Review of the public-health evidence of flour fortification impacting serum folate, neural tube defects, serum ferritin, and hemoglobin

Flour Fortification Initiative
A Public-Private-Civic Investment in Each Nation

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Cost Benefit Analysis training in Dar –es-Salaam

Acknowledgements

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Study types

EFFICACY

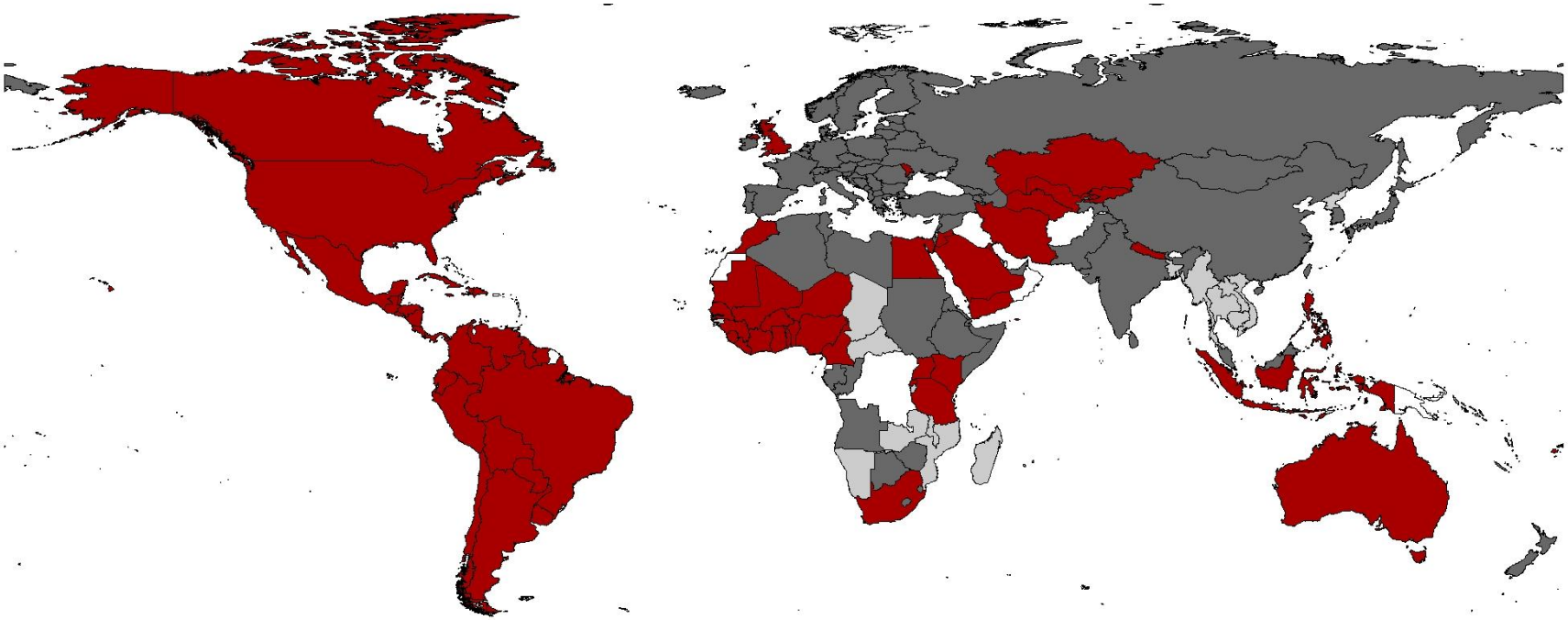
"The extent to which a specific intervention, procedure, regimen, or service produces a beneficial result under ideal conditions …Ideally, the determination of efficacy is based on the results of a randomized controlled trial."

EFFECTIVENESS

"**…**it is a measure of the extent to which a specific intervention, procedure, regimen, or service, when deployed in the field in the usual circumstances, does what it is intended to do for a specified population. A measure of the extent to which a health care intervention fulfills its objectives in practice."

This presentation will summarize results from effectiveness trials, conducted before and after fortification programs were initiated in countries. None of these results are from efficacy trials.

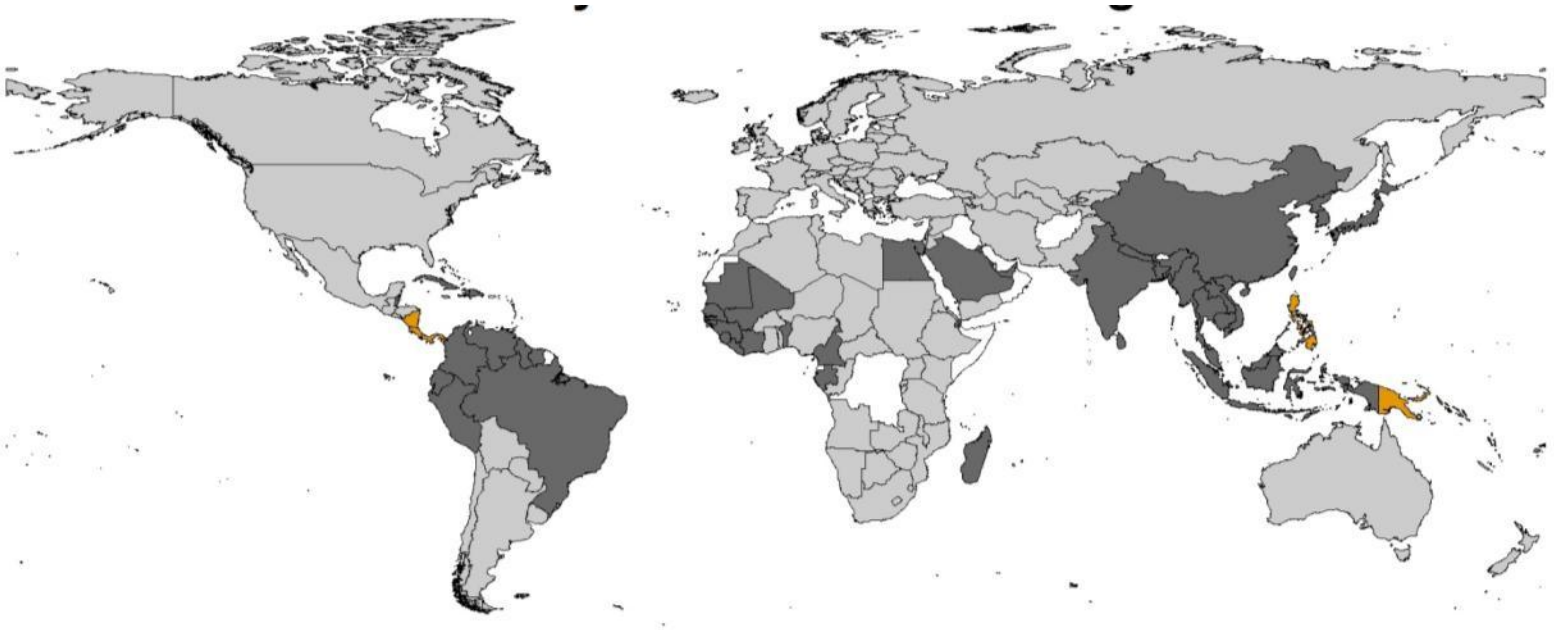
Wheat Availability and Fortification Legislation



75 or more grams available per person per day	Mandatory fortification legislation * 78 countries
Less than 75 grams available per person per day	No availability or legislation data

* Legislation has effect of mandating grain fortification with at least iron or folic acid; does not reflect how much grain is available .
Grain availability data from the Food and Agriculture Organization (2009).
Legislation status from the Flour Fortification Initiative (www.FFInetwork.org) November 2013

Rice Availability and Fortification Legislation

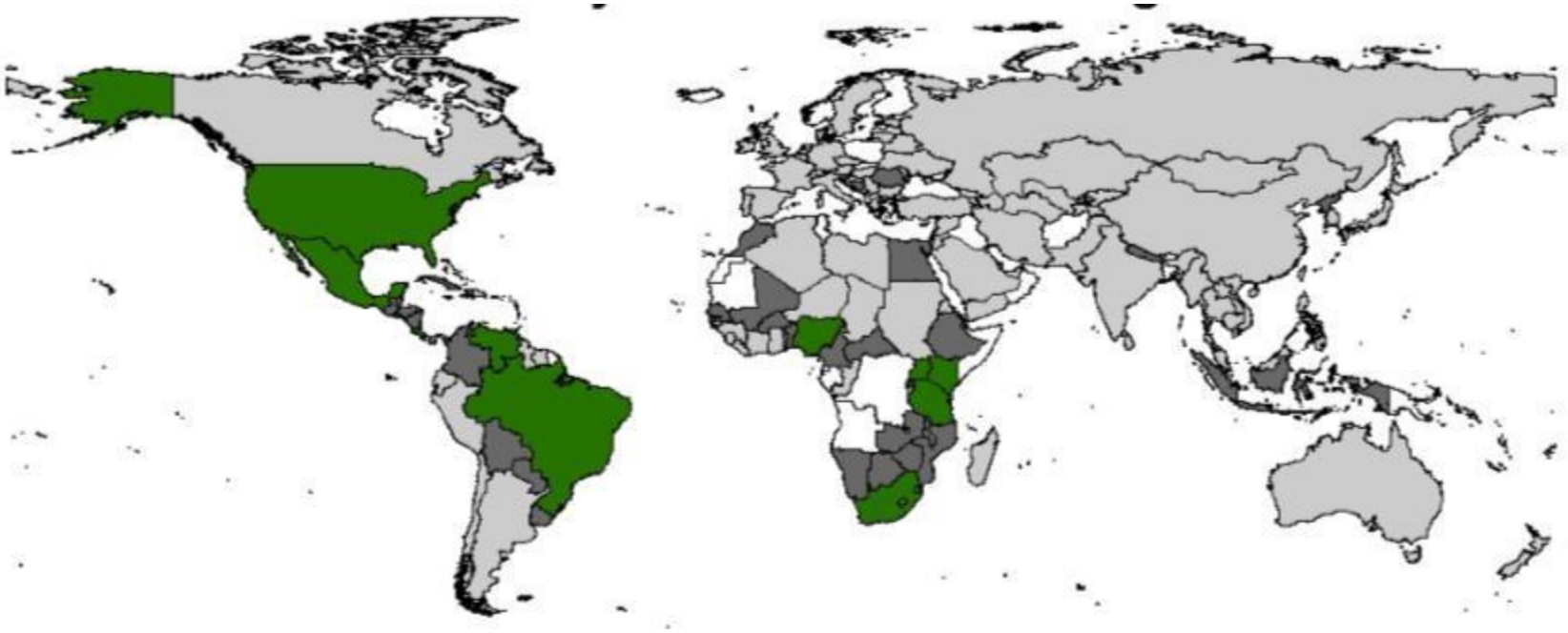


	75 or more grams available per person per day
	Less than 75 grams available per person per day

	Mandatory fortification legislation * 5 countries
	No availability or legislation data

* Legislation has effect of mandating grain fortification with at least iron or folic acid; does not reflect how much grain is available .
Grain availability data from the Food and Agriculture Organization (2009).
Legislation status from the Flour Fortification Initiative (www.FFInetwork.org) November 2013

Maize Availability and Fortification Legislation



	75 or more grams available per person per day
	Less than 75 grams available per person per day

	Mandatory fortification legislation * 12 countries
	No availability or legislation data

* Legislation has effect of mandating grain fortification with at least iron or folic acid; does not reflect how much grain is available .
Grain availability data from the Food and Agriculture Organization (2009).
Legislation status from the Flour Fortification Initiative (www.FFInetwork.org) November 2013

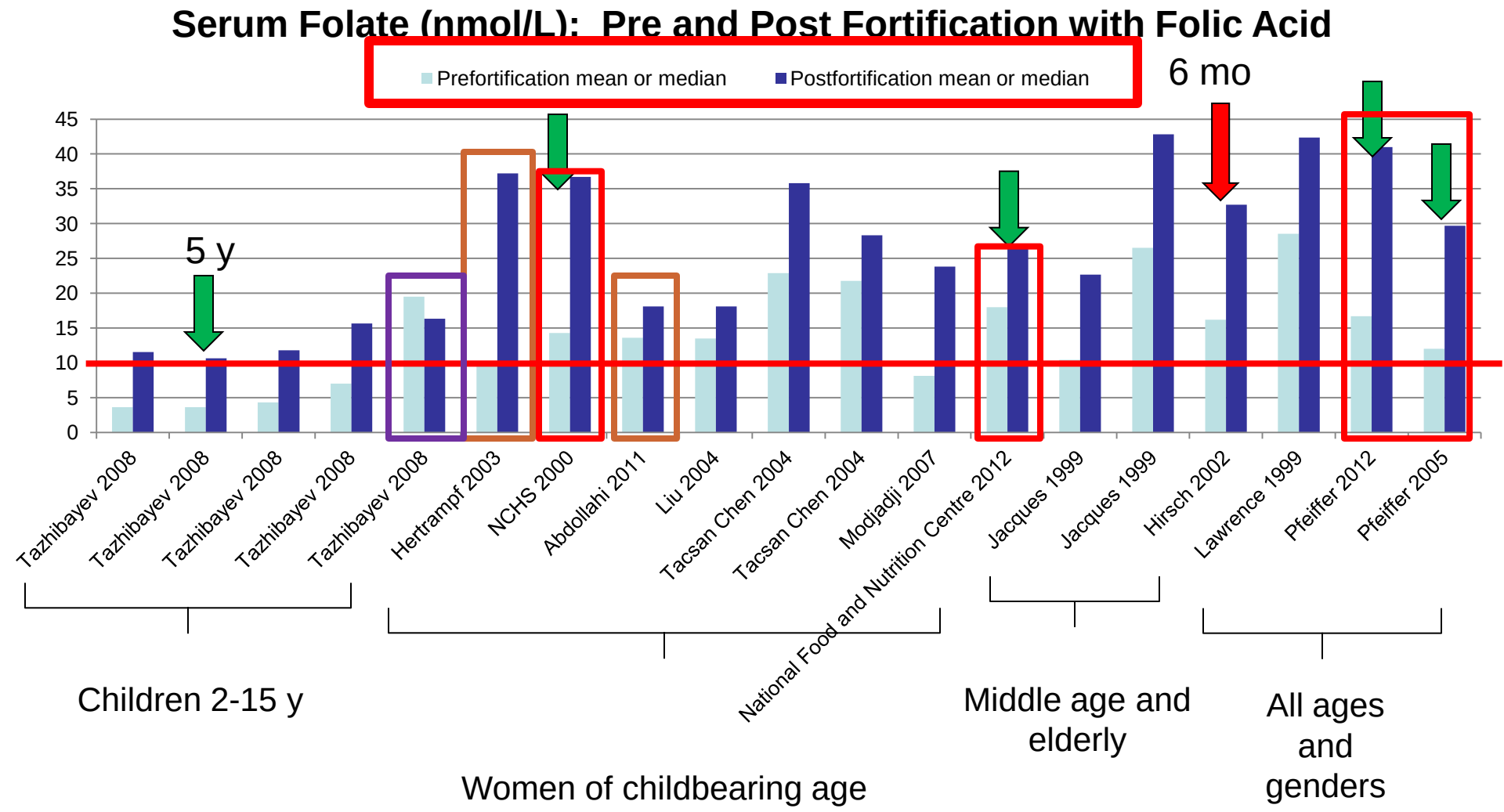
Recommendations on wheat and maize flour fortification

Table 1. Average levels of nutrients to consider adding to fortified wheat flour based on extraction, fortificant compound, and estimated *per capita* flour availability

Nutrient	Flour Extraction Rate	Compound	Level of nutrient to be added in parts per million (ppm) by estimated average per capita wheat flour availability (g/day)[1]			
			<75[2] g/day	75-149 g/day	150-300 g/day	>300 g/day
Iron	Low	NaFeEDTA	40	40	20	15
		Ferrous Sulfate	60	60	30	20
		Ferrous Fumarate	60	60	30	20
		Electrolytic Iron	NR[3]	NR[3]	60	40
	High	NaFeEDTA	40	40	20	15
Folic Acid	Low or High	Folic Acid	5.0	2.6	1.3	1.0
Vitamin B_{12}	Low or High	Cyanocobalamin	0.04	0.02	0.01	0.008
Vitamin A	Low or High	Vitamin A Palmitate	5.9	3	1.5	1
Zinc[4]	Low	Zinc Oxide	95	55	40	30
	High	Zinc Oxide	100	100	80	70

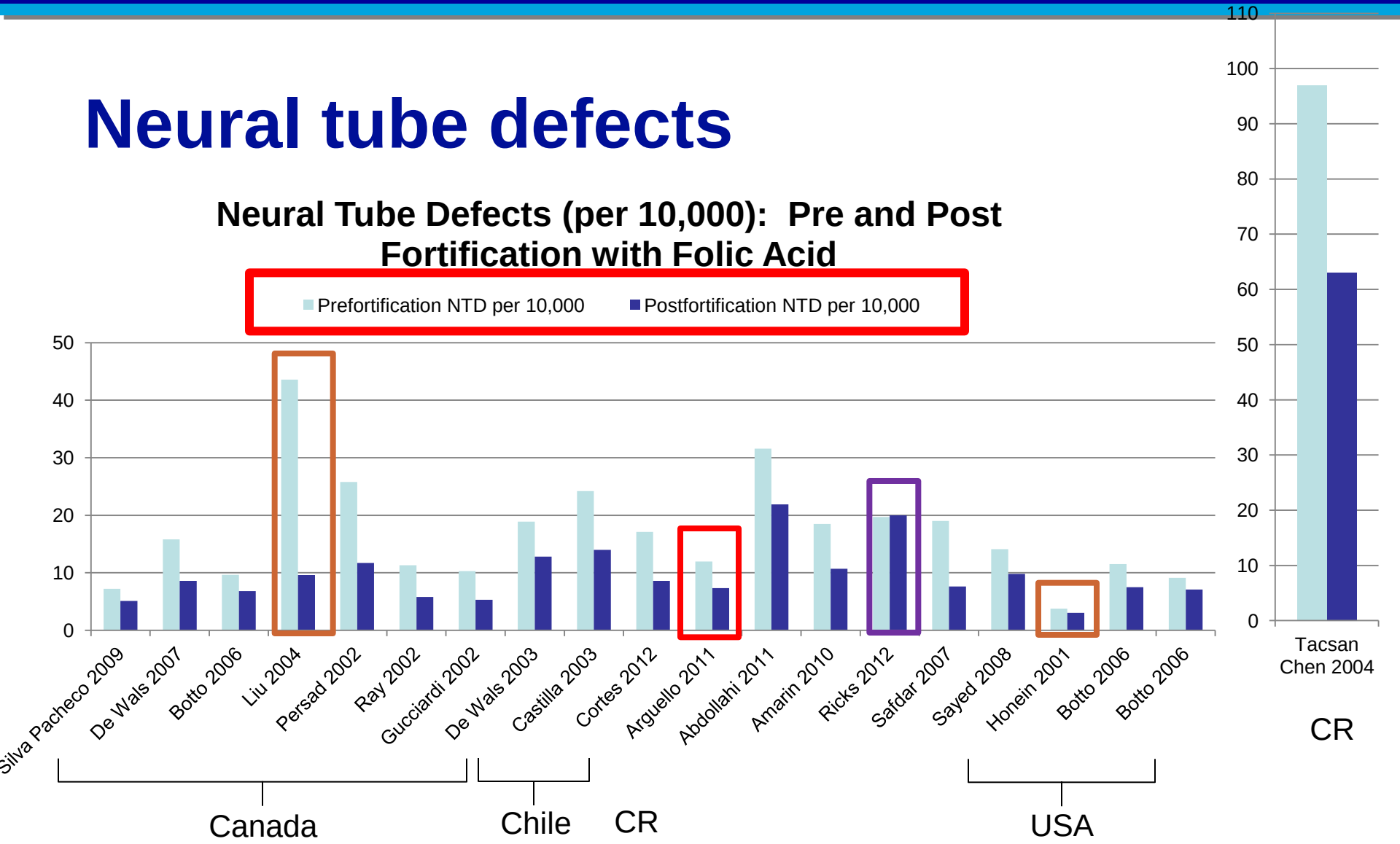
WHO and partners 2009

Serum folate



FFI review 2013. Folic acid in flour ranged from 1.2-2.2 mg/kg.

Neural tube defects



Brazil, Canada, Chile, Costa Rica, Iran, Jordan, Peru, Saudi Arabia, South Africa, USA

Adapted from FFI 2013

Folic acid in flour ranged from 1.2-2.2 mg/kg.

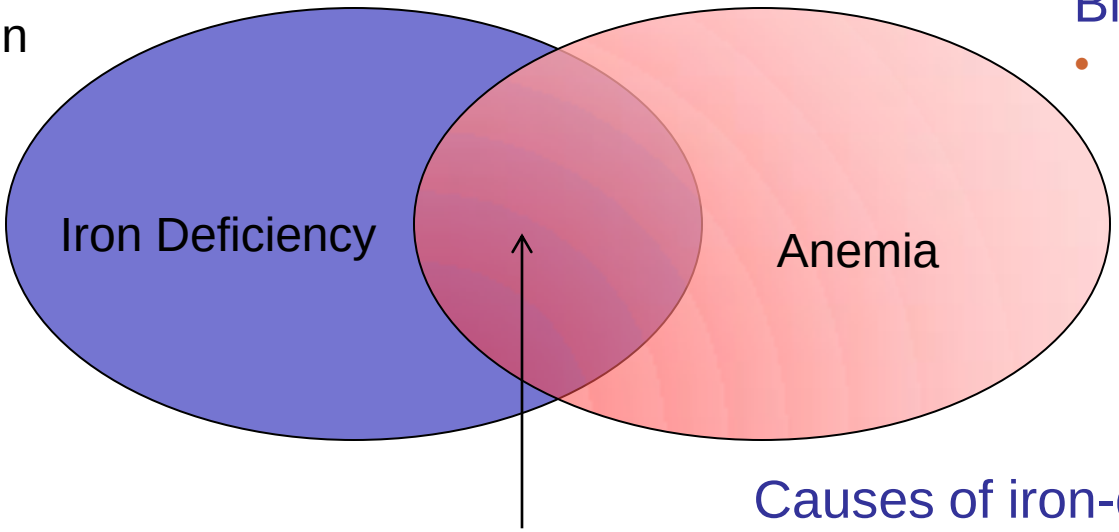
Iron deficiency vs anemia vs iron-deficiency anemia

Causes of iron deficiency:
- Deficient iron intake
- Excessive iron loss

Biological marker:
- Serum ferritin

Causes of anemia:
- Deficiency of iron, vitamin B12, folate, vitamin A
- Hemoglobinopathies
- Infections

Biological marker:
- Hemoglobin

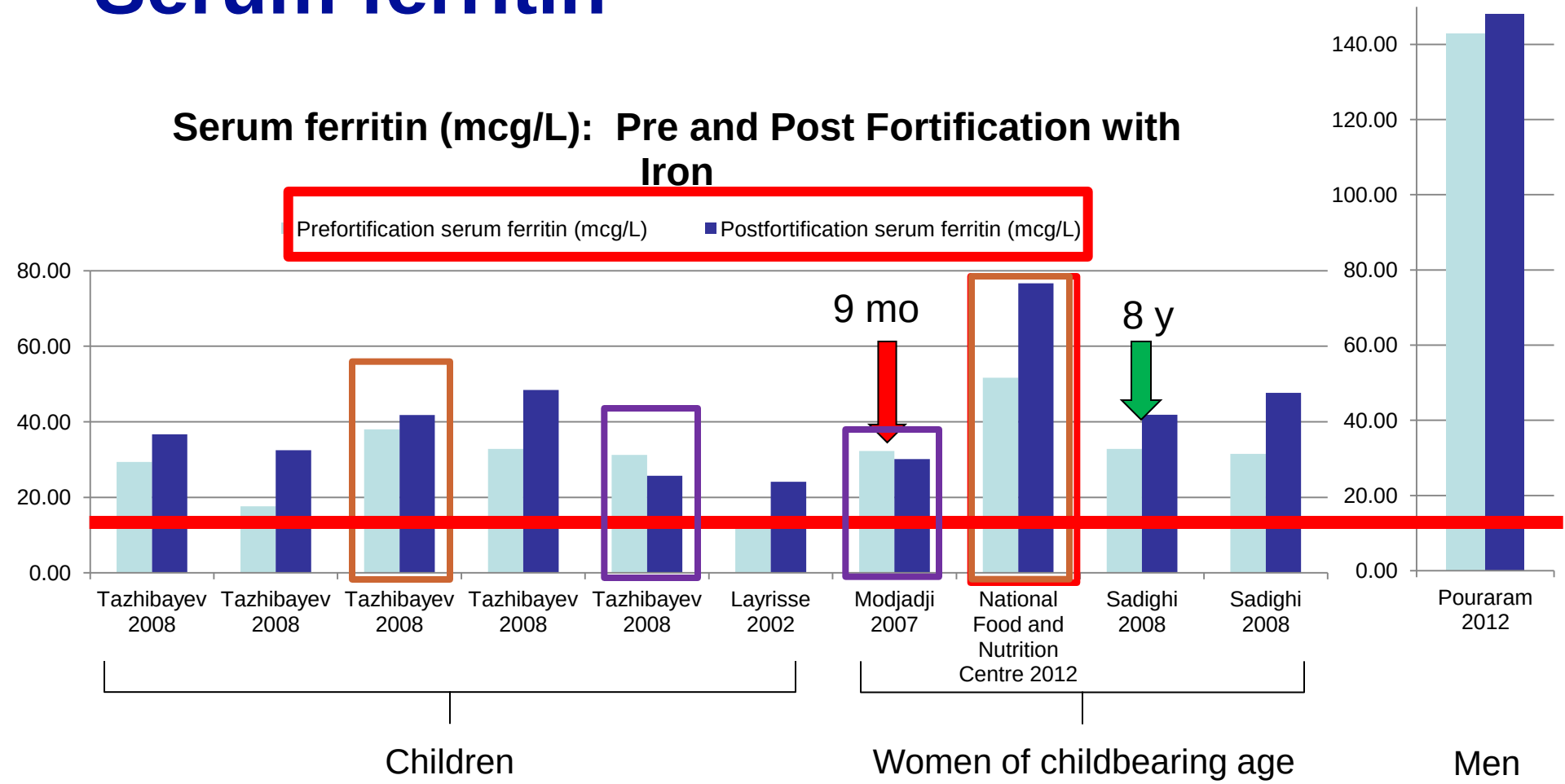


Causes of iron-deficiency anemia:
- Iron deficiency

Biological marker:
- Serum ferritin & hemoglobin

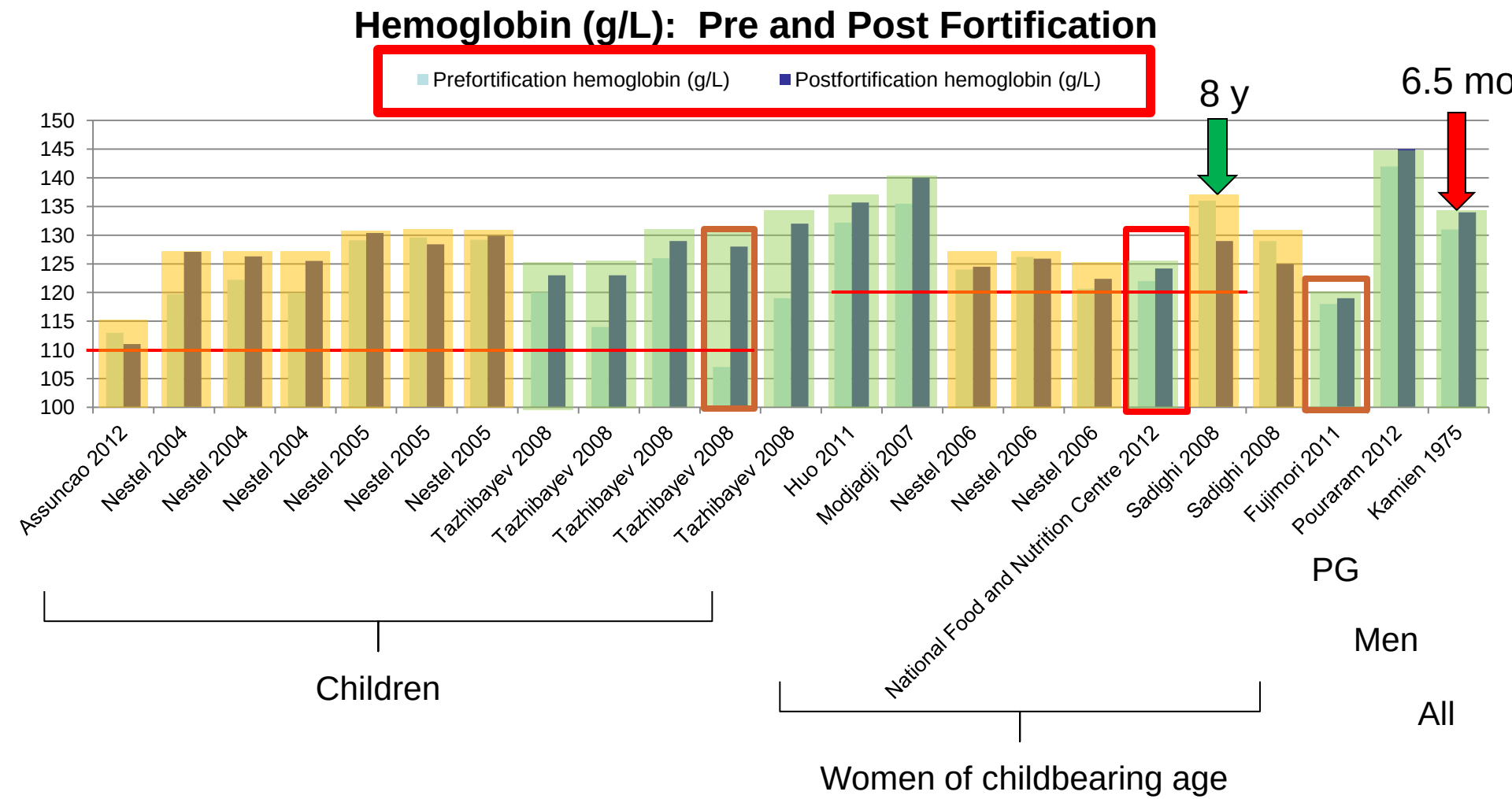
Zimmermann 2008; Gleason 2007; Scott 2007; West 2007; Cameron 2011

Serum ferritin



FFI review 2013. Iron in flour ranged from 30-60 mg/kg. Iron compounds used were ferrous sulfate, ferrous fumarate, elemental iron, and electrolytic iron.

Hemoglobin



FFI review 2013. Nutrients added to flour were iron, zinc, folic acid (B9), thiamin (B1), riboflavin (B2), niacin (B3), pyridoxine (B6), and vitamin A

Effectiveness of National Flour Fortification Programs

National Program Evaluations Prevalence of Iron Deficiency and Anemia					
Country	**Risk Group**	**Condition**	**Pre**	**Post**	**% Reduction**
Venezuela	Children > 5yrs	Iron Deficiency	37.2%	15.5%	**58.3%**
		Anemia	18.1%	17.1%	**5.5%**
Costa Rica	Adult Women		18.4%	10.2%	**45%**
Kuwait			33%	24%	**27%**
Oman	Pregnant Women		49%	31%	**37%**

Summary

Outcome	Favorable Result (n)*	Total Evaluated (n)**
Serum folate	18	19
Neural tube defects (NTDs)	19	20
Serum ferritin	9	11
Hemoglobin	11	23

* Favorable result (increased folate, ferritin, hemoglobin; decreased NTDs) in sub-group analyses
** Total number of sub-groups analyzed

Large Scale Effectiveness Trial Darjeeling, India

Prevalence of Vitamin A Deficiency (Serum Retinol < 0.70 umol/l)			
	Pre	**Post**	**% Reduction**
Pregnant Women	24.5%	23.2%	5%
School Age Children	34.5%	18.7%	46%
Adolescent Girls	30.1%	12.5%	58%
Pre-School Children	26.5%	22.5%	15%

Conclusions

Effectiveness studies of wheat and maize flour fortification programs reveal:

- Folic-acid fortification increases serum folate levels
- Folic-acid fortification decreases risk of neural tube defects (NTDs)
- Iron fortification increases serum ferritin levels
- Effect of fortification with one or multiple nutrients on hemoglobin levels is equivocal

For more information

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References for download

http://www.sph.emory.edu/~hpacho2/

References for slides 3, 5, and 8

Miquel Porta, Dictionary of Epidemiology, 2008. http://jpkc.fudan.edu.cn/picture/article/189/c4/24/81c086374fd8a31d9be7208bbb80/eb7e72b0-3b41-4b6b-8b23-168950e0e794.pdf

WHO and partners. Recommendations on wheat and maize flour fortification: Interim consensus statement. 2009. http://www.who.int/nutrition/publications/micronutrients/wheat_maize_fort.pdf

Cameron BM, Neufeld LM. Estimating the prevalence of iron deficiency in the first two years of life: technical and measurement issues. Nutrition Reviews 69(S1):S49-56, 2011.

Gleason G, Scrimshaw NS. An overview of the functional significance of iron deficiency. In: Nutritional anemia. Basel: Sight and Life Press; p.45-58, 2007.

Scott JM. Nutritional anemia: B-vitamins. In: Nutritional anemia. Basel: Sight and Life Press; p.111-132, 2007.

West KP Jr, Gernand AD, Sommer A. Vitamin A in nutritional anemia. In: Nutritional anemia. Basel: Sight and Life Press; p.133-154, 2007.

Zimmermann MB. Methods to assess iron and iodine status. British Journal of Nutrition 99(S3):S2-9, 2008.

References for serum folate (1)

Abdollahi Z, Elmadfa I, Djazayery A, Golalipour MJ, Sadighi J, Salehi F, Sadeghian Shariff S. Efficacy of flour fortification with folic acid in women of childbearing age in Iran. Annals of Nutrition and Metabolism 58:188-96, 2011.

Hertrampf E, Cortés F, Erickson JD, Cayazzo M, Freire W, Bailey LB, Howson C, Kauwell GPA, Pfeiffer C. Consumption of folic acid-fortified bread improves folate status in women of reproductive age in Chile. Journal of Nutrition 133:3166-9, 2003.

Hirsch S, de la Maza P, Barrera G, Gattás V, Petermann M, Bunout D. The Chilean flour folic acid fortification program reduces serum homocysteine levels and masks vitamin B-12 deficiency in elderly people. Journal of Nutrition 132:289-91, 2002.

Jacques PF, Selhub J, Bostom AG, Wilson PWF, Rosenberg IH. The effect of folic acid fortification on plasma folate and total homocystein concentrations. New England Journal of Medicine 340:1449-54, 1999.

Lawrence JM, Petitti DB, Watkins M, Umekubo MA. Trends in serum folate after food fortification. Lancet 354:915-6, 1999.

Liu S, West R, Randell E, Longerich L, Steel O'Connor K, Scott H, Crowley M, Lam A, Prabhakaran V, McCourt C. A comprehensive evaluation of food fortification with folic acid for the primary prevention of neural tube defects. BMC Pregnancy and Childbirth 4:20, 2004.

Modjadji SEP, Alberts M. Folate and iron status of South African non-pregnant rural women of childbearing age, before and after fortification of foods. South Africa Journal of Clinical Nutrition 20:89-93, 2007.

References for serum folate (2)

National Food and Nutrition Centre. Impact of iron fortified flour in child bearing age (CBA) women in Fiji, 2010 report. 2012.

NCHS. Folate status in women of childbearing age--United States, 1999. MMWR 49:962-5, 2000.

Pfeiffer CM, Caudill SP, Gunter EW, Osterloh J, Sampson EJ. Biochemical indicators of B vitamin status in the US population after folic acid fortification: results from the National Health and Nutrition Examination Survey 1999-2000. American Journal of Clinical Nutrition 82:442-50, 2005.

Pfeiffer CM, Hughes JP, Lacher DA, Bailey RL, Berry RJ, Zhang M, Yetley EA, Rader JI, Sempos CT, Johnson CL. 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. Journal of Nutrition 142:886-93, 2012.

Tacsan Chen L, Ascencio Rivera M. The Costa Rican experience: reduction of neural tube defects following food fortification programs. Nutrition Reviews 62:S40-3, 2004.

Tazhibayev S, Dolmatova O, Ganiyeva G, Khairov K, Ospanova F, Oyunchimeg D, Suleimanova D, Scrimshaw N. Evaluation of the potential effectiveness of wheat flour and salt fortification programs in five Central Asian countries and Mongolia, 2002-2007. Food and Nutrition Bulletin 29:255-265, 2008.

WHO. Serum and red blood cell folate concentrations for assessing folate status in populations. Vitamin and Mineral Nutrition Information System. WHO: Geneva, 2012.

References for neural tube defects (1)

Abdollahi Z, Djazayery A, Golalipour MJ et al. Efficacy of flour fortification with folic acid in women of childbearing age in Iran. *Annals of Nutrition and Metabolism* 58(3):188-196, 2011.

Arguello LB, Umana Solis LM. Impact of the fortification of food with folic acid on neural tube defects in Costa Rica. Revista Panamericana de Salud Publica 30(1):1-6, 2011.

Botto LD et al. Trends of selected malformations in relation to folic acid recommendations and fortification: an international assessment. Birth Defects Research (Part A) 76:693-705, 2006.

Castilla EE, Oriolo IM, Lopez-Camelo JS, Dutra MDG, Nazer-Herrera J. Preliminary data on changes in neural tube defect prevalence rates after folic acid fortification in South America. American Journal of Medical Genetics Part A 123A:123-8, 2003.

Cortes F, Mellado C, Pardo RA. Wheat flour fortification with folic acid changes in neural tube defects rates in Chile. American Journal of Genetics 158A(8):1885-1890, 2012.

De Wals P, Rusen ID, Lee NS, Morin P, Niyonsenga T. Trend in prevalence of neural tube defects in Quebec. Birth Defects Research (Part A) 67:919-23, 2003.

De Wals P, Tairou F, Van Allen MI, Uh SH, Lowry B, Sibbald B, Evans JA, Van den Hof MC, Zimmer P, Crowley M, Fernandez B, Lee NS, Niyonsenga T. Reduction in neural-tube defects after folic acid fortification in Canada. New England Journal of Medicine 357:135-42, 2007.

FFI. Public Health Impact of Fortifying Flour With Folic Acid To Prevent Neural Tube Defects. 2012. http://www.ffinetwork.org/why_fortify/documents/FortifyToPreventNTDs.pdf

Gucciardi E, Pietrusiak MA, Reynolds DL, Rouleau J. Incidence of neural tube defects in Ontario, 1986-1999. Canadian Medical Association Journal 167:237-40, 2002.

References for neural tube defects (2)

Honein MA, Paulozzi LJ, Mathews TJ, Erickson JD, Wong LYC. Impact of folic acid fortification of the US food supply on the occurrence of neural tube defects. JAMA 285:2981-6, 2001.

Liu S, West R, Randell E, Longerich L, Steel O'Connor K, Scott H, Crowley M, Lam A, Prabhakaran V, McCourt C. A comprehensive evaluation of food fortification with folic acid for the primary prevention of neural tube defects. BMC Pregnancy and Childbirth 4:20, 2004.

Persad VL, Van den Hof MC, Dubé JM, Zimmer P. Incidence of open neural tube defects in Nova Scotia after folic acid fortification. Canadian Medical Association Journal 167:241-5, 2002.

Ray JG, Meier C, Vermeulen MJ, Boss S, Wyatt PR, Cole DEC. Association of neural tube defects and folic acid food fortification in Canada. Lancet 360: 2047-8, 2002.

Ricks DJ, Rees CA, Osborn KA, Crookston BT, Leaver K, Merrill SB, Velásquez C, Ricks JH. Peru's national folic acid fortification program and its effect on neural tube defects in Lima. Rev Panam Salud Publica 32:391-8, 2012.

Safdar OY, Al-Dabbagh AA, AbuElieneen WA, Kari JA. Decline in the incidence of neural tuve defects after the national fortification of flour (1997-2005). Saudi Medical Journal 28:1227-9, 2007.

Sayed A-R, Bourne D, Pattinson R, Nixon J, Henderson B. Decline in the prevalence of neural tube defects following folic acid fortification and its cost-benefit in South Africa. Birth Defects Research (Part A) 82:211-6, 2008.

Silva Pacheco S, Braga C, Impieri de Souza A, Natal Figueiroa J. Effects of folic acid fortification on the prevalence of neural tuve defects. Rev Saúde Pública 43:1-6, 2009.

Tacsan Chen L, Rivera MA. The Costa Rican experience: Reduction of neural tube defects following food fortification programs. Nutrition Reviews 62(6):S40-43, 2004.

References for serum ferritin

Assuncao MCG, Santos IS, Barros AJD, Gigante DP, Victora CG. Flour fortification with iron has no impact on anaemia in urban Brazilian children. Public Health Nutrition 16(1):188, 2012.

Huo J, Sun J, Huang J, Li W, Wang L, Selenje L, Gleason GR, Yu X. The effectiveness of fortified flour on micro-nutrient status in rural female adults in China. Asia Pacific Journal of Clinical Nutrition 20:118-24, 2011.

Layrisse M, García-Casal MN, Méndez-Castellano H, Jiménez M, Olavarría H, Chávez JF, González E. Impact of fortification of flours with iron to reduce the prevalence of anemia and iron deficiency among school children in Caracas, Venezuela: a follow-up. Food and Nutrition Bulletin 23(4):384-9, 2002.

Modjadji SEP, Alberts M. Folate and iron status of South African non-pregnant rural women of childbearing age, before and after fortification of foods. South Africa Journal of Clinical Nutrition 20:89-93, 2007.

National Food and Nutrition Centre. Impact of iron fortified flour in child bearing age (CBA) women in Fiji, 2010 report. 2012.

Pouraram H, Elmadfa I, Dorosty AR, Abtahi M, Neyestani TR, Sadeghian S. Long-term consequences of iron-fortified flour consumption in nonanemic men. Annals of Nutrition and Metabolism 60(2):115-21, 2012.

Sadighi J, Mohammad K, Sheikholeslam R, Amirkhani MA, Torabi P, Salehi F, Abdolahi Z. Anaemia control: lessons from the flour fortification programme. Public Health 123:794-9, 2009.

Tazhibayev S, Dolmatova O, Ganiyeva G, Khairov K, Ospanova F, Oyunchimeg D, Suleimanova D, Scrimshaw N. Evaluation of the potential effectiveness of wheat flour and salt fortification programs in five Central Asian countries and Mongolia, 2002-2007. Food and Nutrition Bulletin 29:255-265, 2008.

References for hemoglobin (1)

Assuncao MCG, Santos IS, Barros AJD, Gigante DP, Victora CG. Flour fortification with iron has no impact on anaemia in urban Brazilian children. Public Health Nutrition 16(1):188, 2012.

Fujimori E, Sato APS, Szarfarc SC, da Veiga GV, de Oliveira VA, Colli C, dos Reis Moreira-Araújo R. Anemia in Brazilian pregnant women before and after flour fortification with iron. Rev Saúde Publica 45:1027-35, 2011.

Huo J, Sun J, Huang J, Li W, Wang L, Selenje L, Gleason GR, Yu X. The effectiveness of fortified flour on micro-nutrient status in rural female adults in China. Asia Pacific Journal of Clinical Nutrition 20:118-24, 2011.

Kamien M, Woodhill JM, Nobile S, Cameron P, Rosevear P. Nutrition in the Australian aborigines-effects of the fortification of wheat flour. Australian and New Zealand Journal of Medicine 5:123-33, 1974.

Modjadji SEP, Alberts M. Folate and iron status of South African non-pregnant rural women of childbearing age, before and after fortification of foods. South Africa Journal of Clinical Nutrition 20:89-93, 2007.

National Food and Nutrition Centre. Impact of iron fortified flour in child bearing age (CBA) women in Fiji, 2010 report. 2012.

Nestel P, Nalubola R, Sivakeneshan R, Wickramasinghe AR, Atukorala S, Wickramanayake T. The use of iron-fortified wheat flour to reduce anemia among the estate population in Sri Lanka. International Journal of Vitamin Nutrition Research. 74:35-51, 2004.

References for hemoglobin

Pouraram H, Elmadfa I, Dorosty AR, Abtahi M, Neyestani TR, Sadeghian S. Long-term consequences of iron-fortified flour consumption in nonanemic men. Annals of Nutrition and Metabolism 60(2):115-21, 2012.

Sadighi J, Mohammad K, Sheikholeslam R, Amirkhani MA, Torabi P, Salehi F, Abdolahi Z. Anaemia control: lessons from the flour fortification programme. Public Health 123:794-9, 2009.

Tazhibayev S, Dolmatova O, Ganiyeva G, Khairov K, Ospanova F, Oyunchimeg D, Suleimanova D, Scrimshaw N. Evaluation of the potential effectiveness of wheat flour and salt fortification programs in five Central Asian countries and Mongolia, 2002-2007. Food and Nutrition Bulletin 29:255-265, 2008.