gora
SIMP
Società Italiana di Medicina Perinatale
27-29 novembre
2014Milano
Presidente: Prof. Irene Cetin

Irene Cetin
Professore di Ostetricia e Ginecologia
Università degli Studi di Milano
Direttore Clinica Ostetrica e Ginecologica
Ospedale Luigi Sacco di Milano

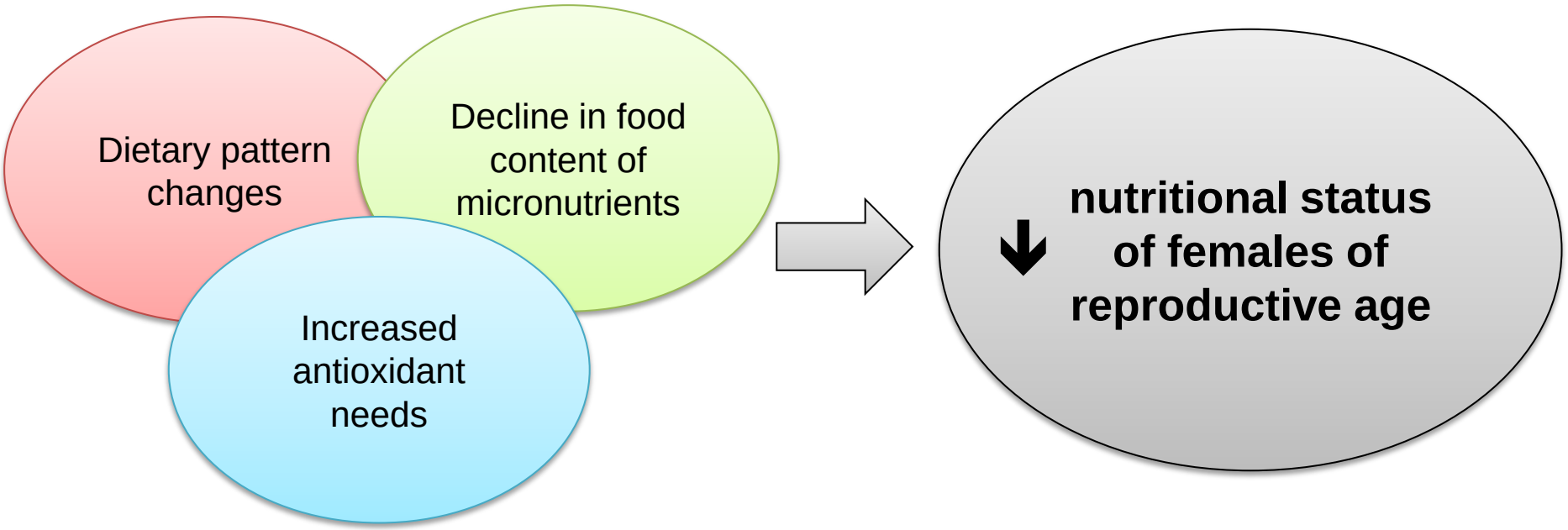
Necessità nutrizionali e integrazione *in gravidanza*

The Telegraph Tuesday 25 November 2014

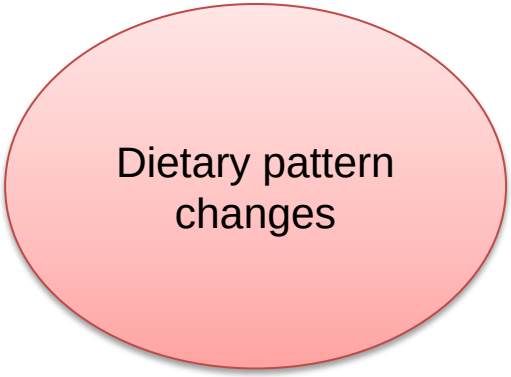
There is little chance of leading a truly simple life today because so much of it is done with the advice of experts. When it comes to safe driving, it is the likes of the Department of Transport or the AA; with food, we are bombarded with nutritional tips; and there is no shortage of instruction on how to bring up our children.

Do we need nutritional advice in pregnancy?

Are we meeting nutrients needs in pregnancy?



Are we meeting nutrients needs in pregnancy?



Dietary pattern changes

Public Health Nutrition: 12(9A), 1676–1684

Worldwide variation of adherence to the Mediterranean diet, in 1961–1965 and 2000–2003

Data obtained from the "***FAO food balance sheets***" (FBS)
→ reflecting production, supply and different human utilization of foodstuff during a certain time period in a specific country.

41 Countries included worldwide, two periods analyzed:
1961–1965 and 2000–2003.

Trends of adherence to the Mediterranean diet (MD)
Mediterranean Adequacy Index

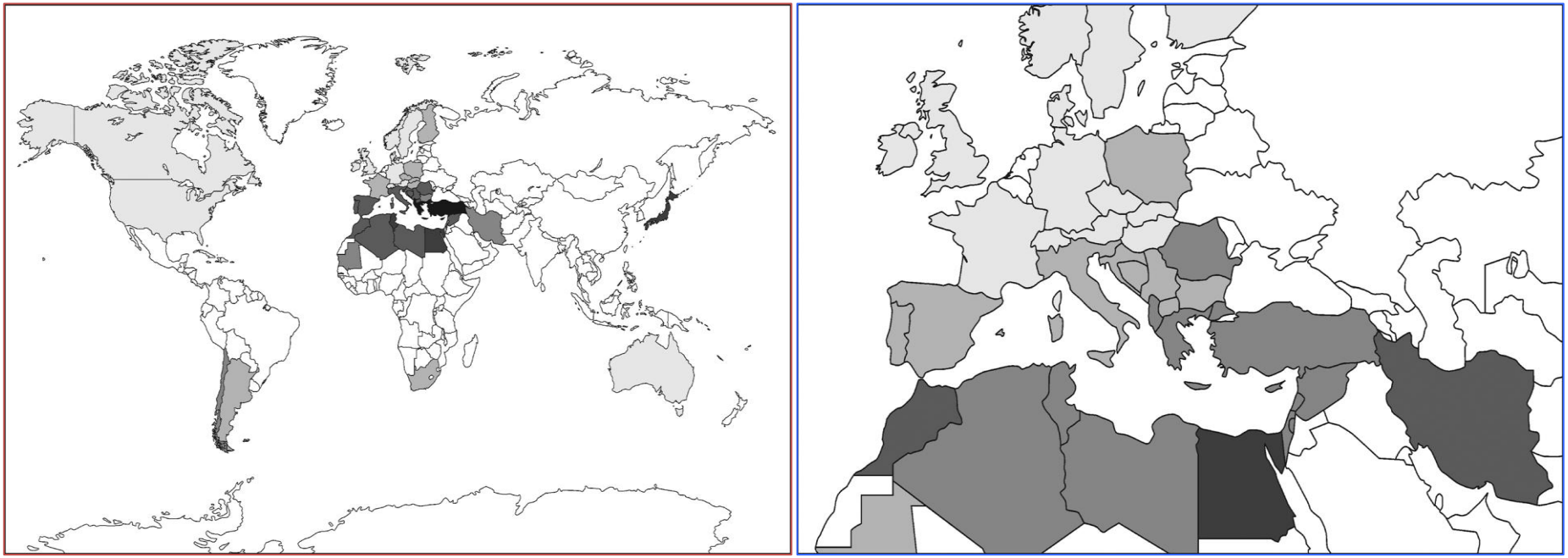
$$\text{MAI} = \frac{\text{daily energy derived from "mediterranean food"}}{\text{daily energy not derived from "mediterranean food"}}$$

Olive oil, olives, cereals, root vegetables, herbs and spices, fruits, vegetables, nuts, fish and seafood, legumes, wine…

Animal fats, sugar, sweets, alcoholic beverages (except wine), meat, beer, stimulants (coffee, tea)…

Da Silva et al., Public Health Nutrition 2009

Dietary pattern changes



Map of the adherence to the Mediterranean dietary pattern, comparing Mediterranean adequacy index value

(□, 0·00–0·99; □, 1·00–1·99; □, 2·00–2·99; □, 3·00–3·99; □, 4·00–4·99; □, 5·00–5·99)

1961-1965

MAI Worldwide: 2.86
MAI Mediterranean Countries: 3.44
MAI Italy: 3.30

2000-2003

MAI Worldwide: 2.03
MAI Mediterranean Countries : 1.98
MAI Italy: 1.62

Da Silva et al., Public Health Nutrition 2009

Decline of the Mediterranean diet at a time of economic crisis. Results from the Moli-sani study **21,001 citizens from southern Italy**

High adherence to the Mediterranean Diet (IMI ≥ 5) in relation to socio economic status

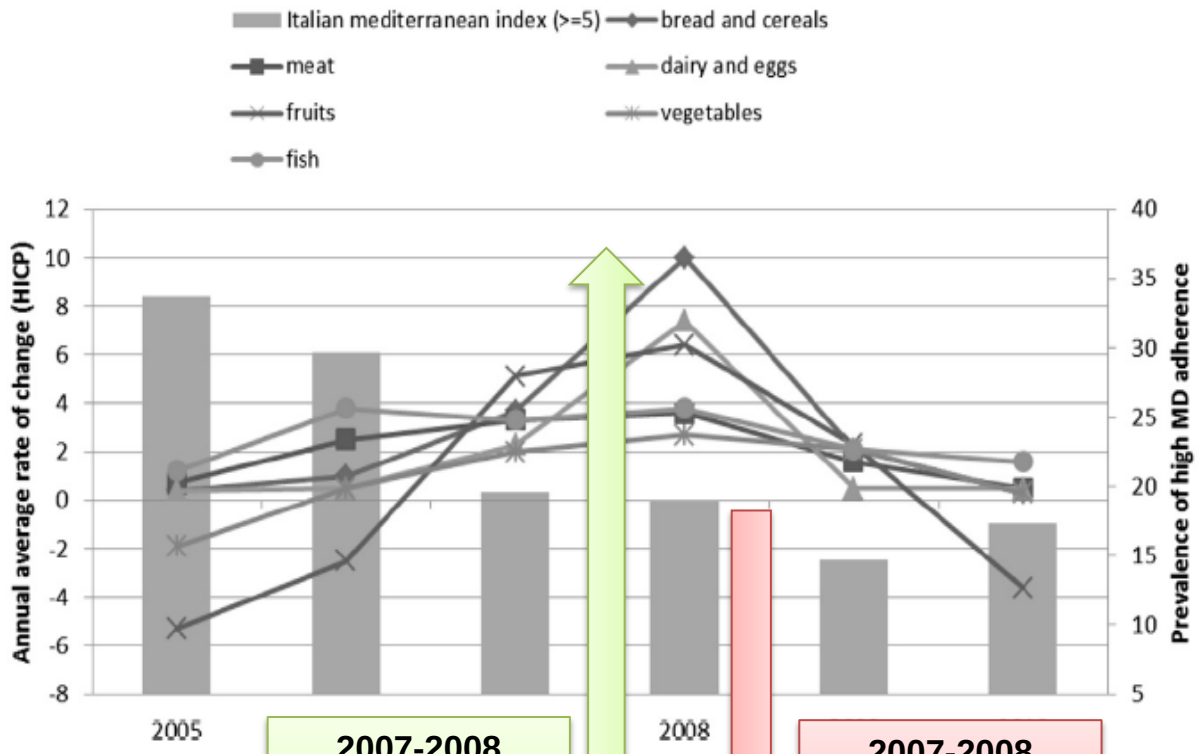
in the whole and by recruitment periods.

IMI≥ 5points	Overall	By recruitment period		Difference[a]	P value[b]
	2005–2010	2005–2006	2007–2010		
Whole sample	4755 (22.6	**31.3% in 2005-06**	**18.3% in 2007-10**	**- 13%!**	<0.0001
Age groups (*n*, %)					
35–43	807 (20.8			−8.6	<0.0001
44–53	1428 (21.7)	640 (31.3)	788 (17.4)	−13.9	<0.0001
54–59	923 (25.3)	403 (33.9)	520 (21.1)	−12.8	<0.0001
60–70	1147 (25.1)	541 (35.8)	606 (19.8)	−16.0	<0.0001
>70	450 (19.4)	240 (27.8)	210 (14.4)	−13.4	<0.0001
	$P<0.0001$[c]	$P<0.0001$	$P<0.0001$	P for interaction = 0.026	
Sex (*n*, %)					
Women	2567 (23.2)	1203 (32.4)	1364 (18.5)	−13.9	<0.0001
Men	2188 (22.0)	988 (30.1)	1200 (18.0)	−12.1	<0.0001
	$P=0.04$	$P=0.04$	$P=0.45$	P for interaction = 0.29	
Wealth score (*n*, %)					
Low	970 (21.2)	432 (30.2)	538 (17.1)	−13.1	<0.0001
Medium	1083 (23.5)	535 (31.7)	548 (18.8)	−12.9	<0.0001
High	1347 (26.9)	687 (33.0)	660 (22.6)	−10.4	<0.0001
Non-respondent	1355 (19.9)	537 (29.8)	818 (16.3)	−13.5	<0.0001
	$P<0.0001$	$P=0.09$	$P<0.0001$	P for interaction = 0.032	
Education (*n*, %; years)					
≤8	2234 (20.8)	989 (30.7)	1245 (16.5)	−14.2	<0.0001
>8≤13	1792 (23.9)	839 (30.7)	953 (20.1)	−10.6	<0.0001
>13	728 (26.5)	363 (34.7)	365 (21.4)	−13.3	<0.0001
	$P<0.0001$	$P=0.014$	$P<0.0001$	P for interaction = 0.016	
Profession (*n*, %)					
Not manual	1232 (24.5)	609 (31.4)	623 (20.1)	−11.3	<0.0001
Manual	460 (19.2)	188 (31.4)	272 (15.1)	−16.3	<0.0001
Other (retired, housewife, etc.)	3059 (22.6)	1392 (31.2)	1667 (18.3)	−12.9	<0.0001

Panagiotakos et al., Nutrition Metab Cardiovasc Diseases, 2014

Changes in nutritional habits: Moli-sani Study

HICP
Indice dei prezzi al consumo armonizzato = "paniere" di beni e servizi, tra cui alimenti



IMI
Italian Mediterranean Index,
Prevalenza IMI ≥ 5
= alta aderenza Dieta Med

2007-2008
Sale il prezzo di alimenti "base" della dieta mediterranea

2007-2008
Crolla la prevalenza di alta aderenza alla DM

Figure 1 Bars (vertical axis on the right) repr… adheren… o I… ≥ 5) over time as observed in our sample. Each line (vertical axis on the left) re… a… rate of ch… ge… x of Consumer Prices of selected foods typical of the Mediterranean dietary p… h… dramatic … op… e Mediterranean diet was firstly recorded in 2007 when the cost of some key …

Bonaccio et al., Nutrition Metab Cardiovasc Disease 2014

Applied nutritional investigation

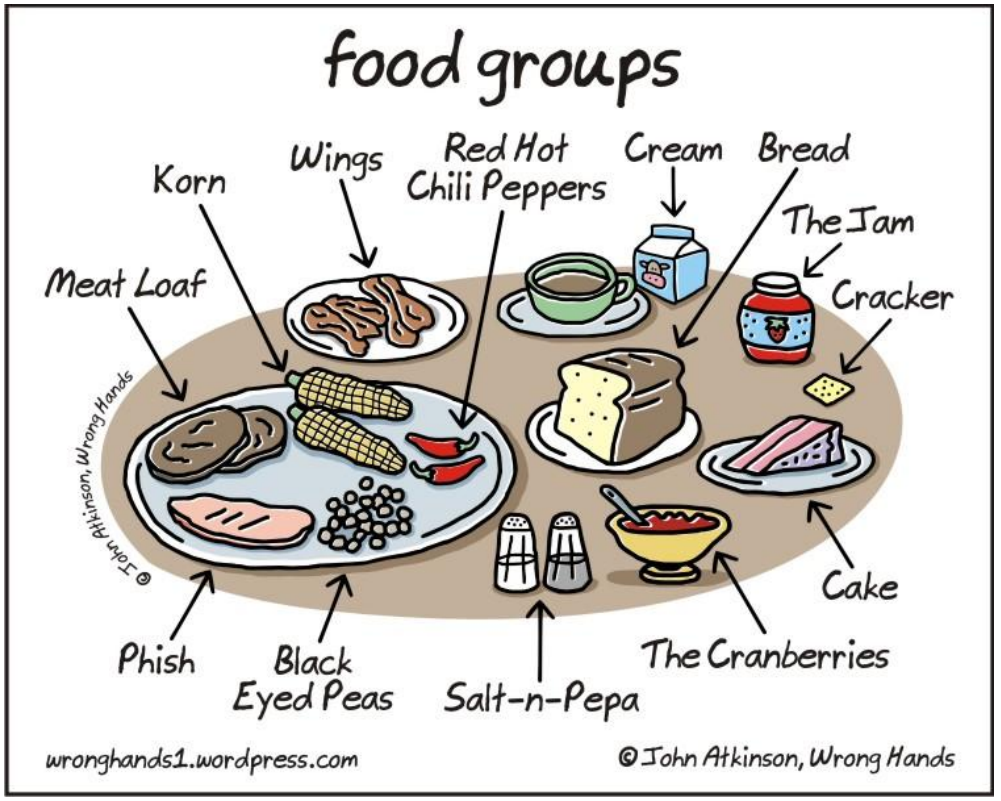
Adherence to Mediterranean diet in a sample of Tuscan adolescents

1127 studenti (16.8 ± 1.6 anni)

questionario KIDMED:
adeguatezza dieta mediterranea

Punteggio finale
>4 scarsa aderenza
4-7: aderenza media
≥ 8: buona aderenza

good in 16.5%,
average in 60.5%,
and poor in 23%



Santomauro et al., Nutrition 2014

Changes in nutritional habits: age matters

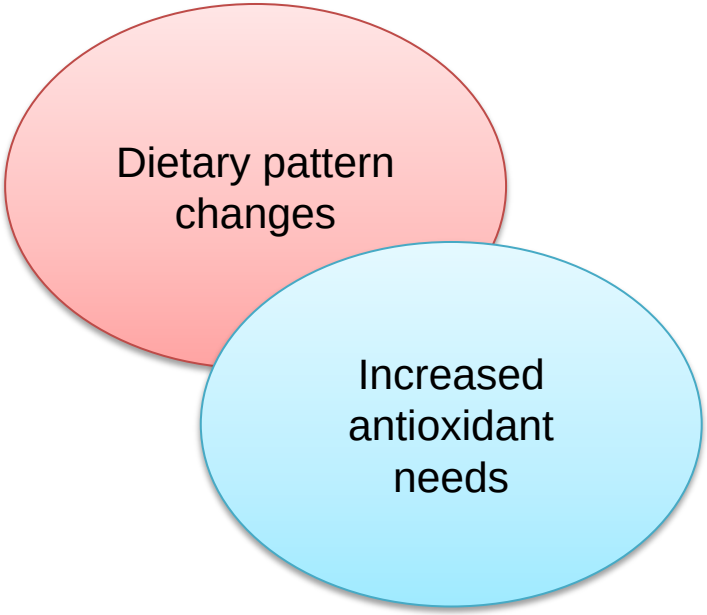
KIDMED: Percentage of "Yes" answers*

KIDMED test	Yes (%)
Takes a fruit or fruit juice every day	78.0
Consumes a second fruit every day	40.4
Consumes fresh or cooked vegetables regularly 1×/d	64.3
Consumes fresh or cooked vegetables >1×/d	29.8
Consumes fish regularly (at least 2–3×/wk)	42.6
Eats at a fastfood restaurant >1×/wk	10.4
Likes pulses and eats them >1×/wk	48.2
Consumes pasta or rice almost every day (≥5×/wk)	84.3
Consumes cereals or grains (bread, etc.) for breakfast	42.9
Consumes nuts regularly (≥2–3×/wk)	24.5
Uses olive oil at home	96.1
Skips breakfast	31.4
Consumes a dairy product for breakfast (yogurt, milk, etc.)	66.6
Has commercially baked goods or pastries for breakfast	55.0
Consumes 2 yogurts and/or some cheese (40 g) daily	33.2
Consumes sweets and candy several times every day	34.5

* "Yes" answers in the white rows have a positive score (+1); "yes" answers in the grey rows have a negative score (−1).

Santomauro et al., Nutrition 2014

Are we meeting nutrients needs in pregnancy?



Changes in nutritional habits: Moli-sani Study

Macro and micro nutrient Intake

Table 4 Differences in micronutrient and macronutrient intake over time

Grams/day (means ± SD)	Period of recruitment		
	2005–2006	20	
Decreased intake			
Vegetarian proteins	29.6 (11.1)		
Ve			
F			
Ca			01
Fats (%)	31.8	32.5	<0.0001
Alcohol (%)	5.0	4.9	0.39

[a] Means and *P* value adjusted for sex, age and energy intake.

↑ Antioxidant needs for
- Stress
- Sedentary life
- Smoke, pollution……

↓ energy intake but…

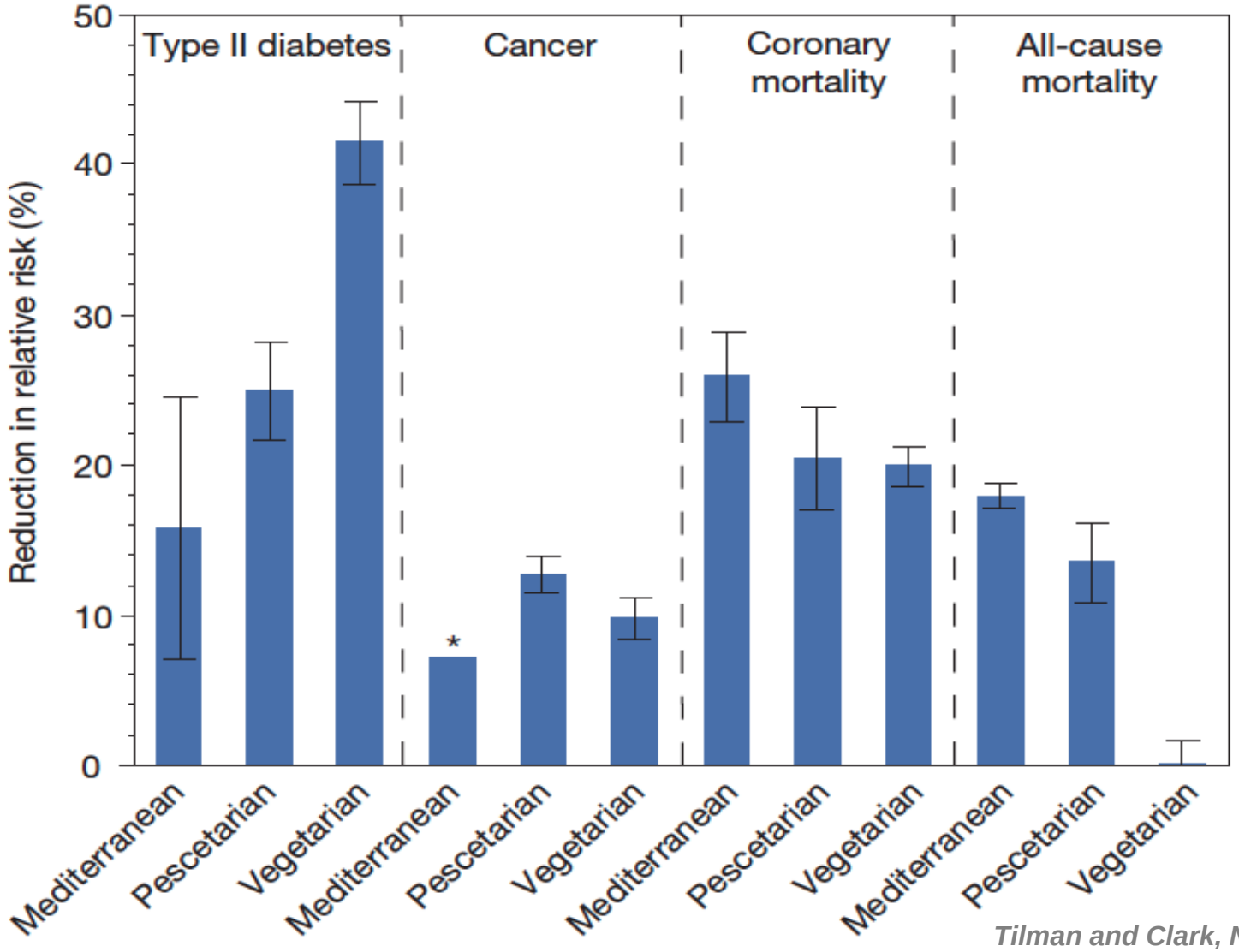
↓ antioxidants, fibers and folate in the diet …

↑ intake of animal proteins, animal fat and saturated fats …

Bonaccio et al., Nutrition Metab Cardiovasc Disease 2014

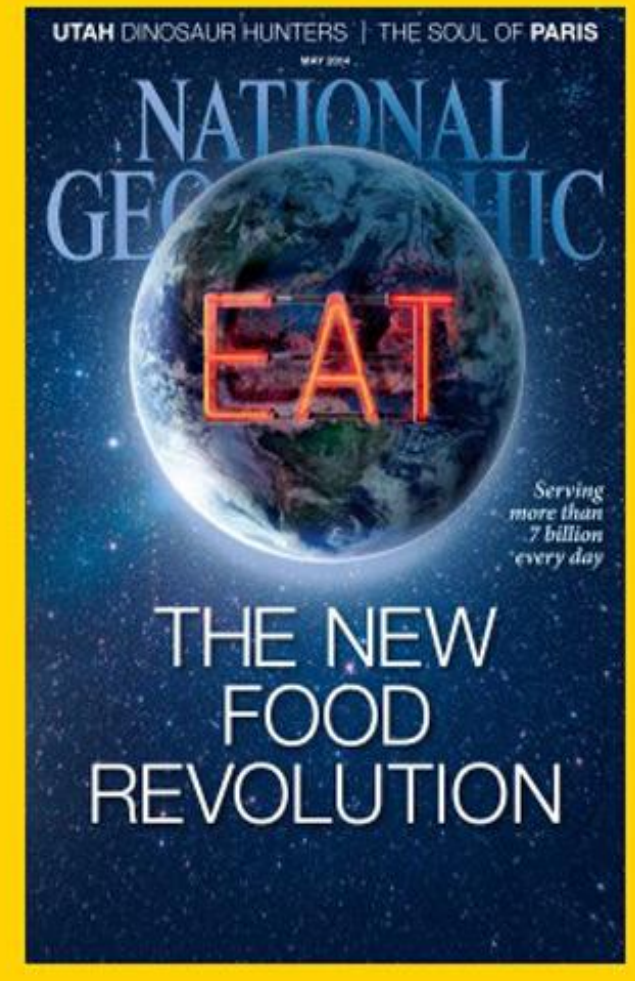
Global diets ➔human health

Diet-dependent percentage reductions in relative risk of type II diabetes, cancer, coronary heart disease mortality and of all-cause mortality

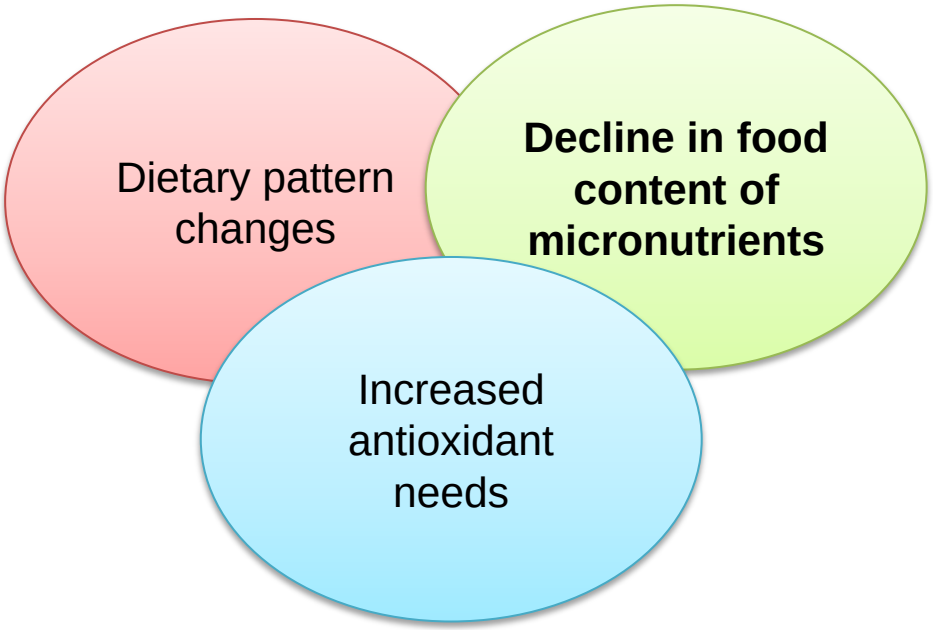


Tilman and Clark, Nature 2014

Beyond the health benefits of the Mediterranean diet…



Are we meeting nutrients needs in pregnancy?



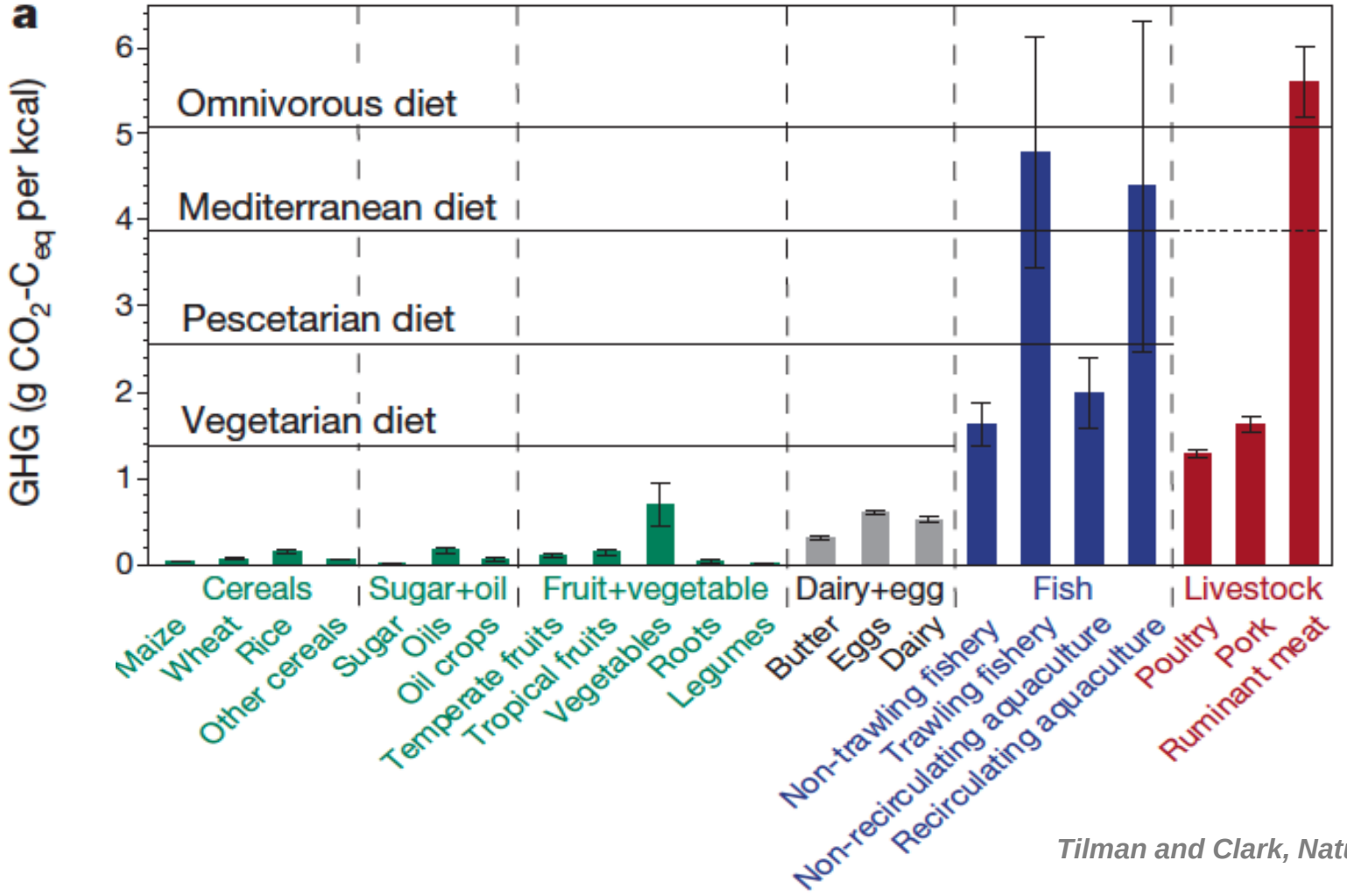
ARTICLE

doi:10.1038/nature13959

Global diets link environmental sustainability and human health

David Tilman[1,2] & Michael Clark[1]

Greenhouse gas emissions



Tilman and Clark, Nature 2014

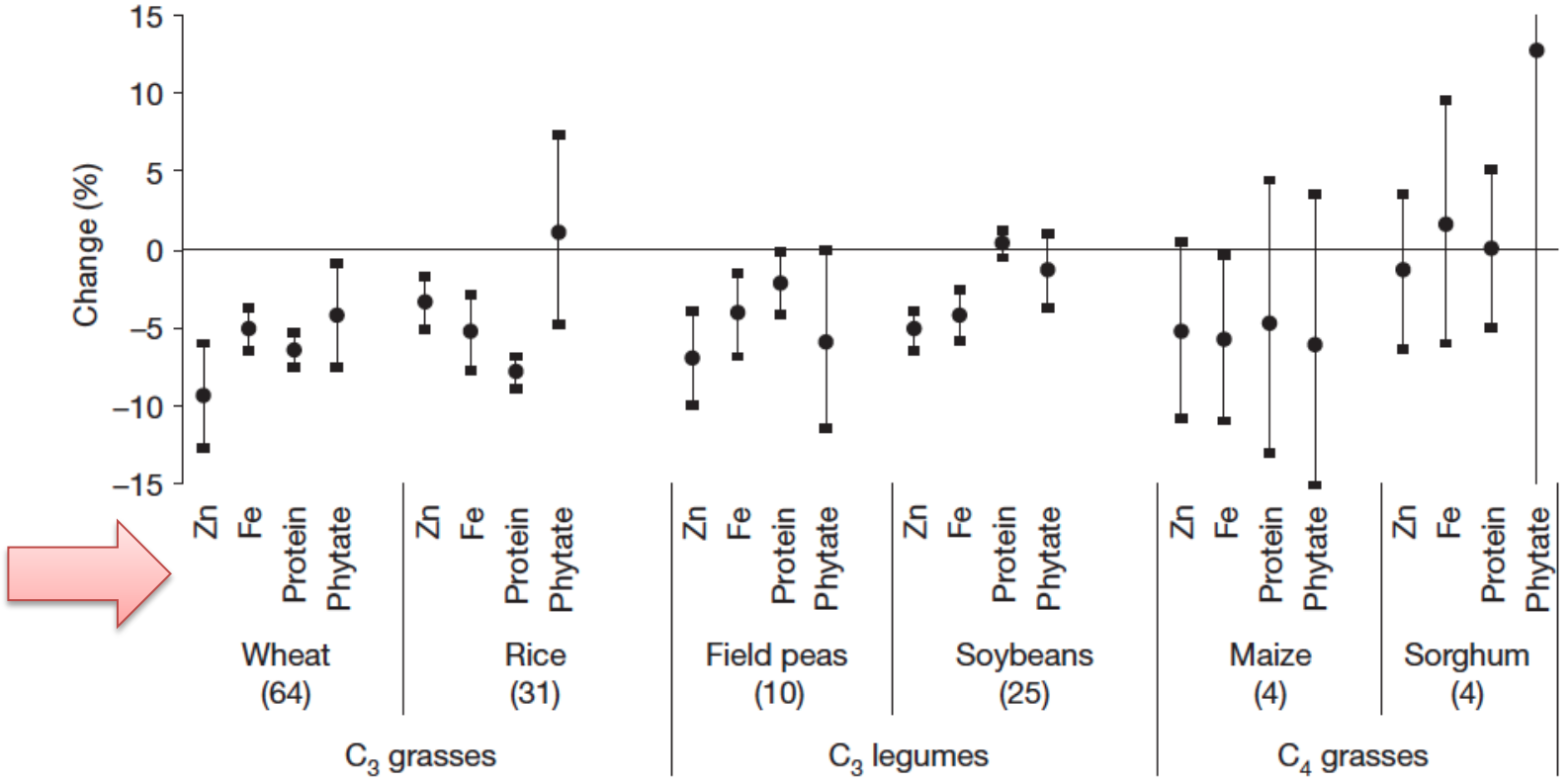
Decline in food content of micronutrients

LETTER

doi:10.1038/nature13179

Increasing CO_2 threatens human nutrition

Percentage change in nutrients at elevated [CO2] relative to ambient [CO2]



Mayers et al., Nature 2014

Declining Fruit and Vegetable Nutrient Composition: What Is the Evidence?

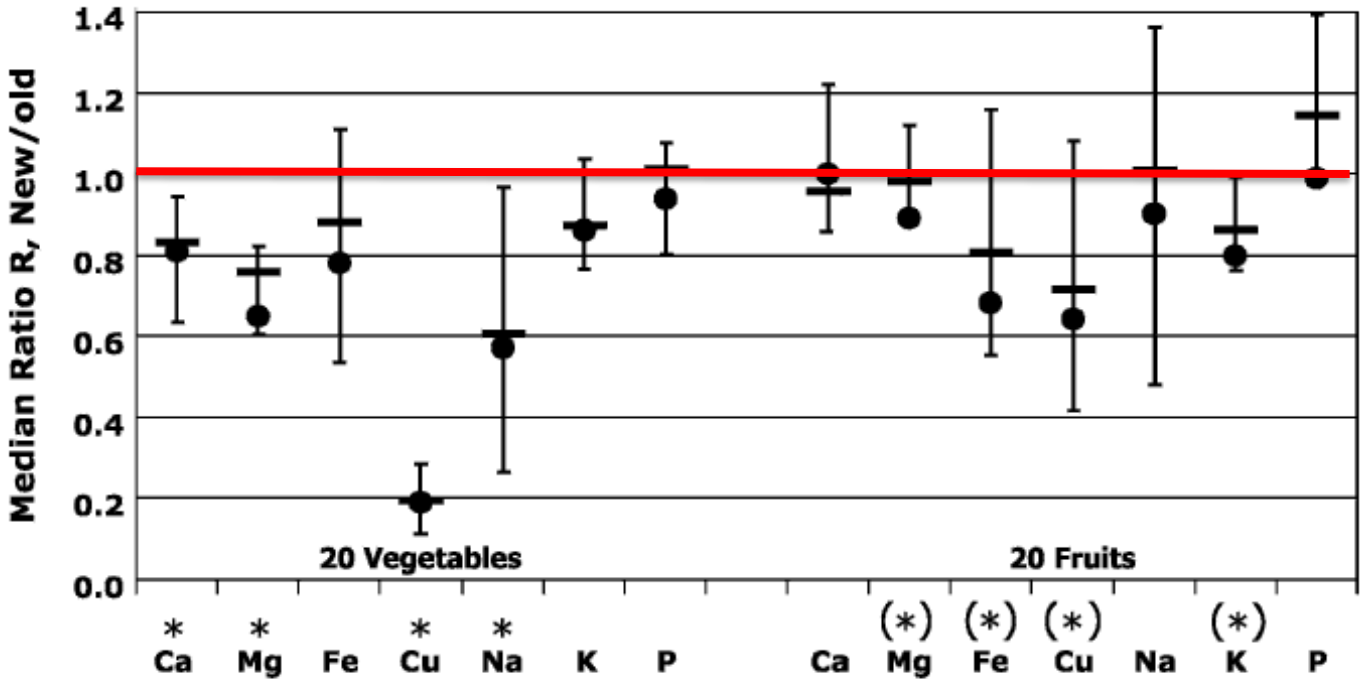
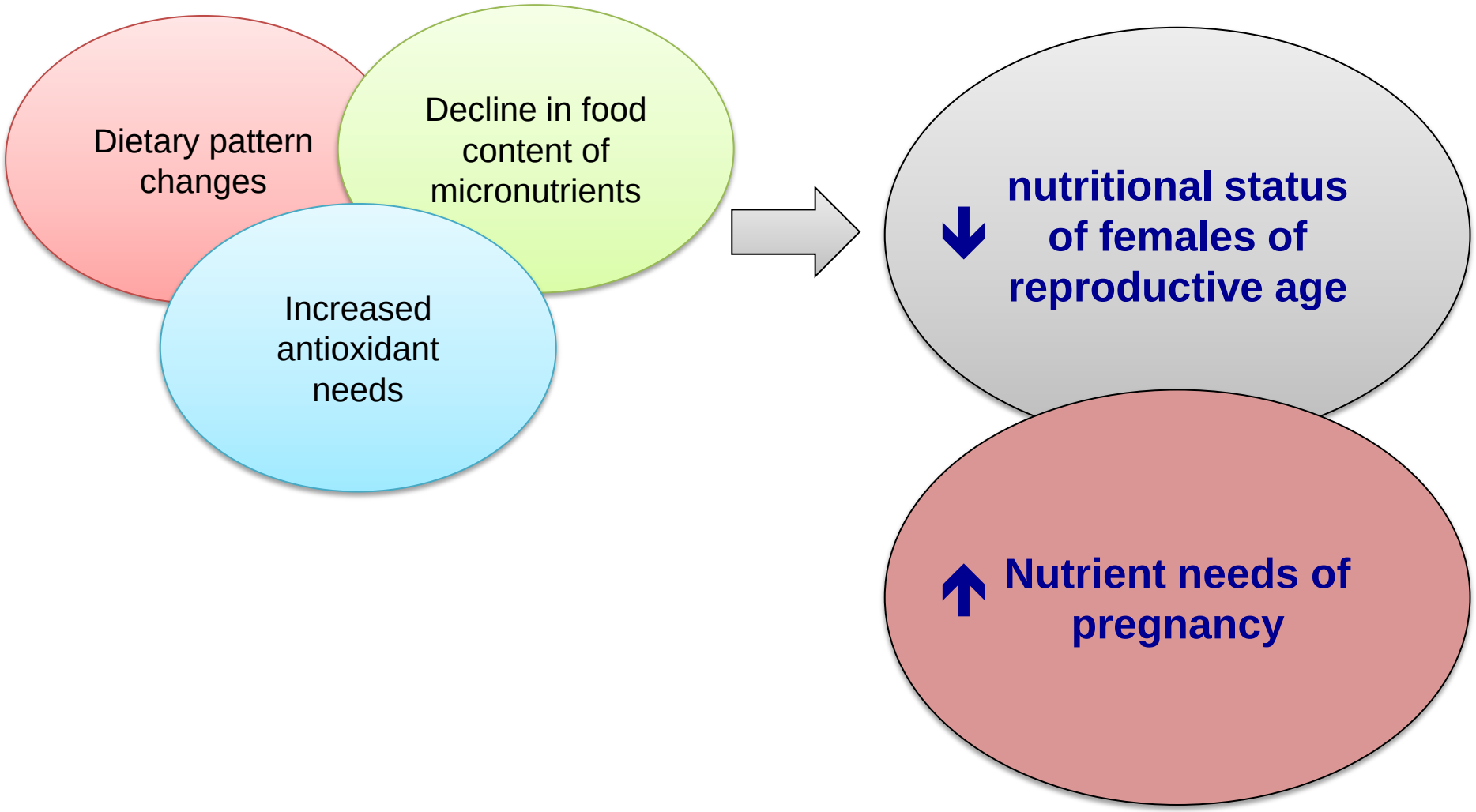


Fig. 2. Apparent changes in nutrient concentrations in 20 vegetables and 20 fruits with 95% confidence intervals (partially recalculated from Mayer, 1997; U.K. data, 1930s to 1980s). ● Originally published geometric mean R values, fresh weight basis. *Originally published geometric mean R < 1 by *t* test, $P \leq 0.014$ (fresh weight basis) confirmed except for sodium by median R < 1 by sign test (dry weight basis), $P = 0.041$ for calcium, 0.0026 for magnesium, 0.0000 for copper, 0.096 for sodium. (*) Originally published geometric mean R < 1 by *t* test, $P \leq 0.016$ (fresh weight basis), not confirmed by median R < 1 by sign test (dry weight basis), $P > 0.05$, mainly because of adjustment for increased water in the recent fruits (median 7% difference).

Davis, HortScience 2009

Are we meeting nutrients needs in pregnancy?



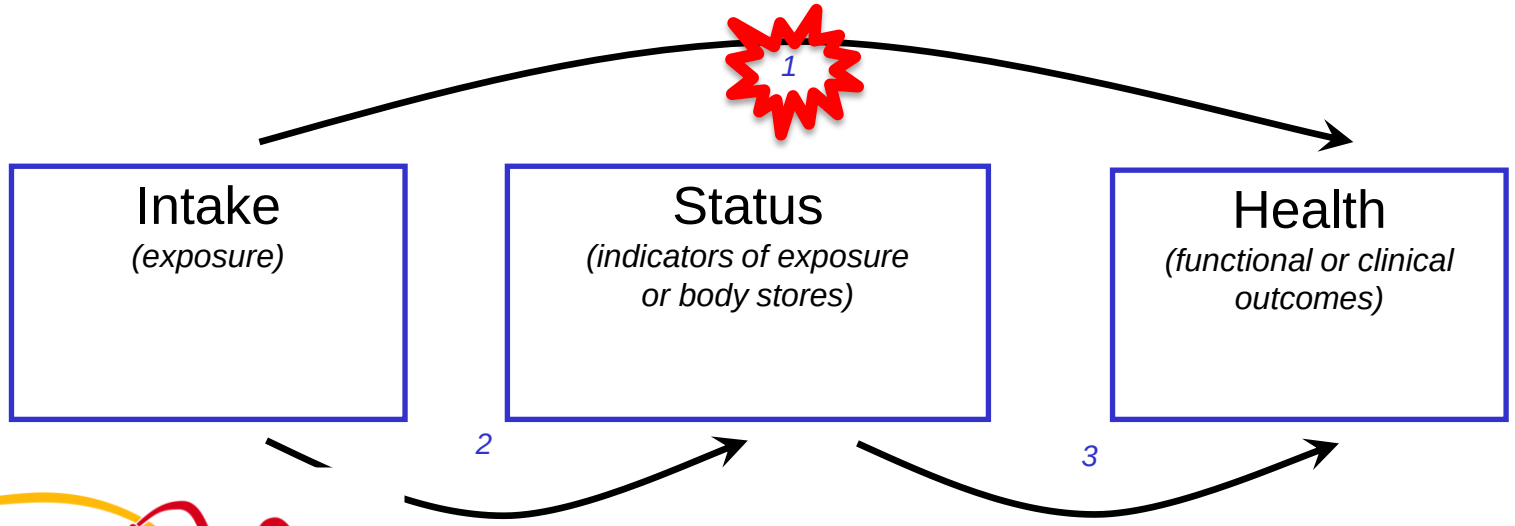
INTAKE - STATUS - HEALTH RELATIONSHIP

Intake: data based on FFQuestionnaires

Status: markers (of exposure or body store)

- iron (ferritin, Hb, …)
- folate (RBC folate, homocysteine…)
- vit D (25(OH)D)
- iodine (UI 24 hours)

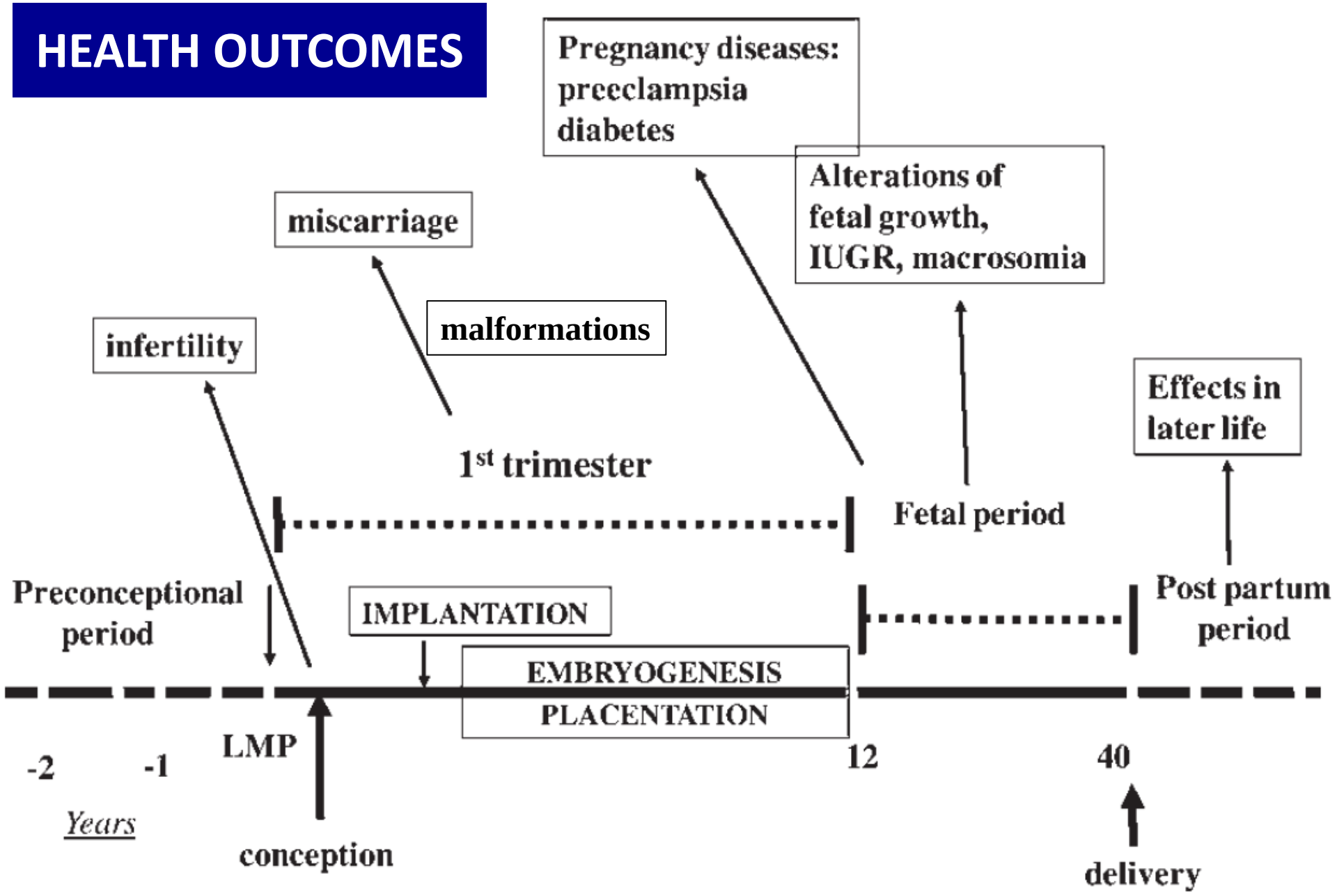
Health: outcomes of interest.



eurreca

EURopean micronutrient RECommendations Aligned

HEALTH OUTCOMES



Cetin et al, Hum Reprod Update 2010

intake-health

Strong adherence of the couple to the preconception diet

Mediterranean

Pregnancy chance **OR 1.4 (1.0-1.9)**

The preconception Mediterranean dietary pattern in couples undergoing in vitro fertilization/ intracytoplasmic sperm injection treatment increases the chance of pregnancy

Marijana Vujkovic, B.Sc.,[a] Jeanne H. de Vries, Ph.D.,[g] Jan Lindemans, Ph.D.,[b] Nick S. Macklon, Ph.D.,[a,h,i] Peter J. van der Spek, Ph.D.,[c] Eric A. P. Steegers, Ph.D.,[a] and Régine P. M. Steegers-Theunissen, Ph.D.[a,d,e,f]

Generation R Study - Rotterdam

Vujkovic et al. 2010

intake-health

Strong adherence of the woman to the preconception diet

Mediterranean

Spina Bifida **OR 0.3 (0.1 - 0.9)**

One carbon metabolism

Congenital heart disease **OR 0.4 (0.2 - 0.7)**

Western

Cleft lip- and/or palate **OR 1.9 (1.2 - 2.9)**

Generation R Study - Rotterdam

Vujkovic et al. 2007, 2008, 2009; Obermann-Borst et al. 2011

Maternal dietary patterns: NTD and CHD

Maternal Dietary Patterns are Associated With Risk of Neural Tube and Congenital Heart Defects

Daniela Sotres-Alvarez*, Anna Maria Siega-Riz, Amy H. Herring, Suzan L. Carmichael, Marcia L. Feldkamp, Charlotte A. Hobbs, Andrew F. Olshan, and the National Birth Defects Prevention Study

US National Birth Defects Prevention Study (1997–2005)
1,047 with an NTD

A dietary pattern rich in fruits, vegetables and fish, and low in fat, even with folate fortification, may decrease the risk of NTDs and some heart defects

Prudent ➔ fish, fruits and vegetables, low fat

Western
low-calorie Western
Mexican

x 1.5 times more likely to have NTD
and x 2.0 to have CHD

Sotres- Alvarez et al., Am J Epidemiol 2013

intake-health

Poor adherence of the woman to the preconception diet



Mediterranean

Growth restriction **OR 2.8 (1.6 - 4.8)**

Generation R Study - Rotterdam

Timmermans et al., 2009

BMJ

BMJ 2014;348:g1446 doi: 10.1136/bmj.g1446 (Published 4 March 2014)

Maternal dietary patterns and preterm delivery: results from large prospective cohort study

66000 women, FFQ in the first 4-5 mts of pregnancy

Linda Englund-Ögge *medical doctor*[1], Anne Lise Brantsæter *senior scientist*[2], Verena Sengpiel *medical doctor*[1], Margareta Haugen *senior scientist*[2], Bryndis Eva Birgisdottir *associate professor*[2 3], Ronny Myhre *senior scientist*[4], Helle Margrete Meltzer *professor*[2], Bo Jacobsson *professor*[1 4]

- ↓ high scores on the "prudent" dietary pattern were associated with significantly **reduced risk of preterm delivery** hazard ratio (0.88, 95% confidence interval 0.80 to 0.97).

➔ dietary advice to eat a balanced diet including **vegetables**, **fruit**, **whole grains**, and **fish** and to drink **water**.

Maternal dietary patterns: Preeclampsia

A Dietary Pattern Characterized by High Intake of Vegetables, Fruits, and Vegetable Oils Is Associated with Reduced Risk of Preeclampsia in Nulliparous Pregnant Norwegian Women[1–3]

23,423 women, FFQ at 17-22 wks

Norwegian Mother and Child Cohort Study (MoBa)
40.6% of pregnancies from all over Norway in the years 1999– 2008.

Pregnancy outcomes were obtained from the Medical Birth Registry of Norway
→ 1267 patients **(5.4%) developed preeclampsia**

4 p
Veg

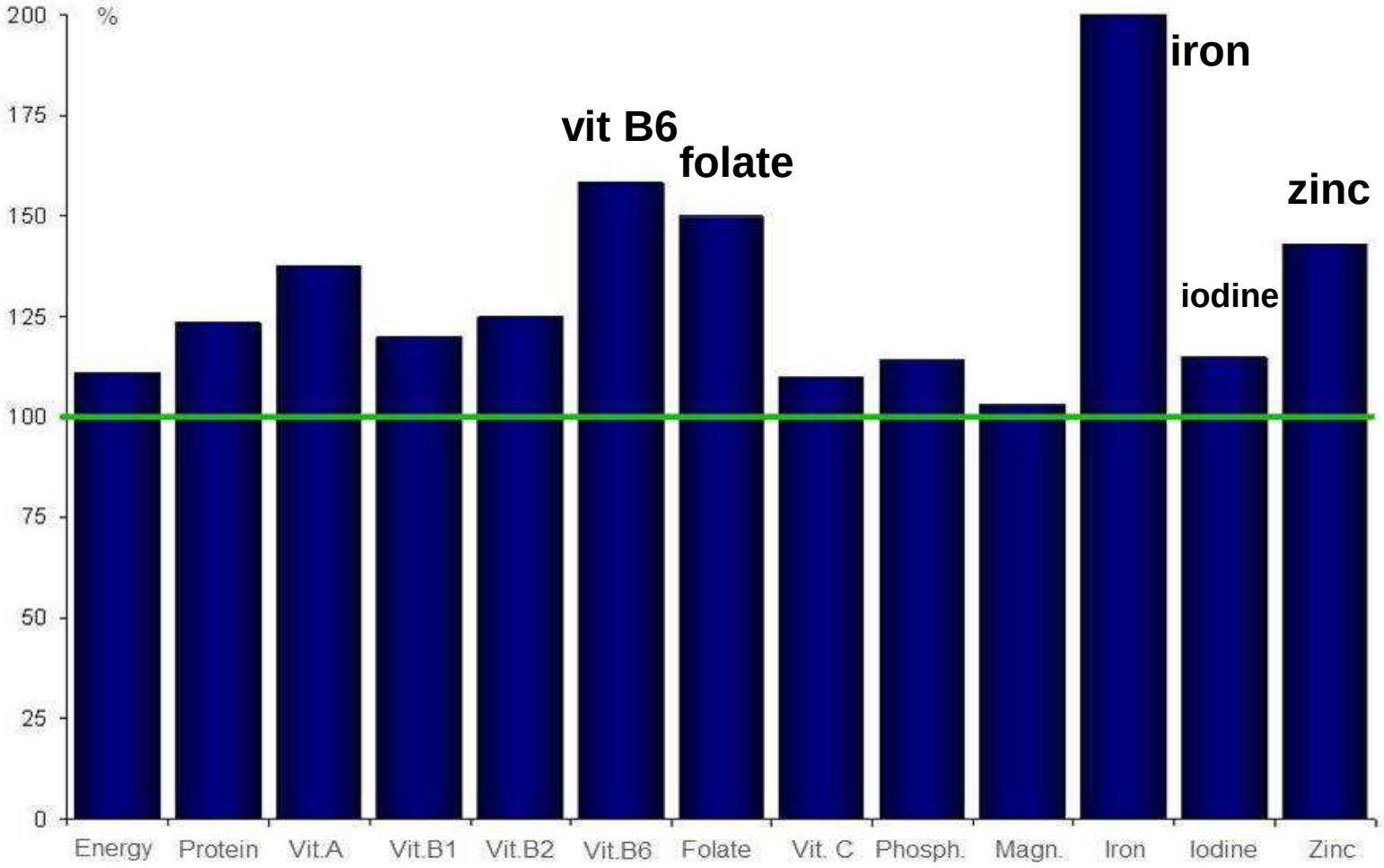
A dietary pattern characterized by **high intake of vegetables, plant foods, and vegetable oils decreases the risk of preeclampsia**,

whereas a dietary pattern characterized by **high consumption of processed meat, sweet drinks, and salty snacks increases the risk**

Brantsæter et al., J Nutr 2009

Reference nutrient intakes for pregnant women expressed as percentage of reference intake values non-pregnant women.

The recommended intake for several nutrients shows a much greater increase than the recommended energy intake



Koletzko B et al, Ann Nutr Metab 2013

Maternal micronutrient status – current knowledge

Micronutrient deficiencies are very common even in developed countries

most prevalent (known) are iron, vitamin D, folate, iodine

Parisi F, Laoreti A, Cetin I, Ann Nutr Metab. 2014

INTAKE - STATUS - HEALTH RELATIONSHIP

Intake: data based on FFQuestionnaires
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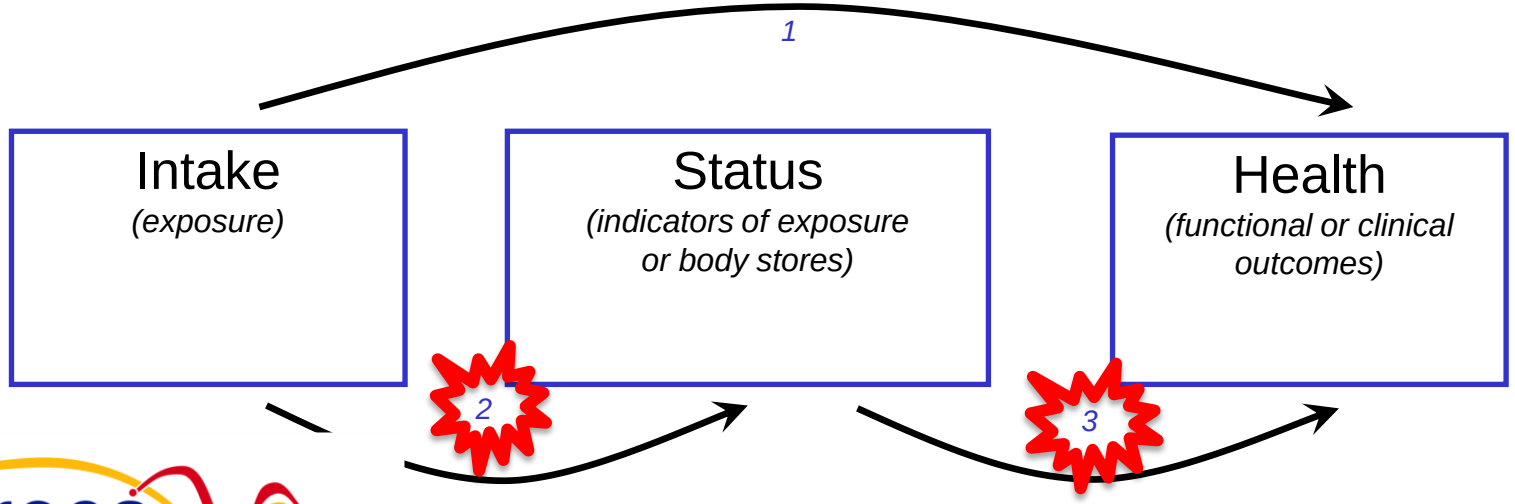
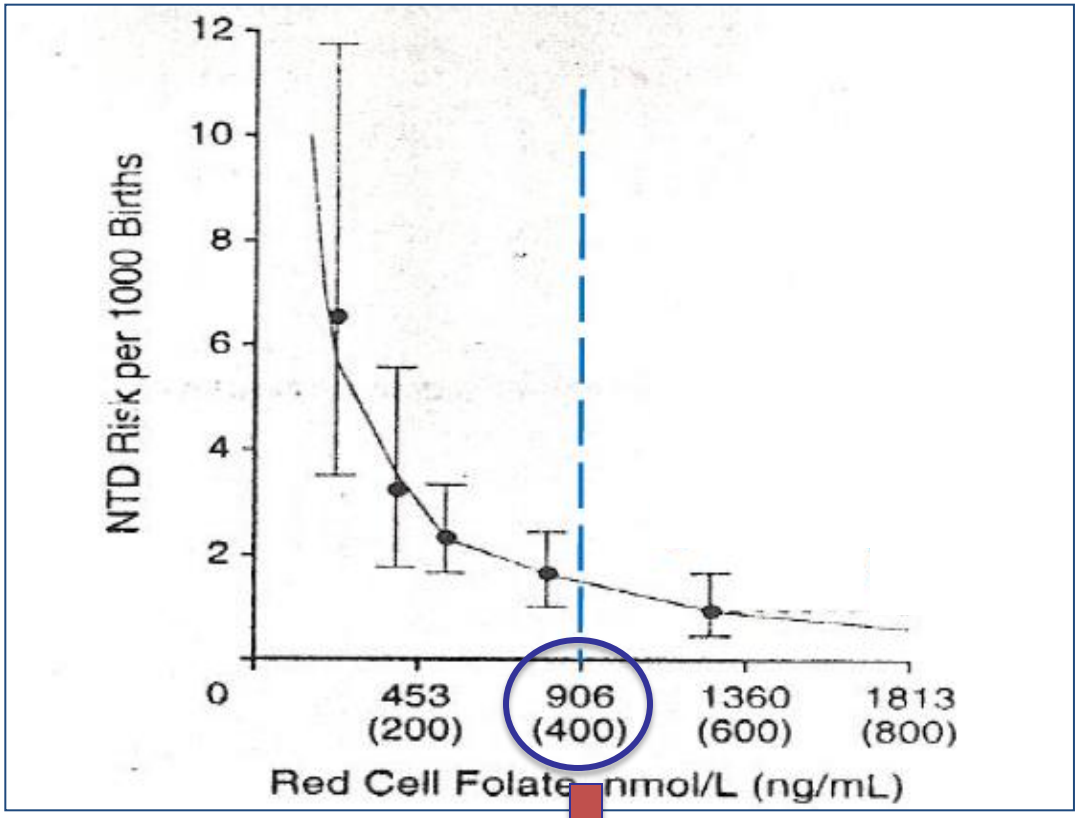
- iron (ferritin, Hb, …)
- folate (RBC folate, homocysteine…)
- vit D (25(OH)D)
- iodine (UI 24 hours)

Health: outcomes of interest.



eurreca
EURopean micronutrient RECommendations Aligned

FOLATE: WHY TO SUPPLEMENT?

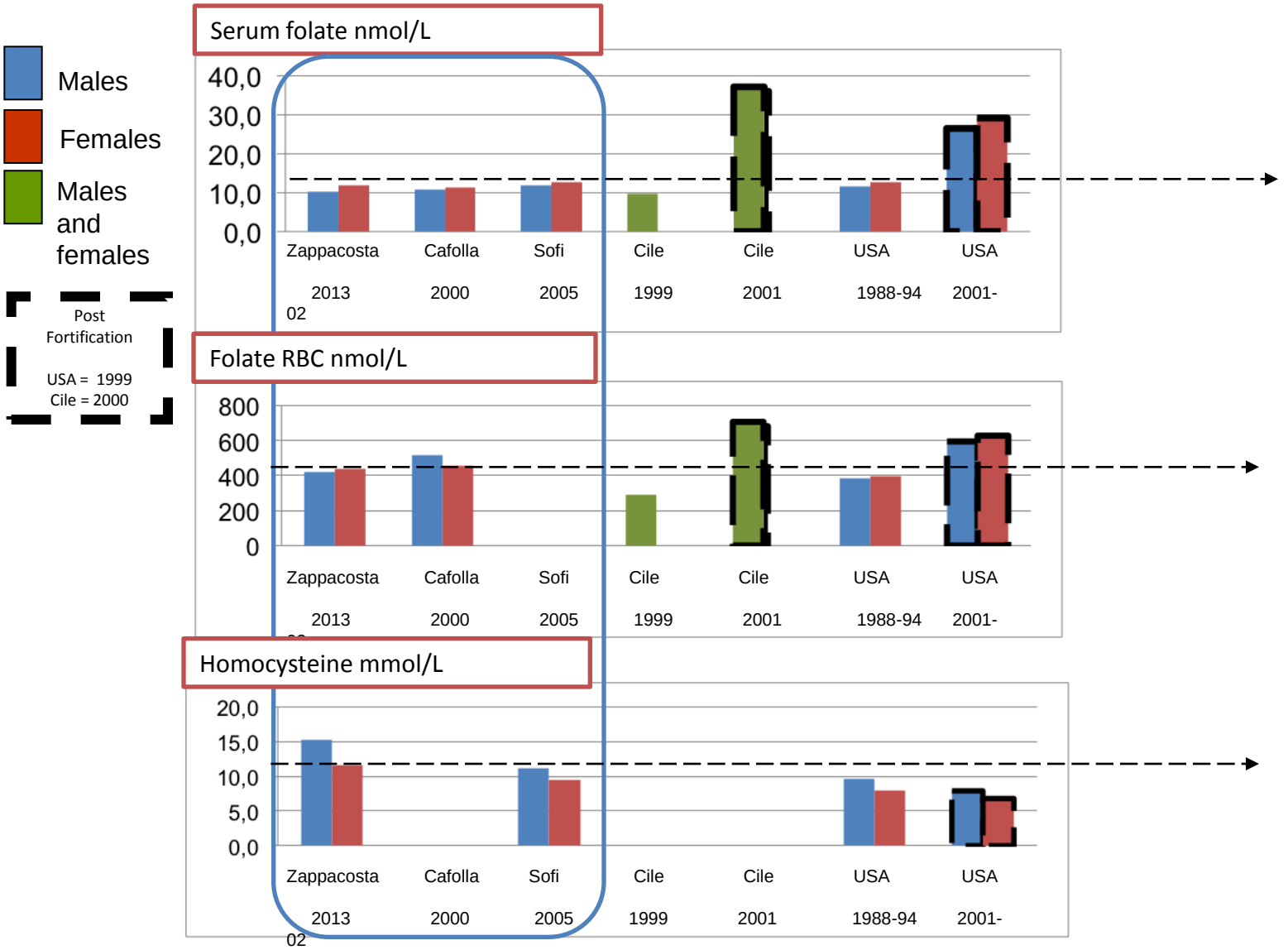


Inverse relationship between RBC folate and NTDs risk

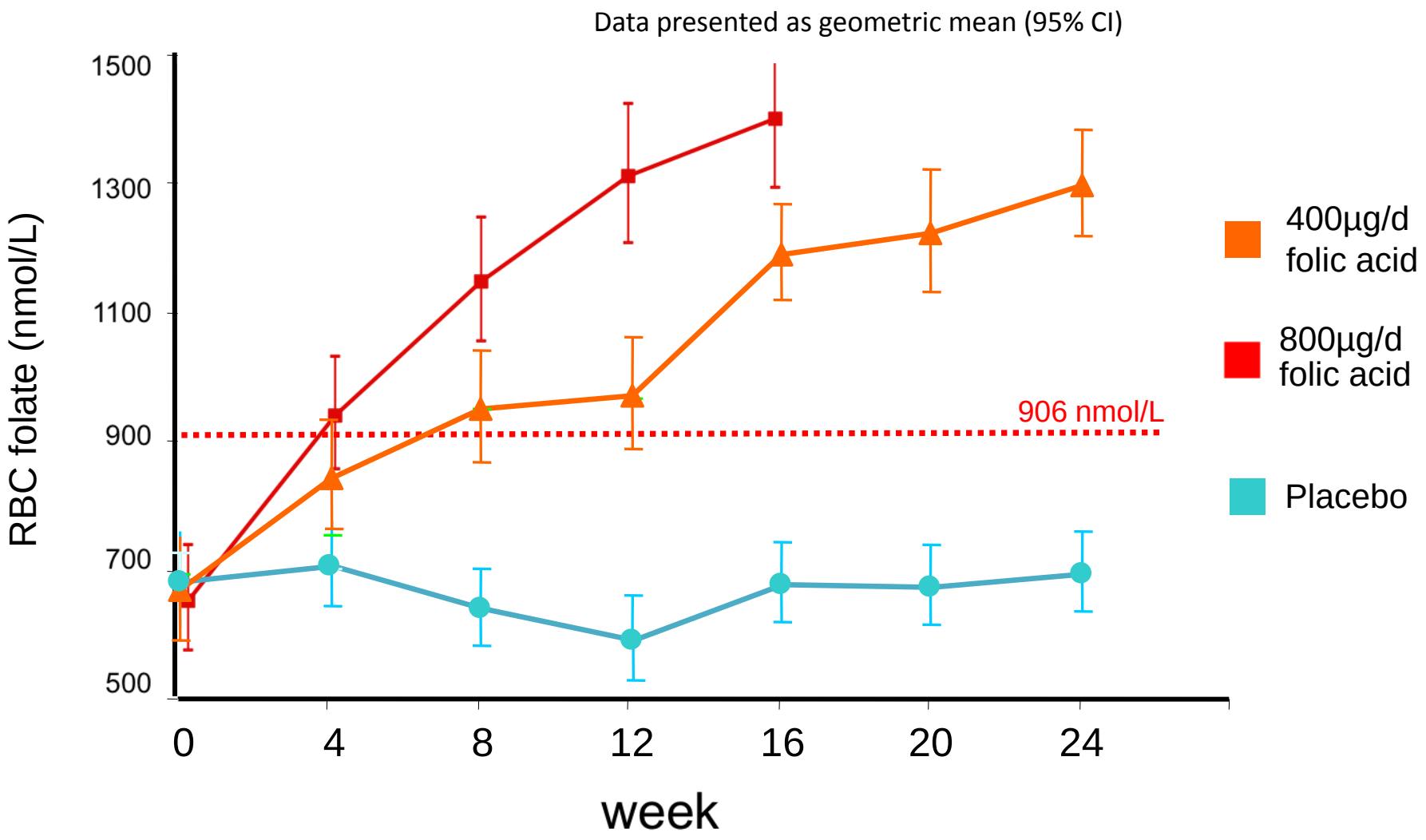
Minimum optimal level at the time of conception and in the 42 days preceding the gestation in order to minimize the risk of NTD

Daly et al., JAMA, 1995

Italian population



FOLATE: effect of supplementation on hematological status



BERTI C, BIESALSKI HK, GARTNER R, LAPILLONNE A, PIETRZIK K, POSTON L, REDMAN C, KOLETZKO B, CETIN I.
Micronutrients in pregnancy: Current knowledge and unresolved questions.
Clin Nutr 2011; 30:689-701

Iron deficiency anemia and adverse pregnancy outcomes

MATERNAL IDA

In industrialized countries:

25-50% in pregnancy

> 50% in post-partum

→ **MOTHER**
- Preeclampsia
- ↑ Mortality

→ **FETUS**
- Low birth weight (LBW)
- Prematurity - IUGR
- Reduced iron stores

→ **OFFSPRING**
- Metabolic syndrome
- Schizofrenia

Milman H, Ann Hematol 2008, 2011

RCT with oral iron in pregnancies with Hb> 10.5 g/dl

	Gestational wks at delivery	Birthweight (g)	Placental weight (g)	Umbilical pH	Blood losses (ml)
Controls	39.1 (2.3)	3092.9 (469.5)	513 (105.0)	7.27 (0.1)	350 (125.8)
Ferrous Iron 30 mg	40.1 (1.2)	3253 (323.8)	482.6 (46.8)	7.24 (0.1)	416 (355.9)
Liposomial Iron 14 mg	39.1 (1.1)	3280 (312.1)	514 (73.5)	7.29 (0.08)	350 (180)
Liposomial Iron 28 mg	39.3 (1.4)	3479.3 (588.0)	488.8 (48.3)	7.28 (0.09)	300 (150)
	ns	**p<0.05**	ns	ns	ns

Parisi F, Mandò C, Martinelli A, Cetin I, in press 2014

vitamin D

✓**support maternal and fetal bone health**

increased vitamin D status during pregnancy may enhance bone mineralization in the offspring *Bischoff-Ferrari HA 2011*

✓**enable the maternal immunological adaptation required to mantain a normal pregnancy**

observational and intervention studies have suggested that vitamin D supplementation benefits immune function and the loss of tolerance of preeclampsia

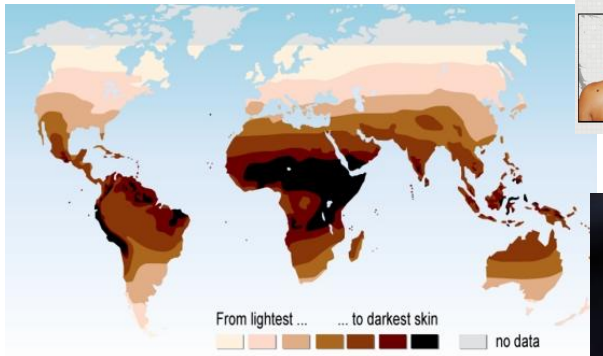
Hypponen E 2011

increased levels are associated with long-term protection against immunological diseases (allergies, type 1 diabetes, asthma)

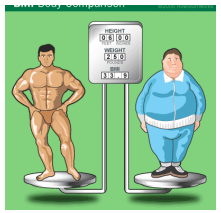
Bischoff-Ferrari HA 2011

What determines **vitamin D** status?

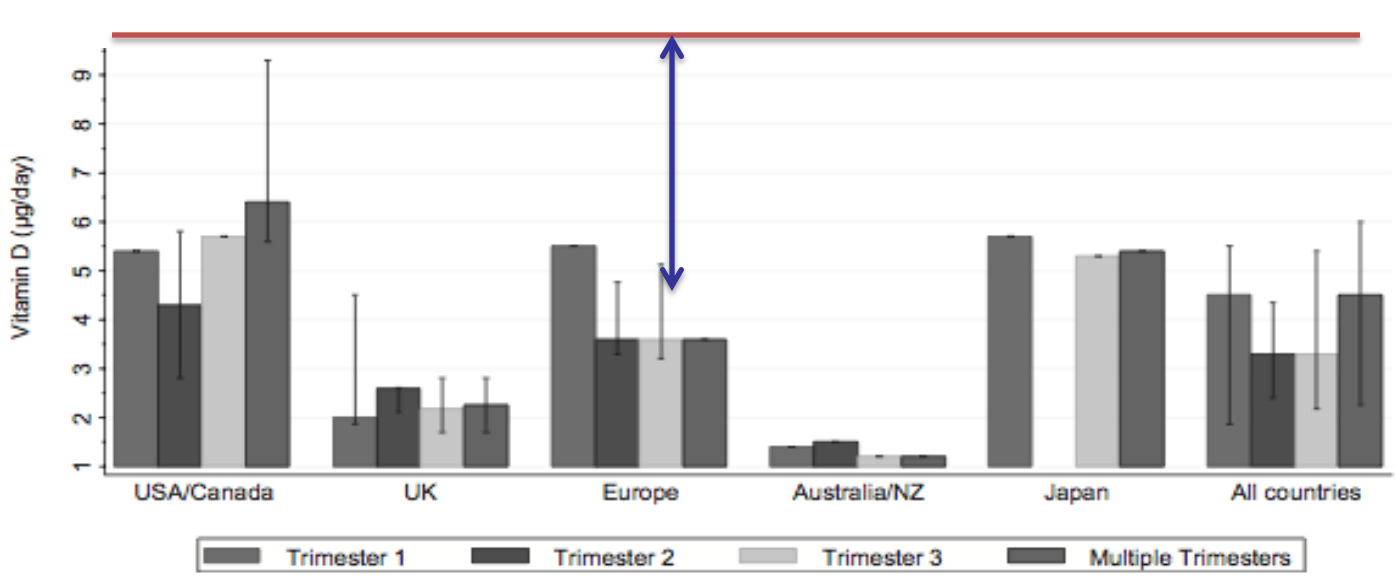
- Sunlight exposure
  - Degree of skin pigmentation
  - Use of sunscreen
  - Latitude
  - Season
  - Time spent outdoors
  - Protective clothing: type of clothing and degree of body covered



- Body mass and percentage body fat
- Diet
  - intake of fish oil, oily fish,
  - foods with vitamin D fortification
  - Vitamin D supplements



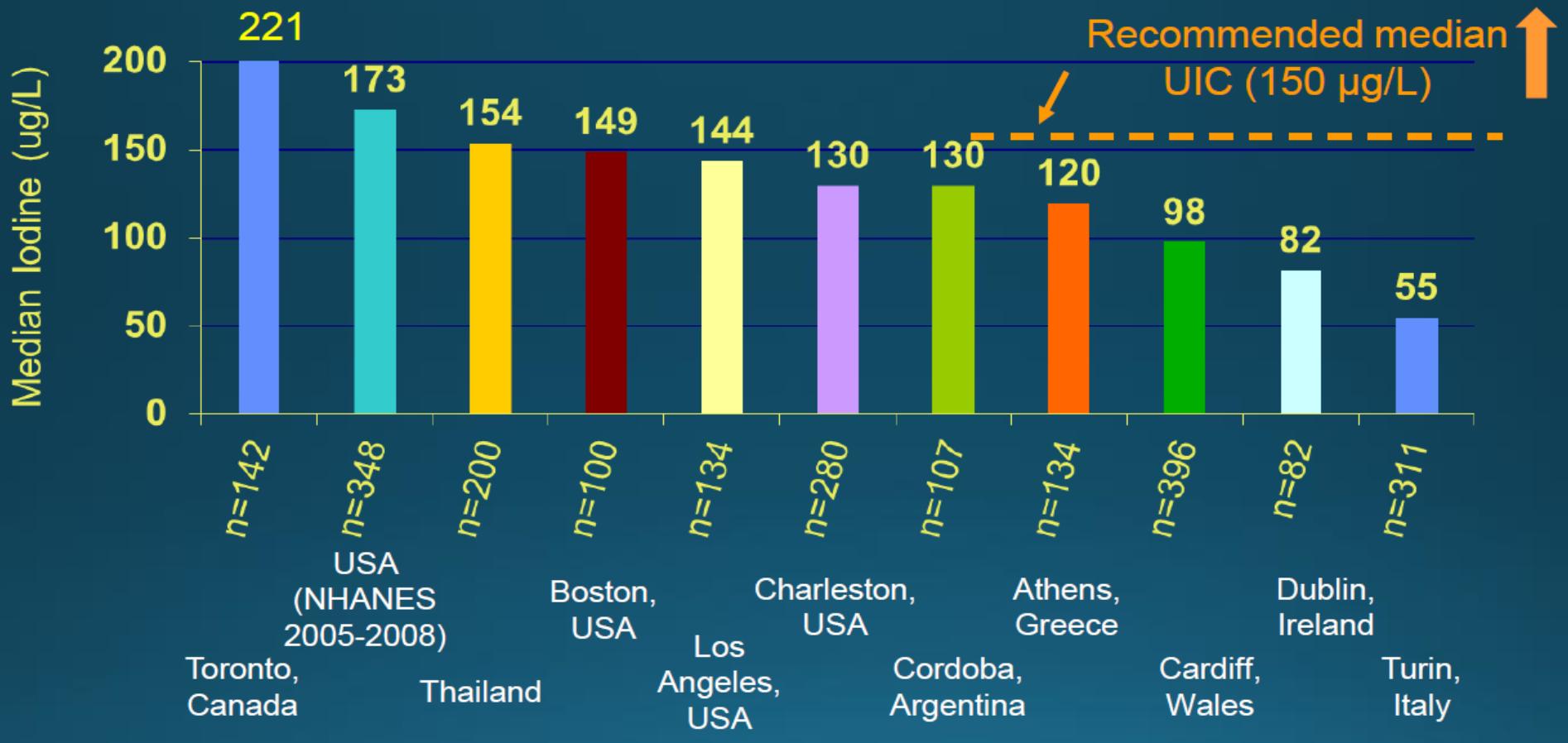
vitamin D intake



Intakes were below recommendations for all regions; however, with ARI 0-10.0 Europe was reported as an adequate intake (compared with European recommendations)

Blumfield M et al, Nutr Rev 2013

Median Urine Iodine in Pregnant Women in Canada, USA, Thailand, Argentina, Wales, Italy, Ireland, and Greece



Pearce EN et al. *Thyroid* 2004
KL Caldwell KL et al, *Thyroid* 2005
Pearce EN et al. *J Clin Endo Metab* 2010

Pearce EN et al. *Endo Pract* 2011
Pearce EN et al. *Clin Endocrinol (Oxf)* 2012

Sullivan S et al. *Ob Gyn* 2012
Katz PM et al. *Endo Pract* 2013
Charatcharoenwitthaya N. et al. ATA 2013

Effects of mild-moderate I deficiency in pregnancy

Effect of inadequate iodine status in UK pregnant women on cognitive outcomes in their children: results from the Avon Longitudinal Study of Parents and Children (ALSPAC)

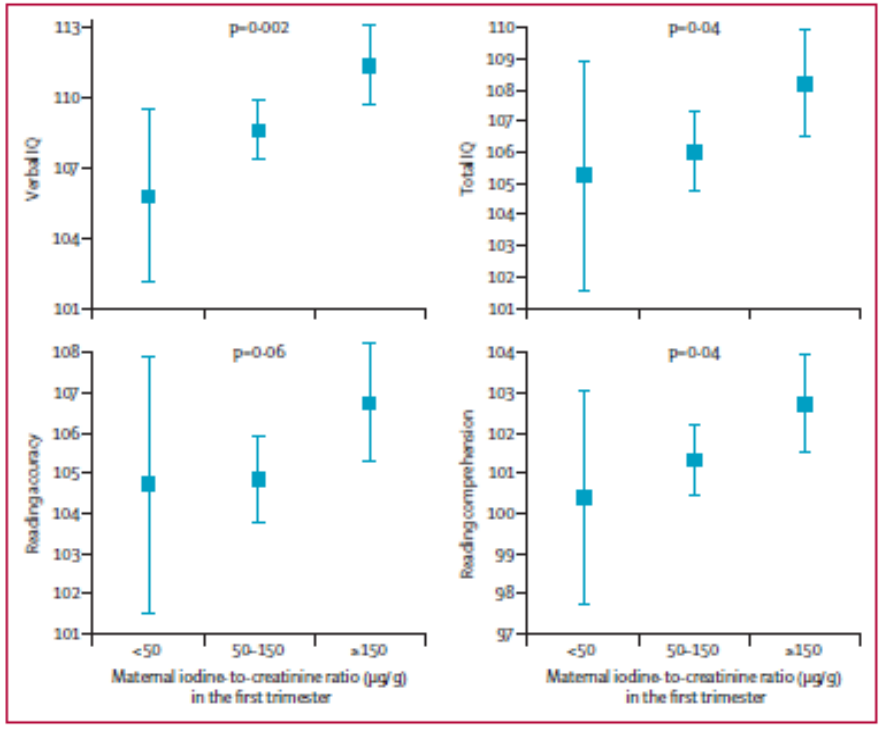


Figure: **Means (95% CIs) for child cognitive outcomes according to maternal iodine status in the first trimester**
Values are adjusted for the effect of confounders (model three). Child verbal and total IQ were assessed at age 8 years and reading accuracy and comprehension at age 9 years. IQ=intelligence quotient.

Offspring of women with UI between 50-150 µg/l in 1st trimester

studied at 8-9 yrs

- ↓ IQ
- ↓ Reading accuracy
- ↓ Reading comprehension

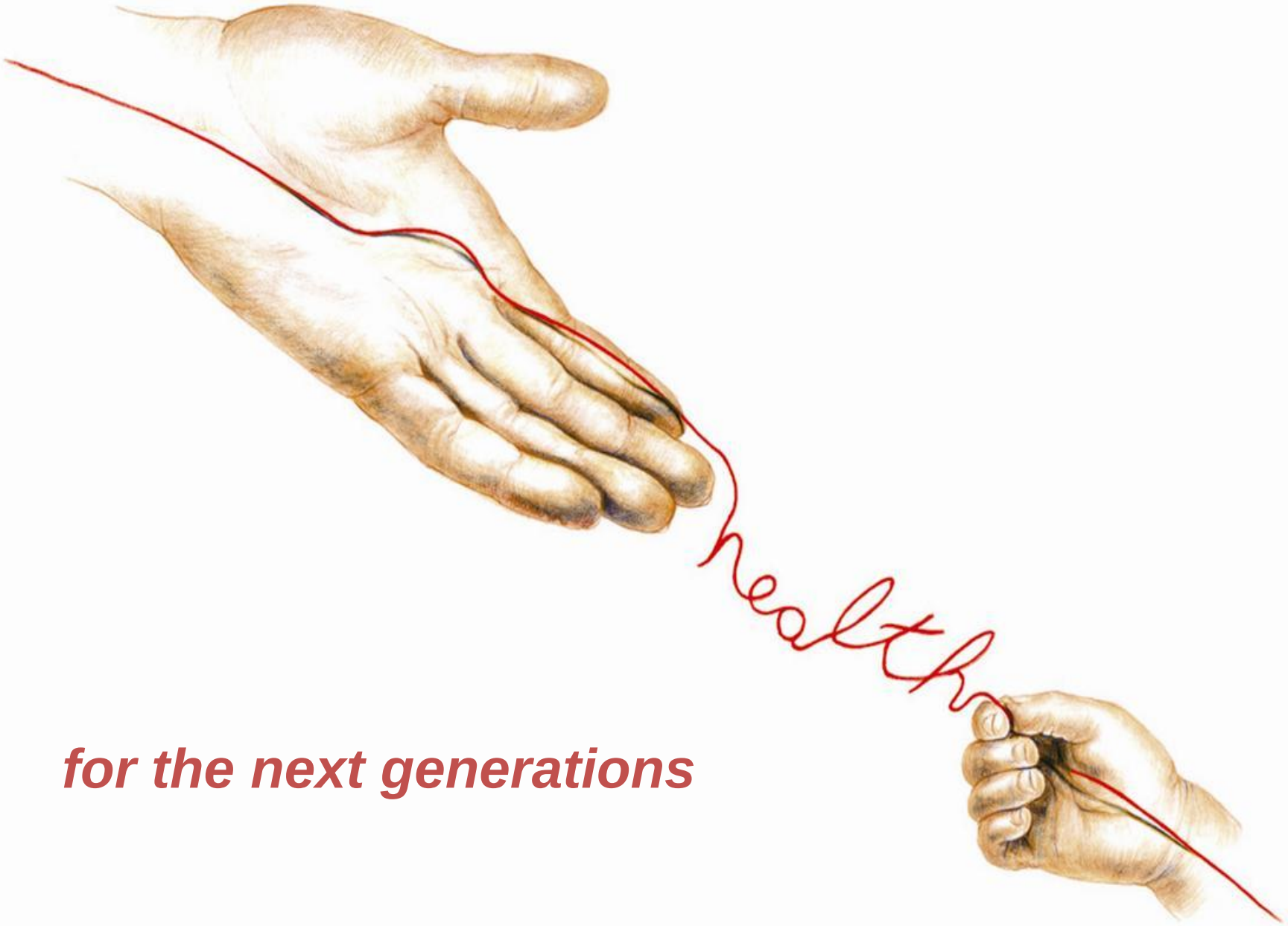
Sara Bath et Al. Lancet 2013

final thoughts

- ✓ Nutritional inadequacies are very likely to occur in the pre-conceptional period as well as in pregnancy, particularly for **IRON, FOLATE, IODINE, vitamin D**
- ✓ Encourage women to establish healthy dietary practice before conception
- ✓ Folate: routine periconceptional supplementation – *starting before conception, at least 400 µg/day*
- ✓ Iron, vitamin D and iodine intakes and biomarkers should be evaluated with more attention to **high risk women** (i.e. adolescents, advanced maternal age, twins,….)
- ✓ Individualization of supplementation: obesity, adolescents, vegetarians, twins, celiac disease, specific pregnancy risks…….

ADVICE for SUPPLEMENTATION

	AI	SUPPLEMENTATION
DHA	AI LC-PUFA 250 mg/die	All pregnant women that do not eat fish, particularly those at **risk for preterm delivery, OBESITY**
FOLIC ACID	600 µg/die	**400 µg/die: all women periconceptionally** 4 mg/die for women at high risk?
IRON	27 mg/die	**ferritin <70 µg/L**
IODINE	220 µg/die	**150 µg/die** - 3 months before conception - in iodine deficient areas
VITAMIN D	15 µg/die – 600 UI/die	**People with darker skin; people who have low or no SUN exposure; OBESITY, risk of preeclampsia vitamin D < 75 nmol/l**
CALCIUM	1000 mg/die	**pregnant women at risk for PE, OBESITY** **No intake of dairy foods**
VITAMIN B12	2,6 µg/die	**vegetarian diet**
ZINC	11 mg/die	**Women at risk for GI malabsorption**
SELENIUM **MAGNESIUM**	55 µg/die 240 mg/die	**?? RISK OF PREECLAMPSIA**



for the next generations

Courtesy of David Barker