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Nutritional status & phenotyping

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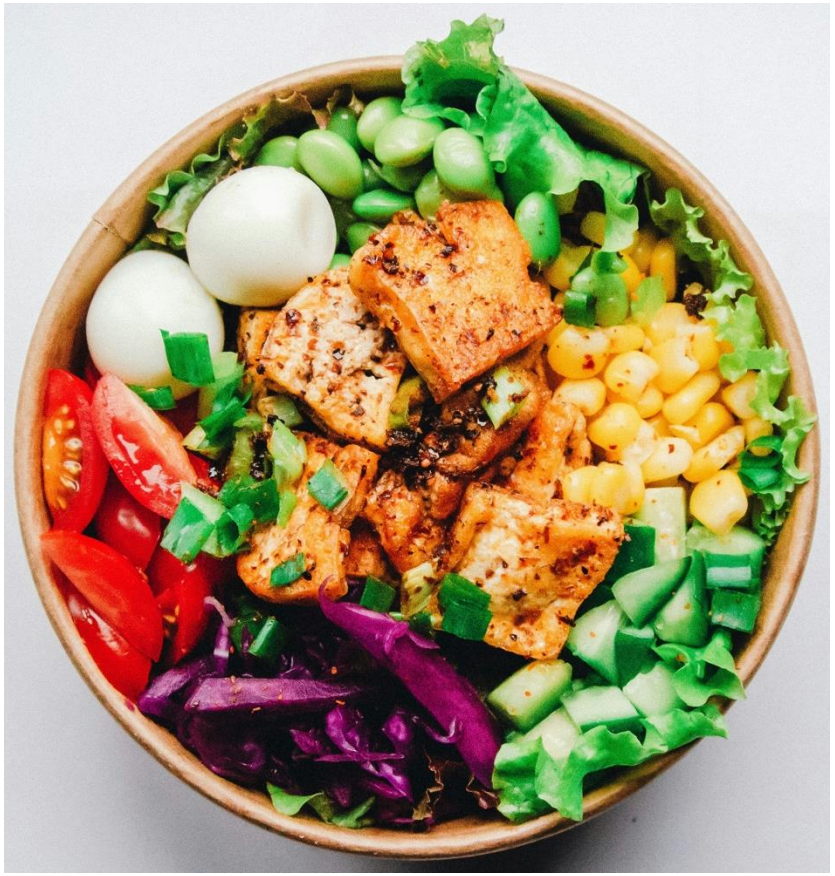
Nutrition



The biochemical and physiological process by which an organism uses food to support its life.
It includes ingestion, absorption, assimilation, biosynthesis, catabolism and excretion of nutrients and related molecules

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Nutritional status to define nutrient needs

Nutritional status is the balance between the intake of nutrients by an organism and the expenditure of these in the processes of growth, reproduction, and health maintenance

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Nutrients and micronutrients

Water

MACRONUTRIENTS
(required in relatively high amounts)

- PROTEINS
  - Amino acids
- CARBOHYDRATES
  - Complex sugars (starch, fibers)
  - Simple sugars (fructose / saccharose)
- LIPIDS
  - Triglycerides and insaturated fatty acids
  - Triglycerides and saturated fatty acids
  - Other lipids (phospholipds, cholesterol…)

MICRONUTRIENTS
(required in relatively low amounts)

- VITAMINS
  - Hydrosoluble C, B1, B2, B3, B6..
  - Liposoluble A, D, E, K
- MINERALS / TE
  - Iron (Fe), Calcium (Ca), Potassium (K), Zinc (Zn)…
- PHYTOCHEMICALS
  - Lutein, zeaxanthin, lyopene, ployphenols…

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Measurement of nutritional status needs a multi-disciplinary approach

Nutritional status is multifactorial

- Food intake
- Socio-economics status
- Genetics
- Microbiome
- Metabolism
- Health status
- Physiological status
- Environment
- Lifestyle

Dietary assessment

FFQ
24H recall

Clinical assessment

Anthropometry
Symptomology

Laboratory tests

Current gaps

Accuracy (i.e. poorly quantitative)
Validation in specific population
Electronic version not always available

Accuracy (i.e. poorly quantitative)
Specificity
Based on short term symptomology

Accuracy (i.e. poorly quantitative)
Single nutrient-based
Standardization
Reliable biomarkers
Interpreted vs. population reference values
Knowledge on long term effects

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Self-Reported Dietary Assessment methods

		24-Hour Recall	Food Record	Food Frequency Questionnaire	Screener or History
Scope of interest	Total diet	X	X	X	
	One or a few components			X	X
Time frame of interest	Short term	X	X		
	Long term			X	X
Can be used to query diet in distant past	Yes			X	X
	No	X	X		
Allows cross-cultural comparisons	Yes	X	X		
	No			X	X
Main type of measurement error	Random	X	X		
	Systematic			X	X
Potential for reactivity	High		X		
	Low	X		X	X
Time required to complete	<15 minutes				X
	>20 minutes	X	X	X	
Memory requirements	Specific	X			
	Generic			X	X
	None		X		
Cognitive difficulty	High			X	X
	Low	X	X		
Study Design	Cross-sectional	X	X	X	X
	Retrospective			X	X
	Prospective	X	X	X	X
	Intervention	X		X	X

Bailey RL et al. Curr Opin Biotechnol. 2021 Aug;70:91-96.

Nutritional recommendations in Switzerland

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Le Conseil fédéral › DFI › OSAV

Contact Médias Extranet DE FR IT EN

Schweizerische Eidgenossenschaft
Confédération suisse
Confederazione Svizzera
Confederaziun svizra

Office fédéral de la sécurité alimentaire et des affaires vétérinaires

Recherche ...

Aliments et nutrition | Objets usuels | Animaux | Importation et exportation | L'OSAV

OSAV › Aliments et nutrition › Nutrition › Recommandations et informations › Aliments et nutriments › Besoins en nutriments

‹ Recommandations et informations

Aliments et nutriments

- Aliments sélectionnés
- Besoins en nutriments
- Base de données des valeurs nutritives
- Allergies et intolérances

Besoins en nutriments

L'OSAV publie des recommandations sur les besoins journaliers en protéines, en glucides et en graisses, ainsi que sur les nutriments nécessaires aux personnes ayant des besoins nutritionnels particuliers.

Actuel

Les poissons des lacs, une bonne source de vitamine D

La carence en vitamine D est très répandue en Suisse comme au niveau mondial. Même si chez l'homme les besoins sont en majorité couverts par la synthèse endogène de vitamine D au niveau de la peau, les apports alimentaires sont aussi importants au bon fonctionnement de l'organisme.

A balanced diet to diversify and optimize nutrient intakes

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Swiss food pyramid

Source: SSN - Food Pyramid

Optimal dishes

Balanced meal

Food nutrient contents

Swiss food composition database

https://valeursnutritives.ch

Food/nutrients intakes

Nutrients needs

sge Schweizerische Gesellschaft für Ernährung
ssn Société Suisse de Nutrition
ssn Società Svizzera di Nutrizione

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Dietary supplements

Definition

Food supplements are foodstuffs intended to supplement the normal diet. They constitute a concentrated source of vitamins, minerals or other substances having a nutritional or physiological effect, alone or in combination, marketed in the form of doses.

Ordinance of the Federal Department of Home Affairs on food supplements, December 16th 2016

Article 3

The labeling must mention the content of vitamins, minerals and other substances at the time of delivery to the consumer. The values indicated must be based on the average values referred to in art. 26, al. 4, OIDAl

Ordinance of the Federal Department of Home Affairs about the information on foodstuffs (OIDA1), article 26
The energy value and nutrient content of the food ***must be indicated on the date of delivery to consumers****.*
For mandatory indications, can use mean values from: ***analysis from the manufacturer****, calculation made from the values relating to the used ingredients, calculation made from generally established and recognized data.*

Article 4

The labeling, presentation and advertising of food supplements **may not bear any statement asserting or suggesting that a balanced and varied diet is not a sufficient source of nutrients in general**.

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Dietary supplements, several facts…

- France, Study NutriNet-Santé (2009)
  - 15 % of men and 28 % of women took dietary suplements (DS) at least 3 days a week
  - 60 % of DS regularly consumed for one year
  - In 55 % of cases, products recommended or prescribed by a medical doctor
- Switzerland, study on CoLaus cohort (around 6000 subjects)
  - 26% consumed a DS (vitamins/mineerals: 16,8%)
  - Women consumed more DS than men
  - DS consumption associated with a better helath profile

P Marques-Vidal et al. European Journal of Clinical Nutrition (2009) 63, 273–281

Dietary supplements pitfalls on quality

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US

JAMA Network | Open

Original Investigation | Public Health

Analysis of Select Dietary Supplement Products Marketed to Support or Boost the Immune System

Cindy Crawford, BA; Bharathi Avula, PhD; Andrea T. Lindsey, MS; Abraham Walter, MS; Kumar Katragunta, PhD; Ikhlas A. Khan, PhD; Patricia A. Deuster, PhD, MPH

Crawford C et al. JAMA Netw Open. 2022;5(8):e2226040.

- 17 / 30 products with inaccurate labels
- 13 products with labelled ingredients not detected by laboratory analysis
- 9 products had substances detected that were not on the labels
- None of the products had third-party certification seals present on the packaging

CH

Source: https://www.frc.ch/complement-alimentaire/

- 10 products (vitamins & minerals, positioned to support immune function) purchased in pharmacies
- Differences in measured and declared values in 50% of products
- One product reported as iron containing product was not found to contain iron
- Large variability of compositions and relatively to RVs

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What efficacy and for what goal ?

- In general, lack of high quality scientific studies demostrating clinical effects
  - Randomized clinical studies, double blind

- Different scenarios leading to DS consumption:
  - Medical prescriptions:
    - Based on credible diagnostic and demonstrated nutritional needs
    - Management of deficiencies, insuffisencies and possible toxicity
  - « Self-medication »
    - Driven by expectations on maintaining health, improvement of physical or cognitive performance, disease prevention or management of disease/therapy side effects

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Study SU.VI.MAX (Supplémentation en Vitamines et Minéraux Anti-oXydants)

- Interventional double blind clinical study
- Research team (Prof. Hercberg Serge et al.), 12’000-15’000 subjects
- Intervention: beta-carotene (6mg), vitamine C (120mg), vitamine E (30mg), zinc (20mg), selenium (100mg) / day (period: 8 years) vs. Placebo
- Study of effects on cancer incidence, cardiovascular diseases, death
- Results:
  - No effect on cardiovascular diseases incidence
  - Effect on cancer incidence, in men only
  - Effect on mortality, on men only

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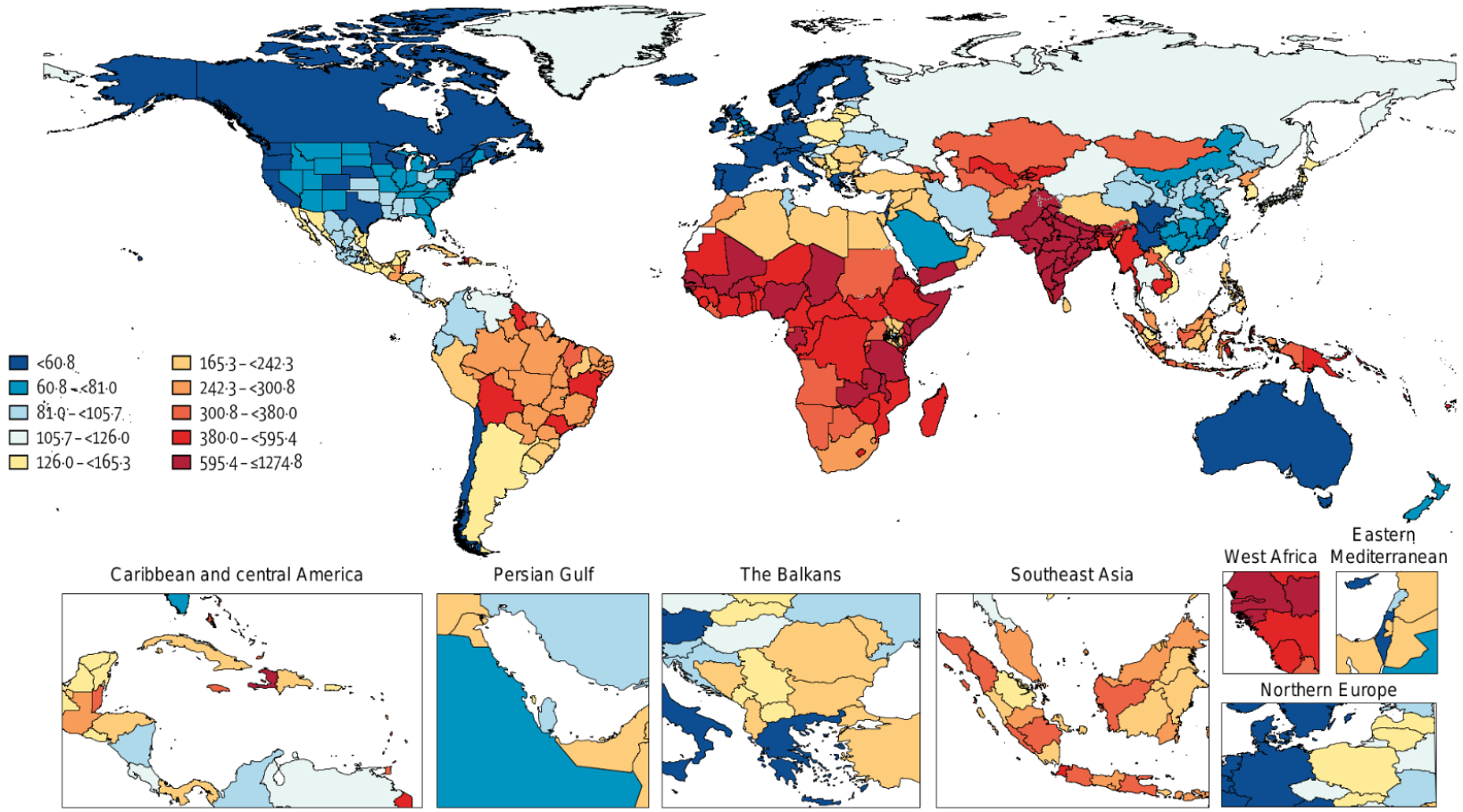
Dietary iron deficiency

Age-standardised DALY rates (per 100 000) by location, both sexes combined, 2019

Global prevalence of 14·4% (14·1–14·6) and accounted for 28·5 million (19·1–41·1) disability-adjusted life year (DALYs) globally in 2019.



One DALY represents the loss of the equivalent of one year of full health.

Source: https://www.healthdata.org/results/gbd_summaries/2019/dietary-iron-deficiency-level-3-cause

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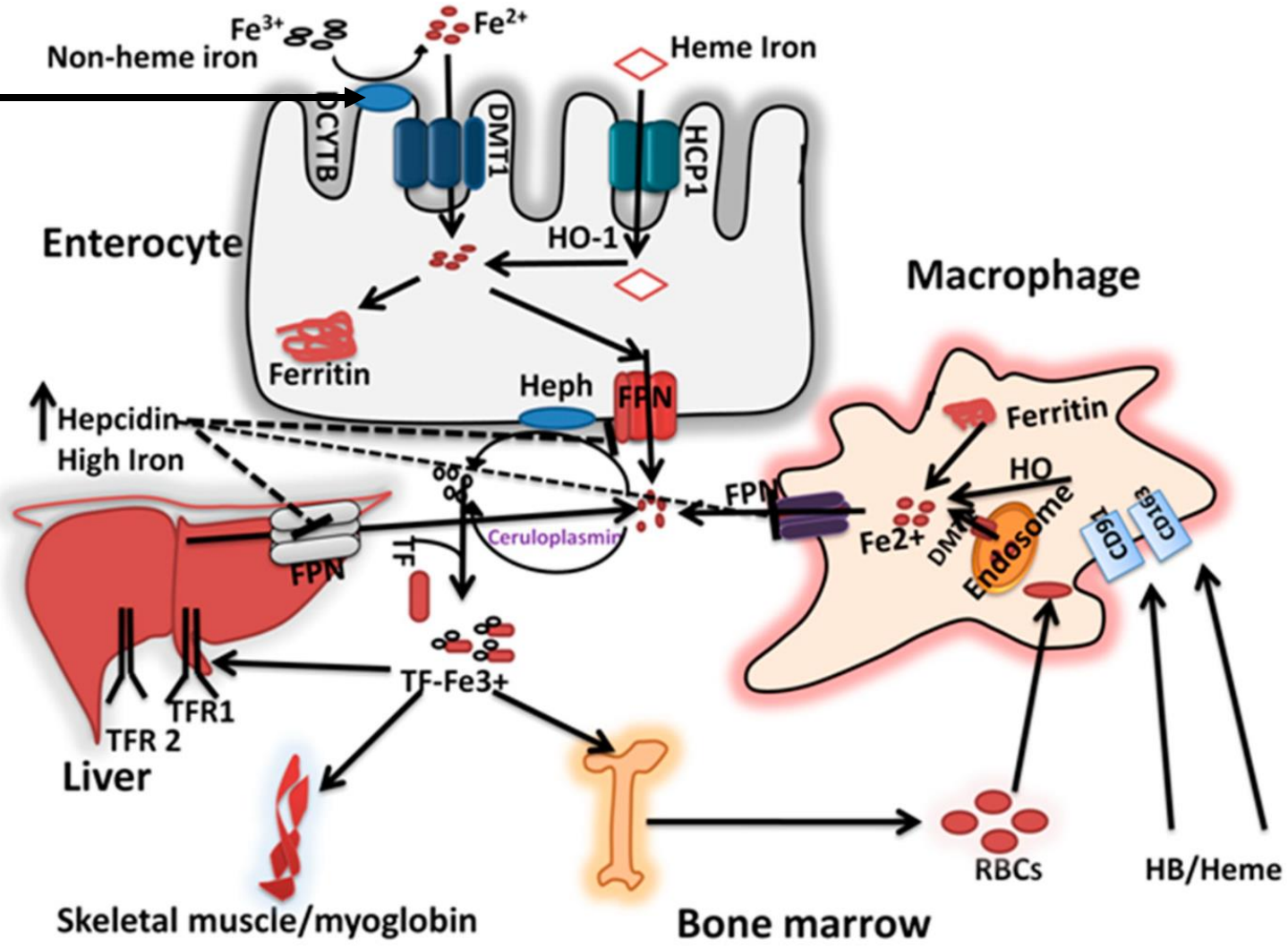
Iron metabolism

Vitamin C (ascorbate)
ferrireductase
Duodenal cytochrome B
reductase 1 (DCYTB)



Kondaiah P et al. Nutrients. 2019 Aug 13;11(8):1885.

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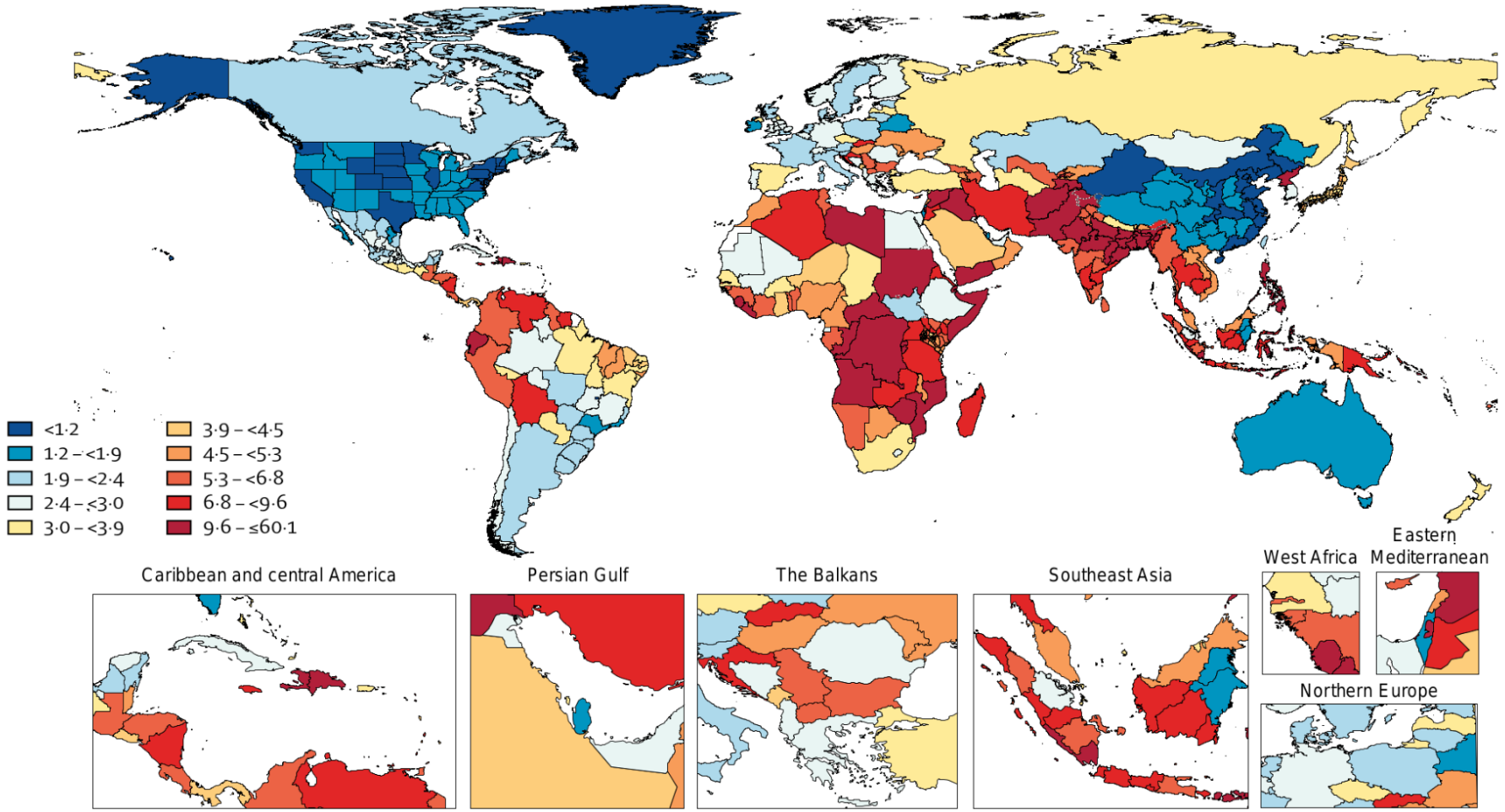
Dietary zinc deficiency

Age-standardised all-cause summary exposure values, SEV, by location, both sexes combined, 2019

Zinc deficiency is defined as zinc consumption (in mg/day) less than 2–3 mg from all dietary sources.



Source: https://www.healthdata.org/results/gbd_summaries/2019/zinc-deficiency-level-3-risk

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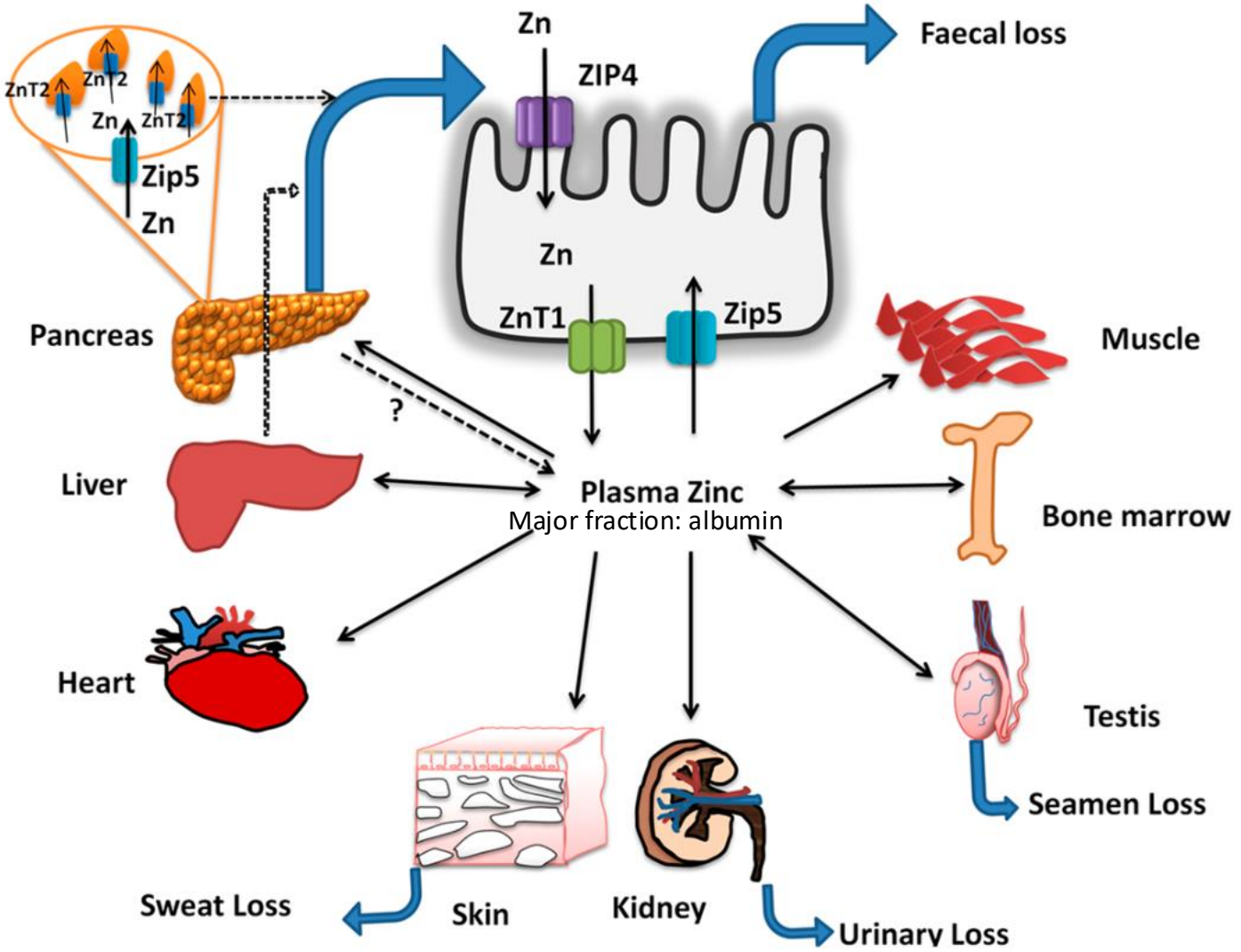
Zinc metabolism



Kondaiah P et al. Nutrients. 2019 Aug 13;11(8):1885.

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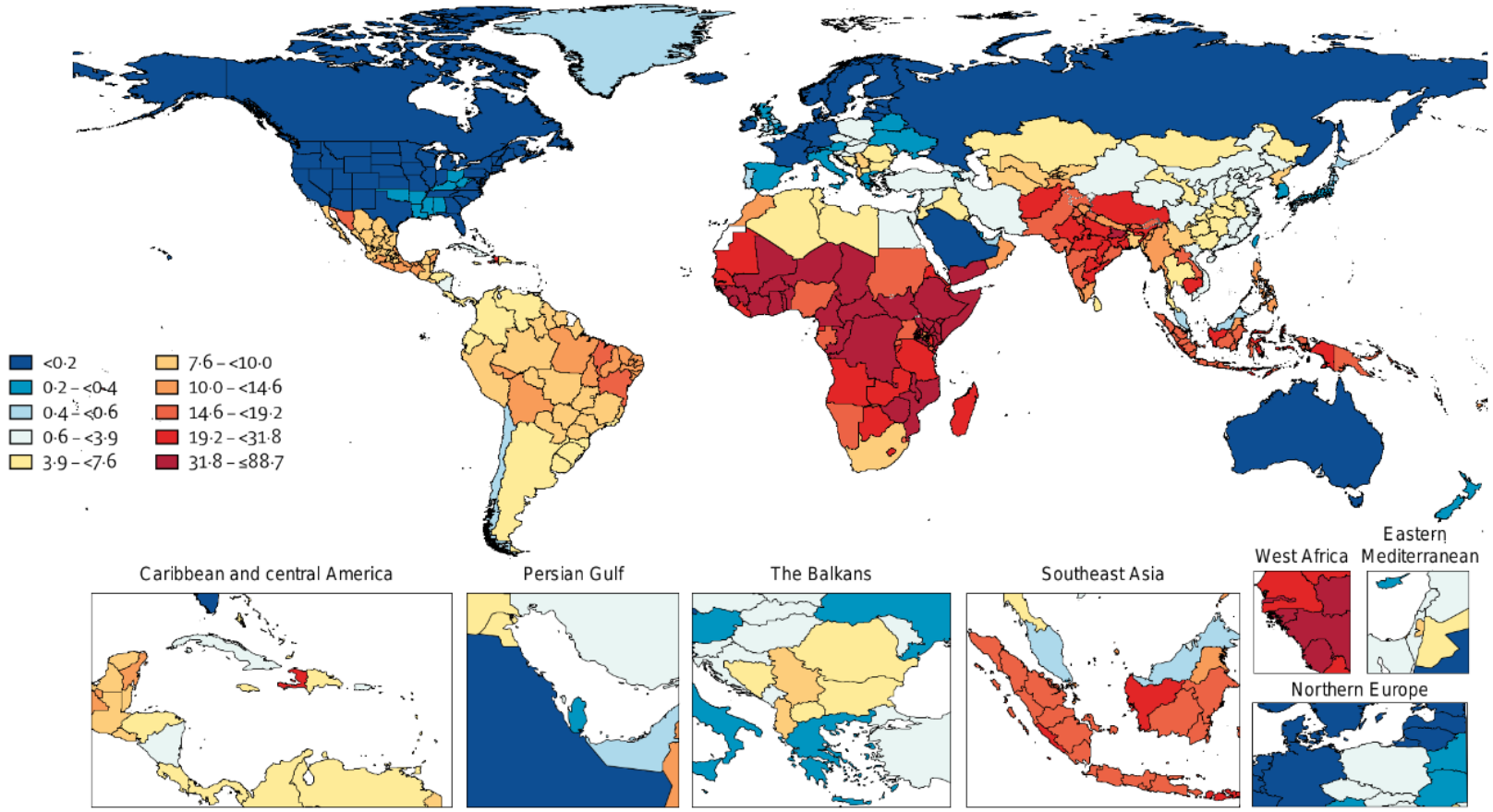
Vitamin A deficiency

Age-standardised DALY rates (per 100 000) by location, both sexes combined, 2019

Vitamin A deficiency was responsible for 1·18 million DALYs globally, including 506 000 DALYs in children under the age of 5. Total vitamin A deficiency (defined as serum retinol <0.70 µmol/L) and disability from blindness and vision loss due to vitamin A deficiency



Source: https://www.healthdata.org/results/gbd_summaries/2019/vitamin-a-deficiency-level-3-cause

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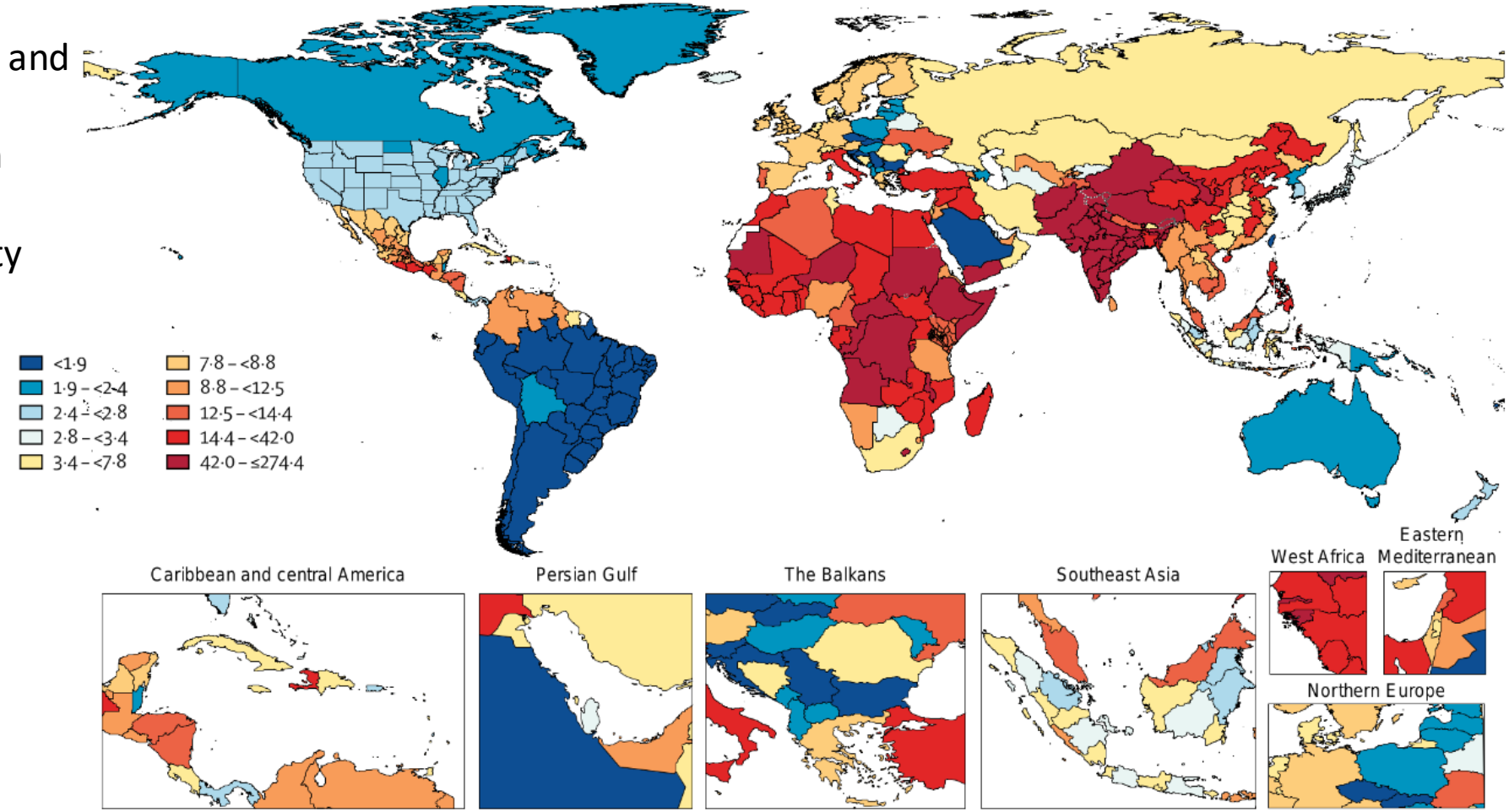
Iodine deficiency

In 2019, iodine deficiency had a global prevalence of 2·4% and accounted for 2·44 million DALYs globally.

visible goiter (grade 2) and associated sequelae:

- thyroid dysfunction
- heart failure
- intellectual disability



Source: https://www.healthdata.org/results/gbd_summaries/2019/iodine-deficiency-level-3-cause

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Nutrient needs and nutritional biomarkers

A useful biomarker of micronutrient status must:

- Correlate with the rate of vitamin intake, at least within the nutritionally significant range, and respond to deprivation of the vitamin
- Relate to a meaningful period of time
- Relate to normal physiologic function
- Be measurable in an accessible specimen
- Be technically feasible, reproducible, and affordable l have an available base of normative data

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Vitamin status biomarkers

Liposoluble vitamins

Vitamin	Functional parameters	Tissue levels
A		**Serum retinol** **Total body store using stable isotopes (heavy to implement)** *Change in serum retinol after oral load* *Liver retinyl esters*
D		**Serum total 25-(OH)-vitamin D (sum of D2 and D3 forms)** *Serum vitamin D3* *Serum 1,25-(OH)2-D3* *Serum alkaline phosphatase*
E	Erythrocyte hemolysis	**Serum tocopherols (often α- and γ-tocopherol) not corrected and corrected to blood lipids (cholesterol and triglycerides)** *Serum malondialdehyde, Serum 1,4-isoprostanes* *Breath alkanes*
K	Clotting time **Prothrombin time** **Uncarboxylated Gla-proteins (PIVKA-II)**	***Serum vitamin K***

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Vitamin status biomarkers

Hydrosoluble vitamins

Vitamin	Functional parameters	Tissue levels	Urinary excretion
C (ascorbic acid)		**Serum ascorbic acid** Leukocyte ascorbic acid	Ascorbic acid Ascorbic acid after load
B1 (thiamin)	**Erythrocyte transketolase stimulation**	**Blood thiamin** Blood pyruvate	Thiamin (thiochrome) Thiamin after load
B2 (riboflavin)	**RBC glutathione reductase stimulation**	Blood riboflavin	Ribloflavin
B3 (niacin)		**RBC nicotinamide (NAD)** RBC NAD:NADP ratio Plasma tryptophan	**1-methylnicotinamide** **1-methyl-6-pyridone-3- carboxamide**
B5 (pantothenic acid)	RBC sulfanilamide acetylase	**Serum/plasma pantothenic acid** RBC pantothenic acid	Pantothenic acid

RBC: red blood cells.

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Vitamin status biomarkers

Hydrosoluble vitamins

Vitamin	Functional parameters	Tissue levels	Urinary excretion
B6*	RBC transaminase	**Plasma pyridoxal phosphate** RBC transaminase stimulation RBC pyridoxal phosphate Plasma pyridoxal	**Xanthurenic acid after tryptophan load** Quinolinic acid 4-Pyridoxic acid
B7 (biotin)		**Blood biotin** **Serum/plasma biotin**	Biotin **3-hydroxyisovalerylcarnitine and acylcarnitines**
B9 (folic acid)	Plasma homocysteine	**Serum folates** **RBC folates** Leukocyte folates, liver folates	FIGLU after histidine load Urocanic acid after histidine load
B12 (cobalamin)	Plasma homocysteine	**Serum vitamin B12** **Serum holoTC 2** RBC vitamin B12	FIGLU **Methylmalonic acid**

*Vitamin B6 refers to six common forms: pyridoxal, pyridoxine (pyridoxol), pyridoxamine, and their phosphorylated forms.
RBC: red blood cells; FIGLU: formiminoglutamic acid; holoTC2: holotranscobalamin 2

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Limitations of some biomarkers of vitamin status

Vitamin	Biomarker	Limitations
A	Plasma retinol	Reflects body vitamin A stores only at severely depleted or excessive levels; confounding effects of protein and zinc deficiencies and renal dysfunction
D	Plasma alkaline phosphatase	Affected by other disease states
E	Plasma tocopherol	Affected by blood lipid transport capacity
B1	Plasma thiamin	Low sensitivity to changes in thiamin intake
B2	Plasma riboflavin	Low sensitivity to changes in riboflavin intake
B6	RBC glutamic-pyruvic	Genetic polymorphism transaminase
B9	RBC folates Urinary FIGLU	Also reduced in vitamin B12 deficiency Also increased in vitamin B12 deficiency
B12	Urinary FIGLU	Also increased in folate deficiency

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Several mineral / trace element status biomarkers

Element	Status biomarker	Remark
Fe	**Serum ferritin**	Affected by inflammation other biomarker: hepcidin
Se	**Plasma selenium** Selenoprotein P	
I	**Urinary iodine**	Other biomarker: serum thyroglobulin
Zn	**Serum/plasma Zn**	New biomarkers required
Cu	**Serum ceruloplasmin** Serum Cu	

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Nutrient needs and nutritional biomarkers

Overall limitations		Possible ways forward
Single nutrient-based biomarkers, lack of specificity and sensitivity	☞	Novel nutrient pattern signatures or integrative biomarkers (Metabolomics)
Neglect kinetic / nutrient bioavailability aspects	☞	Assess individual nutrient bioavailability capabilities (Nutrikinetics)
Accessible testing matrix (plasma…) might not relate to intracellular pools	☞	Assess intracellular nutrient status with highly sensitive techniques (mass spectrometry)
Indicative of depletion/repletion (short term exposure)	☞	Build scientific evidence on long term health effects
Neglect interactions with the gut	☞	Nutrient pattern signatures or integrative biomarkers
Reference ranges based on population studies	☞	Develop individual-specific targets (precision nutrition)

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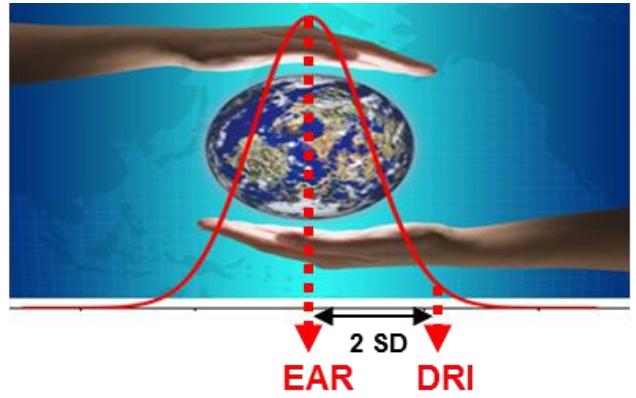
Meeting individual needs requires individual nutritional phenotyping

- Nutritional reference systems (DRI, RDA, EAR) are population-based and limited to the study of acute nutritional deficiencies (i.e. vitamin C and scurvy)
- Need to capture and understand nutrient biology in its inherent complexity and at the individual scale (i.e. genetic variants and nutrikinetics, nutridynamics, nutrient-nutrient interactions)



The EAR is based on a specific criterion of adequacy, derived from a careful review of the literature. Reduction of disease risk is considered along with many other health parameters in the selection of that criterion.
- From USDA

Nutritional phenotyping

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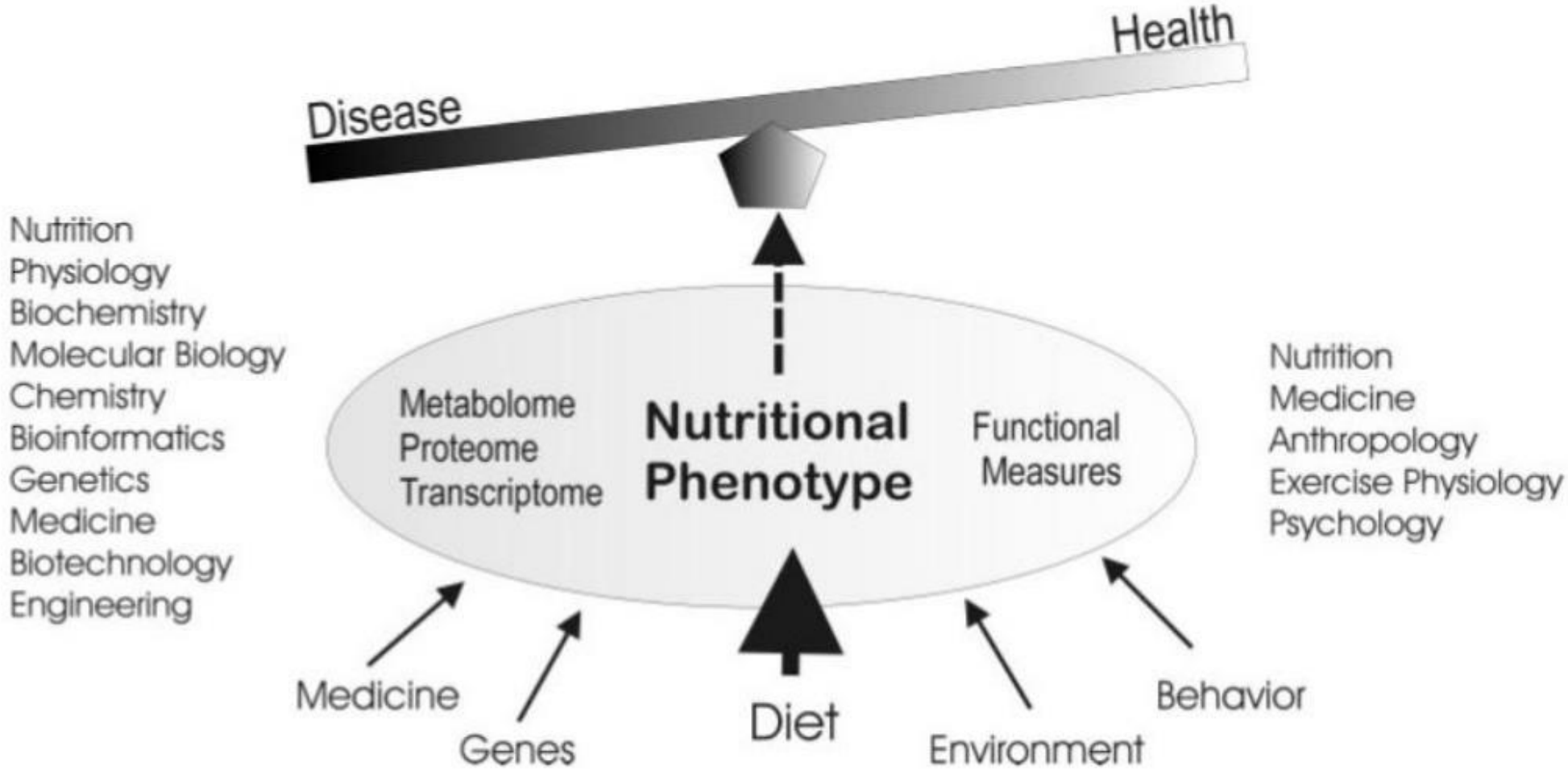
Nutritional phenotype



Zeisel SH et al. J Nutr. 2005 Jul;135(7):1613-6.

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Genetics and micronutrient status

Am J Clin Nutr. 2005 Mar;81(3):624-32.

Influence of apolipoprotein E genotype on fat-soluble plasma antioxidants in Spanish children.

Ortega H, Castilla P, Gómez-Coronado D, Garcés C, Benavente M, Rodríguez-Artalejo F, de Oya M, Lasunción MA.

Nimitphong *et al. Nutrition Journal* 2013, **12**:39
http://www.nutritionj.com/content/12/1/39

NUTRITION JOURNAL

RESEARCH Open Access

Changes in circulating 25-hydroxyvitamin D according to vitamin D binding protein genotypes after vitamin D_3 or D_2 supplementation

Intra- and Inter-Individual Variations of Blood and Urinary Water-Soluble Vitamins in Japanese Young Adults Consuming a Semi-Purified Diet for 7 Days

J Nutr Sci Vitaminol, **55**, 459–470, 2009

The Journal of Nutrition
Nutrient Requirements and Optimal Nutrition

J. Nutr. 138: 67–72, 2008

Folate Intake at RDA Levels Is Inadequate for Mexican American Men with the Methylenetetrahydrofolate Reductase 677TT Genotype[1–3]

Claudia Solis,[4] Kristin Veenema,[4] Alexandre A. Ivanov,[4] Sally Tran,[4] Rui Li,[4] Wei Wang,[5] David J. Moriarty,[6] Charles V. Maletz,[7] and Marie A. Caudill[8]*

The Journal of Nutrition
Nutritional Epidemiology

J. Nutr. 142: 866–871, 2012.

Genome-Wide Association Study Identifies Three Common Variants Associated with Serologic Response to Vitamin E Supplementation in Men[1–4]

Jacqueline M. Major,[5] Kai Yu,[5] Charles C. Chung,[6] Stephanie J. Weinstein,[5] Meredith Yeager,[6] William Wheeler,[7] Kirk Snyder,[7] Margaret E. Wright,[8] Jarmo Virtamo,[9] Stephen Chanock,[5, 6] and Demetrius Albanes[5]*

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The complex interplay of drugs with nutrients

DRUGS

NUTRIENTS

Food intake

Appetite, taste

Absorption

Binding, stomach acidity, transport

Stomach empting rate, acidity, binding

Metabolism

Enhance/inhibit enzyme activities

Modulate bioavaibility, efficacy

Excretion

Alter mineral reabsorption (kidneys), urinary nutrient losses (folate, B_2,B_6, Mg, Zn)

Modulate xenobiotic excretion (urine acidity)

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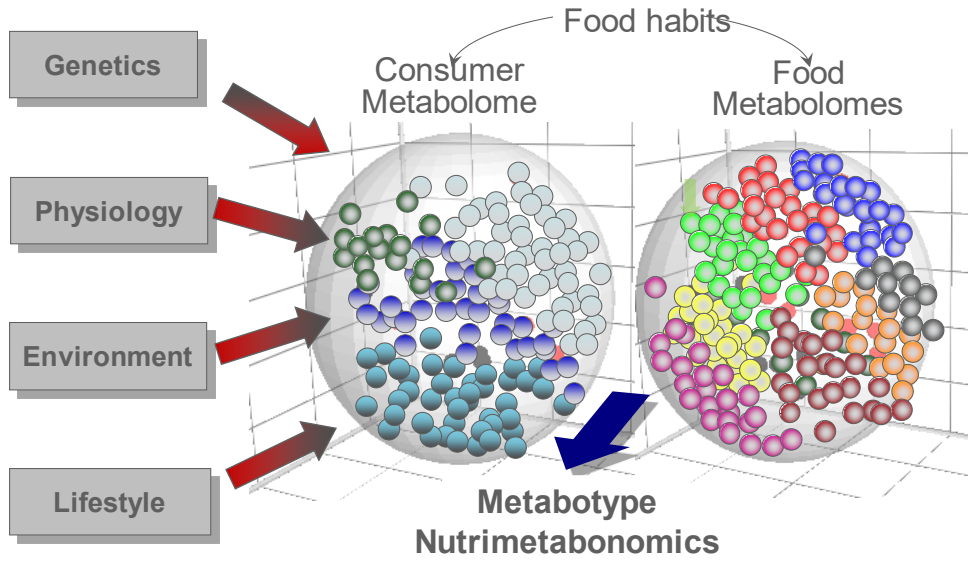
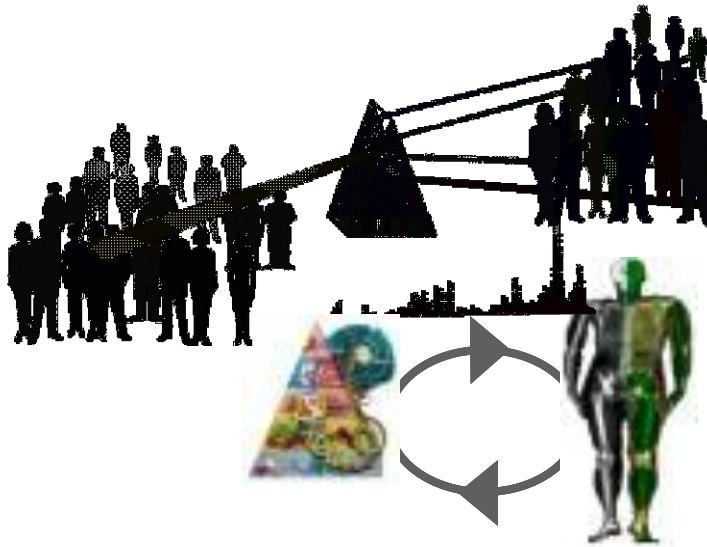
Workflow in precision nutrition

1 - Understanding of the nutrient-organism interaction and impact on health status
Nutrikinetics & nutridynamics

2 - Quantification of health optimization: Nutrition and health indicators (nutrition status)

3 - Implement personalized nutrition and monitor for efficacy





Precision Nutrition

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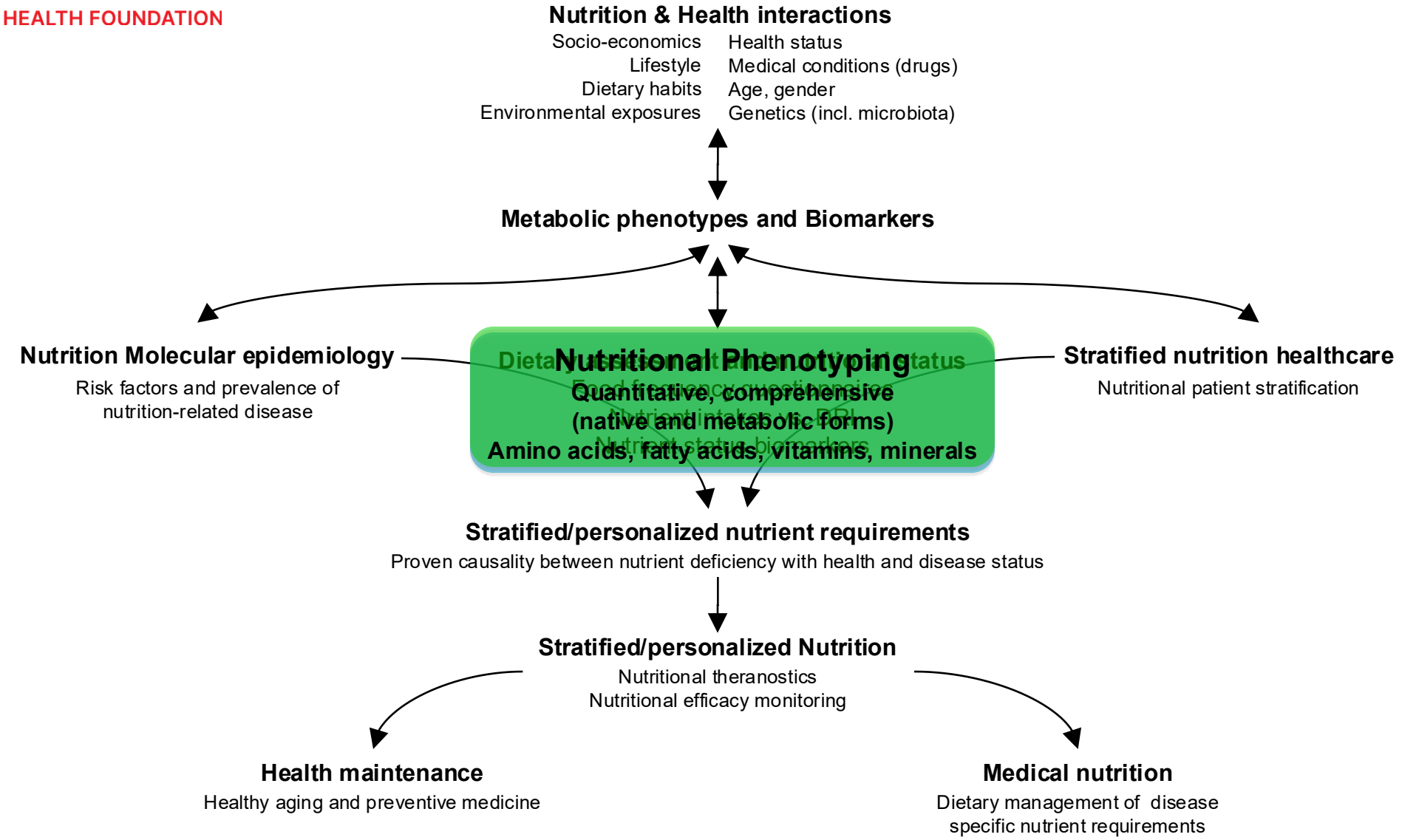
Towards Precision Nutrition



* From Rezzi et al. Trends in Analytical Chemistry, 2013