

# Sources of Folic Acid, Supplement Use, and the Relationship Between Intake and Blood Levels

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*Views expressed are my own and do not reflect the views of ODS, NIH, CDC, HHS, or any other entity of the U.S. Government*

# Disclosures and Disclaimers

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- I have no conflicts of interests and nothing to disclose
- Unpublished Data
- Views expressed are my own and do not reflect the views of ODS, NIH, HHS, or any other entity of the U.S. Government

# Acknowledgements



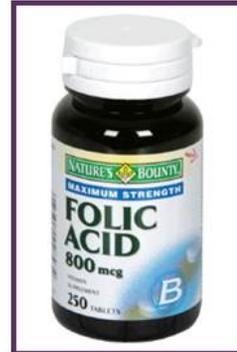
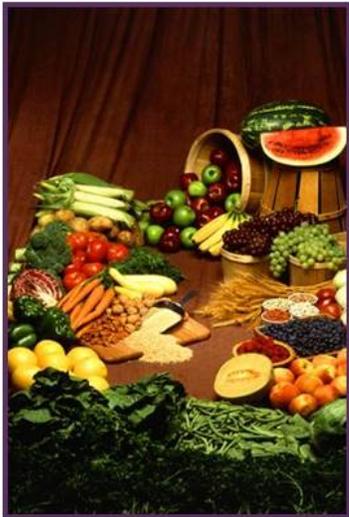
- **Victor Fulgoni III**
  - Usual intake analyses
- **Deborah Keast**
  - Database generation to distinguish intrinsic, added, and total nutrients in foods
- **Louise Berner**
  - Work on food sources of nutrients from children's diet
- **Johanna Dwyer**
  - Co-author extraordinaire
- **Christine Pfeiffer, Anne Molloy, Jim Mills**
  - Help with biomarkers and cut-points

Folate

Folic Acid

*Dihydrofolate reductase*

Dihydrofolate



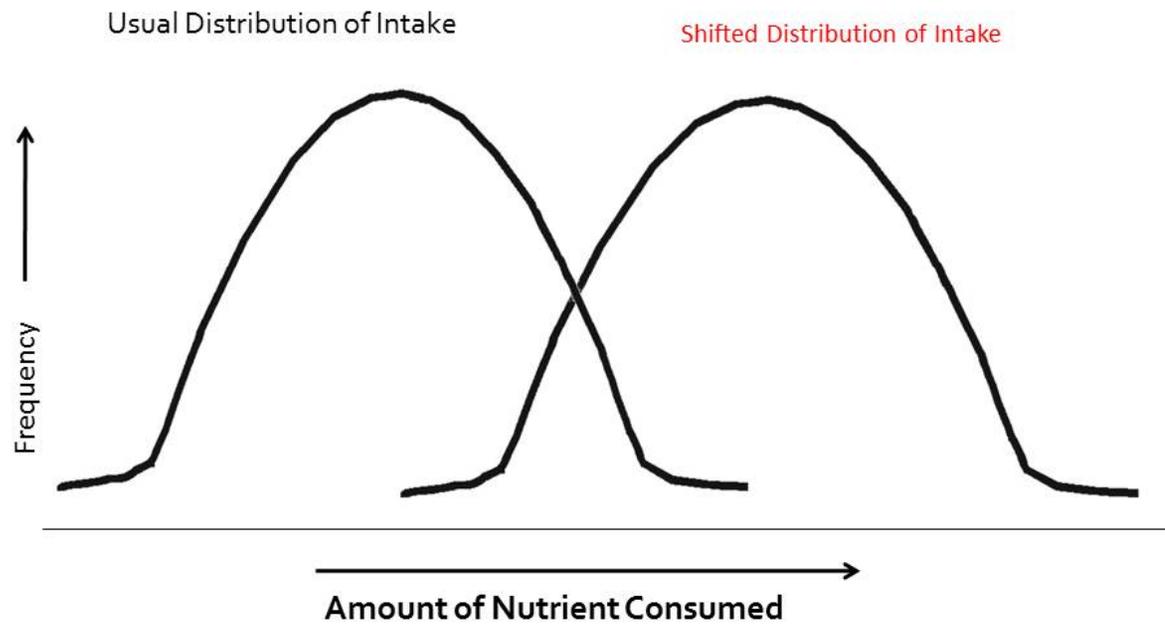


# Current Status

~ 70 countries require folic acid in flour

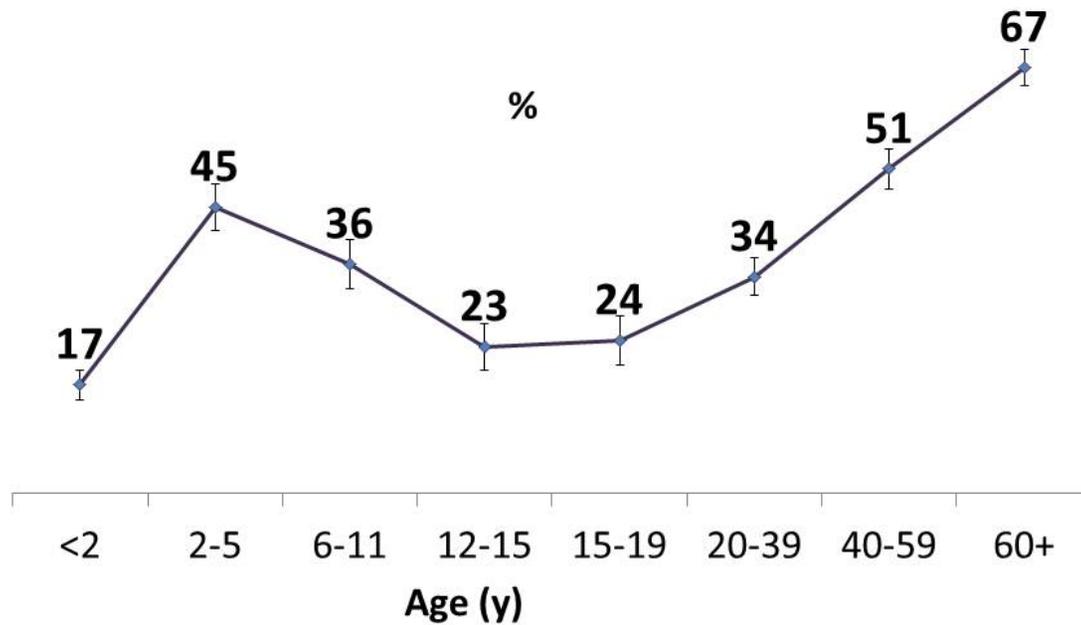


# Fortification shifts intake for all persons, but not systematically



# Prevalence of Use of Any Dietary Supplement

NHANES 2007-2010

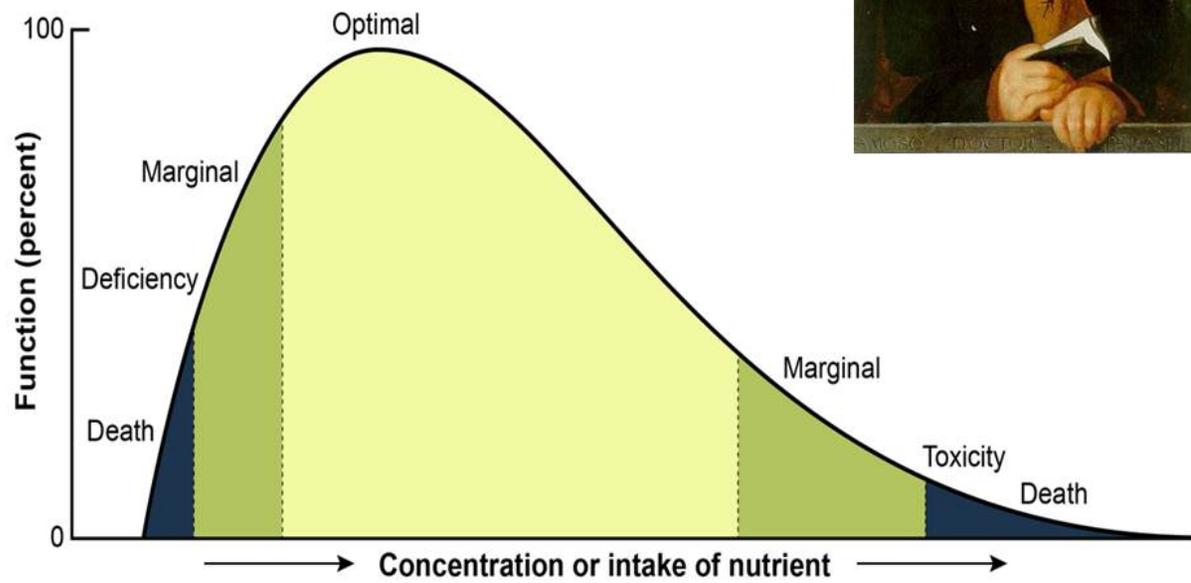


Error bars represent 95% confidence intervals.

SOURCES: CDC/NCHS, National Health and Nutrition Examination Survey, 2007-2010.

“The dose is the poison”

Paracelsus (1493-1541)



# Institute of Medicine Dietary Reference Intakes

Adapted from the IOM/FNB: Dietary reference intakes applications in dietary assessment, 2000.

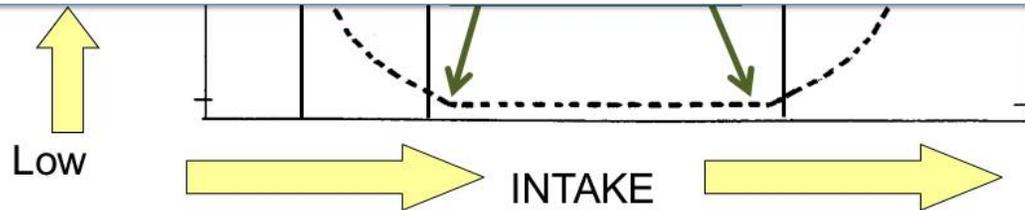
High

Likely Inadequate for  
'healthy' population

Tolerable Upper Intake Level (UL) >  
levels increase potential risk for harm

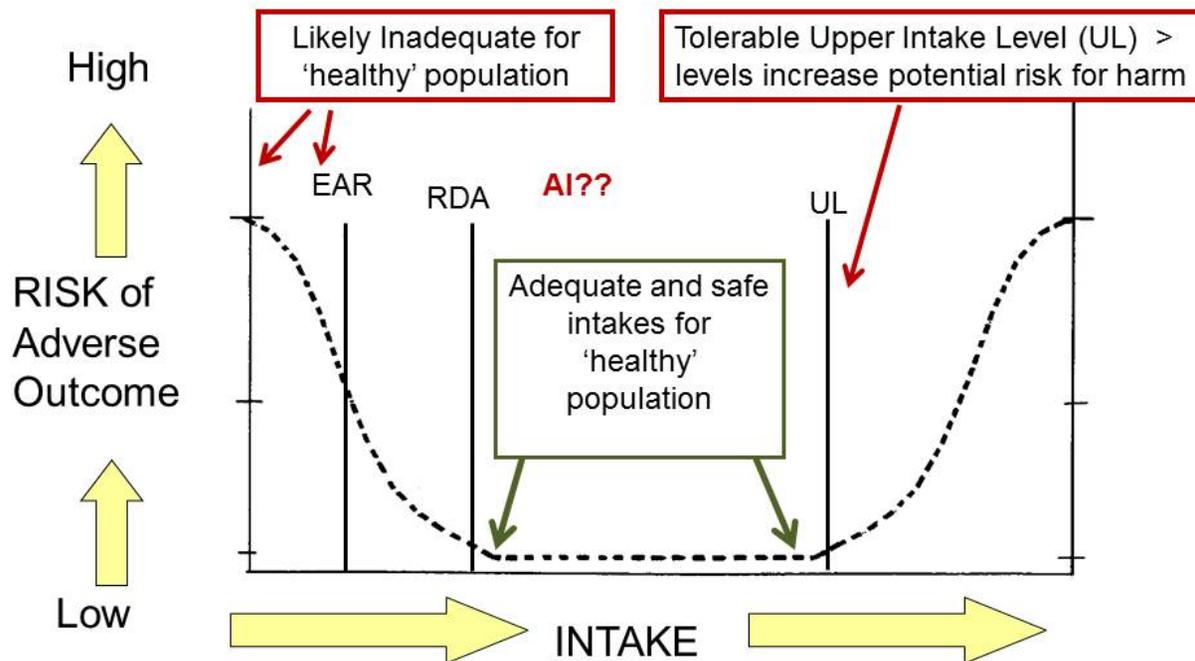
The DRIs are built upon the notion of dual risk

Others refer to it a U or J shaped curve



# Institute of Medicine Dietary Reference Intakes

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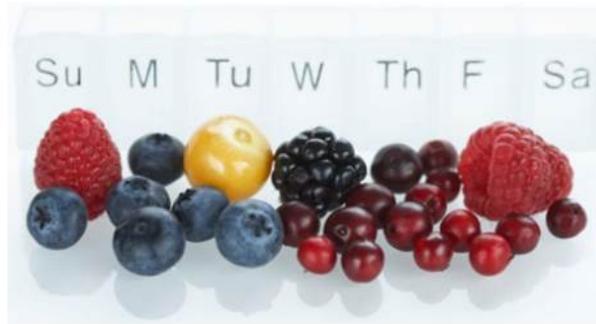


# Dietary Folate Equivalents

- The FNB/IOM developed the Dietary Folate Equivalent (DFE)
- Folate bioequivalence
  - 1 DFE = 1  $\mu\text{g}$  food folate = 0.6  $\mu\text{g}$  folic acid from supplements and fortified foods
  - EAR is in terms of DFE, but UL is ONLY for folic acid

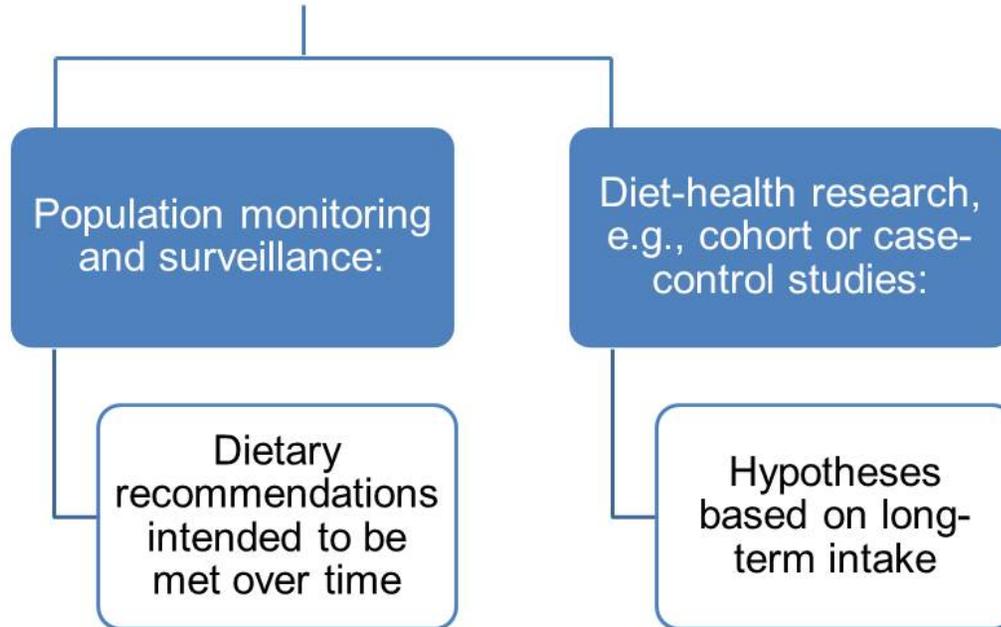
## Usual dietary intake

- Usual nutrients intakes distributions are necessary to describe the prevalence of inadequate or excessive nutrient intakes (i.e. the tails of the distribution).



## Usual dietary intake

Average or long-run intake (*habitual intake*)  
over a specific period of time

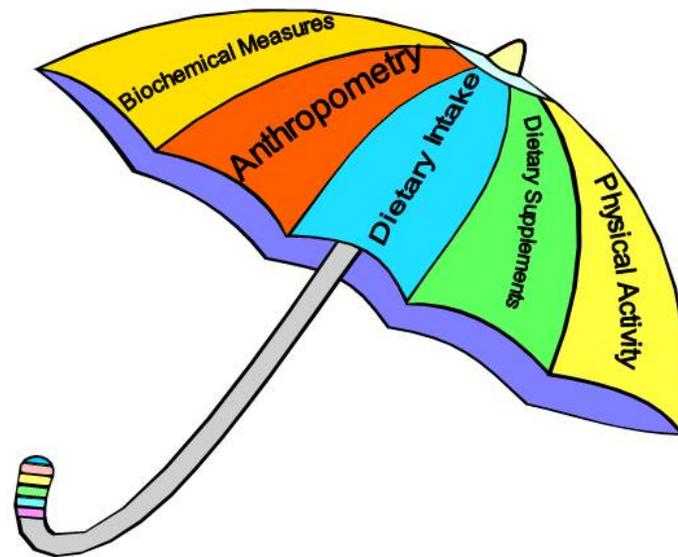


Slide courtesy of the National Cancer Institute Measurement Error Webinar Series

## Usual intakes are not directly observable

- Self-report dietary assessment instruments measure usual intake with error
  - If ignored, this error can bias results
- Statistical modeling methods can be used to correct this bias
  - Requires repeat measurements
  - Estimate distribution of usual intake by removing within-person variation
  - May also account for nuisance effects (e.g., day of week, recall sequence, interview mode)

# National Health and Nutrition Examination Survey (NHANES)



To assess the health and nutritional status of adults and children in the United States.



## National Health and Nutrition Examination Survey

- Dietary Intakes
  - 2, 24-hour recalls
- Supplement Intakes
  - 30 day frequency questionnaire
- NCI Method
  - Covariates
- Biomarkers
  - Serum Folate
  - RBC Folic
  - Serum Folic Acid (aka unmetabolized folic acid)

# Folate/Folic Acid in Diets and Blood of Toddlers, Children, Adolescents, and Teens in the U.S.



## NHANES 2003-2006: Impact of Added Folic Acid

1-3 years 120 mcg DFE 1-3 years 300 mcg  
4-8 years mcg  
9-13 y mcg  
14-18 y mcg

Before fortification half to all children were not achieving recommended levels; however, after fortification is considered we almost ~10% of children (2-8y) exceeding the UL from foods alone and 70% exceeding the UL among children using supplements.

Data shown for females and males combined 2-8 years; females only for 9-18 years



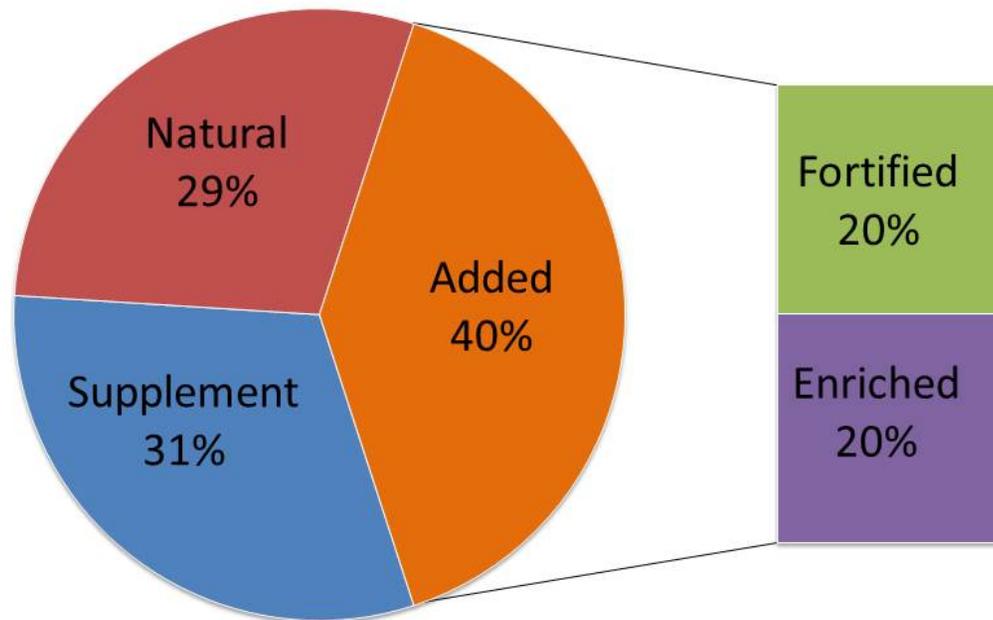
**% >UL by Nutrition Source,  
Children 2-8 y  
Users and Non-Users Combined**



<b>Nutrient Source</b>	<b>Folic Acid</b>
<b>Intrinsic Only</b>	N/A
<b>+ Fortification</b>	9.7%
<b>+ Supplements</b>	30.3%

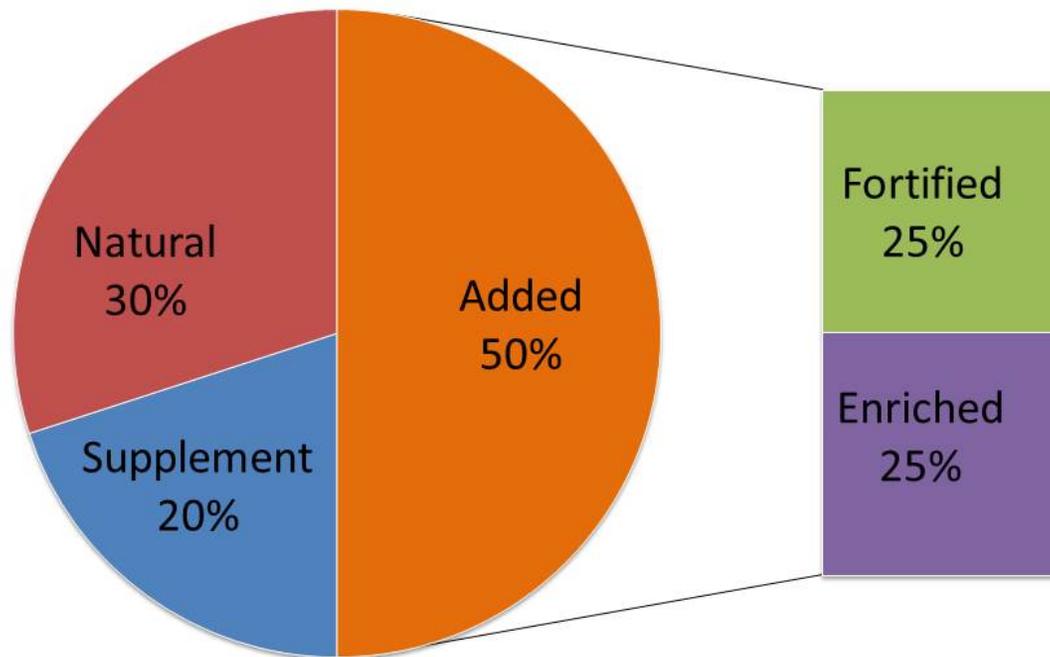
## Sources of Folate & Folic Acid (DFE)

### 2-3 year olds



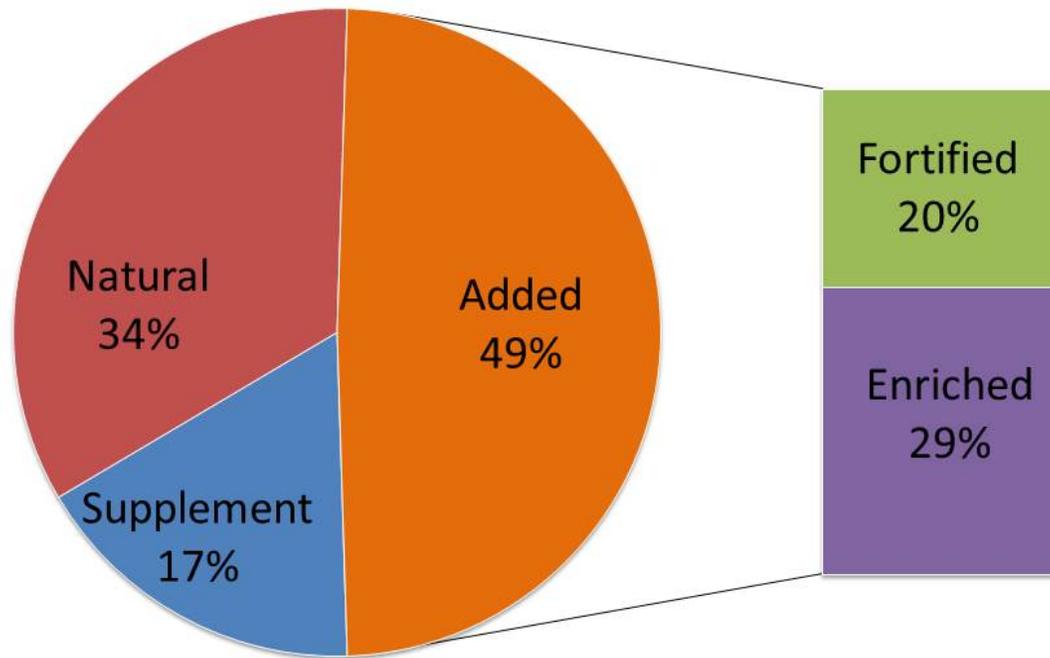
## Folate & Folic Acid (DFE)

### 4-8 year olds



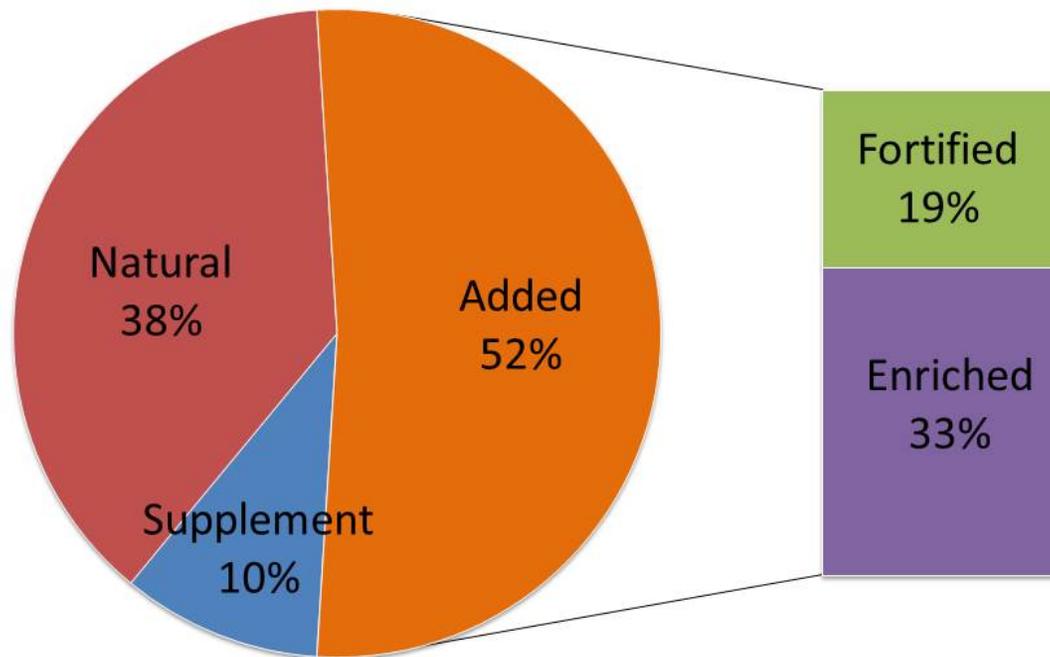
## Folate & Folic Acid (DFE)

### 9-13 year olds



## Folate & Folic Acid (DFE)

### 14-18 year olds



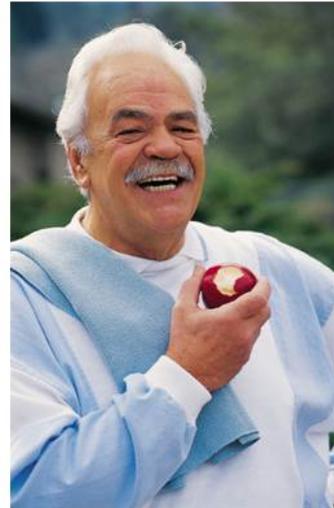
## Food Sources of Folate/Folic Acid: Total vs Added

Children 2-8 years (n = 2601)					
Food Sources of Both Intrinsic and Added Folate			Food Sources of Only Added Folate		
Rank and Food Grouping	%	Cum. %	Rank and Food Grouping	%	Cum. %
1 RTE cereal	30.5	30.5	1 RTE cereal	48.2	48.2
2 Yeast bread, rolls	9.7	40.2	2 Yeast bread, rolls	11.2	59.4
3 Pizza, turnovers	6.0	46.2	3 Pasta dishes	7.7	67.1
4 Pasta dishes	6.0	52.2	4 Pizza, turnovers	6.5	73.6
5 Crackers, popcorn, pretzels, chips	4.5	56.7	5 Cake, cookie, quick bread, pastry, pie	4.6	78.2

## Food Sources of Folate: Total vs Added

Children/Adolescents 9-18 years (n = 4649)					
Food Sources of Both Intrinsic and Added Folate			Food Sources of Only Added Folate		
Rank and Food Grouping	%	Cum. %	Rank and Food Grouping	%	Cum. %
1 RTE cereal	22.0	22.0	1 RTE cereal	36.1	36.1
2 Yeast bread, rolls	13.3	35.3	2 Yeast bread, rolls	16.3	52.4
3 Pizza, turnovers	9.7	45.0	3 Pizza, turnovers	10.9	63.3
4 Pasta dishes	5.0	50.0	4 Pasta dishes	6.6	69.9
5 Crackers, popcorn, pretzels, chips	4.4	54.4	5 Cake, cookie, quick bread, pastry, pie	5.1	75.0

## Folate/ Folic Acid in the Diets of Adults (19+ years) in the U.S.



## Summary and Considerations

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- Children exceed the UL from diet alone, not true in adults
  - About 50% of folate/folic acid intakes among US children are added to foods through fortification and enrichment
- Discrepancy between who is at risk by diet and by biomarker; but, they are measuring very different constructs
- Diet and biomarkers agree more at the high ranges



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ODS Web site: <http://ods.od.nih.gov>



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