

# Vitamin supplementation during pregnancy What is reasonable?

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# Disclosure

- Financial: *I was invited from EFFIK to the CampusPharma Lunch Symposium*
- Nonfinancial: *I have no relevant nonfinancial relationships to disclose*



- Energy requirement in pregnancy
- Needs for vitamins and omega three fatty acid
  - Action profile
  - Food source
  - Deficiencies
  - Pregnancies at risk
  - Supplementation
- Summary

# Why Switzerland?

Seychelles

Sierra Leone

Singapore

Slovakia

Slovenia

Solomon Islands

Somalia

Non Europeans often confuse Sweden and Switzerland

South Sudan

Spain

Sri Lanka

Sudan

Suriname

Swaziland

Sweden

Switzerland

Syria





# DIET AND NUTRITION DURING PREGNANCY AND WHILE BREASTFEEDING

## Nordic Nutrition Recommendations 2012

Integrating nutrition and physical activity

The central role of nutrition and metabolism in pregnancy for health and **well-being of pregnant women**, pregnancy outcomes, and **long-term health and development of the offspring** has been generally recognized. Cetin I et al, Crit rev food science nutri 2014

Schweizerische Eidgenossenschaft  
Confédération suisse  
Confederazione Svizzera  
Confederaziun svizra

Federal Department of Home Affairs FDHA  
Federal Food Safety and  
Veterinary Office FSVO



# Twice as healthy- not twice as much





# Energy requirement

**250 kcal/d from 2. trimester**



**500 kcal/d from 3. trimester/  
lactation period**

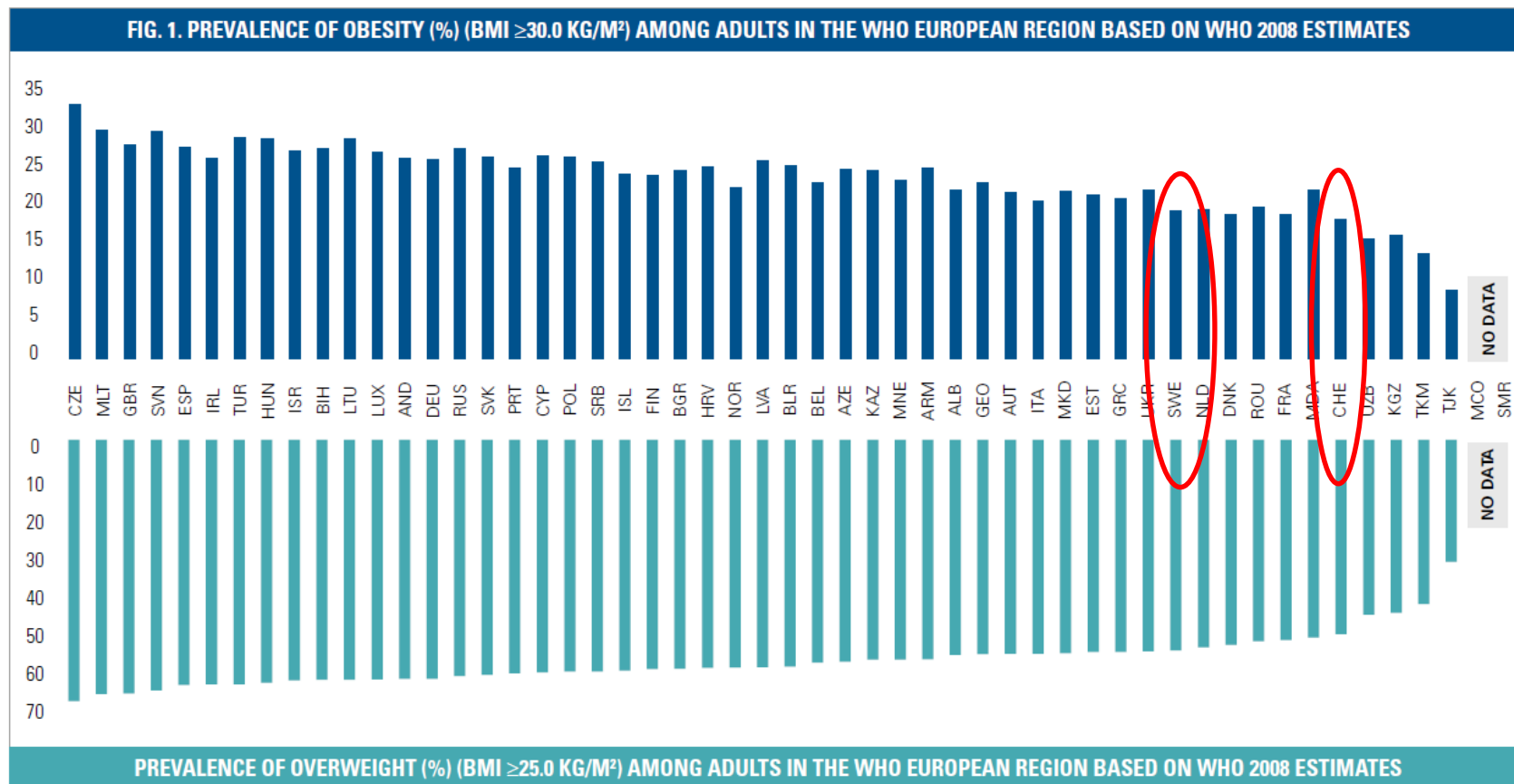




# Weight gain dependent from BMI

	BMI before pregnancy	Recommended weight gain (total in kg)	Recommended weight gain (per week in kg)
Normal weight	18.5 - 24.9	11.5 - 16	0.4 from 12 weeks
Underweight	< 18.5	12.5 - 18	0.5 from 12 weeks
Overweight	25 - 29.9	7 - 11.5	0.3 from 12 weeks
Adipositas	$\geq 30$	5 - 9	
Twins		15.9 - 20.4	0.7 from 12 weeks
Triplets		ca 22	

# BMI > 30 in Switzerland and Sweden non pregnant



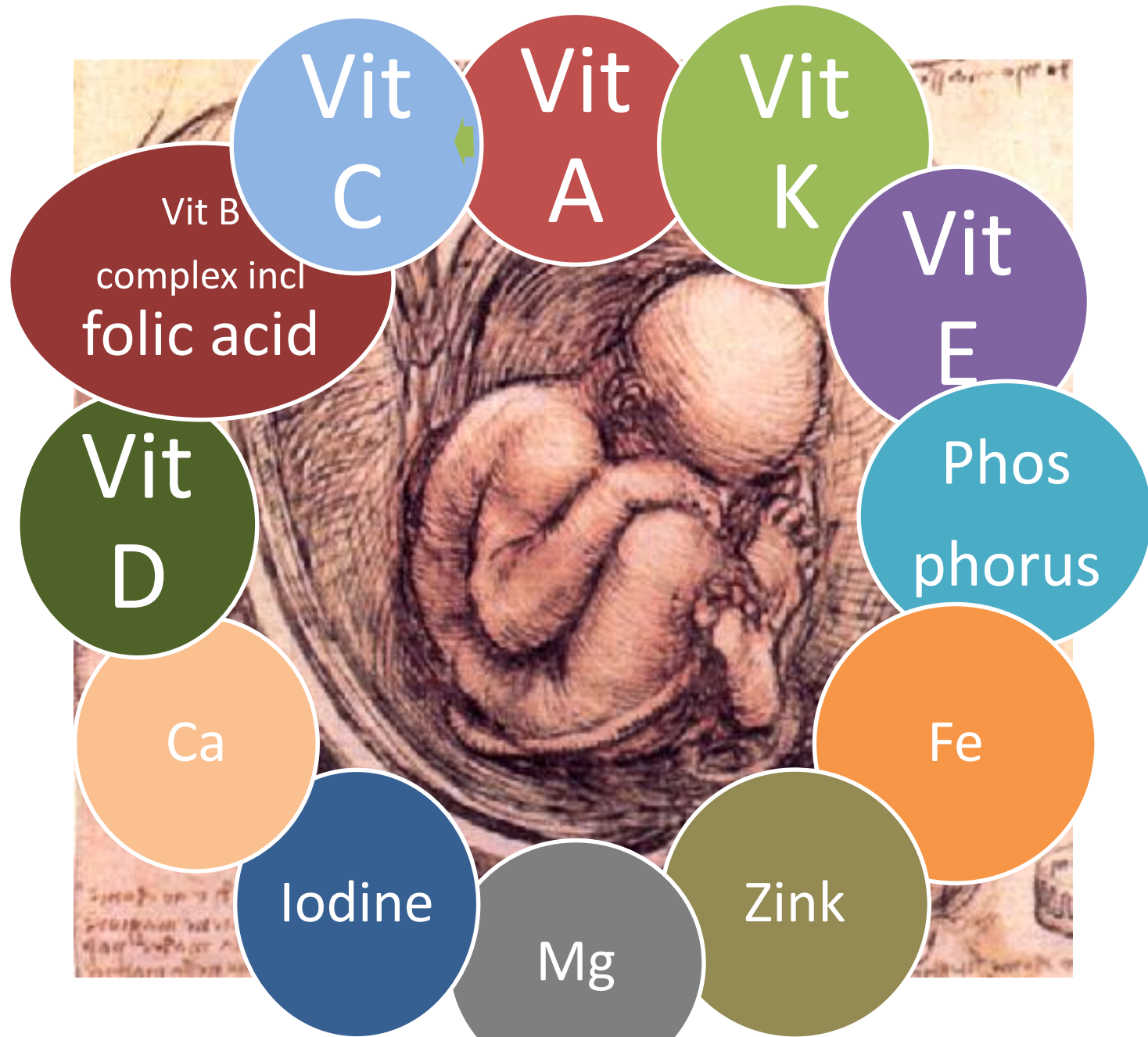
Country profile on nutrition, physical activity and obesity, WHO 2013

# Obstetrical complications and BMI < 16 SSW

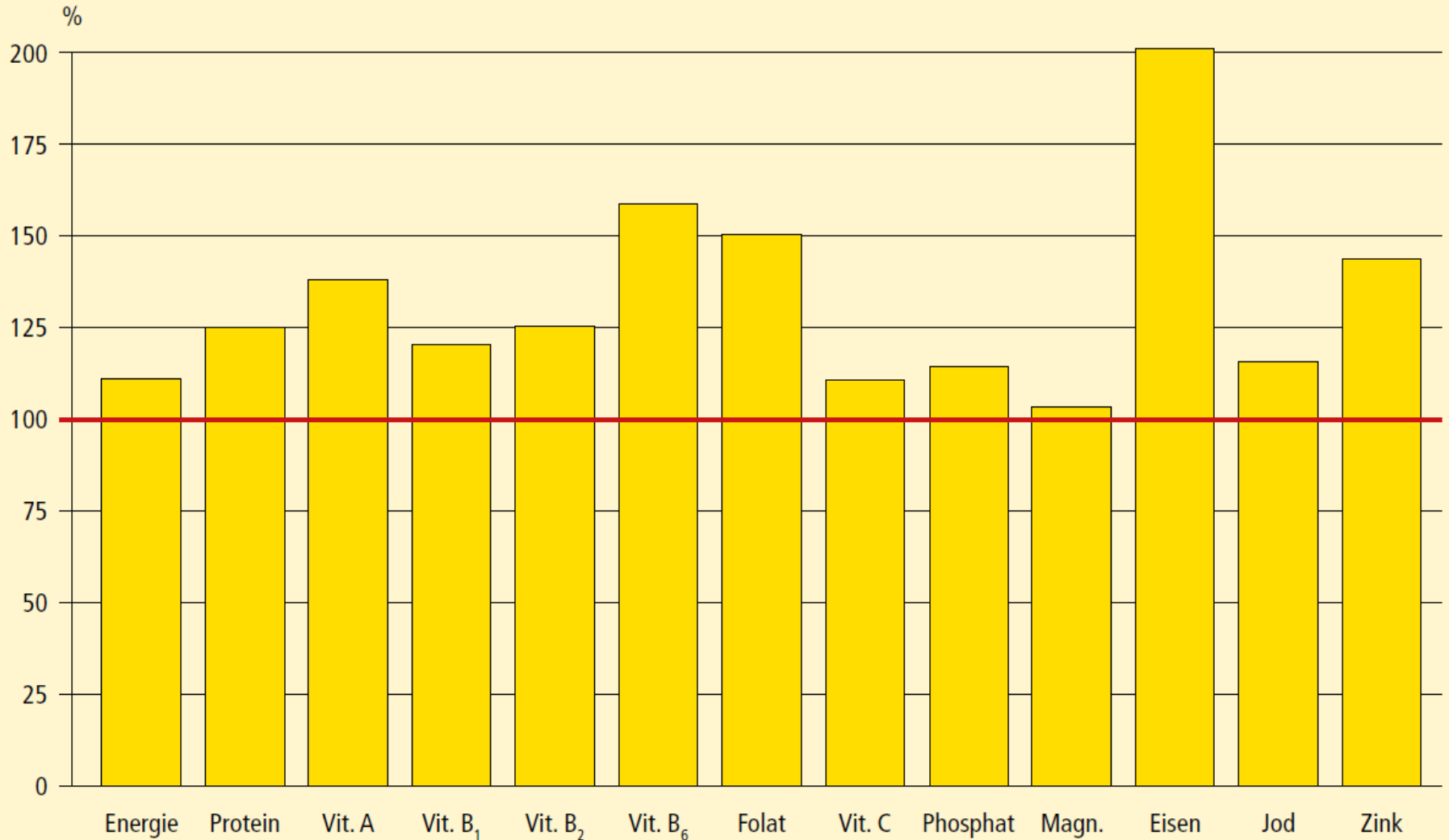
Complications	≤ 18.49 OR	18.5-24.9 OR	25-29.9 OR	30-39.9 OR	≥ 40 OR
Hypertension	0.60	1.0	1.87	11.90	36.10
Gestational diabetes	0.22	1.0	3.39	11.90	67.40
Cesarean section	1.08	1.0	2.06	4.61	17.92
Preterm delivery Medical indicated	1.74	1.0	1.25	1.45	2.12
IUFD	0.92	1.0	1.07	1.43	1.91
Transfer to NICU	1.66	1.0	1.04	1.28	1.87
Adipositas offspring					4.0



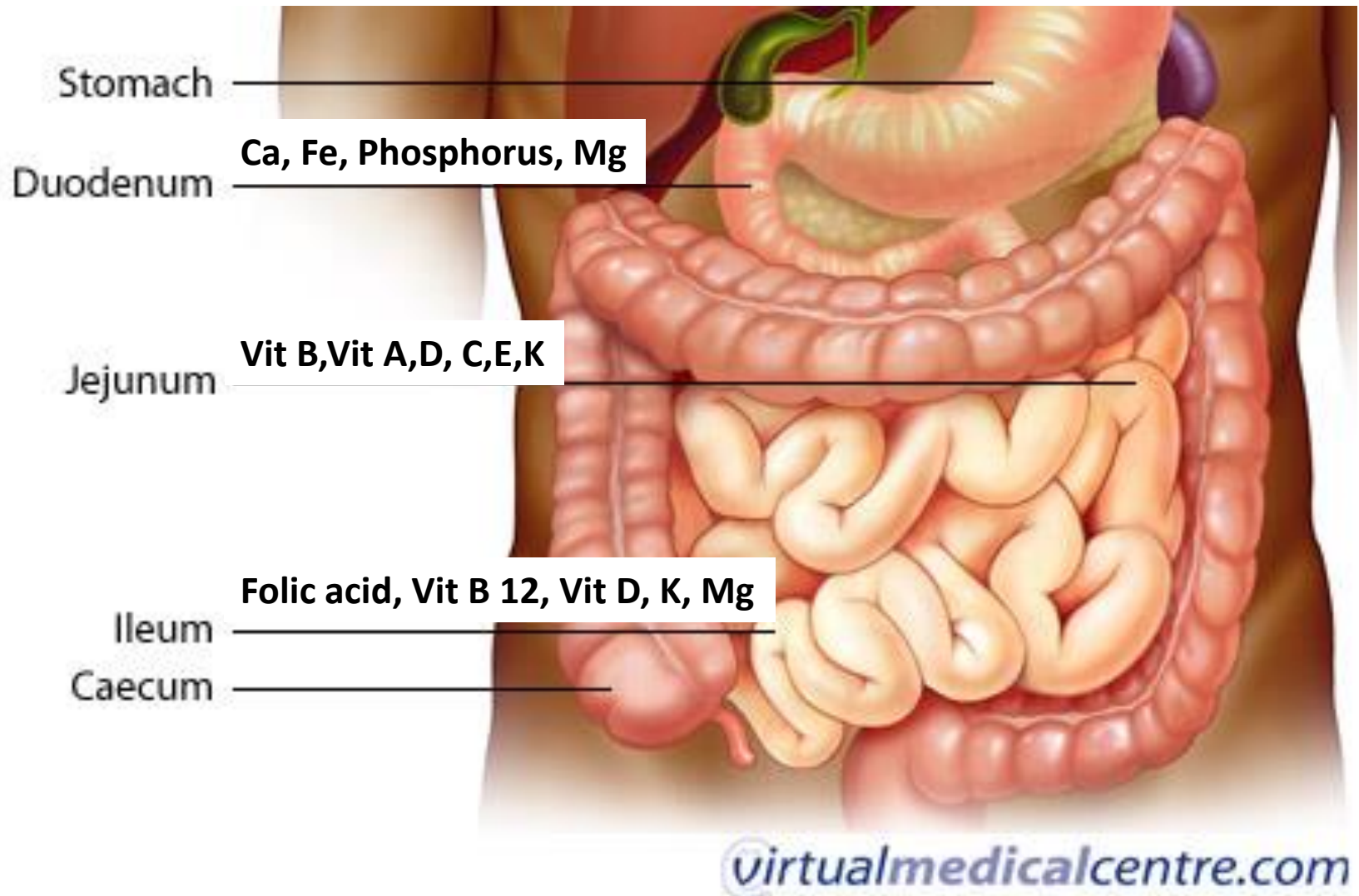
# Vitamins and minerals



# D-A-CH references for nutrients in pregnancy



# Absorption intestinal







**Folic acid**

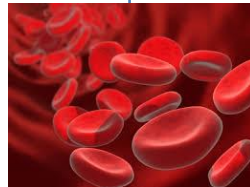
**Vitamin B  
12  
complex**

# Biological function of Vit B12 and folic acid

↓  
Nutrition source



**DNA, RNA Synthesis**  
Cell division, multiplication  
Embryonal period (28 d p.c.)  
Neural tube development



**Production of red blood cells**

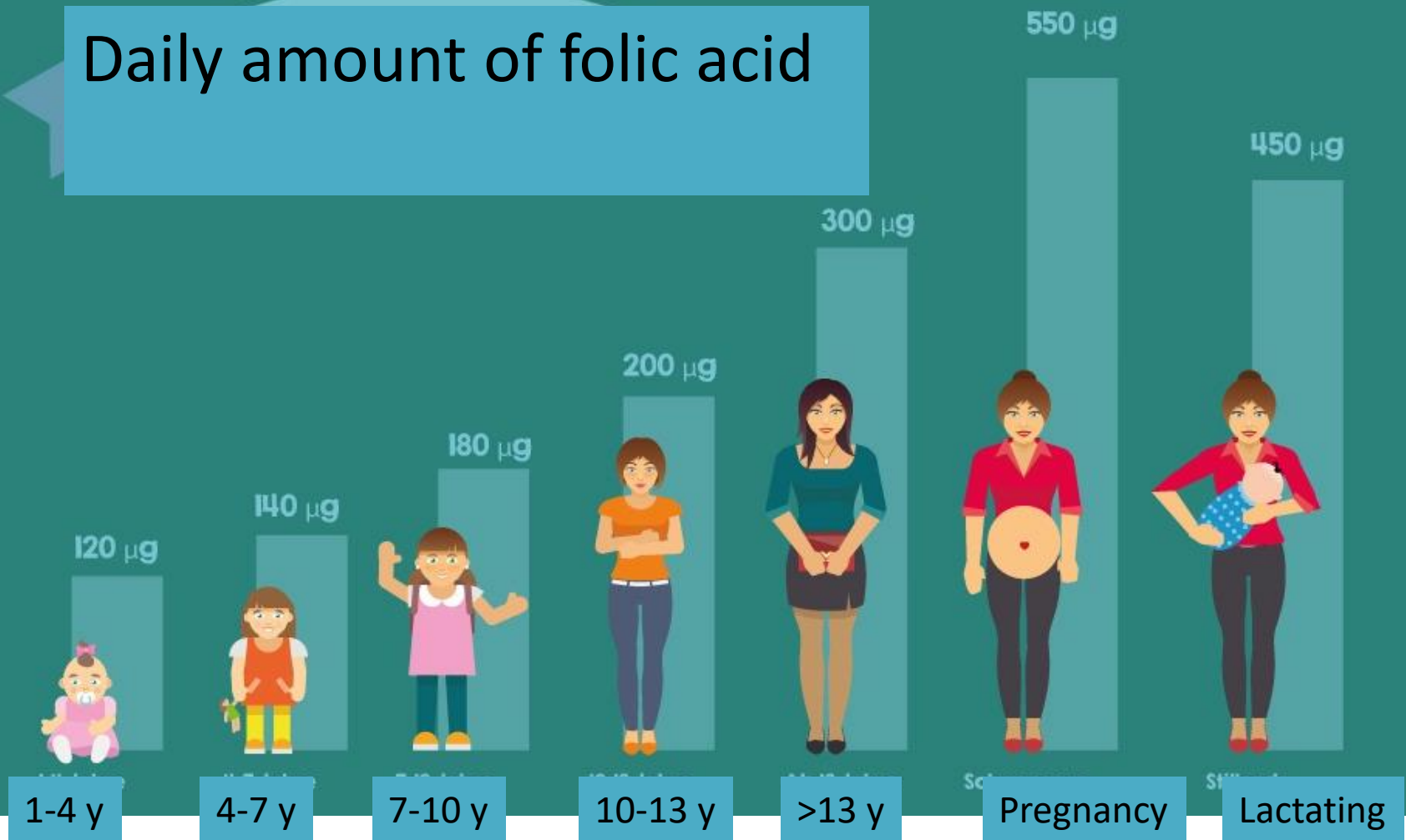


**Myelin**  
Neural myelinisation  
Brain development  
Cognitive functions



**Homocysteine  
Methylation**

## Daily amount of folic acid





# Folic acid deficiency and CA

Table 3. Congenital Malformations, According to Study Group.

MALFORMATION	VITAMIN GROUP	TRACE- ELEMENT GROUP
	2471	2391
	<i>number</i>	
Neural-tube defect	0	6
Congenital hydrocephalus	0	2
Cardiovascular malformation	6	9
Cleft palate	0	2
Cleft lip (with or without cleft palate)	4	3
Hypospadias	1	1
Obstructive defects of urinary system	1	2
Congenital postural deformity	2	0
Limb-reduction defect	1	5
Foramina parietale permagna	0	2
Exomphalos and gastroschisis	1	1
Large hemangioma on face	3	1
Down's syndrome	2	3
Unidentified multiple malformations	3	3
Other*	4	7
Total	28	47

\*Each congenital malformation occurred only once in either

Czeisel AE et al, NEJM, 1992



Congenital abnormality groups (n=7391)	Folic acid / Multivitamin OR 95% CI
<b>Prevention Neural-tube defects</b>	<b>0.28 (0.15 – 0.52)</b>
<b>Recurrence Prevention NTD</b>	<b>0.33 (0.17-0.60)</b>
<b>Cardiovascular abnormalities</b>	ns
<b>Obstructive defects of urinary system</b>	ns
<b>Cleft lip, cleft palate</b>	ns
<b>Miscarriage</b>	ns

**Table.** Dose–Response Relation between Folic Acid and Neural-Tube Defects.

Increase in Daily Folic Acid Intake*	Percentage of Neural-Tube Defects That Would Be Prevented	Effect of an Extra 0.2 mg	Effect of an Extra 1 mg
<i>mg</i>			<i>%</i>
0	0	} 23	} 57
0.2	23		
0.4	36		
0.8	52	} 5	
1.0	57		
4.0	82		} 3
5.0	85		

\* The analysis assumes a base-line serum folate level of 5 ng per milliliter.



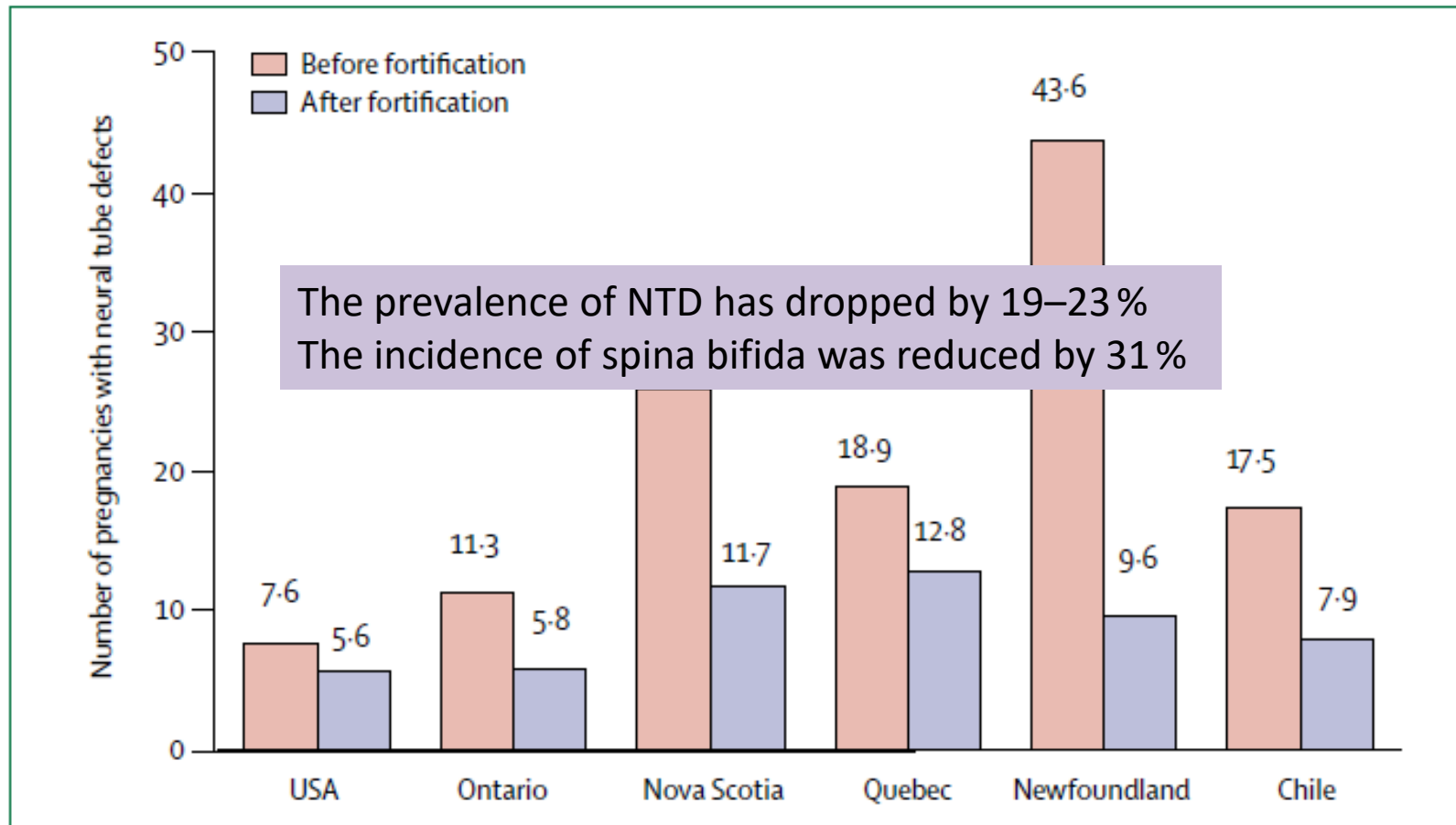
# SWIF: Swiss infant feeding study 2014

- 90% of women take folic acid during pregnancy
- **Only 46% perform preconceptional intake**
- dependent from:
  - Number of pregnancies
  - Socioeconomic status
  - Smoking
  - Region and Nationality

N=1535



# Food Fortification > 50 countries



**Figure: Rates of neural tube defects before and after fortification in regions with mandatory folic acid fortification**

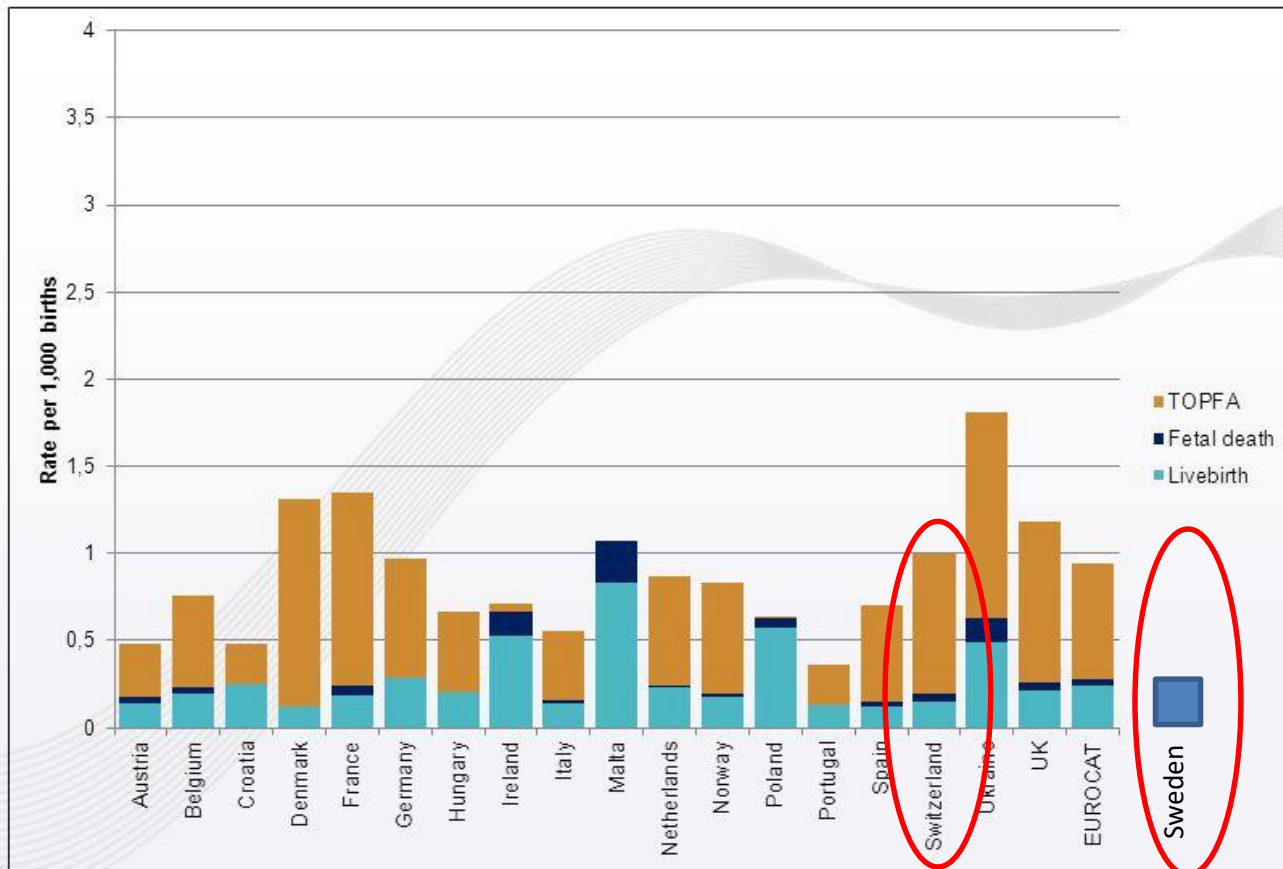
Numbers include livebirths and stillbirths, prenatally diagnosed cases, and elective abortions (Chile with livebirths and stillbirths only, USA with surveillance programmes with and without prenatal assessment).

additional folic acid intake of 80 to 200 µg/d

Eichholzer M et al, The Lancet 2006

# NTD by country

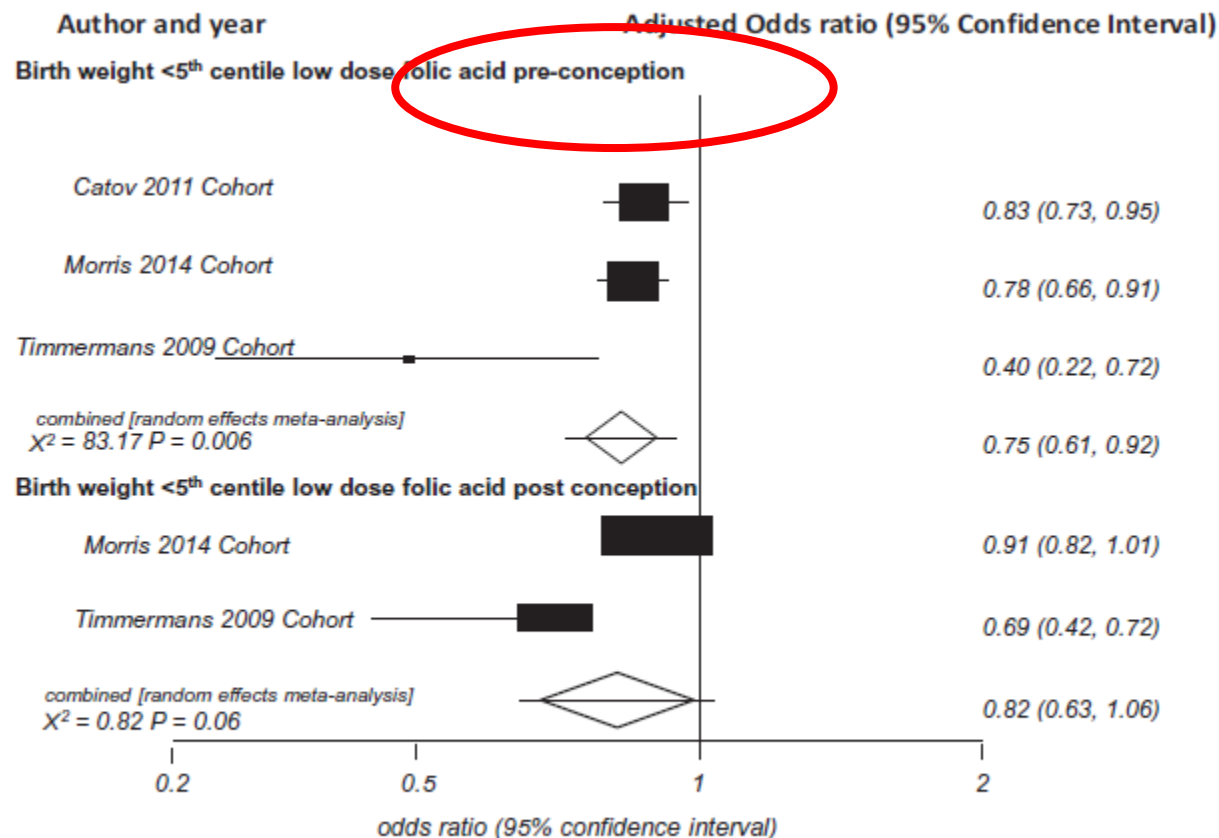
## Neural Tube Defects By Country 2008-2012 (3.6% of all CA)



Swedish Health register 2004

# Effectiveness of folic acid supplementation in pregnancy on reducing the risk of small-for-gestational age neonates: a population study, systematic review and meta-analysis

VA Hodgetts,<sup>a</sup> RK Morris,<sup>b,c</sup> A Francis,<sup>d</sup> J Gardosi,<sup>d</sup> KM Ismail<sup>b,c</sup>

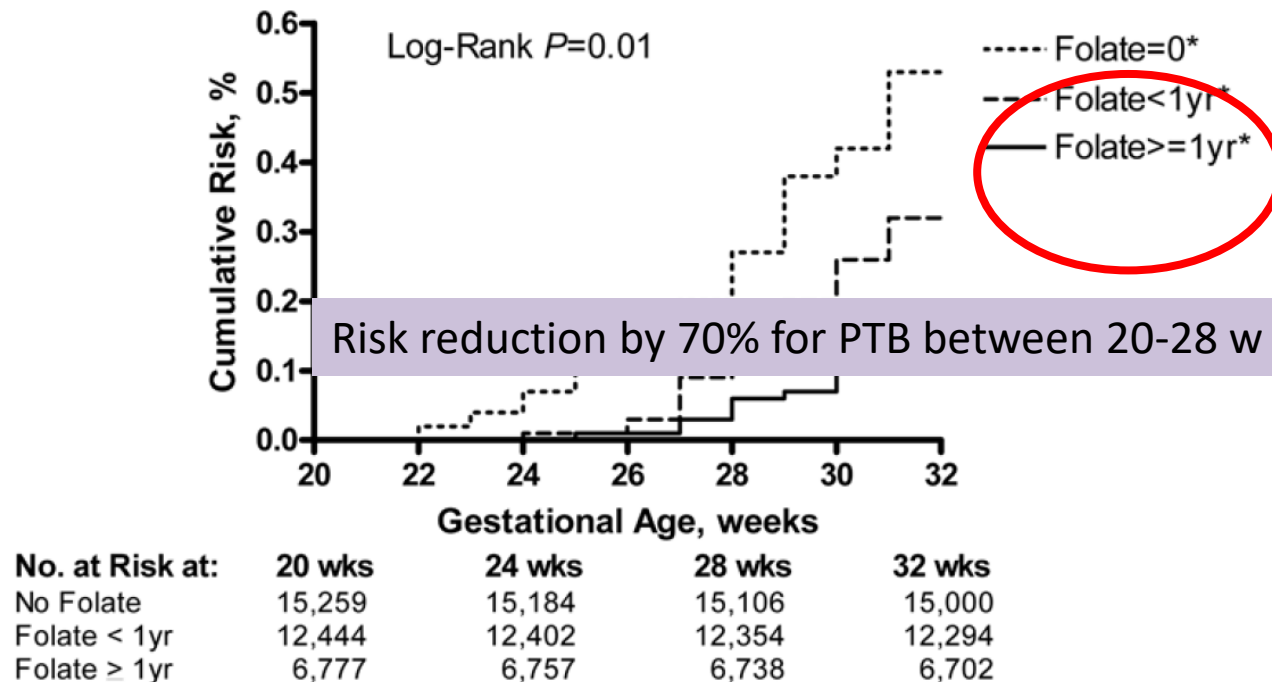


**Figure 2.** Meta-analysis folic acid supplementation and birthweight <5th centile.



# Preconceptional Folate Supplementation and the Risk of Spontaneous Preterm Birth: A Cohort Study

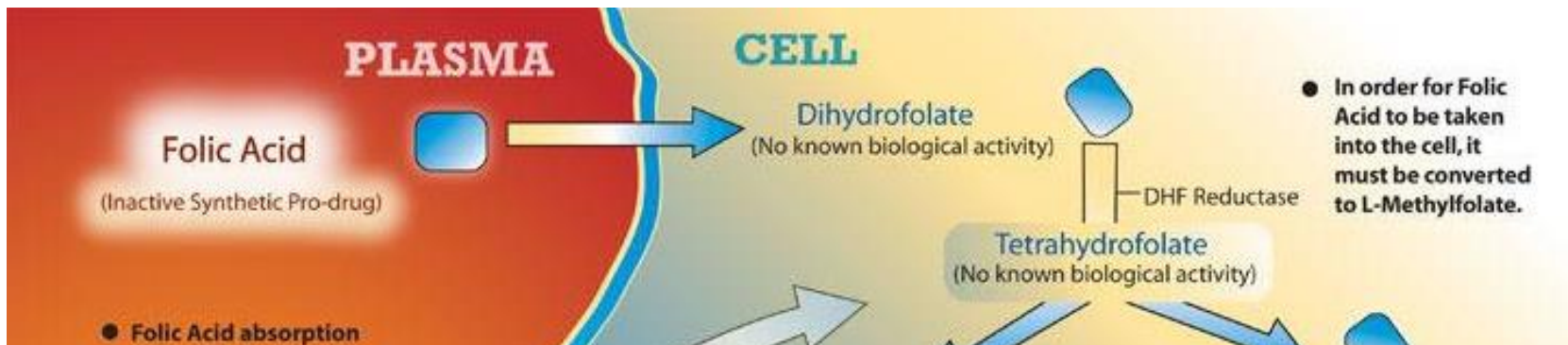
Radek Bukowski<sup>1\*</sup>, Fergal D. Malone<sup>2</sup>, Flint T. Porter<sup>3</sup>, David A. Nyberg<sup>4</sup>, Christine H. Comstock<sup>5</sup>, Gary D. V. Hankins<sup>1</sup>, Keith Eddleman<sup>6</sup>, Susan J. Gross<sup>7</sup>, Lorraine Dugoff<sup>8</sup>, Sabrina D. Craigo<sup>9</sup>, Ilan E. Timor-Tritsch<sup>10</sup>, Stephen R. Carr<sup>11</sup>, Honor M. Wolfe<sup>12</sup>, Mary E. D'Alton<sup>13</sup>



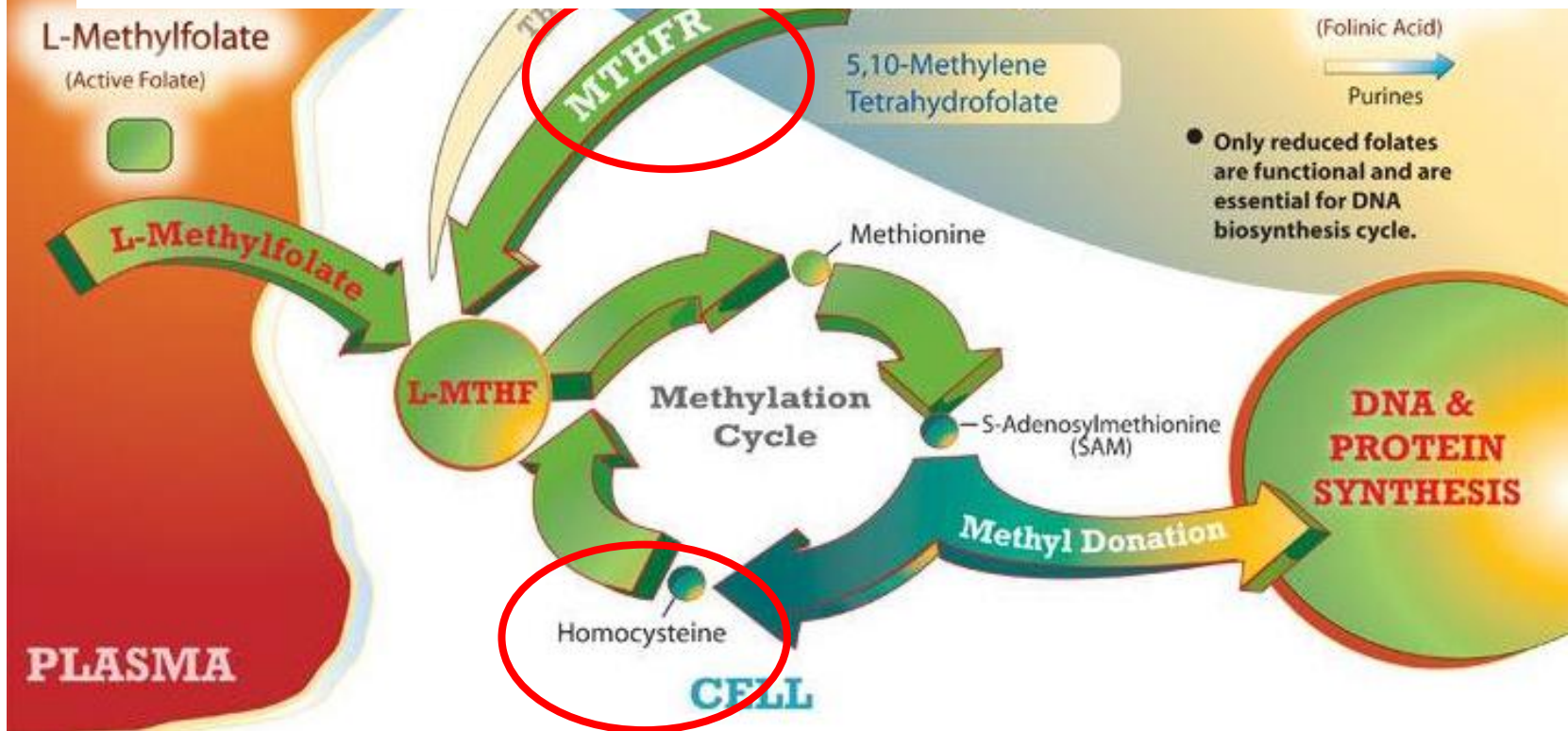
**Figure 1. Cumulative risk of spontaneous preterm birth in relation to duration of preconceptional folate supplementation.** Folate = 0\*, no preconceptional folate supplementation; Folate < 1 yr\*, preconceptional folate supplementation for less than a year; Folate ≥ 1 yr\*, preconceptional folate supplementation for a year or longer. \*Test for trend of survivor functions,  $p=0.01$ . doi:10.1371/journal.pmed.1000061.g001

# 5 Methyl-tetrahydrofolate: an alternative to folic acid

- Synthetic produced folic acid:
  - By itself not active, must be metabolized
  - Higher dosis can mask Vit B 12 deficiency
- Natural form in food: 5-formyl-tetrahydrofolate
  - Bioavailability affected by food preparation
- **5 Methyl-tetrahydrofolate** naturally form of folic acid
  - High bioavailability
  - Can directly enter folate cycle



**In the Caucasian population, around 10% of people are homozygous (677TT) and 40% heterozygous (677CT)**



# **Pre-conception Folic Acid and Multivitamin Supplementation for the Primary and Secondary Prevention of Neural Tube Defects and Other Folic Acid-Sensitive Congenital Anomalies**

## **BOX 1**

**Congenital anomalies which may be sensitive to folate (see text for anomaly detail):**

- Oral facial cleft (and palate)
- Certain cardiac defects
- Certain urinary tract anomalies
- Limb reduction defects

## **BOX 2**

**Practical list of folate-inhibiting medications:**

- Anticonvulsant medications: phenytoin, primidone, phenobarbital, carbamazepine, valproic acid
- Metformin
- Methotrexate (a medication that is highly teratogenic to the fetus).
- Sulfasalazine
- Triamterene
- Trimethoprim (as found in cotrimoxazole)



# Recommendations for Switzerland 2015

General preconceptional (min. 1-2 Mo) preferred 5-methyl-THF	400 µg/d
Intake of folic acid antagonist, DM, previous NTD, multiple pregnancies, BMI > 30 kg/m <sup>2</sup>	5 mg/d

# Recommendations for Sweden 2012

General preconceptionall, during pregnancy and lactation period	500 µg/d
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# Iodine



# Iodine nutrition in non pregnant population

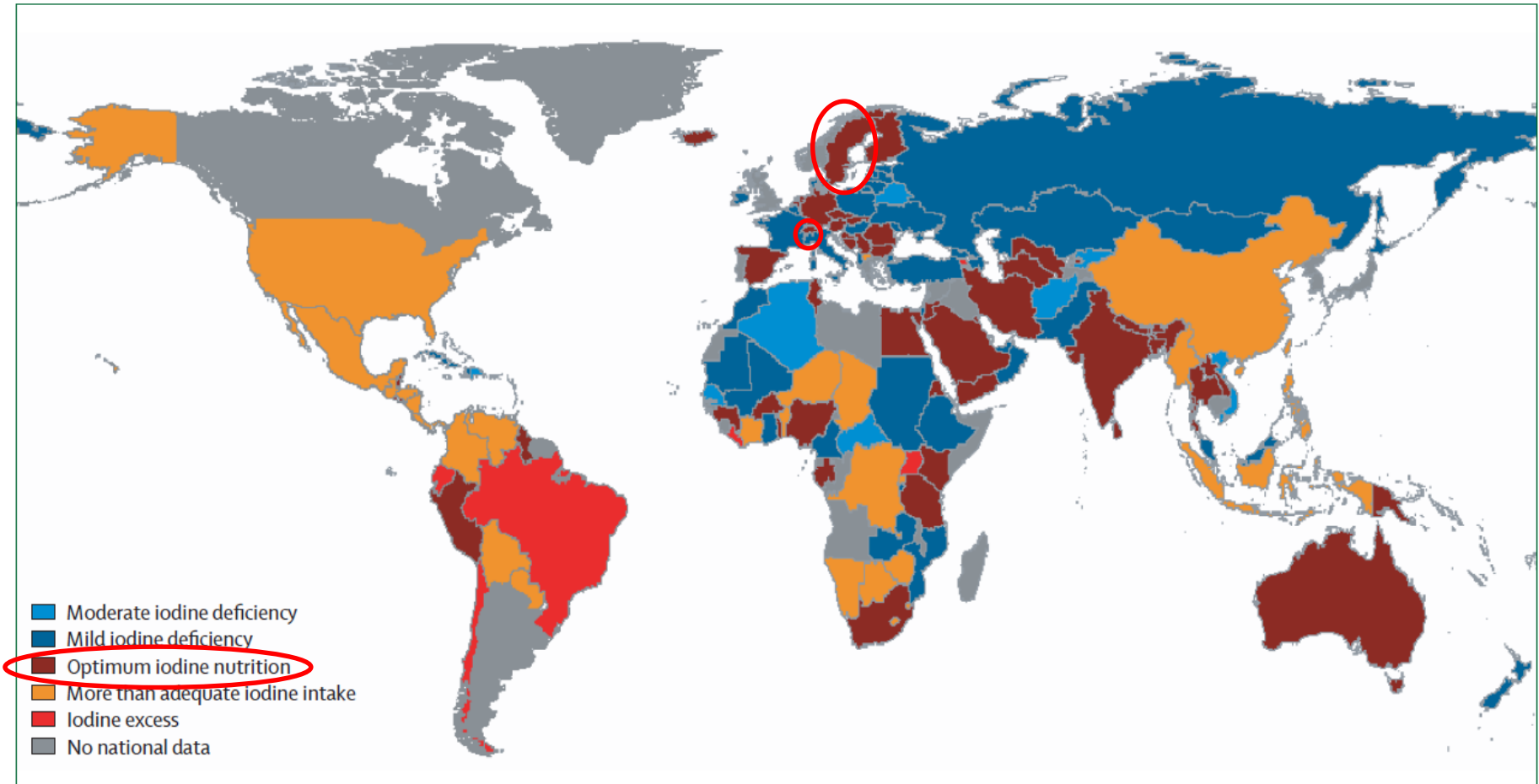
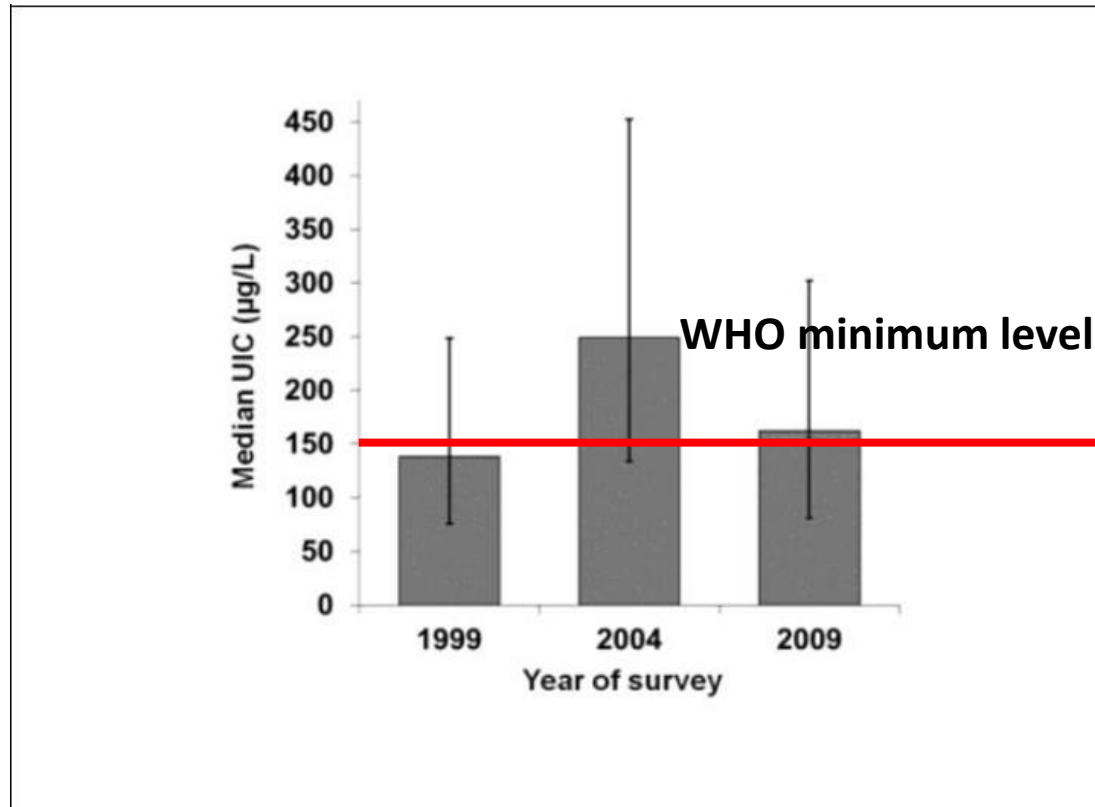


Figure 4: Iodine nutrition based on the median urinary iodine concentration, by country<sup>49,51</sup>

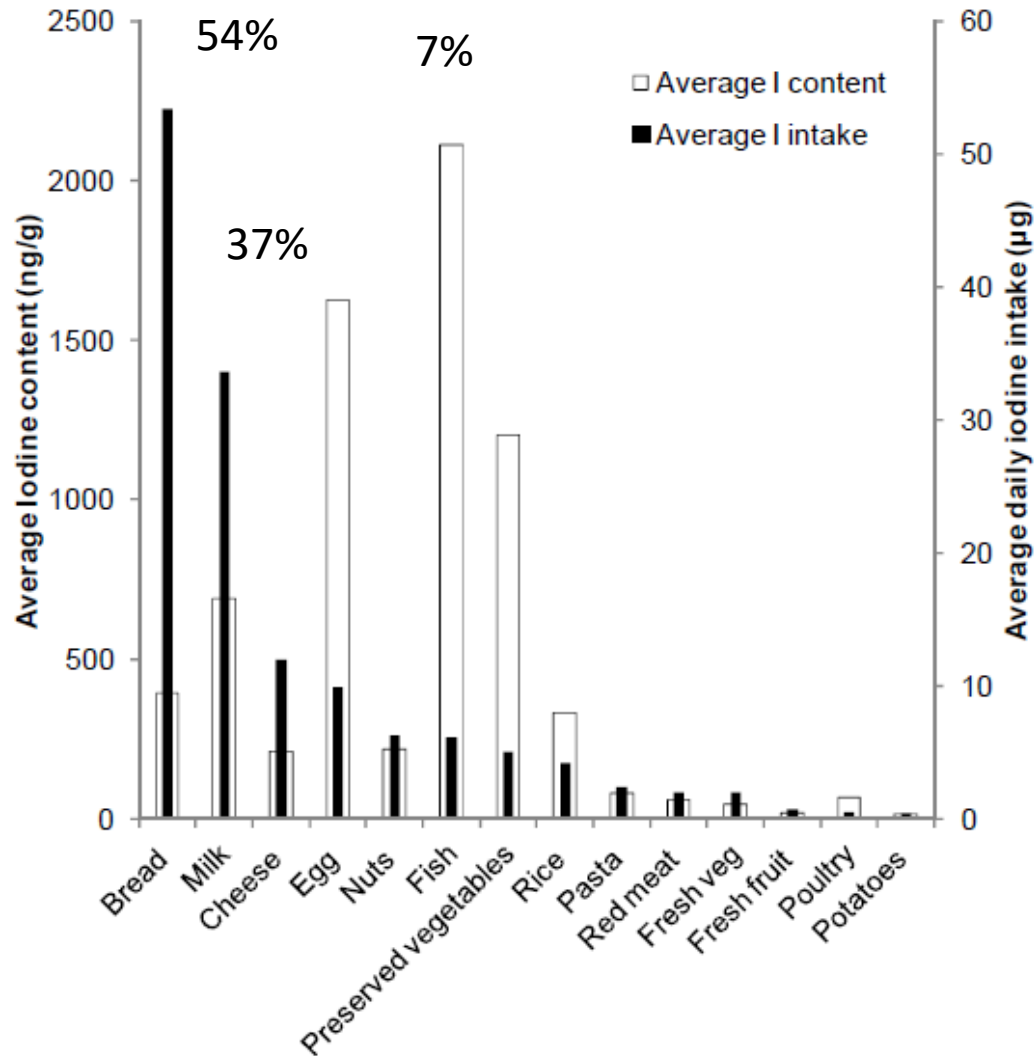
Zimmermann M et al, The Lancet 2008

# Iodine deficiency during pregnancy in Switzerland



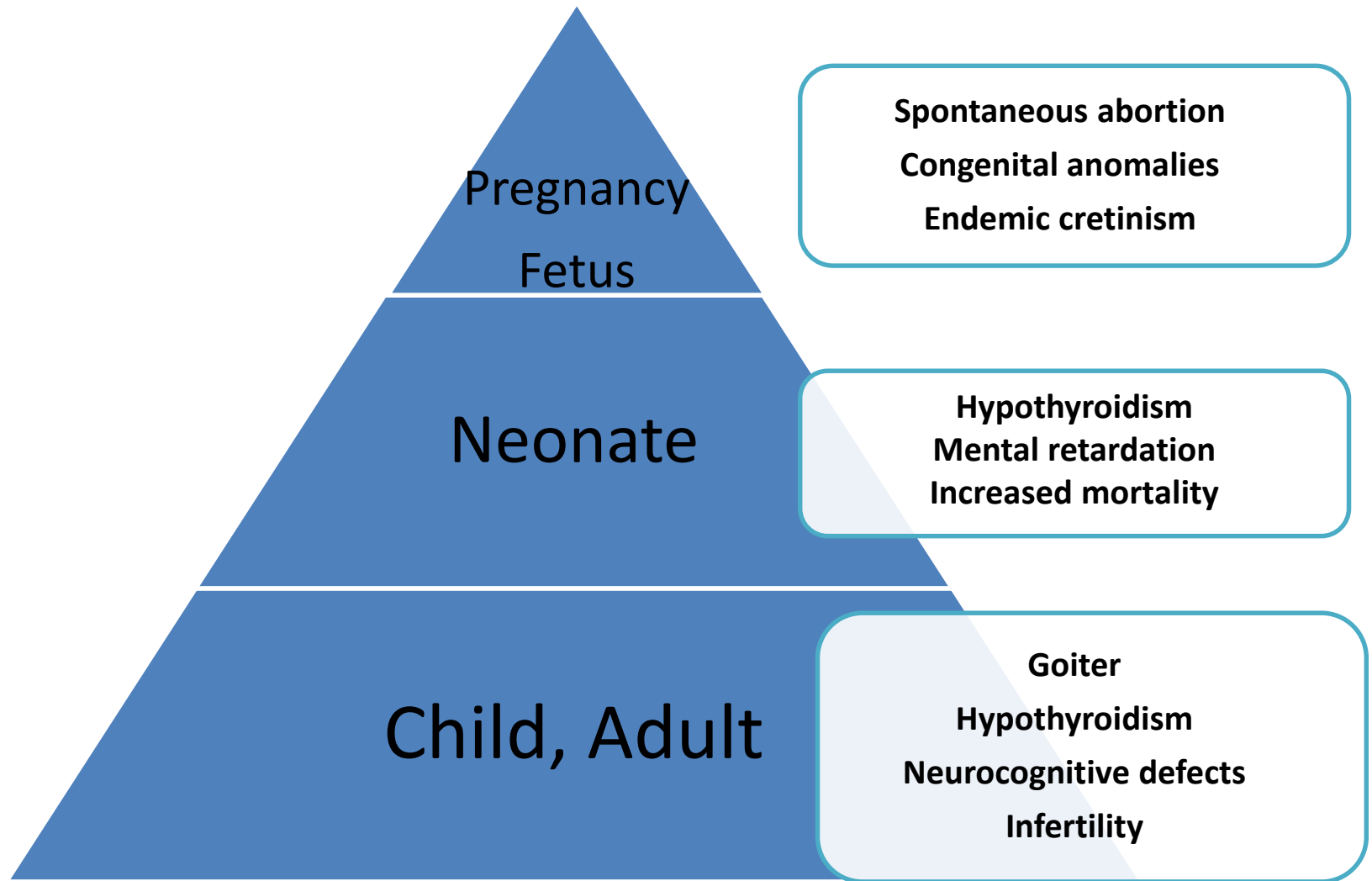
Median (25.,75. percentile) of urinary iodine concentration (UIC)  
Swiss women 1999 (n=511), 2004 (n=279), 2009 (n=648)

# Iodine content in different food





# Consequences of iodine deficiency



# Recommendations for Switzerland 2015

Use of iodine containing salt during pregnancy	
If adequate intake not possible Supplementation of iodine Additional use of iodine salt possible	150-200 µg/d

# Recommendations for Sweden 2012

An extra 25 µg/d is recommended during pregnancy	25 µg/d
An extra 50 µg/d recommended during lactation	50 µg/d



Vit D



# Biologic functions of Vitamin D

Vitamin D<sub>3</sub>: Synthesis from skin with UVB light

Vitamin D<sub>2</sub>: food intake (10-20%)



25 (OH) D



1,25 (OH)<sub>2</sub> D

## Calcium and phosphorus homeostasis

Bone density  
Blood pressure regulation  
Cardiovascular system  
Muscle strength  
Neurological development



1,25 (OH)<sub>2</sub> D

## Immune modulation

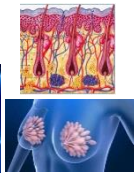
Strengthen auto immune defense



1,25 (OH)<sub>2</sub> D

## Release

**Insulin** secretion

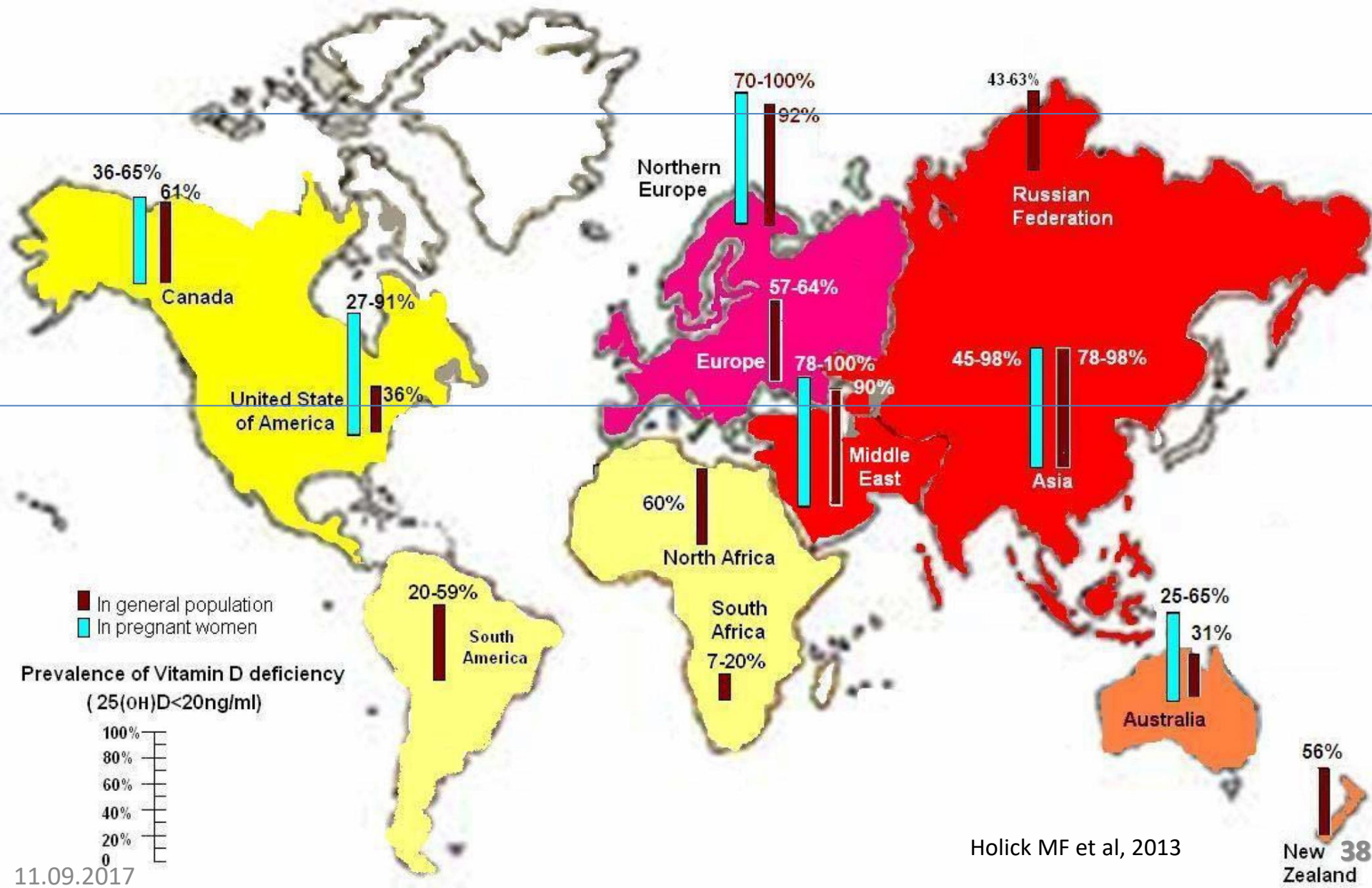


1,25 (OH)<sub>2</sub> D

## Cell cycle regulation

Inhibition of cell proliferation, angiogenesis  
Regulation of Apoptosis

# Prevalence of vitamin D deficiency





- Stay mainly indoors
- Full body clothing
- Veil
- Sun blocker
- Air pollution

### Low sun exposition

- Latitude (higher)
- Season (Winter)
- Day time (before 10 am or after 3pm)
- Time spent outside

### Low UV value

## Risk factors for low 25 (OH) D values

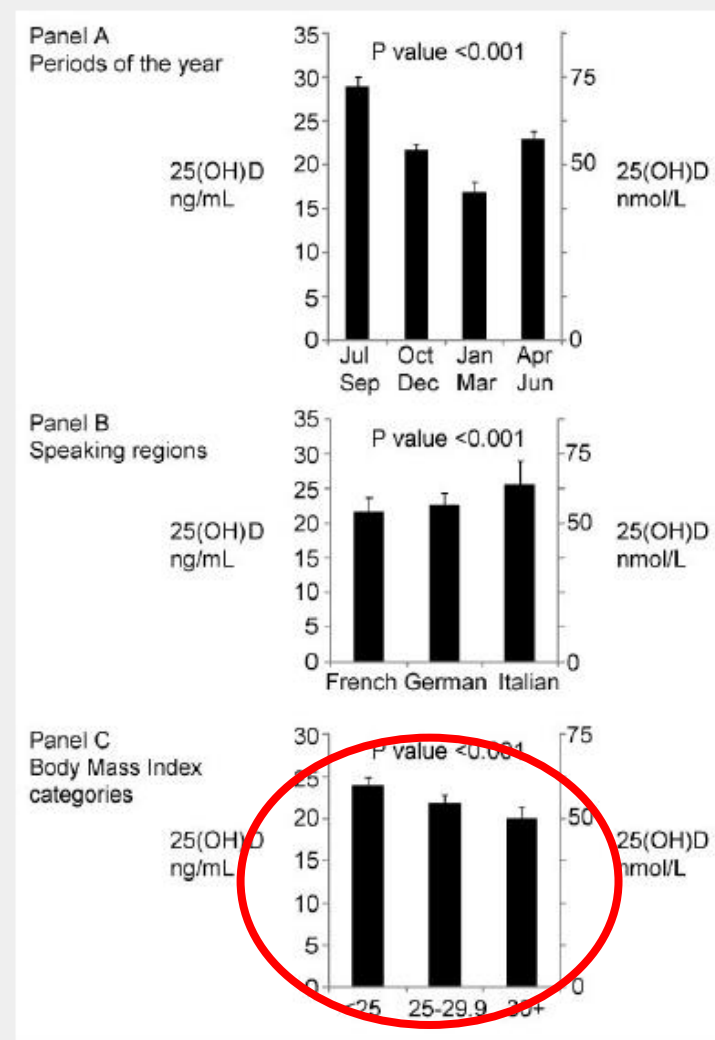
### Physiological factors

- Dark skin
- Malabsorption's syndrome
- BMI >30
- Liver/Kidney disease
- Exclusive breastfeeding
- Pregnancy
- Age

### Low vit D intake

- Vegetarian or vegan nutrition
- Lactose intolerance
- Medication (Cortisone, antiretroviral or antiepileptic med.)
- Socioeconomic status
- Smoking
- VDR polymorphisms
- No vitamin D supplementation

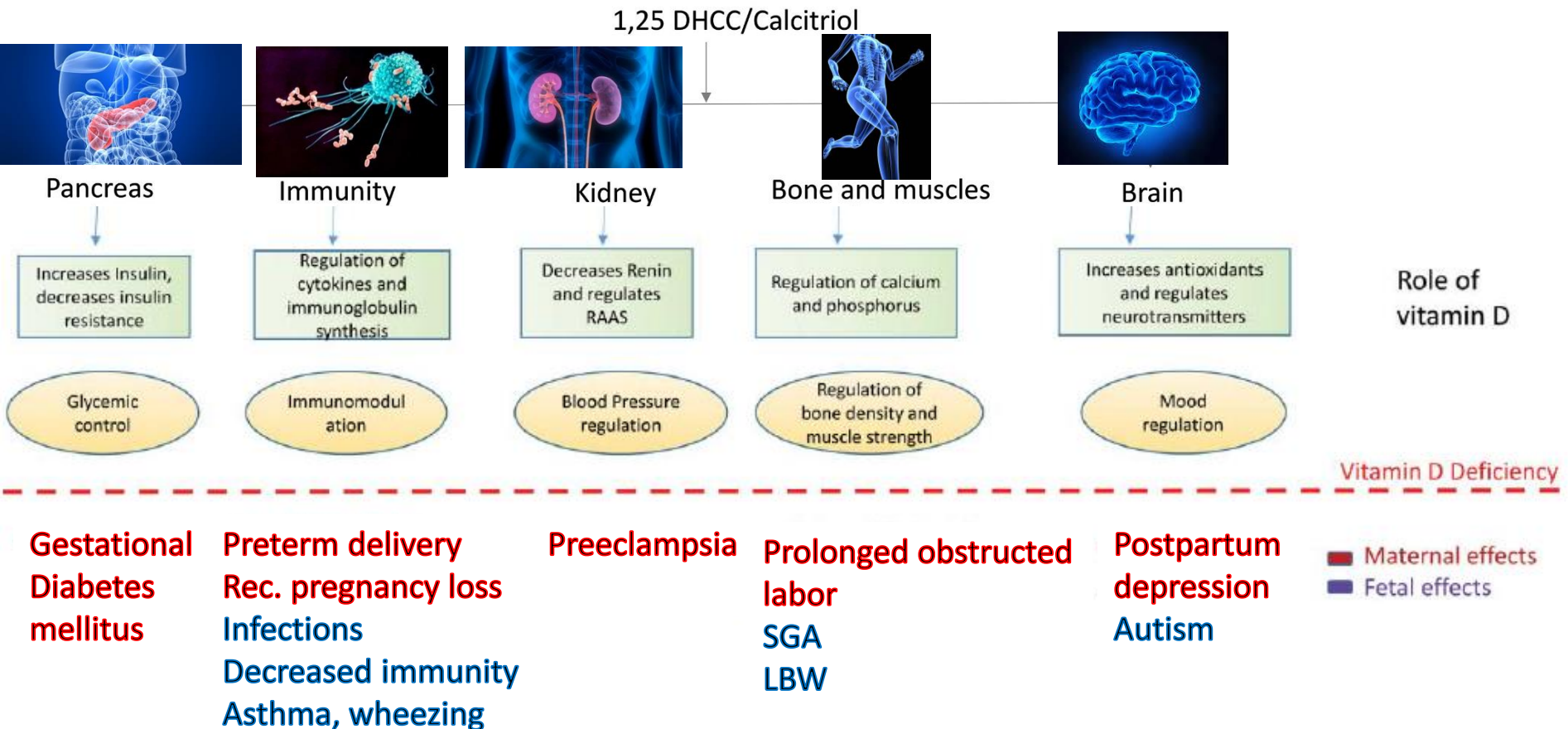
# Vitamin D values in Switzerland



**Figure 1**

Adjusted mean 25(OH)D levels. A By period of the year. B By speaking region. C By BMI categories.

# Role of vitamin D and pregnancy complications



# Vitamin D supplementation



## Vitamin D supplementation for women during pregnancy (Review)

De-Regil LM, Palacios C, Lombardo LK, Peña-Rosas JP

N= 2830	Vitamin D: RR 95% CI	Vitamin D + Ca
<b>Preeclampsia</b>	0.52 (0.25-1.05)	<b>0.51 (0.32-0.80)</b>
Rate of CS	0.95 (0.69-1.31)	
<b>Preterm birth</b>	<b>0.36 (0.14-0.93)</b>	
Gestational diabetes	0.43 (0.05-3.45)	
<b>LBW</b>	<b>0.40 (0.24-0.67)</b>	

# Future studies...

knowledge there are currently 23 ongoing studies that, once published, are likely to double the body of evidence identified for this review. After their publication and overall assessment, conclusions on the effects and safety of this intervention may be updated.

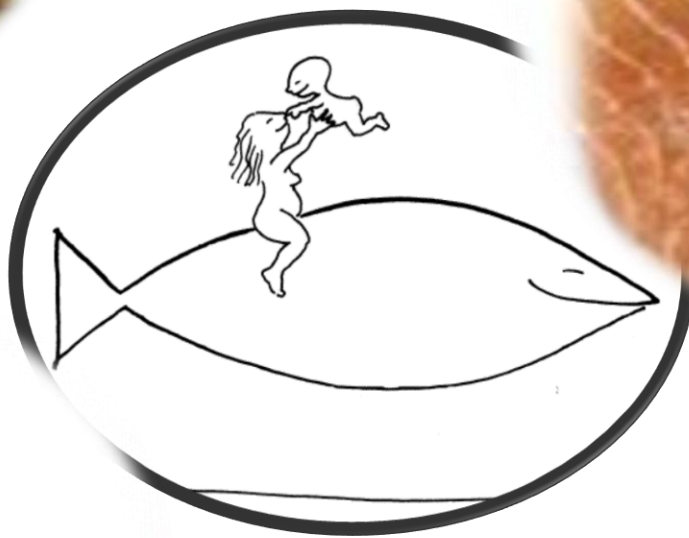


# Recommendations for Switzerland 2015

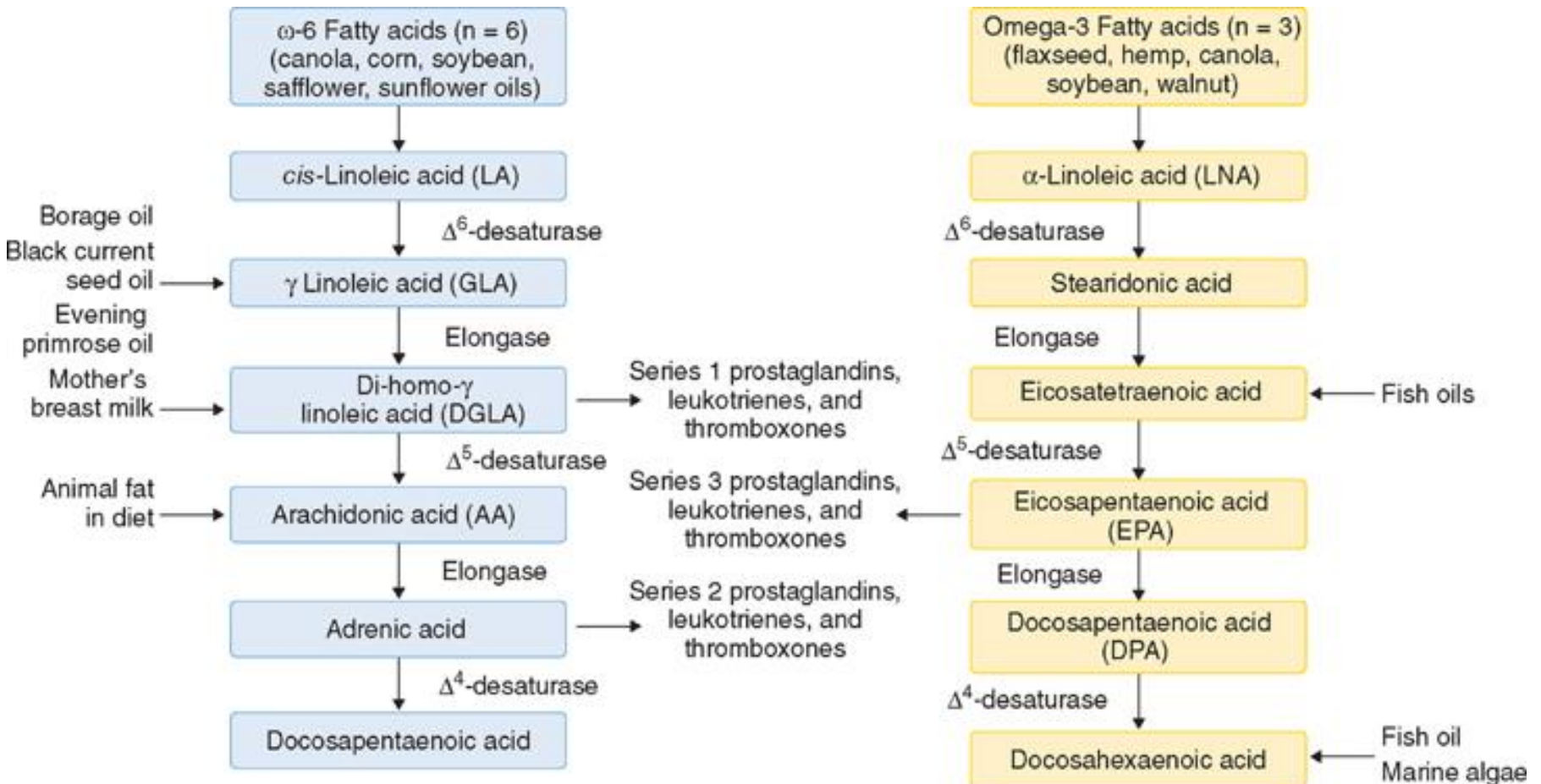
<b>General pregnancy</b> <b>Vitamin D insufficiency: 25- 49 nmol/l</b> <b>Vitamin D deficiency: &lt; 25 nmol/l</b>	<b>600 IE/d (15 µg/d)</b> <b>1000 IE/d</b> <b>1500-2000 IE/d, (37.5-50 µg/d), max. 4000 IE/d (100µg/d)</b>
Selective screening: High risk pregnancies and season, DM, dark skin, adipositas, multiple pregnancies	

# Recommendations for Sweden 2012

Because no new strong evidence has emerged, the recommendation from NNR 2004 is maintained during pregnancy and lactation	<b>400 IE/d (10 µg/d)</b>
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# Omega 3 and Omega 6 fatty acid



# Omega III Fatty acids

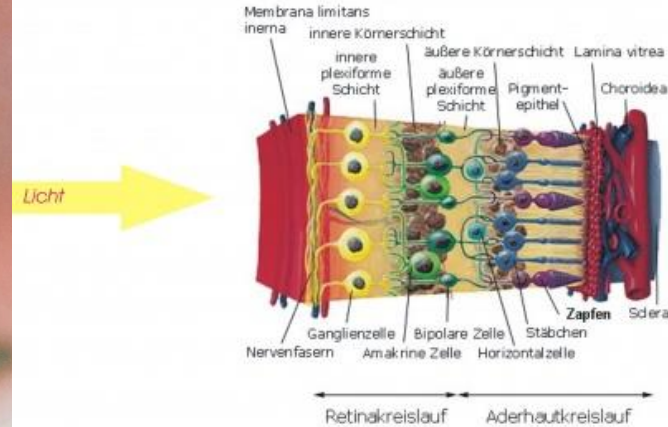
- Reduction of preterm birth after previous preterm
  - Reduction of PG synthesis
- Prolongation of pregnancy
- Influence on fetal growth
  - Reduction of blood viscosity



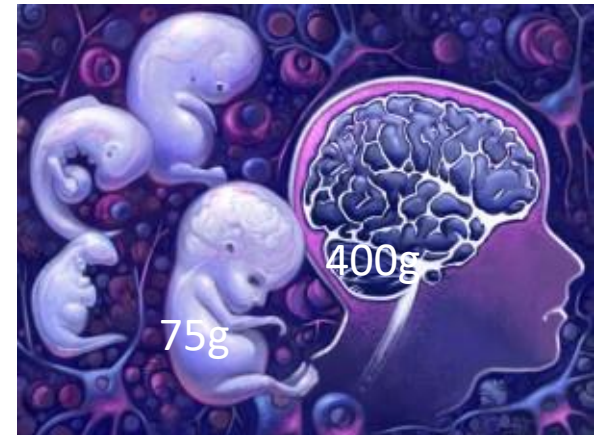


# Omega III Fatty acids

- Visual acuity
- Fine motor skills
- Social development



- Brain development
- Positive influence on post partum depression





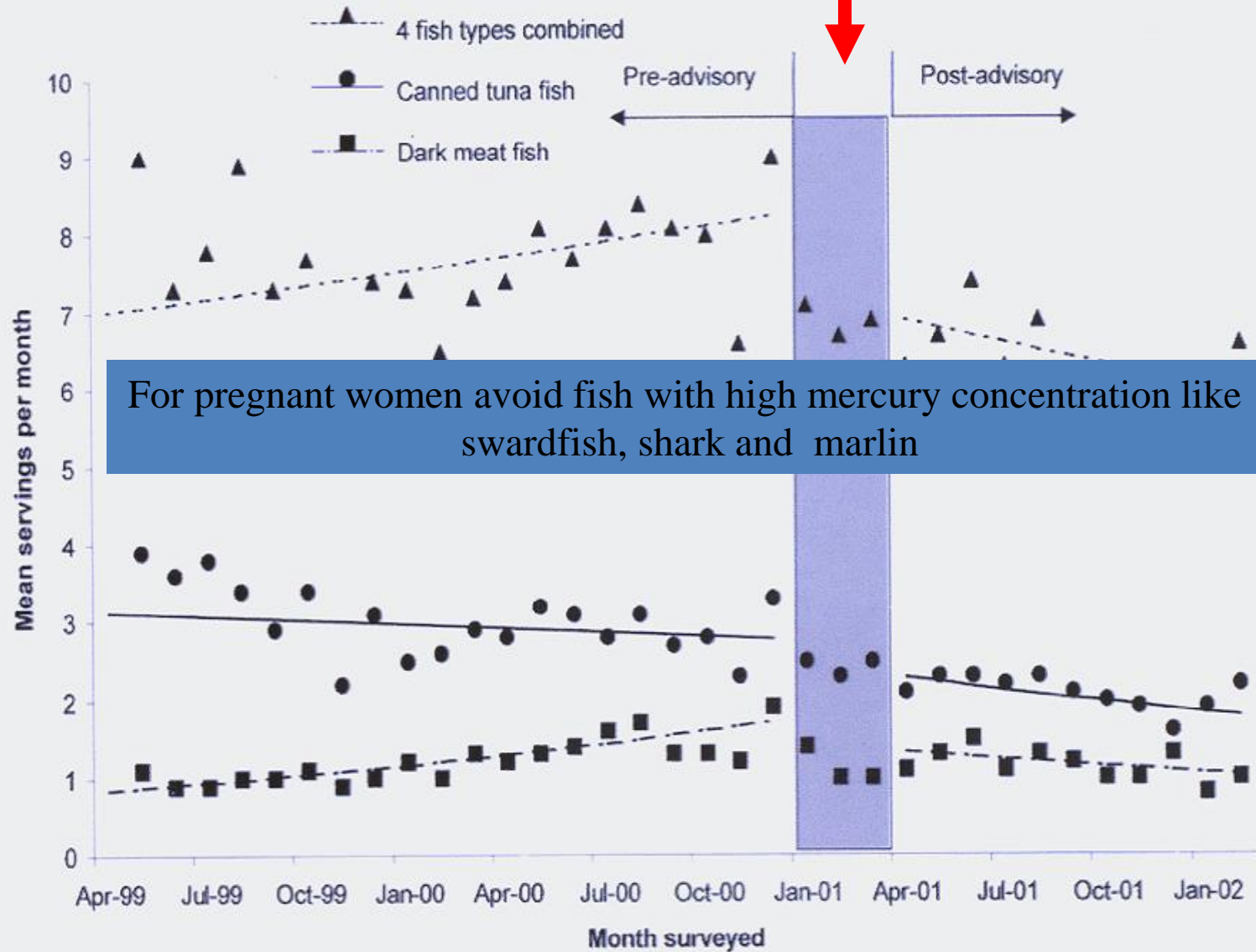
# Global Omega-3 Status Map

shows low levels for most of the world



REFERENCES: Ref. Stark et al., Global survey of the omega-3 fatty acids, docosahexaenoic acid and eicosapentaenoic acid in the blood stream of healthy adults, Progress in Lipid Research, 20 May 2016; doi: 10.1016/j.plipres.2016.05.001.  
[www.sciencedirect.com/science/article/pii/S0163782715300333](http://www.sciencedirect.com/science/article/pii/S0163782715300333).

FSA



# Recommendations for Switzerland 2015

General pregnancy	<p>Eat fish twice weekly, one portion fatty fish like salmon, maquereel or herring</p> <p>Only one portion of tuna fish steak /w</p>
Women who do not eat fish	Supplementation 200 mg/d DHA during pregnancy and lactation

# Summary

- Imbalance in energy and nutritional intake might have long-lasting effects both on maternal health as well as on the long-term health of the offspring
- Most of the requirements in pregnancy can be covered by a healthy diet
- National data confirm a deficiency for vitamin D and iodine (iron)
- Exceptions are vitamin D, iron, iodine, folate and omega three fatty acids
- Evidence exist for preconceptional intake of FA
- 5 –methyl THF has a higher bioavailability and does not need metabolism
- Omega III fatty acid should be supplemented in women avoiding fish during pregnancy



**Thank you for your attention**  
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