Folic acid fortification: The safe and effective action towards spina bifida prevention

Helena Pachón, PhD, MPH
Food Fortification Initiative

Global Alliance for Prevention of Spina Bifida F
24 May 2022

Main messages

Fortifying food with folic acid is

Safe

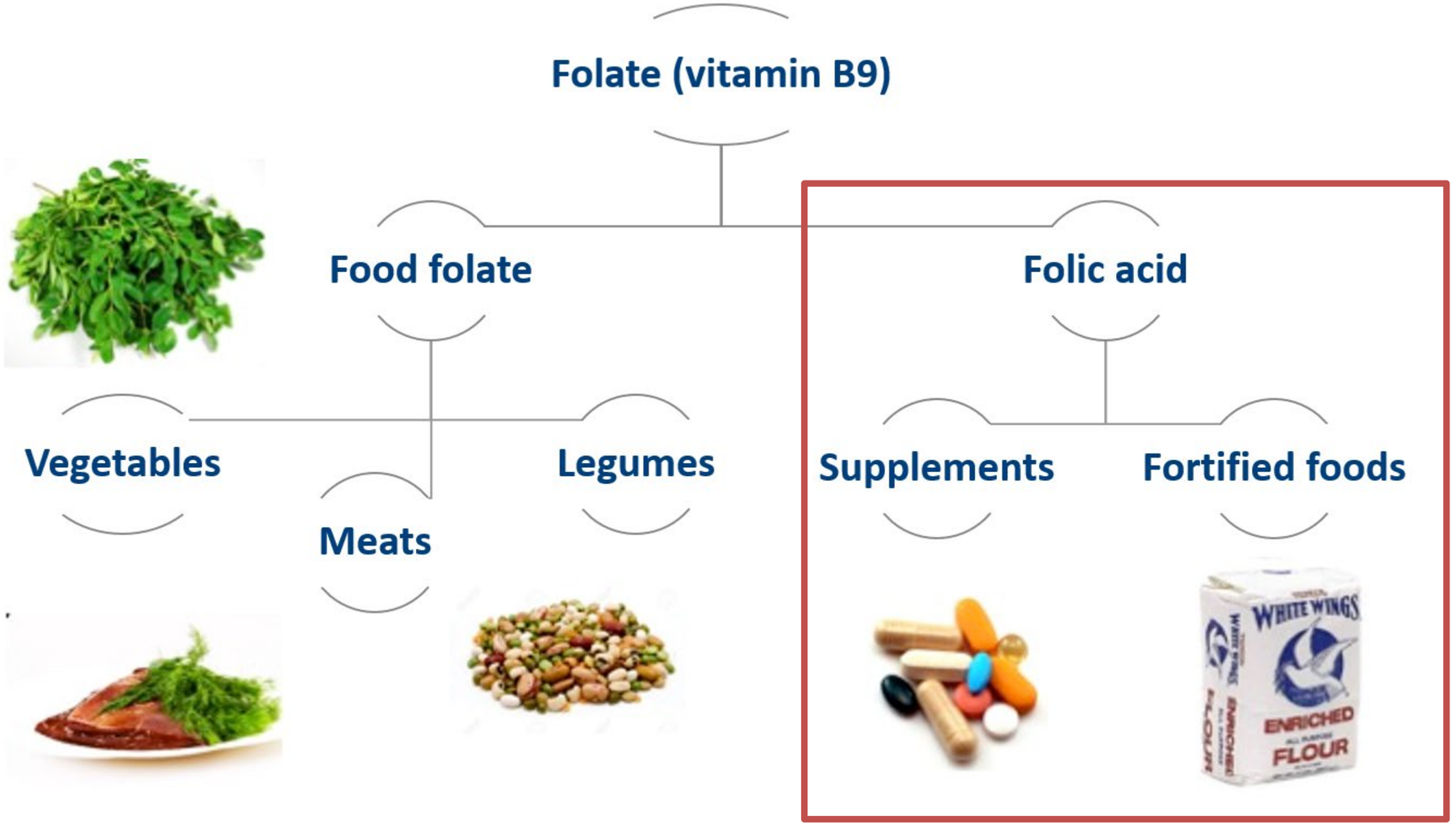
- Fortifying with folic acid does not
  - Mask vitamin B12 deficiency
  - Increase adenoma risk
  - Cause cancer or increase deaths from cancer

Cost-effective

- Fortifying with folic acid
  - Reduces neural tube defects
  - Costs less than treating neural tube defects

Adenomas are benign tumors that can develop into cancer

Folic acid is better absorbed than food folate



Better absorbed by the body

Suitor 2000

What is food fortification (enrichment)?

The addition of vitamins and minerals to foods during their processing

Image

Foods fortified with folic acid

Folic acid in fortification standards

80 countries

18 countries

11 countries

Research


Image


Image


Image

Global Fortification Data Exchange 2022, Tsang unpublished

Fortifying food with folic acid does not mask vitamin B12 deficiency

Folate and vitamin B12 deficiencies cause megaloblastic anemia

Folate deficiency

Causes

Vitamin B12 deficiency

Causes

Megaloblastic Anemia

IOM 2008

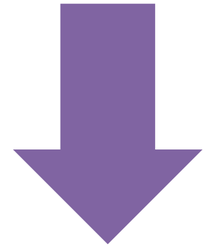
Folic acid masking of vitamin B12 deficiency

Megaloblastic anemia due to vitamin B12 deficiency only

If folic acid is provided

Anemia is corrected

If vitamin B12 is <u>not</u> provided



Vitamin B12 deficiency persists

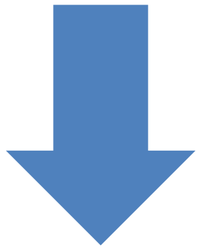
“Folic acid masking of vitamin B12 deficiency”

Berry 2019

Studies to assess if fortification with folic acid causes masking of vitamin B12 deficiency

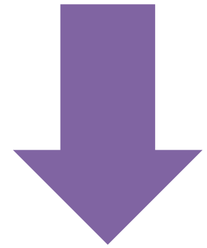
People with vitamin B12 deficiency and no anemia who consume food fortified with folic acid

Folic acid is provided



Anemia does not develop

Vitamin B12 is not provided



Vitamin B12 deficiency persists

Mills 2003, Qi 2014

Fortification with folic acid does not mask vitamin B12 deficiency

People with low vitamin B12 status and no anemia who consume food fortified with folic acid

Folic acid is provided → Anemia does not develop

Vitamin B12 is not provided → Vitamin B12 deficiency persists

If fortification with folic acid masks vitamin B12 deficiency, the percentage of individuals with both of these conditions should increase after fortification with folic acid

Study	Pre-fortification	Post-fortification	Conclusion
Mills 2003	39.2%	37.6%	No masking of vitamin B12 deficiency
Qi 2014	4.0%	3.9%	No masking of vitamin B12 deficiency

Mills 2003, Qi 2014

Free folic acid in the blood does not increase adenoma risk

Adenomas are benign tumors that can develop into cancer

“Free folic acid” is also referred to as “unmetabolized folic acid”

After folic acid consumption, free folic acid appears in the blood

Brazil
(Zanin Palchetti 2017)

Canada
(Plumptre 2015)

Ireland
(Vaish 2016)

USA
(Pfeiffer 2015)

“Free folic acid” is also referred to as “unmetabolized folic acid”

Free folic acid does not increase the risk of adenomas

Free folic acid (nmol/L)	Interval 1: Relative Risk (95% CI)	Interval 2: Relative Risk (95% CI)
0	1.00 (reference)	1.00 (reference)
> 0 - < 3	1.04 (0.81-1.33)	0.88 (0.62-1.25)
3 - < 20	1.00 (0.74-1.35)	1.31 (0.95-1.82)
≥ 20	0.83 (0.58-1.18)	0.96 (0.64-1.43)

Interval 1: three years
Interval 2: an additional three years

Adenomas are benign tumors that can develop into cancer

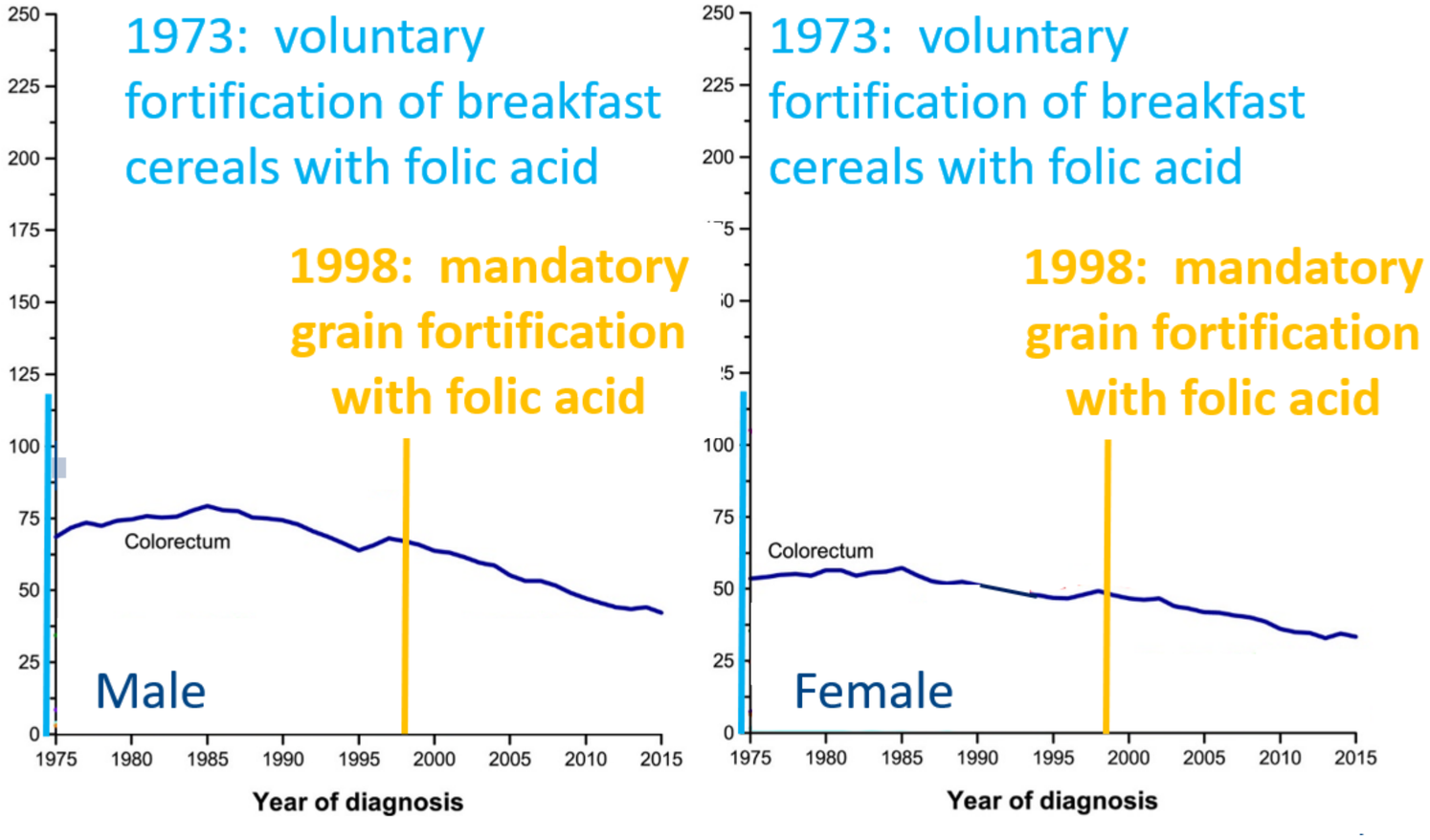
“Free folic acid” is also referred to as “unmetabolized folic acid”

Rees 2017

Fortifying food with folic acid does not cause cancer or increase deaths from cancer

Fortification with folic acid does not cause cancer

Colorectal Cancer Rate per 100,000 Population, USA



Siegel 2019

Fortification with folic acid does not increase deaths from cancer

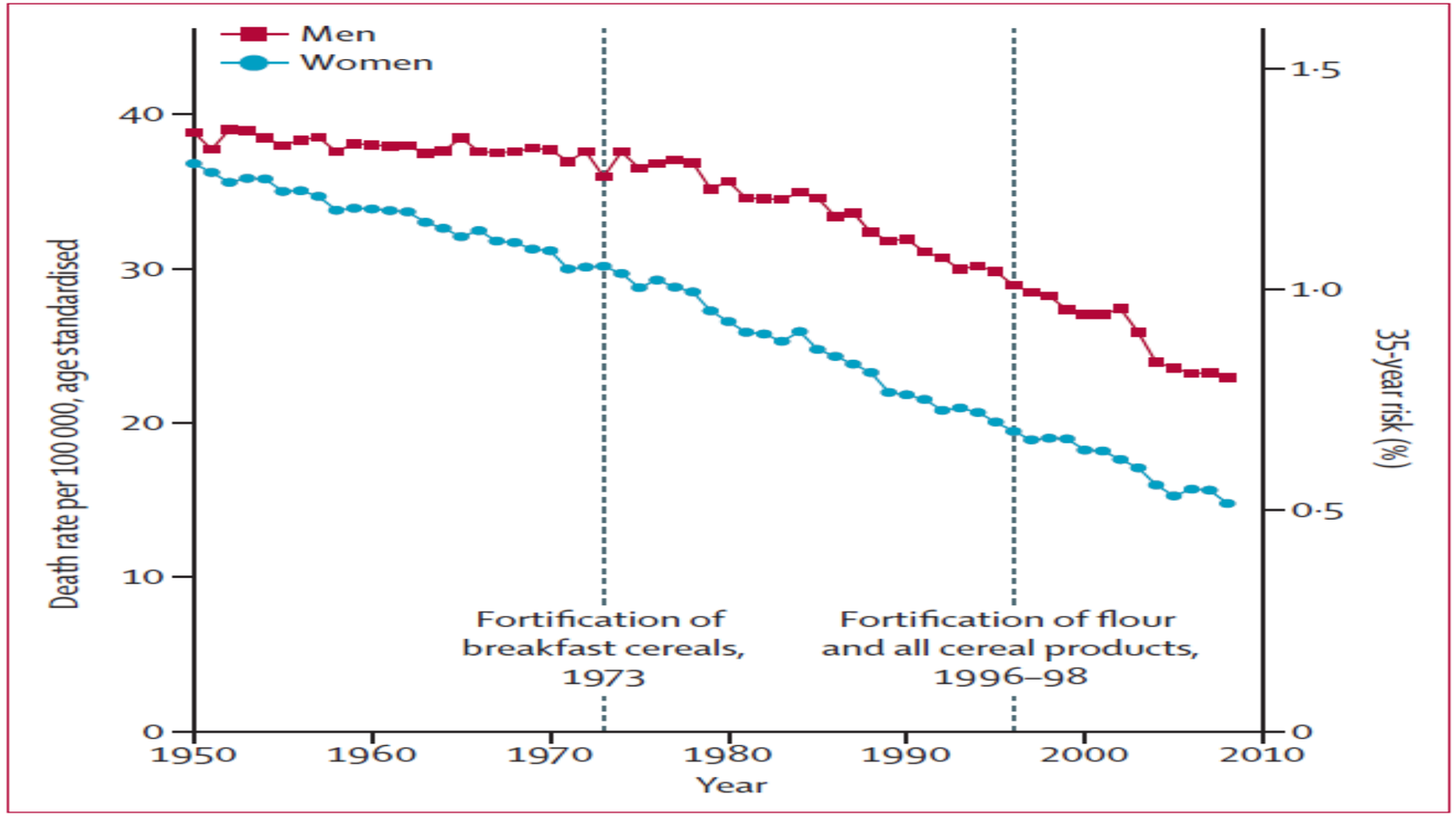


Figure 4: Annual mortality from colorectal cancer in the USA, 1950–2008, at ages 35–69 years

Vollset 2013

Fortifying food with folic acid reduces the risk of neural tube defects and is cost-effective

Fortification with folic acid reduces the risk of neural tube defects: Costa Rica

1997: wheat flour fortification with folic acid 1999: maize flour fortification with folic acid

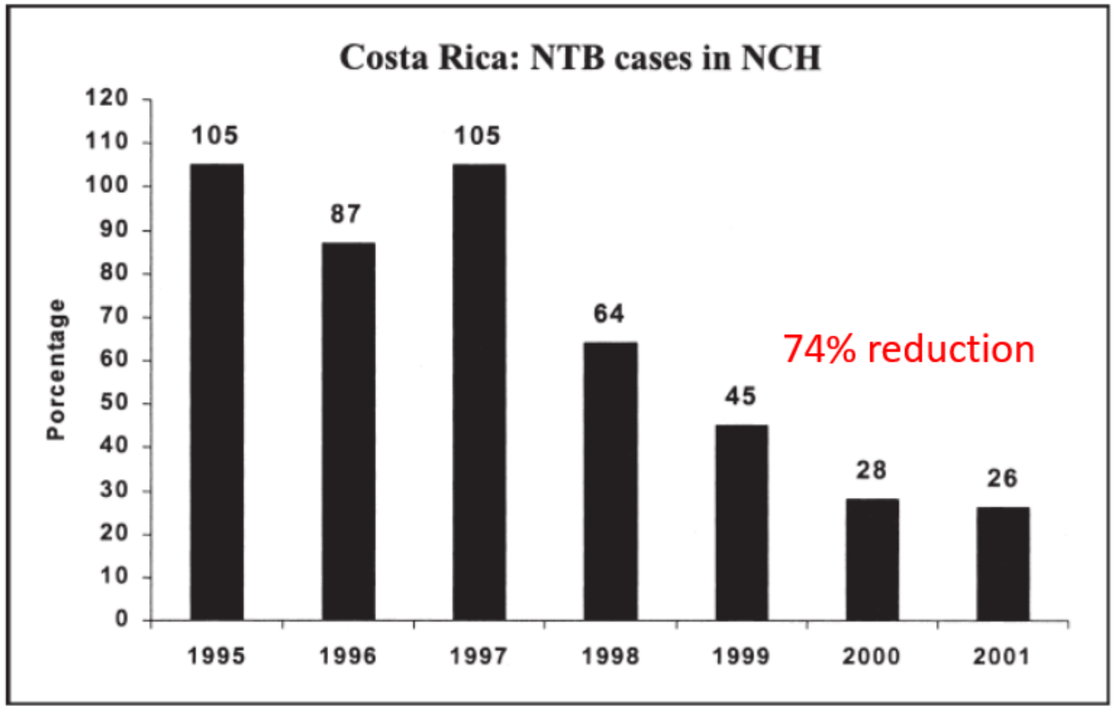


Figure 2. Costa Rica. Neural tube defects cases at National Children's Hospital.

Pre-fortification (1996-1998):

- 9.7 NTDs / 1000 live births

Post-fortification (1999-2000):

- 6.3 NTDs / 1000 live births

Tacsan Chen 2004

Fortification with folic acid reduces the risk of neural tube defects: Canada

1998: wheat flour fortification with folic acid

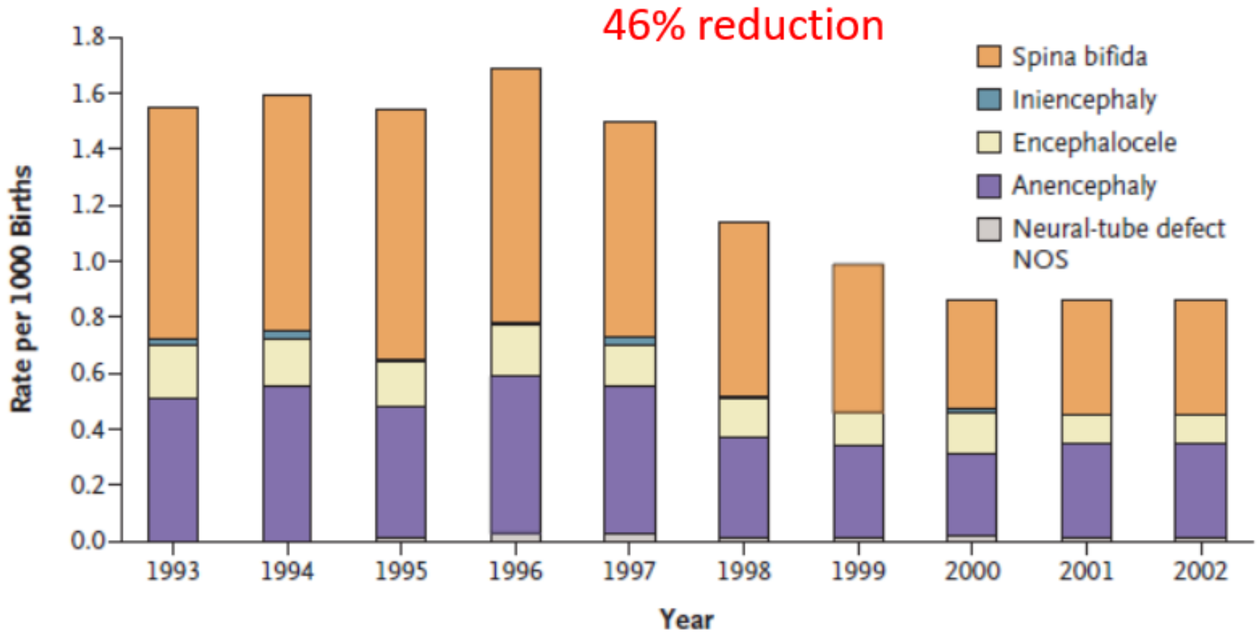


Figure 1. Prevalence of Neural-Tube Defects, According to Diagnostic Category, in Seven Canadian Provinces from 1993 through 2002.

NOS denotes not otherwise specified.

Pre-fortification (1993-1997):

- 1.58 NTDs / 1000 live births

Post-fortification (1998-2002):

- 0.86 NTDs / 1000 live births

De Wals 2007

Fortification with folic acid reduces the risk of neural tube defects: Jordan

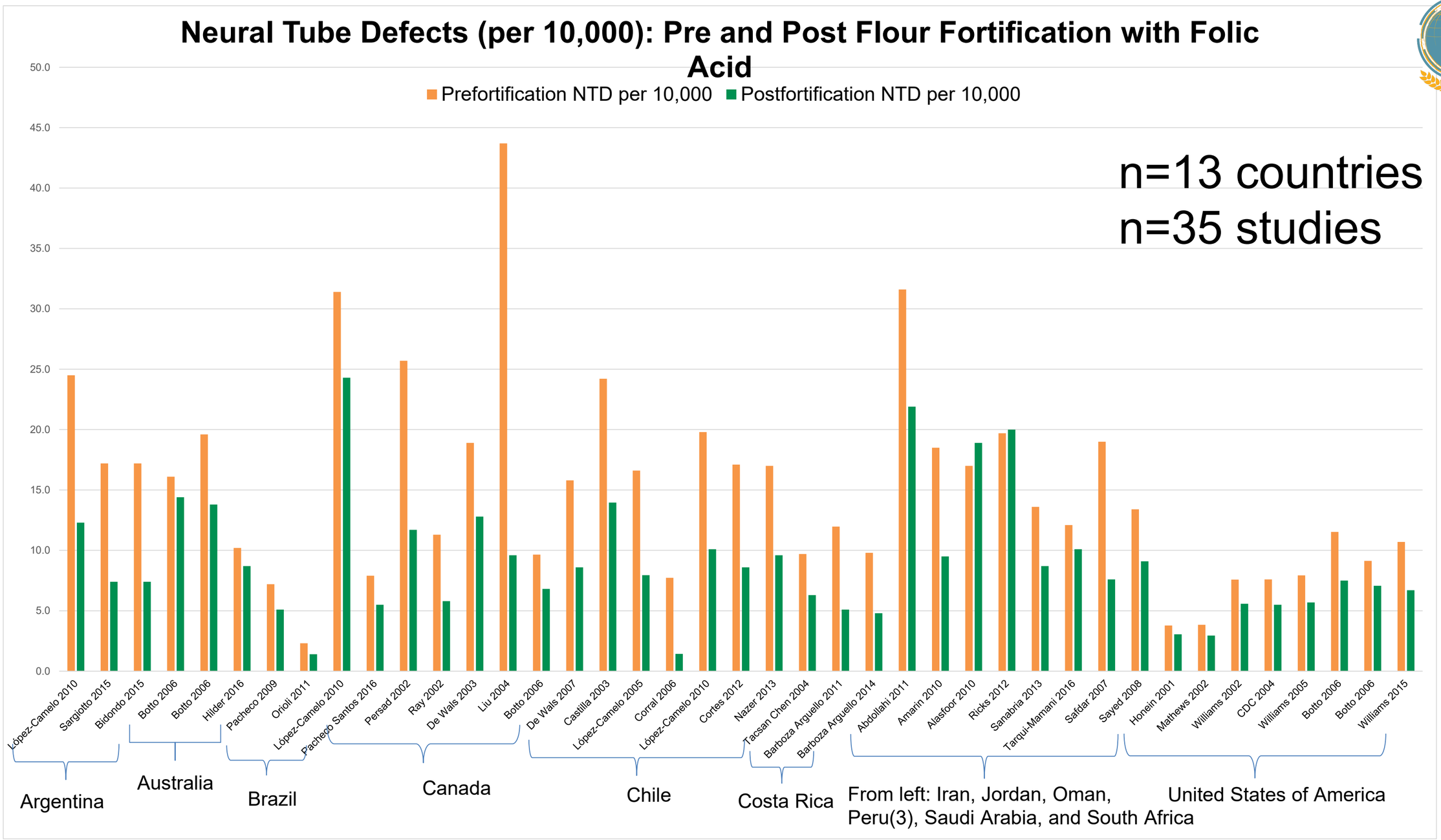
2002: wheat flour fortification with folic acid

Period	Years	Livebirths	NTDs	Rate per 1000	[95% CI]
Before fortification	2000–01	18392	34	1.85	[1.2, 2.4]
Introduction period	2002–04	26286	28	1.07	[0.7, 1.5]
After fortification	2005–06	16769	16	0.95	[0.5, 1.5]

49% reduction

Amarin 2010

Neural Tube Defects (per 10,000): Pre and Post Flour Fortification with Folic Acid



Fortification with folic acid reduces the risk of neural tube defects: meta-analysis

All Neural Tube Defects

Odds Ratio: 0.59 (95% CI: 0.49, 0.70)

n=19,816,008 births (reported in 8 studies)

41% reduction in the odds of neural tube defects after fortification with folic acid

Keats 2019

Fortification with folic acid is cost-effective in reducing the risk of neural tube defects

Annual Net Savings from Adding Folic Acid to Flour

Chile	South Africa	USA
• 2.3 million International Dollars	• 40.6 million Rand	• 603 million US Dollars

Savings in healthcare expenses related to treating people with spina bifida, when spina bifida is prevented

Llanos 2007, Sayed 2008, Grosse 2016

Main messages

Fortifying food with folic acid is

Safe

- Fortifying with folic acid does not
  - Mask vitamin B12 deficiency
  - Increase adenoma risk
  - Cause cancer or increase deaths from cancer

Cost-effective

- Fortifying with folic acid
  - Reduces neural tube defects
  - Costs less than treating neural tube defects

Adenomas are benign tumors that can develop into cancer

Contact details: contact@theg4alliance.org

info@ifglobal.org

gapsbif@uab.edu

Website: www.theg4alliance.org/gapsbif

Helena Pachón
helena.pachon@emory.edu

Food Fortification Initiative
www.FFInetwork.org