

Prevention of Birth Defects: An Emerging Opportunity in the Era of the “Omics”

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Conflicts of Interest

- I have no conflicts of interest related to this presentation



Prevention of Birth Defects: A Historical Perspective

- Before the 20th Century
 - Curiosities. Nothing can be done
 - Cultures in Mesoamerica
- 20th Century: 1950s and forward
 - Genetics and Prenatal Diagnosis
 - Newborn Screening
 - Recognition of birth defects as a public health issue:
Thalidomide & Congenital Rubella Syndrome
 - Folic Acid Prevents Neural Tube Defects
 - Sequencing of the Human Genome



Prevention of Birth Defects: A Historical Perspective (Cont.)

- 21st Century: Emergence of the “Omics”
 - Genomics
 - Proteomics
 - Metabolomics
 - Exposomics



Opportunities for Birth Defects Prevention

- Primary Prevention:
 - Targets Preconceptional Period
 - Folic Acid
 - Rubella Vaccine
- Secondary Prevention
 - Early Detection
 - Prenatal Diagnosis
- Tertiary Prevention
 - Surgery for Oral Clefts and Congenital Heart Disease
 - Newborn Screening



The Case of Prevention of Neural Tube Defects



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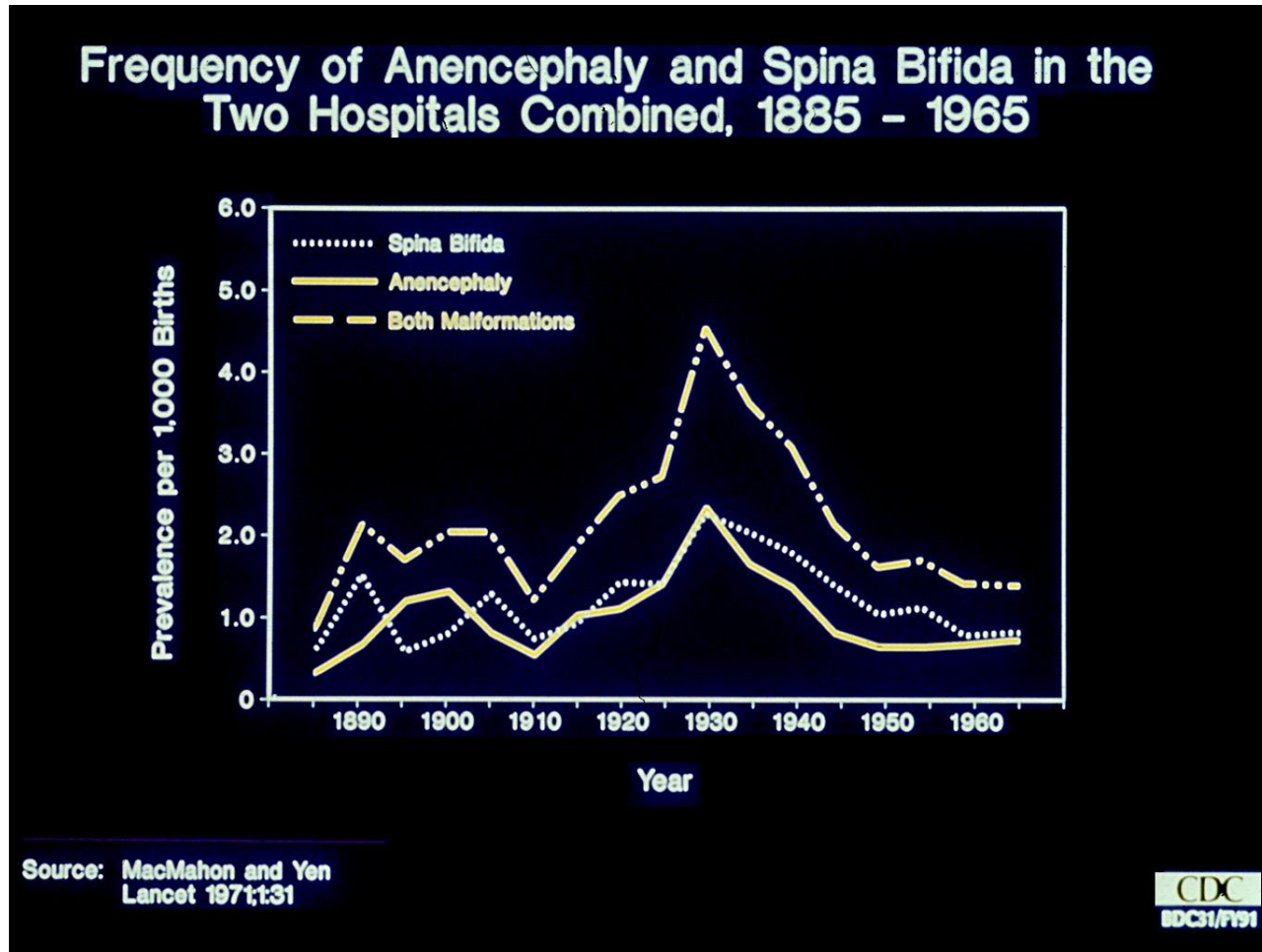
Anencephaly



Spina Bifida (Meningomyelocele)



From McMahon & Yen, 1971



Medical Research Council Folic Acid Randomized Controlled Trial

- **Control: 3.5 % (21/602)**
- **Treated: 1.0 % (6/593)**
**(4,000 mcg synthetic folic acid
and usual diet)**
- **RR = 0.29 (0.12-0.71)**



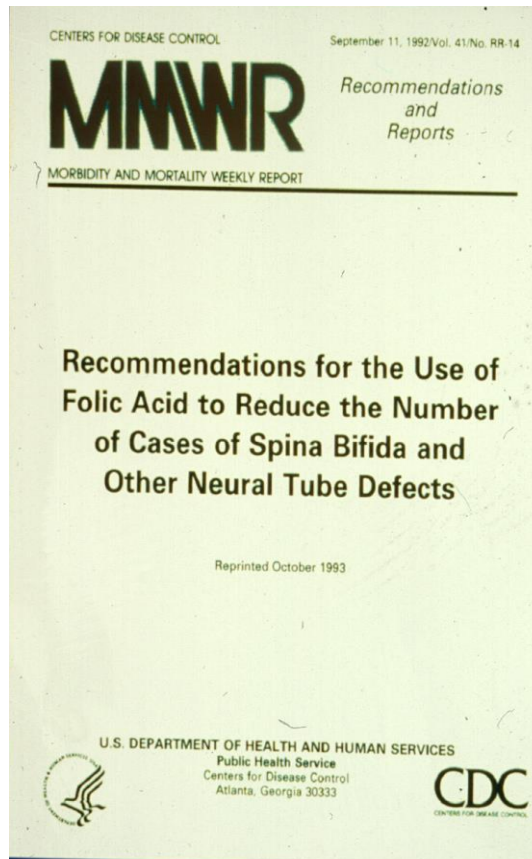
Dr. Nick Wald

Wald et al., Lancet 1991; 338; 131-137



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CDC Recommendations for Increase Consumption of Folic Acid



- Any woman capable of becoming pregnant should consume 0.4 mcg of folic acid daily to reduce the risk of neural tube defects
- If there is a history of a previous affected pregnancy, consumption should be 4 mg daily

Sources of Folic Acid

Diet Changes



Fortification

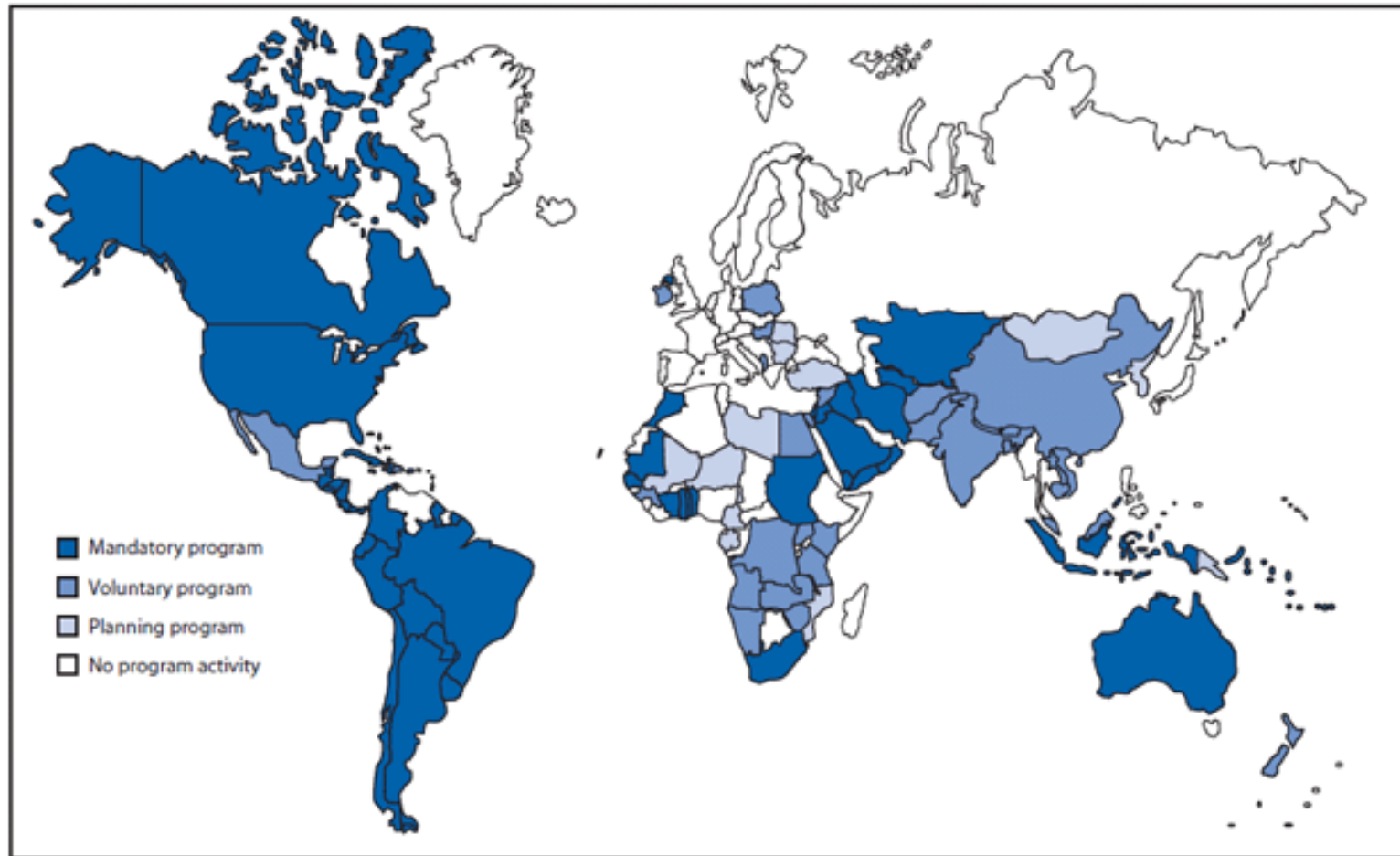


Supplementation

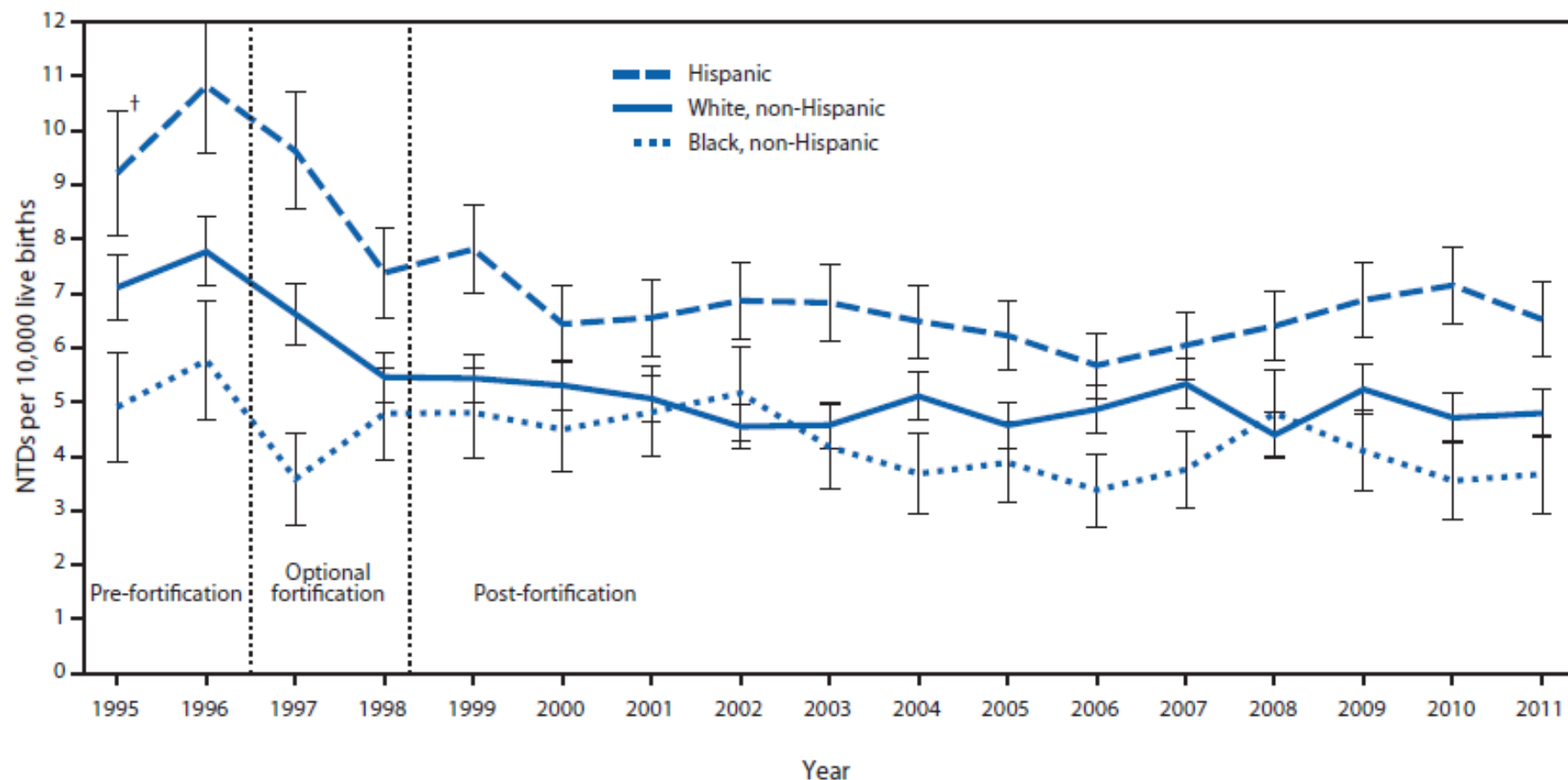


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Fortification Programs Worldwide



Neural Tube Defects in the US: Experience Post-Fortification with Folic Acid



Genomics of Folic Acid MeMTHFR Alleles

- Alleles
 - C, T
 - Genotype TT associated with elevated homocysteine
 - Frequencies of TT varies greatly in populations
 - Very low in Canada (<6%)
 - High in China and Mexico (20%, 32%)
 - Also associated with high rates of NTDs



Summary

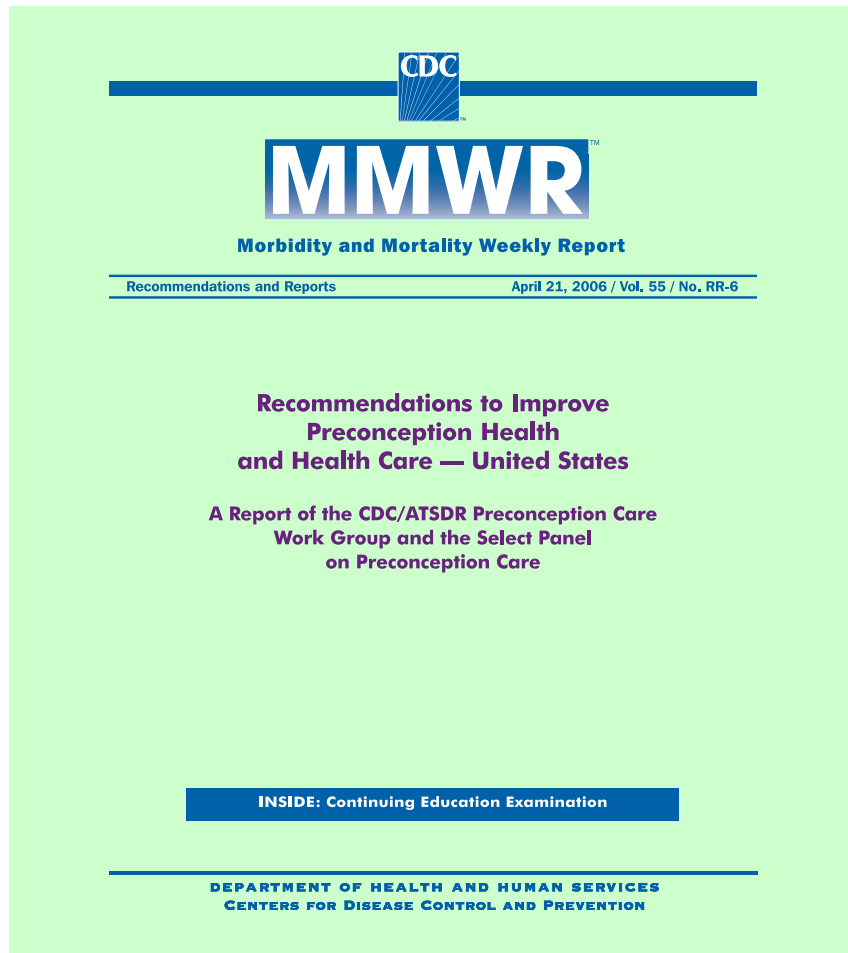
- Fortification is an effective public health strategy that has been implemented in many countries
- It is important to address the genomics of folic acid as well as the need for increased folic acid in corn masa flour in the US

New opportunities in Preconceptional Care in the “Omics” Era

- The key opportunity for primary prevention is before pregnancy begins.
- There are well established recommendations for improving the opportunity of a health pregnancy and a healthy baby through preconceptional strategies



Preconceptional Care



- Identifies opportunities for preconceptional strategies to reduce risk
 - Tobacco
 - Alcohol
 - Control of maternal conditions
 - Addressing family history
 - Endorsed by over 30 organizations

Where is the field going?



- The National Report on Human Exposure to Environmental Chemicals
- Provides data on levels of hundreds of chemicals among a healthy population of adults in the US

The New Technology Opens Opportunities

- Genomics sequencing is getting faster and cheaper
- Manufacturing of chips that do hundreds of test with a single blood specimen using Mass Spectrometry becoming cheaper and larger
- Information on the genome AND the exposome is key to address the interaction of genetic and environmental factors



Summary

- Prevention of Birth Defects is a reality
- The Preconceptional Care should be the target period to address potential pregnancy risks.
- The paradigm shift is:
 - *The time to think about pregnancy is before it begins*

¡Gracias!

Thank you

Merci

