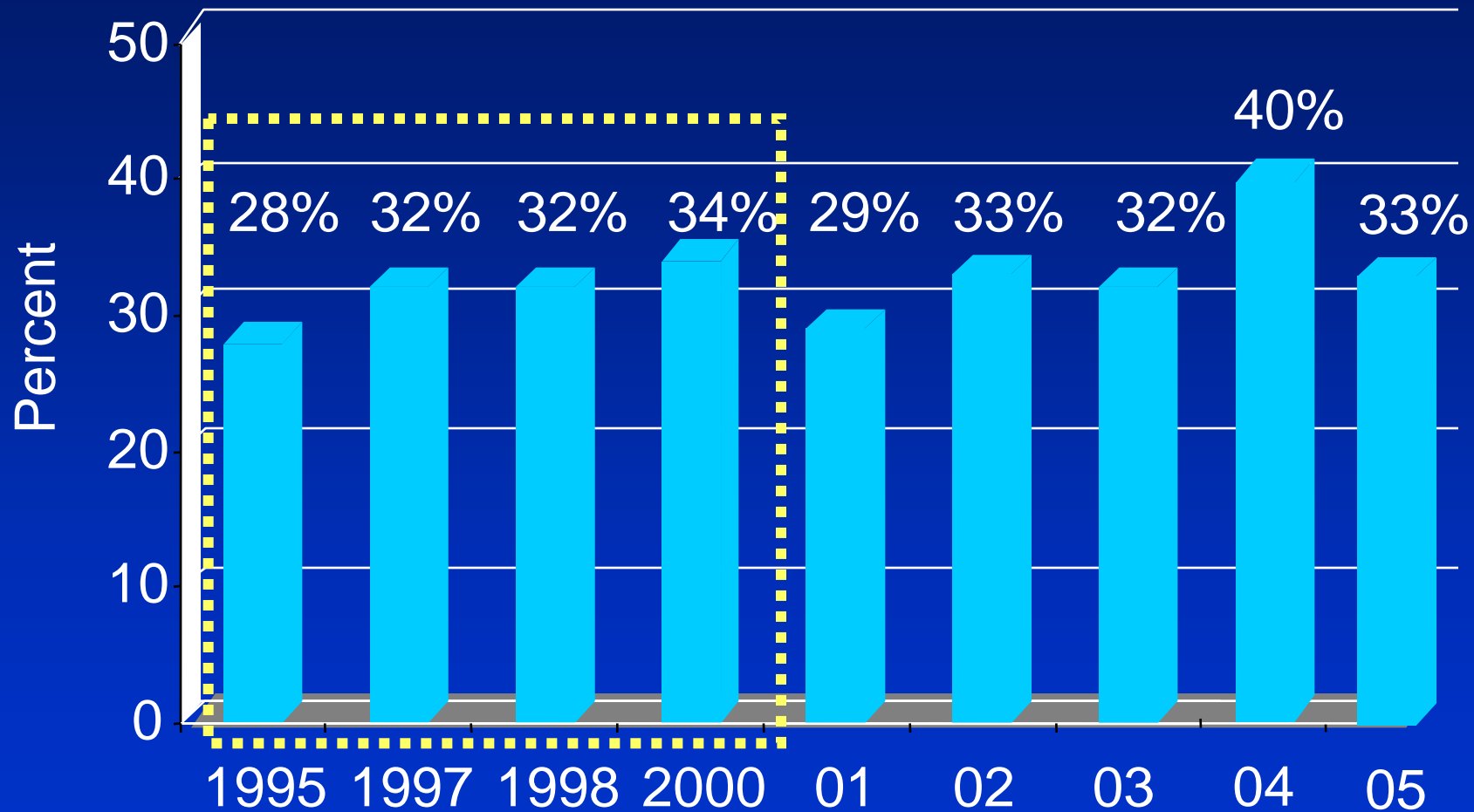
NTD prevalence changes in the Americas before and after mandatory folic acid fortification



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



Percent Women Taking Vitamins with Folic Acid Daily



All women age 18-45,
March of Dimes Gallup Survey, 1995-2005

Conclusions

- **NTD prevalence decreased**
- **Decreasing NTD prevalence consistent with an increase in folic acid from mandatory fortification of “enriched” flour and cereal-grain products**
- **Blood folate concentrations increased**
- **No increase in use of supplements containing folic acid – pill programs fail to reach the majority of women in need**

Sources and Amounts of Folic Acid



**Folic Acid
Enriched Cereal
Grain Products
(**ECGP**)**

**100-150 μg / day
(mandatory)**



**Folic Acid
Fortified
“Ready-to Eat”
Breakfast
Cereals
(**RTE**)**

**Up to 400 μg / serving
(voluntary)**



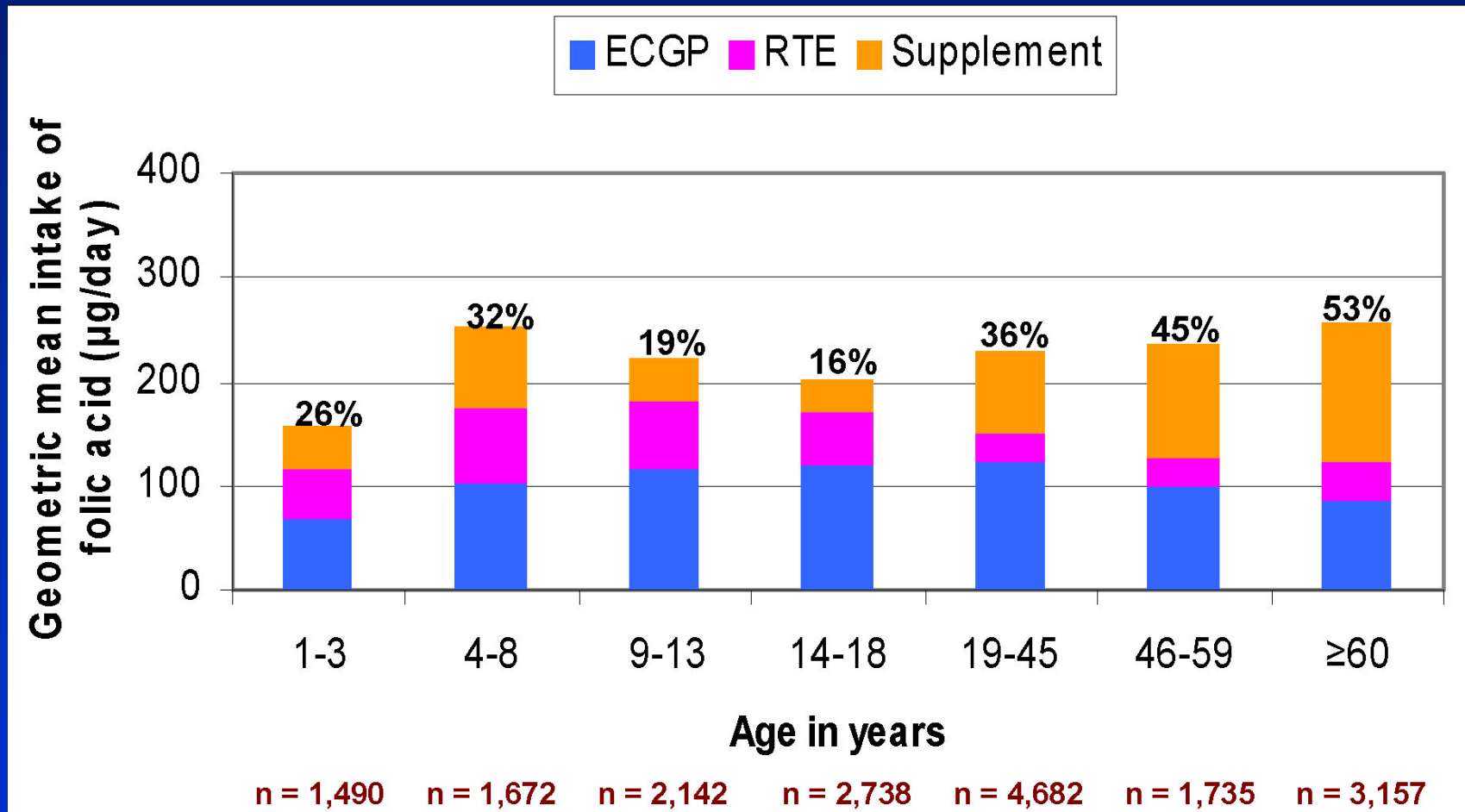
**Folic Acid-
Containing
Supplements**

**~400 μg / supplement
(voluntary)**

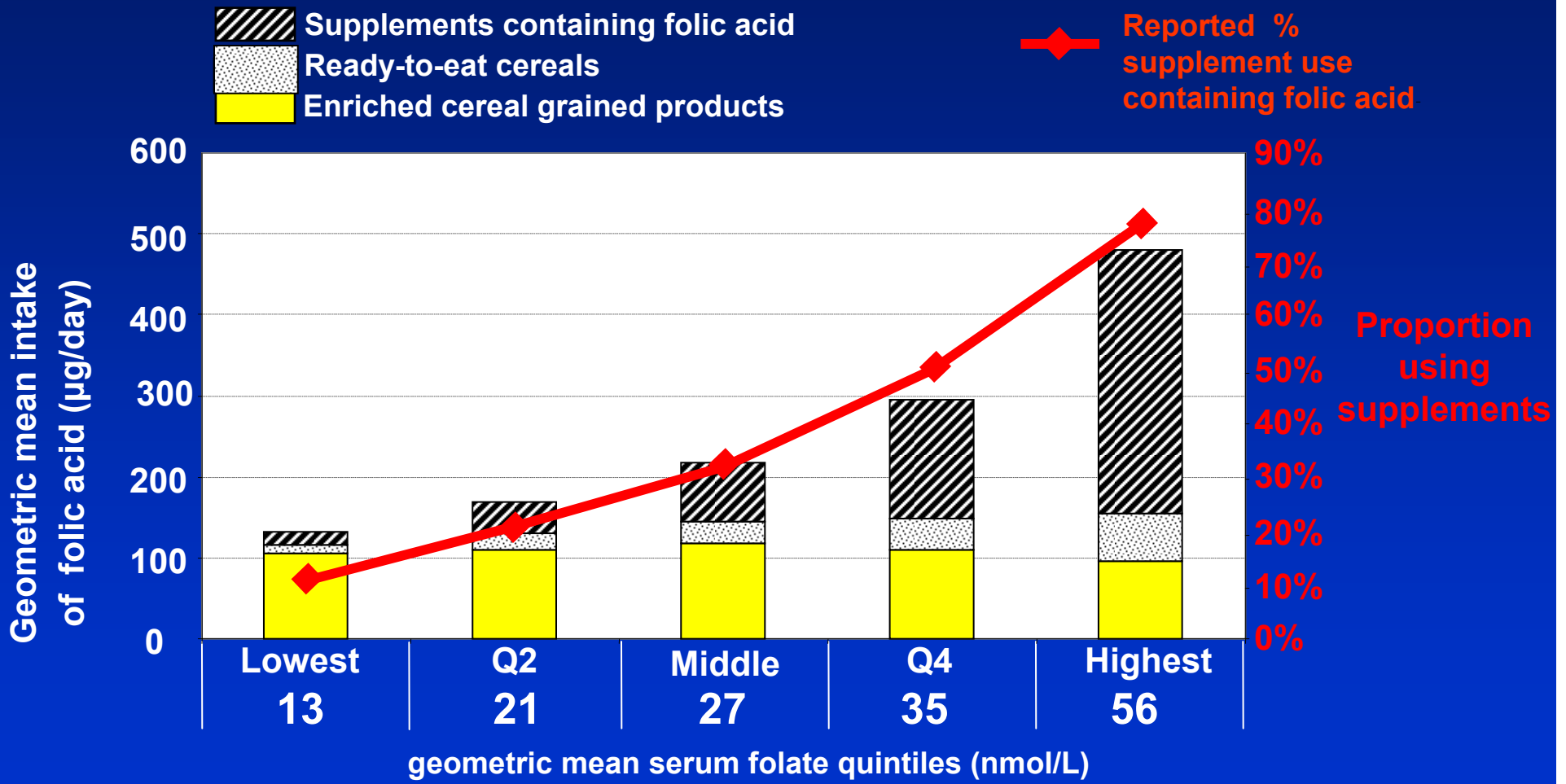
National Health and Nutrition Examination Survey (NHANES)

- **National representative sample of U.S.**
 - **Continuous 2 year cycles since 1999**
- **Interview**
 - **Self-reported dietary assessments using 24 hour recalls**
 - ◆ **Consumption of foods**
 - ◆ **Consumption of every supplement**
- **Laboratory measurements**
 - **Serum and RBC folate**

Geometric Mean Intake from Folic Acid Sources and Percent Contribution of Folic Acid from Supplements by Age Groups, NHANES 2001-2004



Geometric Mean Folic Acid Intake, Enriched Cereal-Grain Products, RTE cereals & Supplements by Serum Folate Quintiles NHANES 2001-2004, ≥19 years, n=8,655



* Percent contribution of folic acid from ECGP

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

Conclusions

- **Supplements main contributor to higher intakes**
- **More than 50% of seniors take supplements containing folic acid**
- **Supplements main contributor to higher blood folate concentrations**

Potential (unproven) adverse health outcomes attributed to FA fortification

- **Limited but suggestive data that excessive folate intake might precipitate or exacerbate neuropathy in vitamin B12 deficient individuals. (IOM DRI B-vitamins)**
- **Findings in RCT of colorectal adenoma theoretically linked results with fortification though research used 1 mg folic acid as exposure. (Cole et al.)**
- **Hypothesis that 1998 mandated FA fortification of flour is correlated with apparent increase in colorectal cancer in NCI SEER data. (Mason et al.)**

Basis of determining the safe level of folic acid to be added to fortify flour

- **Tolerable upper level is maximum average usual intake of folic acid**
- **Average daily consumption of fortified product**

Safe levels of folic acid to be added to flour by per capita consumption of wheat flour

Flour extraction rate	Compound	Level of folic acid in parts per million (ppm) by estimated average per capita wheat flour availability (g/day)			
		<75	75 - 149	150-300	>300
Low or High	Folic acid	5.0	2.6	1.3	1.0

What are the important recommendations to promote fortification of flour with folic acid?

- **Improve monitoring of NTDs and other potential health outcomes potentially associated with fortification.**
- **Establish support for countries preparing to develop plans to fortify flour with folic acid, to enable them to simultaneously implement flour fortification and to collect baseline blood folate concentrations, with which to compare pre-and post-fortification blood folate.**
- **Conduct a workshop to assess possibilities for defining blood folate concentrations that estimate the concentrations at which folic acid preventable NTDs rarely, if ever would occur.**
- **Standardize the measurement of blood folate concentrations for different assays so that results from different assays can be made into equivalent assays so that concentrations can be compared easily.**

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Thank you