

# IMPROVING CHILD SURVIVAL AT THE INTERSECTION OF **NUTRITION** AND **BIRTH DEFECTS**

## INTERACTIVE **WEBINAR**

HOSTED BY THE

## **FOLATE TASK TEAM**

**DECEMBER 4<sup>th</sup>** 2018

10:00AM – 11:30AM EST

For registration

<http://bit.ly/folatewebinar>



Nourish Life



# Folate Task Team



**Dr. Homero Martinez**  
**Senior Technical Advisor**  
**Nutrition International**



**Jessica Poulin**  
**Knowledge Translation**  
**Officer**  
**Nutrition International**



**Alik Pappas Weakland**  
**Project Consultant**  
**Core Engagement LLC**

# List of speakers

## The Science of Prevention

<b>Amy Cordero, MPA</b>	Deputy Team Lead, Prevention Research, Centers for Disease Control and Prevention
<b>Lynn Bailey, PhD</b>	Professor and Head of the Department of Foods and Nutrition, University of Georgia
<b>Scott Montgomery</b>	Director, Food Fortification Initiative
<b>Homero Martinez, MD, PhD</b>	Senior Technical Advisor, Nutrition International

## A Better Life for Everyone

<b>Tom Scott</b>	CEO, Spina Bifida Hydrocephalus Ireland
<b>Ruth Nalugya</b>	Chair, The Spina Bifida and Hydrocephalus Association of Uganda
<b>Elena Záppoli</b>	President, Asociación para Espina Bífida e Hidrocefalia Argentina

# Amy Cordero



Deputy Team Lead, Prevention Research, Centers for Disease  
Control and Prevention



## Neural Tube Defects Overview and Global Prevalence



**Amy Cordero, MPA**

*Prevention Research Team, Prevention Research and Translation Branch,  
Division of Congenital and Developmental Disorders,  
National Center on Birth Defects and Developmental Disabilities, CDC*

4 December 2018

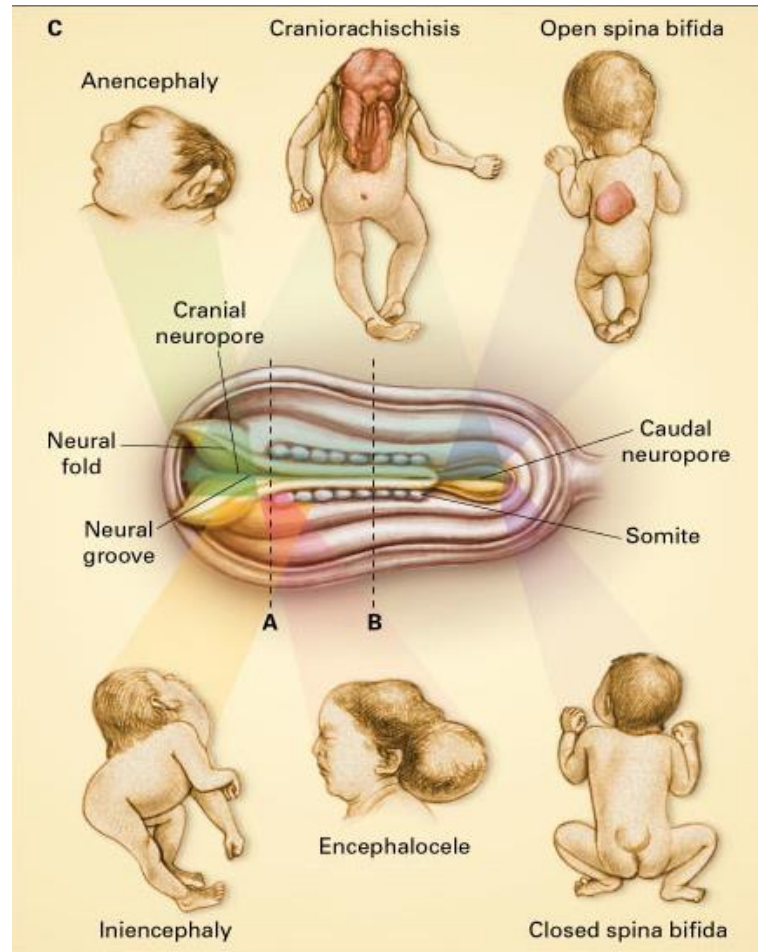
# Outline

- What are Neural Tube Defects (NTDs)?
  - Description
  - Most Common Types
- Mortality and Morbidity
- Global Prevalence
  - Data Limitations
  - Global Burden
- Risk Factors

# Neural Tube Development and Neural Tube Defects



22–26 day old embryo



- **Neural tube defects** are serious birth defects of the brain and spine that occur when the neural tube fails to close properly
- Neural tube formation begins in the first days after conception and is completed by **day 28 of gestation**
- The type and severity of the neural tube defect varies by level of the lesion



# Most Common Types of Neural Tube Defects



**Anencephaly (~39%)**



**Spina Bifida (~49%)**



**Encephalocele (~12%)**

Photos: [who.int/nutrition/publications/birthdefects\\_atlas/en/](http://who.int/nutrition/publications/birthdefects_atlas/en/)

Proportions: Pooled data from EUROCAT; Blencowe et al., Ann N.Y. Acad. Sci. Estimates of global and regional prevalence of neural tube defects for 2015: a systematic analysis, Volume: 1414, Issue: 1, Pages: 31-46, First published: 24 January 2018, DOI: (10.1111/nyas.13548)



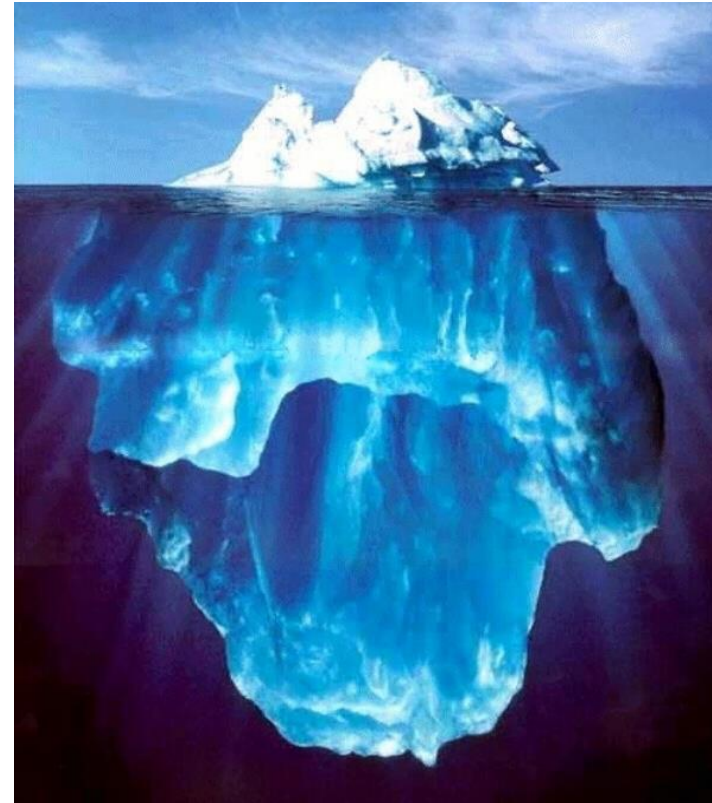
# Mortality and Morbidity of Neural Tube Defects

- Infant mortality (less than 1 year old)
  - Anencephaly – 100%
  - Spina bifida – varies
- Children with spina bifida may live with varying degrees of lifelong disability
  - Paralysis of muscle groups, orthopedic issues
  - Loss of sensation
  - Loss of bladder and bowel control
  - May have hydrocephalus
  - At increased risk of infection
  - Learning and developmental issues
- With access to appropriate services, survival and quality of life for babies born with spina bifida is greatly improved



# Global Prevalence of Neural Tube Defects

- Occur widely
- March of Dimes Global Report on Birth Defects (2006)
  - “There is a paucity of data on the birth prevalence of birth defects in middle- and low-income countries”
  - > 300,000 NTDs globally each year
  - **Systematic underestimation of the toll of birth defects**



Stillbirths

Elective  
terminations of  
pregnancy  
(eTOPFA)

Spontaneous  
abortions

# Estimates of Global and Regional Prevalence of Neural Tube Defects for 2015: A Systematic Analysis

## Global Burden

~260,100 (95% UI: 213,800 – 322,000) NTD-affected birth outcomes

## Prevalence

18.6 (15.3-23.0)/10,000 live births

## Mortality

~ 90% mortality by age 5

(117,900 NTD-associated under 5 deaths among live births + 117,100 stillbirth or eTOPFA)

- Blencowe et al. (2018) built on Modell methodology used by March of Dimes to generate updated global and regional prevalence estimates with uncertainty intervals
- Data sources – birth defects registries, multi-center birth defects monitoring networks, and published literature
- Paucity of high quality data remains, especially in highest burden regions → **Underestimate**

# Risk Factors for Neural Tube Defects

## Multi-factorial

- Nutritional
  - Folate insufficiency
  - Vitamin B-12 deficiency
- Environmental
  - Hyperthermia
  - Environmental toxicants (e.g., high water nitrate)
- Behavioral
  - Maternal medication use (e.g., valproic acid, anti-folates)
- Maternal conditions
  - Obesity, diabetes
- Genetics





# Thank you

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For more information, contact CDC  
1-800-CDC-INFO (232-4636)  
TTY: 1-888-232-6348 [www.cdc.gov](http://www.cdc.gov)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.



# Dr. Lynn Bailey



Professor and Head of the Department of Foods and Nutrition,  
University of Georgia

# **Folate Status in Women: Neural Tube Defect Prevention**

Lynn Bailey, PhD

Flatt Professor in Foods and Nutrition

Head Department of Foods and Nutrition

University of Georgia

Athens, GA, USA

# What is Folic Acid?

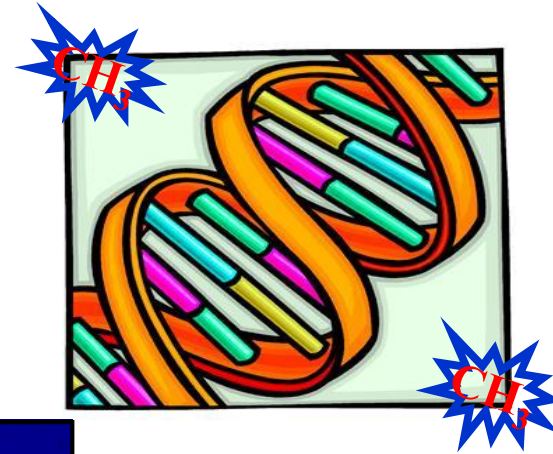
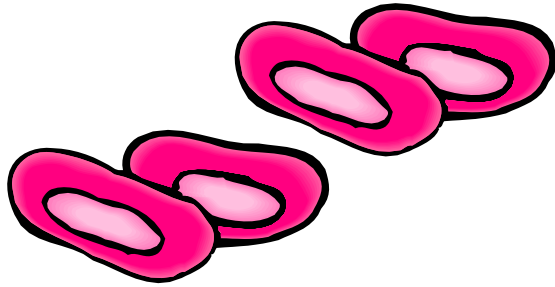
- ▶ Folic acid is one chemical form of vitamin folate
- ▶ Essential nutrient that can't be synthesized by body and must be consumed in diet or in supplements
- ▶ Folic acid is form in supplements and fortified foods





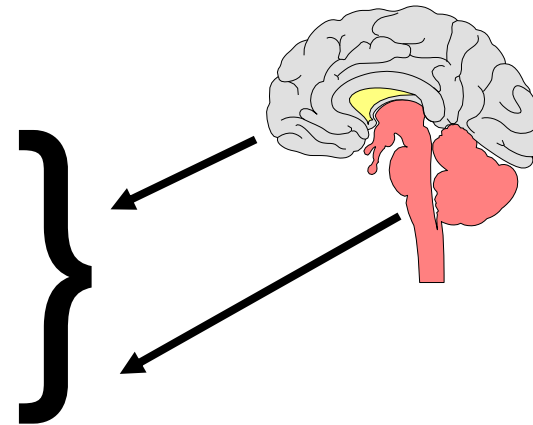
# Functions of Folic Acid

- ▶ DNA synthesis and methylation
- ▶ Cell division and gene regulation for growth and development



11 12 16 20 24 28 32 36 38 Full Term

**Neural tube develops into the fetal spine and brain and requires adequate folic acid**



# Neural Tube Defects



**Spina Bifida**



**Anencephaly**

# Research Evidence: Folic Acid Prevents Neural Tube Defects

Study		% Prevention
Intervention Studies		
<b>Medical Research Council, 1991</b>		<b>72</b>
Czeizel & Dudas, 1992		100
Vergel et al., 1990		100
Prospective Cohort Studies		
Smithells, et al., 1983		86
Mulinaire et al., 1988		60
Bower & Stanley, 1989		75
Milunsky et al., 1989		72
Werler et al., 1993		60
Berry et al., 1999		41 - 85

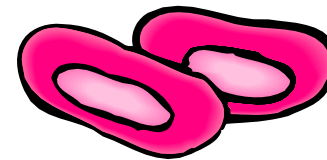


# Folic Acid – NTD Public Health Policies Globally

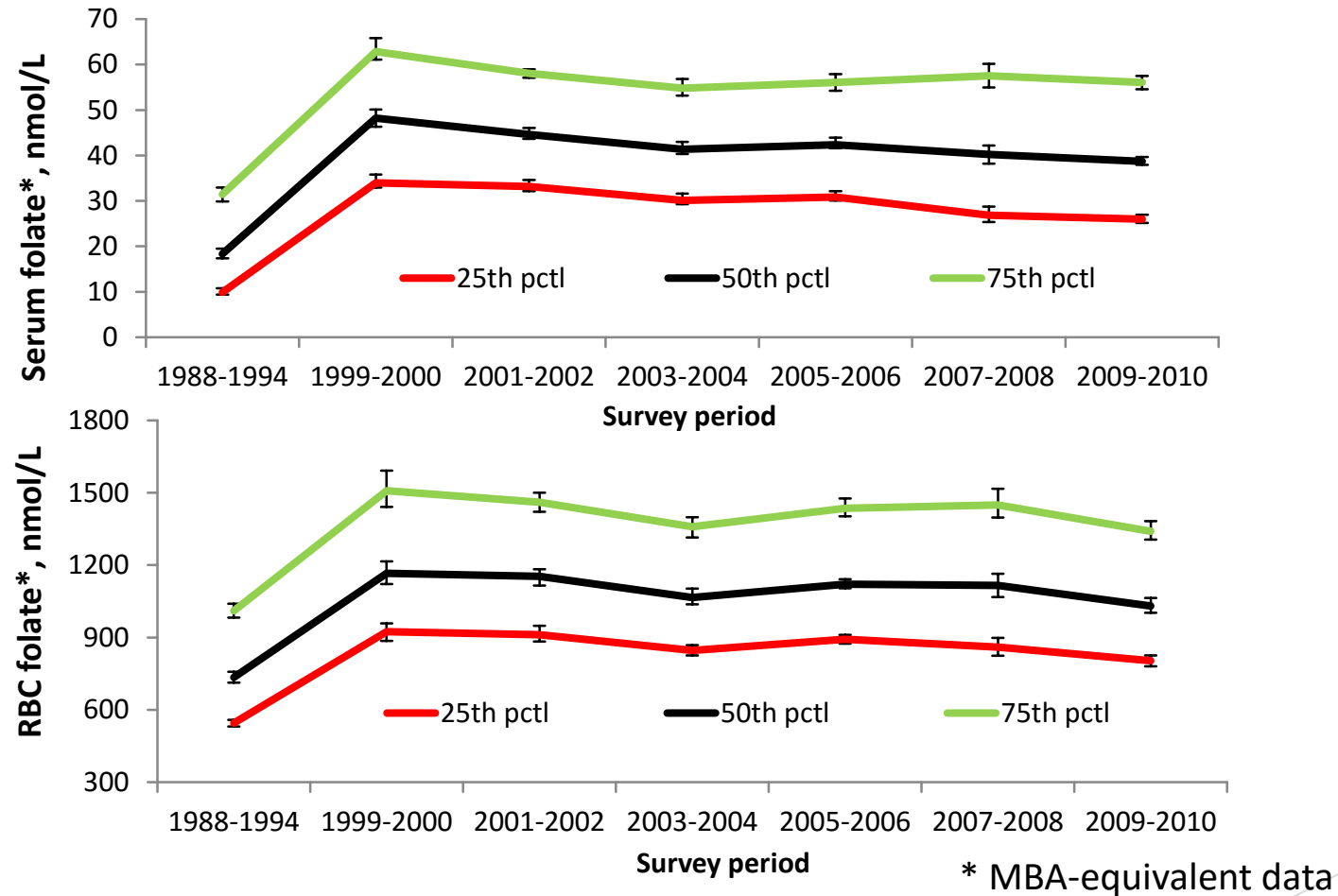
- ▶ Recommendation that all women of reproductive age take 400 micrograms of folic acid daily
- ▶ Folic acid fortification of cereal grain products – policy in 81 countries

# Folate Status Indicators

- ▶ Serum folate very responsive to recent changes in dietary intake
- ▶ Red blood cell (RBC) folate concentration is a sensitive biomarker of longer term folate status and is the only biomarker linked directly to NTD risk



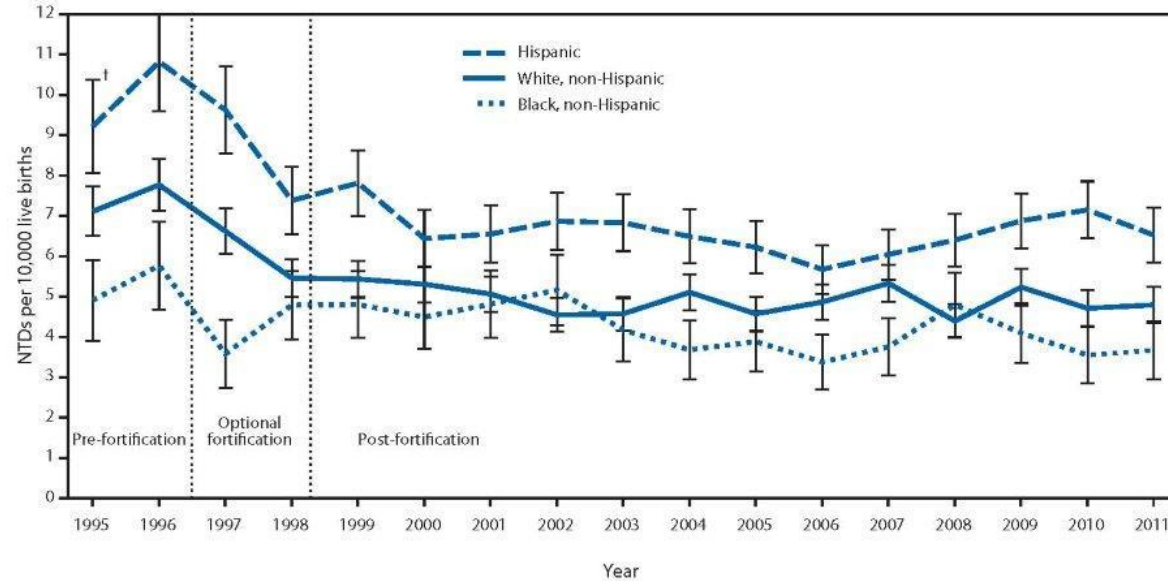
# US Post-fortification Serum and RBC Folate Concentrations were ~ 2.5x and 1.5x Pre-fortification



Pfeiffer et al. Estimation of trends in serum and RBC folate in the US Population from pre-to postfortification using assay-adjusted data from the NHANES 1988-2010, J Nutr 142m 886-93, 2012

# US NTD Rates (1991-2011)

FIGURE. Prevalence of neural tube defects (NTDs) (anencephaly and spina bifida) before and after mandatory folic acid fortification, by maternal race/ethnicity — 19 population-based birth defects surveillance programs,\* United States, 1995–2011



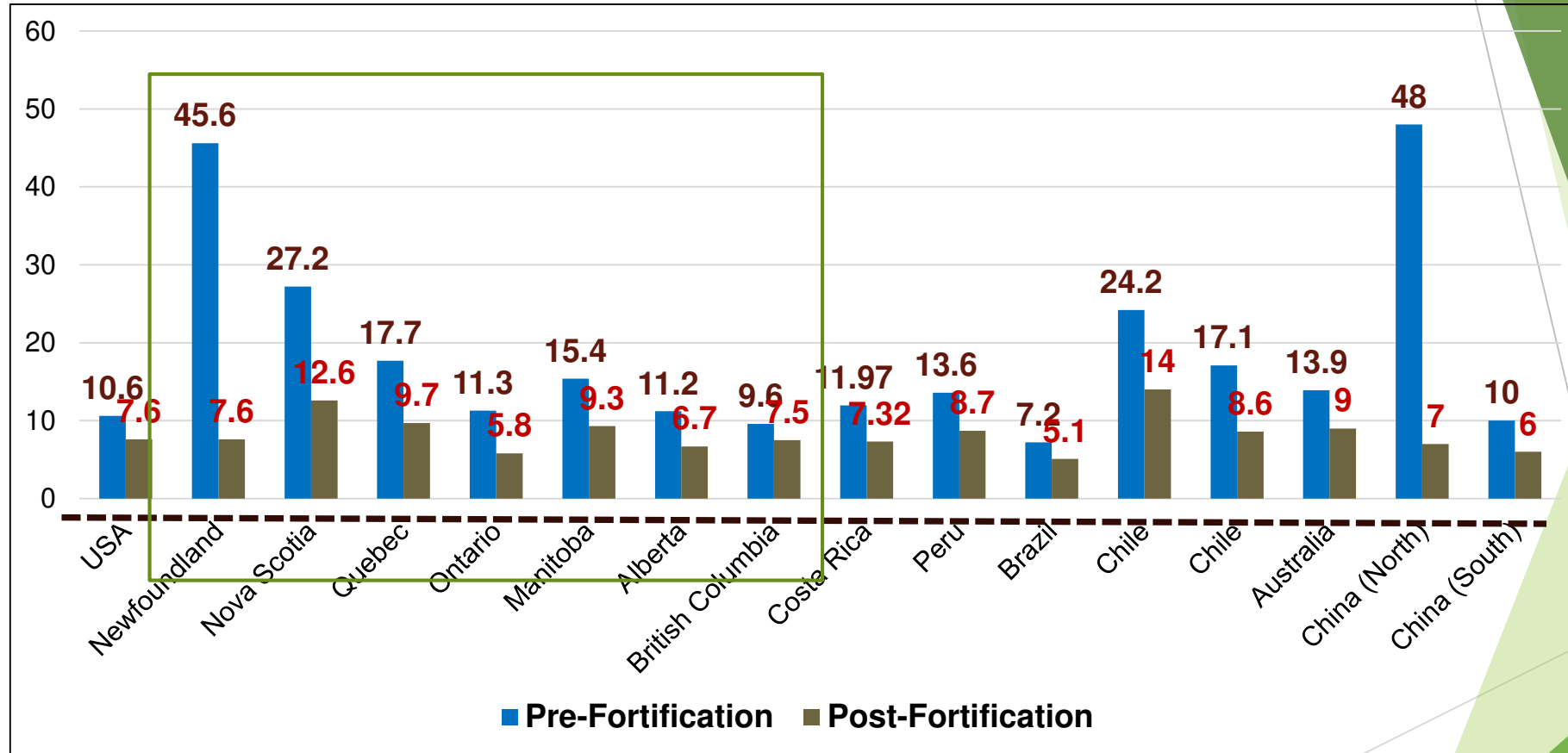
\* Contributing programs are based in Arkansas, Arizona, California, Colorado, Georgia, Illinois, Iowa, Kentucky, Maryland, New Jersey, New York, North Carolina, Oklahoma, Puerto Rico, South Carolina, Texas, Utah, West Virginia, and Wisconsin.

† 95% confidence interval.

After fortification implementation in 1998, NTD rates decreased for all race/ethnic groups. There was a 35% reduction in NTDs including termination and prenatal ascertainment,.



## NTD Prevalence Rates (per 10,000 births) Pre- and Post-Fortification with Folic Acid in Selected Countries



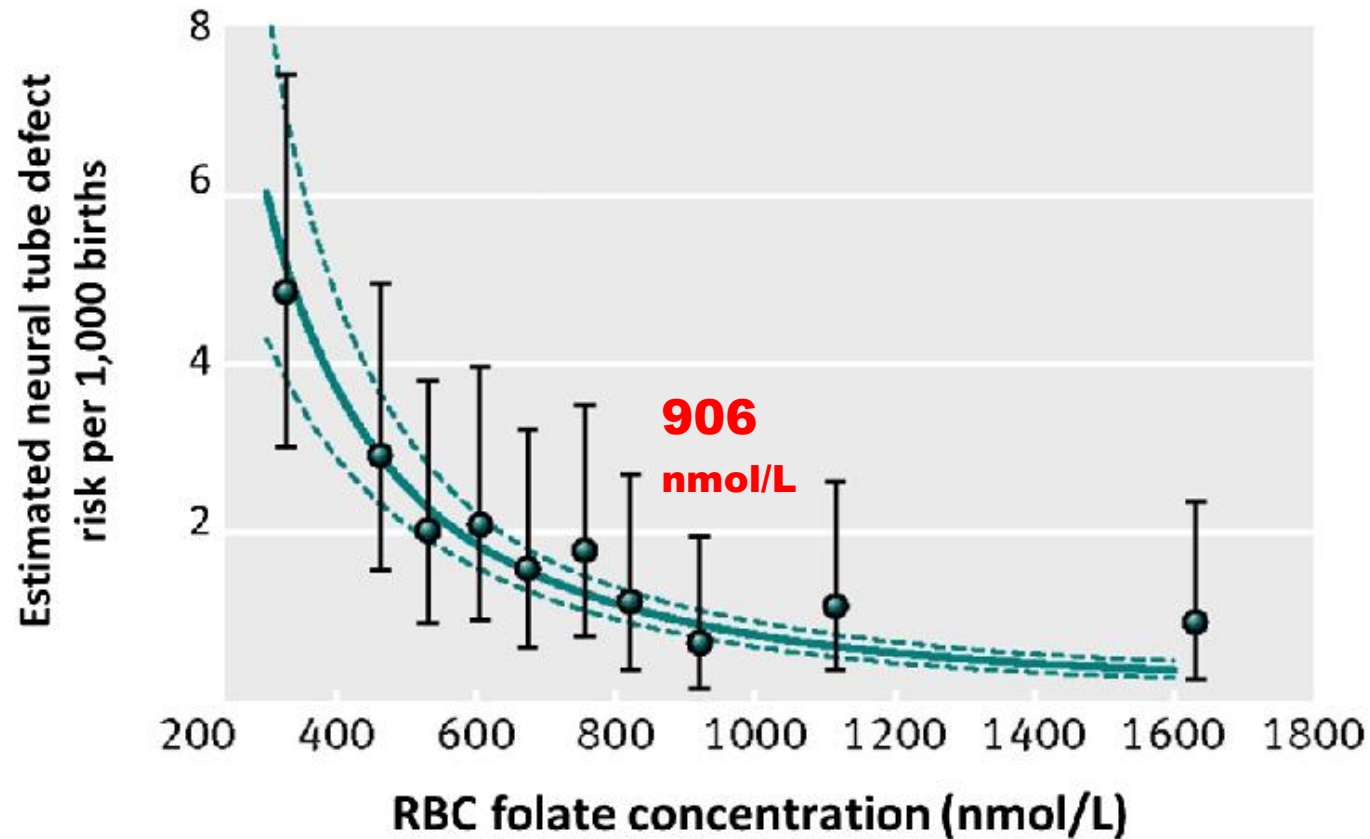
Castilla et al., 2003; Hertrampf et al., 2004; Tacsan et al., 2004; Lopes-Camelo et al., 2005; Silva Pacheco et al., 2009; De Wals et al., 2008; Sayed et al., 2008; Cortes et al., 2012; Ricks et al., 2012; Aña et al., 2016; Santos et al., 2016

# Optimal Blood Folate WHO Guideline



- ▶ RBC folate directly associated with NTD
- ▶ “Optimal” RBC folate defined as 906 nmol/L should be exceeded to achieve greatest reduction in NTDs
- ▶ WHO guideline for “optimal” blood folate meant to be used to assess folate “insufficiency” in populations not individuals
- ▶ Assay of choice is microbiological assay

# Irish Case Control Study Primary Basis of Optimal Blood Folate: Association of RBC Folate with NTD Prevalence



# Microbiological Assay and Need to Harmonize Assays

- ▶ Microbiological assay most reliable method to obtain comparable results for RBC folate across countries and to assess NTD risk within a country
- ▶ For global assessment of NTD risk, there is a need to “harmonize” the MBA through use of consistent key reagents and procedures in selected global regional laboratories conducting the RBC folate analysis



# Assessing NTD Risk: Population-Based RBC Folate Measured by Harmonized Microbiological Assay

- ▶ WHO guideline used to estimate the percentage of women of reproductive age in a population who are folate “insufficient”.
- ▶ This means that this percentage of the population of women of reproductive age are at increased risk for NTD-affected pregnancies.
- ▶ To utilize the WHO guideline to estimate NTD risk in LMI countries, RBC folate in women of reproductive age should be determined with a microbiological assay.



# Global Folate Status of Women of Reproductive Age

- ▶ Systematic review evaluating folate status of women of reproductive age globally based on serum/plasma or RBC folate
- ▶ Results indicate that there are limited data on folate status of women of reproductive age using cut-offs appropriate for the type of assay
- ▶ Disproportionally larger gap in data from LMI countries

# Summary and Conclusions

- ▶ RBC folate predictive of NTD risk defined as folate “Insufficiency” in population groups of women of reproductive age
- ▶ Limited data on folate status in LMI countries
- ▶ Microbiological method recommended
- ▶ Due to methodological differences - great need to “harmonize” microbiological assay to enable comparison within and between countries and regions

# Thank you!



# Scott Montgomery



Director, Food Fortification Initiative

# The Success of Fortifying Grains with Folic Acid

Presented by Scott J. Montgomery  
Director, Food Fortification Initiative  
4 December 2018



**Food  
Fortification  
Initiative**

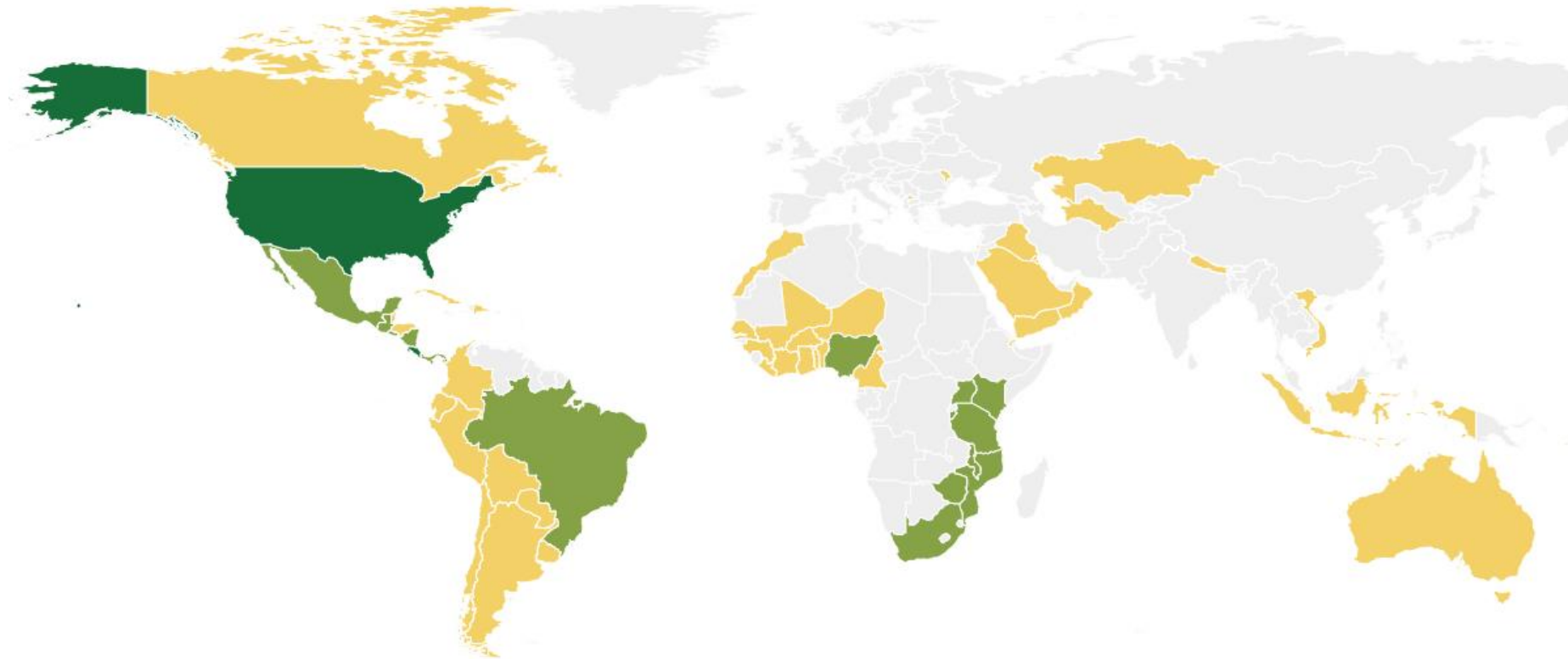
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Enhancing Grains for Healthier Lives





# 62 countries include folic acid in grain fortification mandates



	<b>3 grains fortified with folic acid (wheat flour, maize flour, and rice) Costa Rica and US</b>		<b>2 grains fortified with folic acid (wheat flour and maize flour)</b>		<b>1 grain fortified with folic acid (wheat flour)</b>
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## Advantages of food fortification:

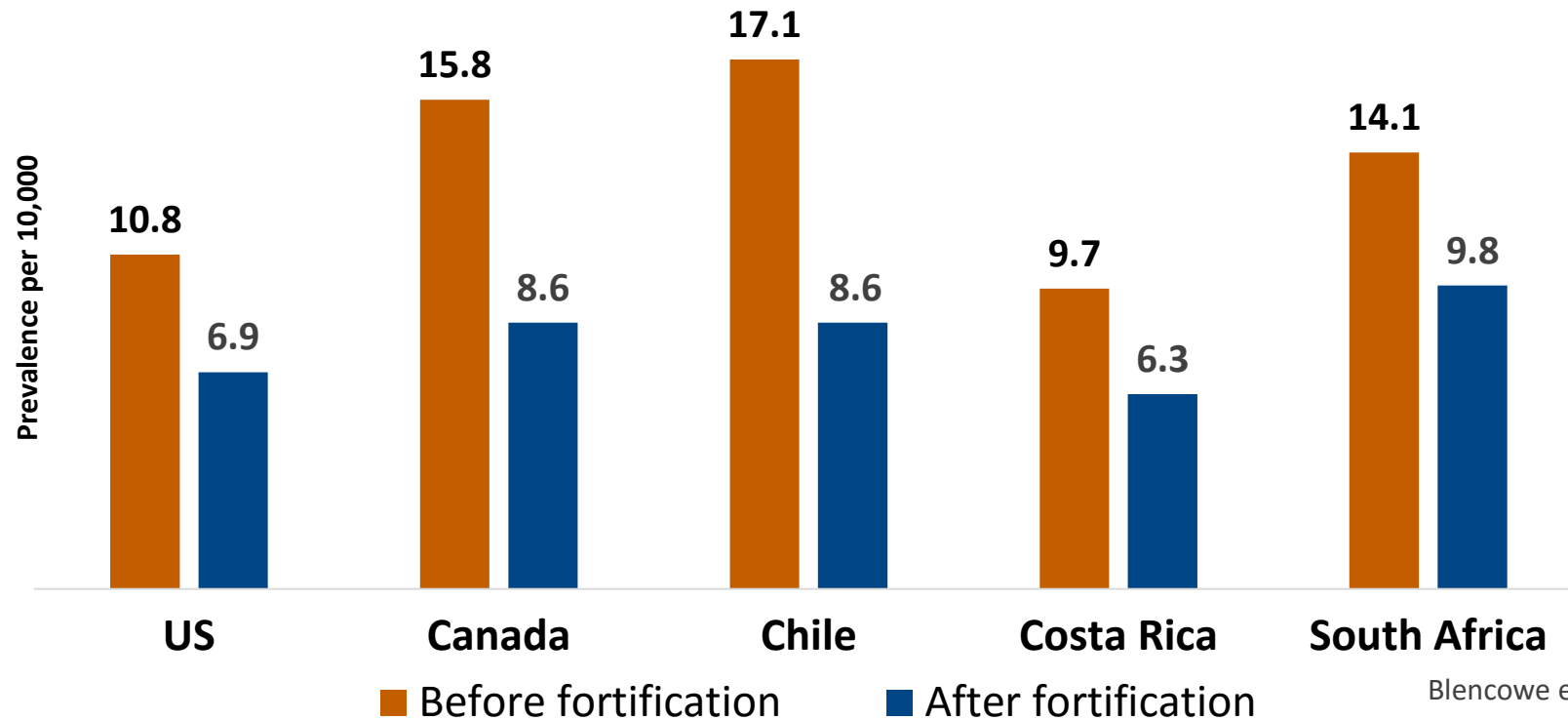
People consume additional folic acid without any behavior change.

Women increase their folic acid intake even if they are not planning a pregnancy.

The private sector provides the product to consumers; a new delivery program is not needed.



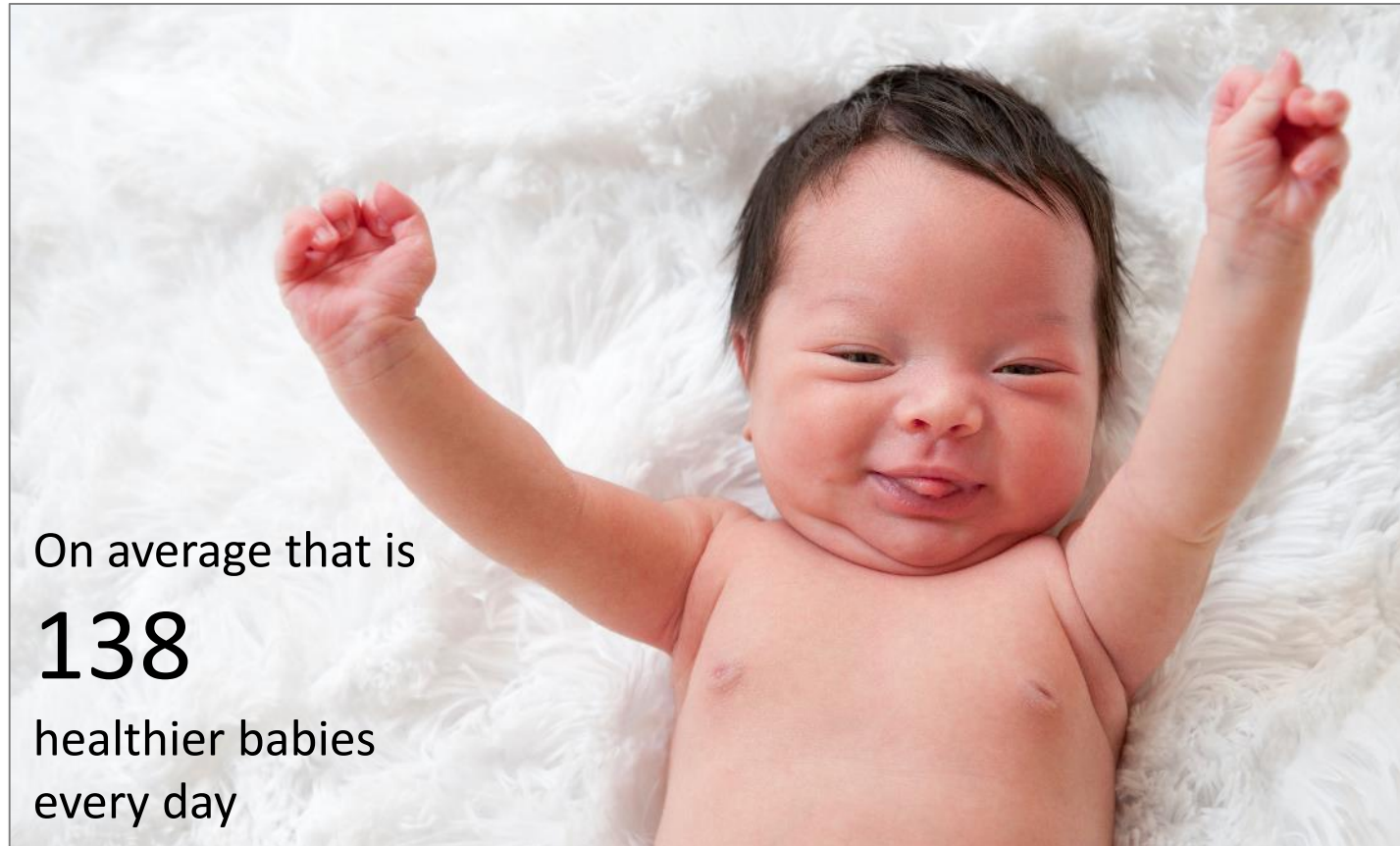
# Countries report decline in NTDs after fortifying flour with folic acid



Blencowe et al. 2010  
CDC 2010  
Cortes et al. 2012  
Sayed et al. 2008  
De Wals et al. 2007  
Rosenthal et al. 2014

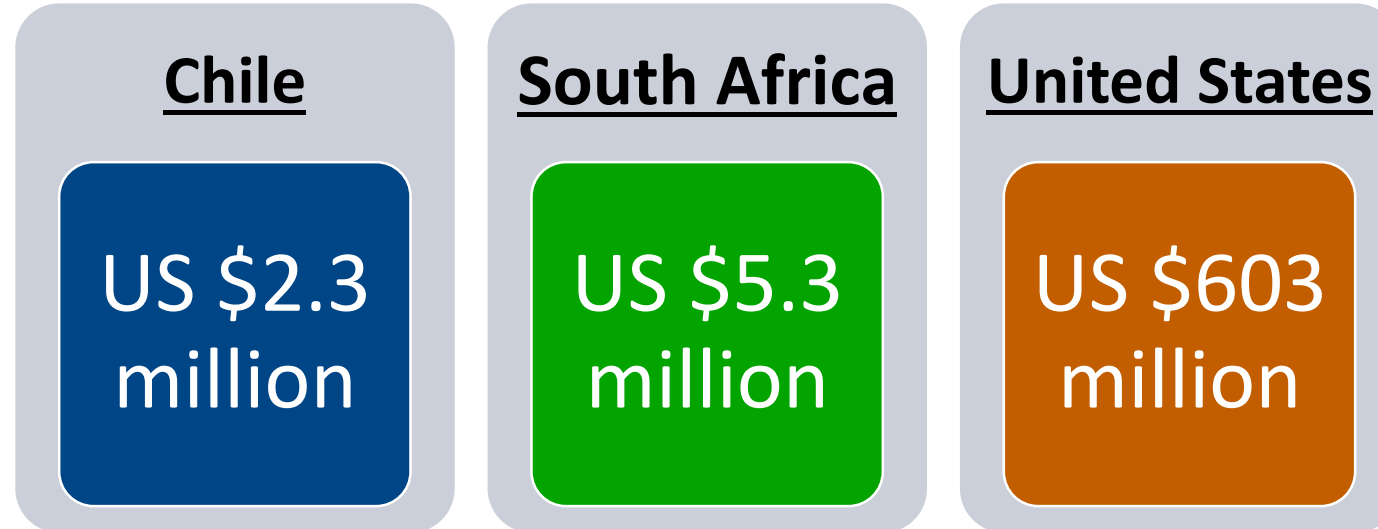


# Globally, fortifying flour with folic acid prevented about 50,270 neural tube defects in 2017





# Preventing spina bifida by fortifying grains averts millions in healthcare expenditures annually

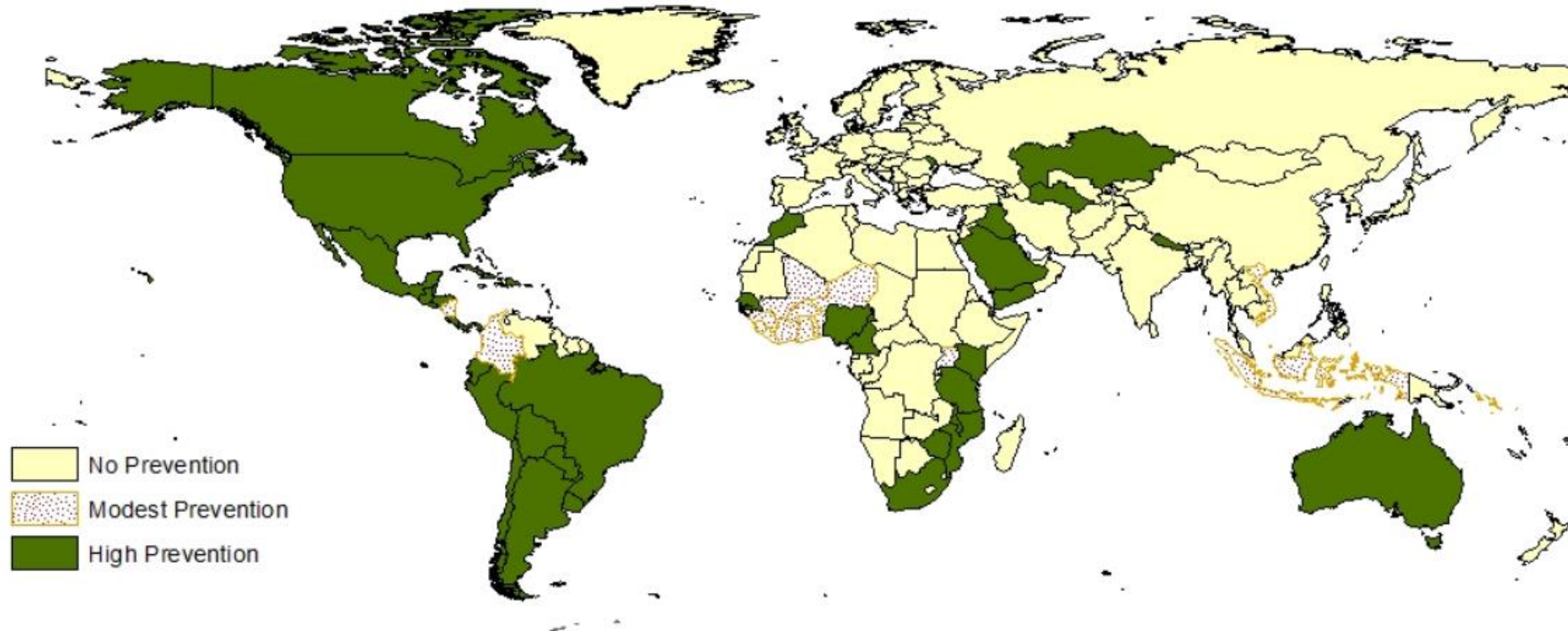


*These are conservative estimates!*





# Only ~18% of NTDs are prevented by fortifying flour with folic acid





# Current NTD prevalence in Haryana is incredibly high



- Approximately 2,400 children born with NTDs annually
  - 41 per 10,000 live births<sup>1</sup>
- Folate interventions could lower this to 350 NTDs annually or 6 per 10,000 live births<sup>2</sup>

<sup>1</sup> Bhide, Birth Defects Research (Part A), 2013; Annual Report on Working of the Registration of Births and Deaths Act, 1969--Haryana, 2013

<sup>2</sup> Crider, British Medical Journal, 2014; Annual Report on Working of the Registration of Births and Deaths Act, 1969--Haryana, 2013

Photo by Ankur P on Flickr



# Haryana began distributing fortified wheat flour in March 2018



- On average, 1,000 metric tons of flour are distributed every month
- Reaches almost 175,000 beneficiaries



# Next steps are to scale up to the rest of Haryana then other states in India

- Reaching all of Haryana would require 50,000 metric tons of fortified flour each month
- Some mills have added equipment to do this (example at right)
- Reach in Haryana would be around 12 million beneficiaries







## Conclusions

- Fortifying flour with folic acid is a proven strategy for preventing neural tube birth defects but it is not being fully utilized.



# Dr. Homero Martinez



Senior Technical Advisor, Nutrition International

# Implementation of an action plan to prevent neural tube defects

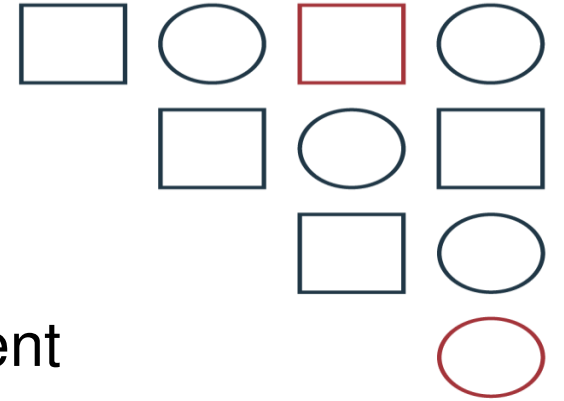
Homero Martinez, MD, PhD

Senior Technical Advisor

Folate Task Team - Nutrition International

[hmartinez@nutritionintl.org](mailto:hmartinez@nutritionintl.org)

# Main challenges remaining to address



- ✓ We know that improving the folate status of women of reproductive age before they are pregnant can help prevent the majority of NTD
- ✓ However, we still need to address:
  - Limited use and availability of valid laboratory methods to assess folate status
  - Monitoring NTD and other health outcomes
  - Effective ways to delivering folic acid to hard to reach populations

## Next Steps.

### With support from BMGF, Nutrition International:

- (1) Established a working group (including a Secretariat, an Expert Advisory Group, and interested partner organizations) to develop, coordinate and prepare for future implementation of a global action plan for NTD prevention
- (2) Continues activities to facilitate access to the scientific and technical conclusions of the recent consultation convened by the Micronutrient Forum for the purposes of planning, implementation and evaluation of NTD prevention programs
- (3) Conducts a landscape analysis to serve as the basis for identifying countries for future advocacy and support for model program development

# Nutrition International:

(4) Supports capacity building in selected LMIC to assess folate status, with a view to establishing a future global network of regional laboratories

- In collaboration with CDC:

- ✓ Identified 4 regional labs to send 8 trainees to CDC
- ✓ Provided these labs with equipment/reagents to conduct MBA to determine RBC folate
- ✓ Produced a training video that will shorten training time (2 weeks to 5 days) and provide support once back at their labs
- ✓ Setting the basis for a future global network of regional labs

(5) Supports folate-relevant research

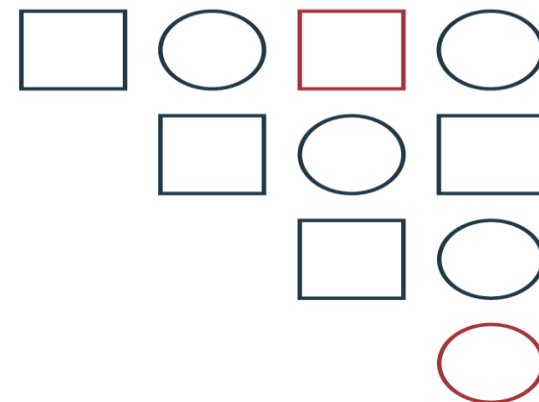
- ✓ Identify actual reach and coverage of mandatory fortified staple foods and identify predicted coverage of alternative food vehicles

# Structure of Folate Task Team









Thank You!

# Tom Scott



CEO, Spina Bifida Hydrocephalus Ireland



Improving child survival at the  
intersection of nutrition and  
birth defects -

Perspectives from Ireland

# High rates of spina bifida

- ▶ Ireland has one of the highest rates of spina bifida in the developed world
  - ▶ Between 30-50 births each year, around 1 in 2000
- ▶ Estimated that between 1000-1500 in Ireland living with spina bifida
- ▶ 65% of people who live with spina bifida in Ireland also have hydrocephalus
- ▶ Hydrocephalus is present in 1 in 1000 live births in Ireland
- ▶ This is due to a variety of factors:
  - ▶ Celtic gene
  - ▶ Limited practice of termination (this is soon to change)
  - ▶ Poor awareness of the benefits of folic acid
  - ▶ Poor awareness of when to take folic acid
  - ▶ Limited action from the Government in terms of taking action to address NTDs

# Action to promote awareness

- ▶ The Government delivers public health messages via the agency, *Safefood*
- ▶ *Safefood* has a wide remit in terms of covering all aspects of public health which means sustained campaigning is not an option
- ▶ This includes the promotion of the information concerning folic acid
- ▶ Typically this involves a 6-week campaign every year, or every two years
- ▶ SBHI has fought to be more involved in the preparation and dissemination of these messages, however this has seen limited success. The messaging is often dictated to SBHI rather than created in consultation with us
- ▶ In the past few years *Safefood* have relied heavily on the resources generated by *Shine* prior to 2015 (the charity for spina bifida and hydrocephalus in England, Wales, and Northern Ireland)
- ▶ I previously worked at *Shine* when Martine Austin was still there, and we developed these resources with various stakeholders



# Changing landscape

- ▶ On 26<sup>th</sup> May 2018 the Irish people voted in a referendum to change the constitution concerning the legalisation of abortion in some circumstances
- ▶ Known as the *Repeal the 8<sup>th</sup>* movement (referring to the relevant amendment) the vote was won by a majority of 66.4% to change the constitution with a record turn out from the electorate
- ▶ The government are working to have the relevant legislation passed by the end of 2018:
  - ▶ “The government will shortly begin work on passing the draft of the proposed law, which will allow for abortion without restriction up to 12 weeks and in limited circumstances after that up to six months.”
  - ▶ [Source: <https://www.thejournal.ie/yes-ireland-votes-to-repeal-eighth-amendment-4034416-May2018/>]

# Fortification

- ▶ Fortification is not really on the agenda of the Irish Government at present
- ▶ If the UK do go ahead with fortification, we think that Ireland, and many other countries as well, will look at the issue more seriously

# SBHI and prevention

- ▶ Although SBHI have been involved in folic acid awareness raising initiatives in the past, the promotion has been limited and only really constitutes information on the SBHI website
- ▶ There are significant issues around messaging in terms of members who take objection to the folic acid message, either because the mother did take folic acid and it didn't prevent their child having spina bifida, or because they didn't take it and they feel blamed for their child having spina bifida
- ▶ We are currently working on a new website and promotion campaign with a GP who is keen to promote the folic acid message. This will launch in 2019
- ▶ Having said this, SBHI, via Tom Scott's interaction as a board member of IF, did work with IF to produce the current folic acid leaflet and we use this as part of our promotional work on the issue

# Communication around ‘prevention’

- ▶ As an organisation working closely with the individuals living with SB/H and their personal networks of family and friends, we do struggle with communication around prevention
- ▶ It is very difficult to promote campaigns which include terms such as ‘prevention’ and ‘defect’, whilst at the same time advocating that we support those living with the conditions to live the most fulfilled lives possible
- ▶ We need to be cognisant of the intersection between the scientific arena and that of the very real, lived experience of those who have been born with SB, and those who work to support these individuals
- ▶ This can be subtle, but phrases such as ‘working to increase awareness’ can offer a similar message than that of ‘working to prevent NTDs’, the detail can be offered but without it needing to be the headline

# Contact

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Twitter: [TomScott\\_SBHI](https://twitter.com/TomScott_SBHI)

# Ruth Nalugya



Chair, The Spina Bifida and Hydrocephalus  
Association of Uganda



**RUTH NALUGYA  
KAMPALA –UGANDA**

## **UGANDA'S EXPERIENCE OF PREVENTING NTDS**

## PERSONAL BACKGROUND

- ❖ The chair of the National Spina Bifida and Hydrocephalus Association of Uganda(SHAU)
- ❖ A member of the National Working Group on Food Fortification(NWGFF), established in 2002 with multidisciplinary public and private sector agency representatives designed to provide leadership in steering the country's food-fortification program.
- ❖ Got involved in prevention of NTDs after giving birth to a child with spina bifida and due to the fact that health workers had not talked to me about the importance of folic acid, and people in my community did not know anything about it, I, through the disability people's organization joined other stakeholders in the awareness and prevention campaigns about prevention of spina bifida.
- ❖ Coordinated the consumer baseline market assessment survey on food fortification that was intended to improve compliance by the industries to the national standards.
- ❖ Currently on the subcommittee reviewing and assembling a targeted advocacy package on food fortification being supported by GAIN through the ENABLE Project.

## Magnitude of micronutrient deficiencies in Uganda

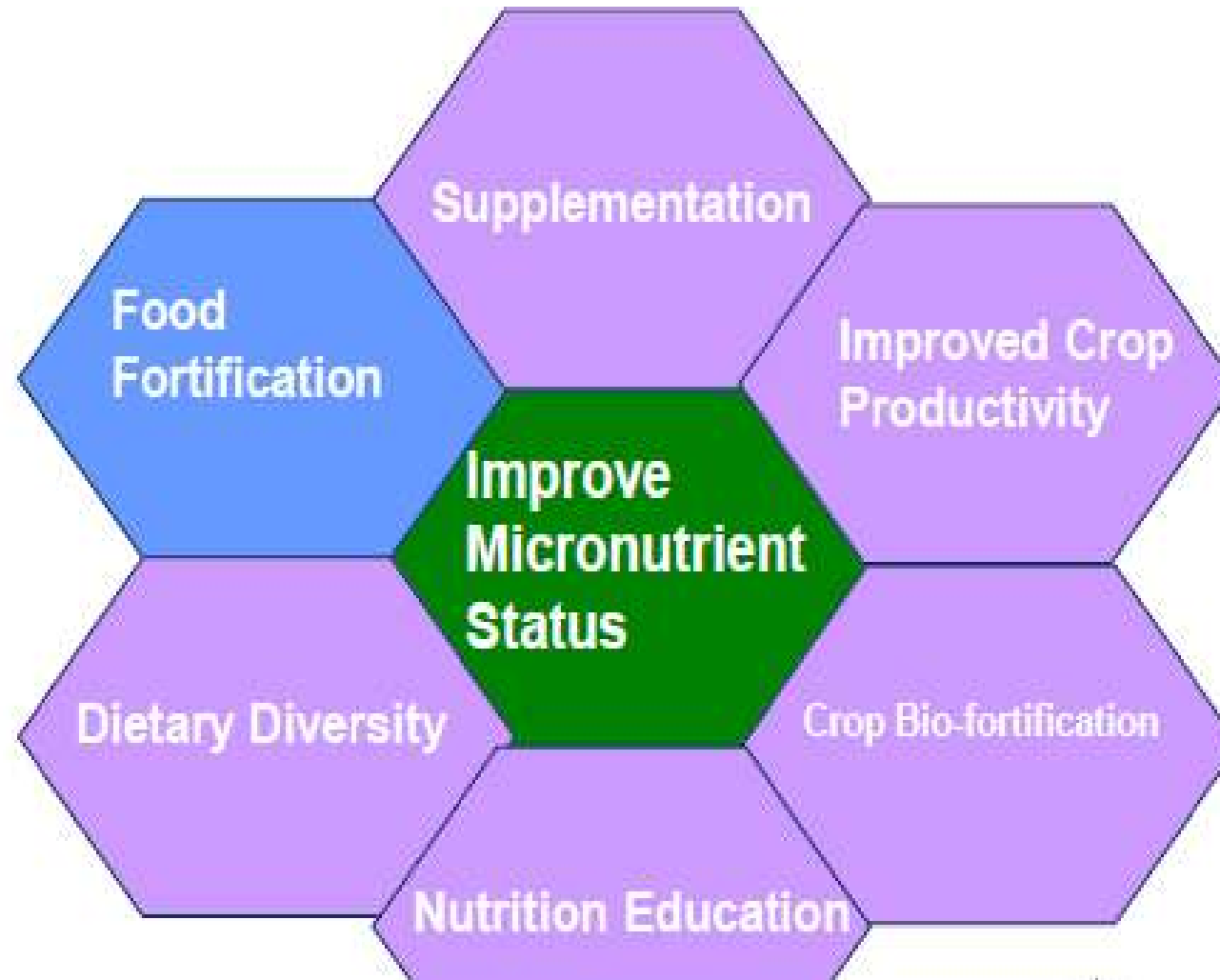
- Micronutrient deficiencies, commonly; Vitamin A, Iron, Iodine, Folic acid, and Zinc are a public health problem in Uganda with a prevalence of 31% (UBOS and ICF International 2012)
- Despite the numerous interventions, Vitamin A deficiency doubled from 19% to 38% in children and from 20% to 36% in WRA (UDHS, 2006 – 2011). There was however an increase in anemia in both WRA and children under 5 from 49% to 53% and 23% to 32% respectively(UDHS 2011 – 2016). And according to the rapid assessment survey on Distribution of IFA through ANC, demand and supply are still constraints.



**National statistics on NTDs is however still limited**



## Interventions to address micronutrient deficiencies in Uganda



# Prevention activities involved with

## 1. Supplementation

National and Community awareness campaigns to improve knowledge about consumption and promote periconceptional use of folic acid.

The WHO guidelines of 2011 are further in line with the Anaemia policy and anaemia strategy which recommend intermittent IFA supplementation for adolescent girls and older women in situations where Anaemia levels are above 20% .

Currently, discussions on the implementation of the intervention on the Intermittent Iron and Folic acid for adolescents is underway by the NTWG.

## 2. Industrial food fortification program.

### Background:

- 1994: Universal Salt Iodization introduced resulted in 99% of the households consuming adequately iodised salt.
- 2000: Maize flour, wheat flour and edible oil fortification were initiated and today have evolved from a voluntary program to a mandatory one.
- Consumer Protection Association and local spina Bifida and Hydrocephalus association conducted a basic market assessment of fortified foods in Uganda.
- Was considered a “Pull” Strategy as it relies on these groups to create a demand for fortification compliance;
- It was intended to complement the government’s “push” strategy of making fortification mandatory

## Likely barriers to prevention/achieving more.

- ❖ limited education and understanding of women and health workers about the importance of early folic acid intake
- ❖ late presentation of women at Antenatal care centres.
- ❖ lack of demand for fortified foods by the consumers due to:
  - i) lack of awareness among consumers on the Rights and benefits of consuming fortified foods.
  - ii) Negative perception by consumers about food fortificants.
- ❖ -Smuggling of food products through porous border and poor enforcement at the importation sites of Uganda and industries.
- ❖ High level of inconsistency among the producers hence cheating the consumers



THANK YOU



# Elena Monzón de Záppoli



President, Asociación para Espina  
Bífida e Hidrocefalia Argentina

# NUTRITION INTERNATIONAL WEBINAR

## **Speaker: Ms. Elena Záppoli**

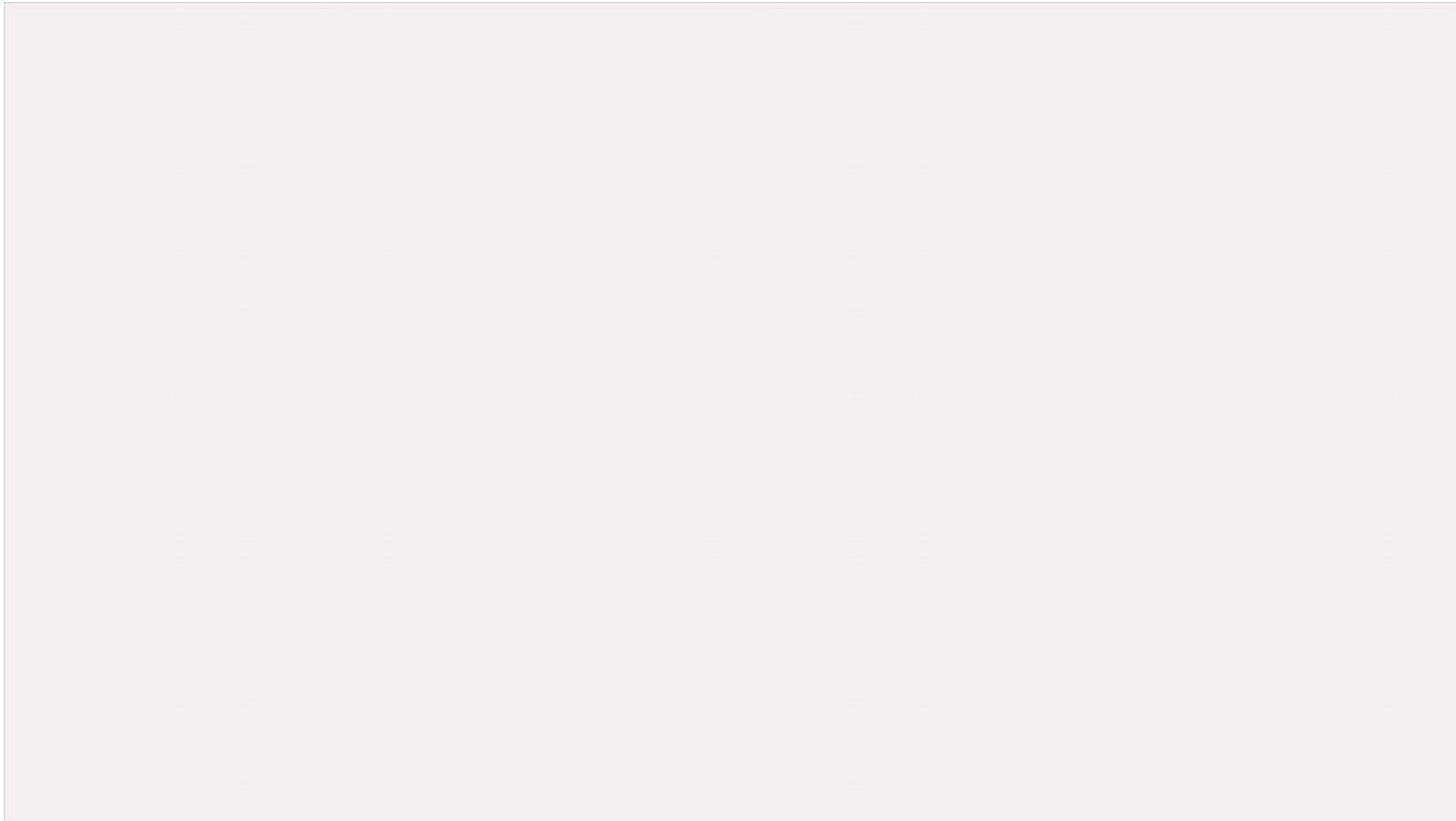
**APEBI President**

**IF Board Member  
LATAM & The Caribbean  
Representative**

**Chair of the Argentine National  
Disability Observatory**



# PREVENTION CAMPAIGN 2018



# FOLIC ACID ACT

Buenos Aires, 5<sup>th</sup> July, 2018.

Buenos Aires City Legislature

hereby enacts with the force of Law

Section 1º - This Law is intended to:

- a). Guarantee free folic acid supplementation, or the medicine which replaces it in the future, for all women of childbearing age - trying to get pregnant - who make an OB-GYN and preconceptional appointment, pregnant women and women who doubt whether they are pregnant until 14 (fourteen) weeks of amenorrhoea.
- b). Create raising-awareness campaigns about the importance of folic acid intake in the preconceptional period and during pregnancy in an effort to promote NTD (Neural Tube Defect) and anaemia prevention and provide health benefits.

Section 2º - Free provision is mandatory at every public healthcare centre in Buenos Aires City.

Section 3º - The implementing and enforcement authority is the Ministry of Health of Buenos Aires City, or the given agency which replaces it in the future.

Section 4º - The Ministry of Health of Buenos Aires City shall introduce every measure to enforce this Law.

Section 5º - Be it thus notified.

DIEGO SANTILLI

CARLOS SERAFIN PEREZ



# **Further discussion**

Please feel free to submit a question via  
the chat box for any of our speakers

# Closing remarks from Dr. Martinez

For more information please contact Dr. Martinez at  
[folatetaskteam@nutritionintl.org](mailto:folatetaskteam@nutritionintl.org)

A recording of this webinar and a PDF of the slides will  
be made available via the Folate Task Team webpage at  
[https://www.nutritionintl.org/what-we-  
do/nteam/folate-task-team/](https://www.nutritionintl.org/what-we-do/nteam/folate-task-team/)



**Thank you!**