UNIVERSITÀ
DI SIENA
1240

GISMO
Gruppo Italiano Studio
Malattie Metabolismo Osseo

Ipovitaminosi D

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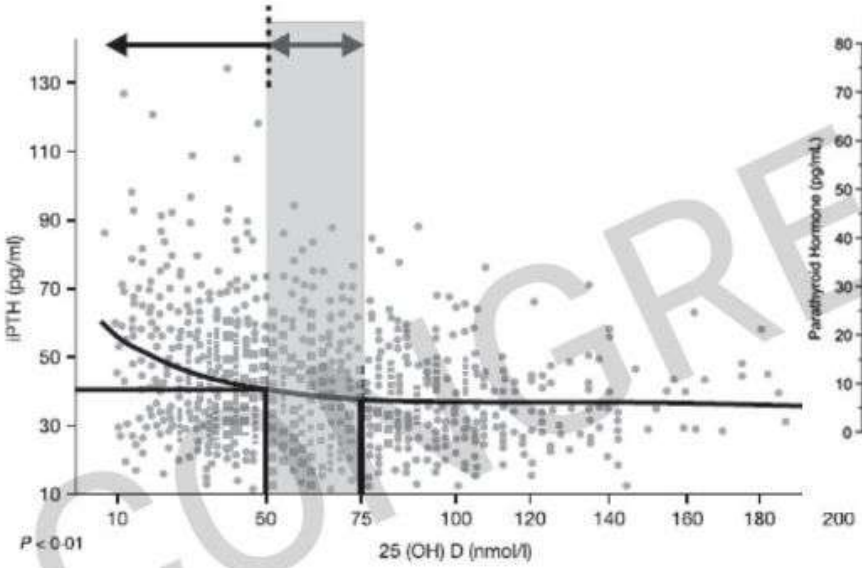
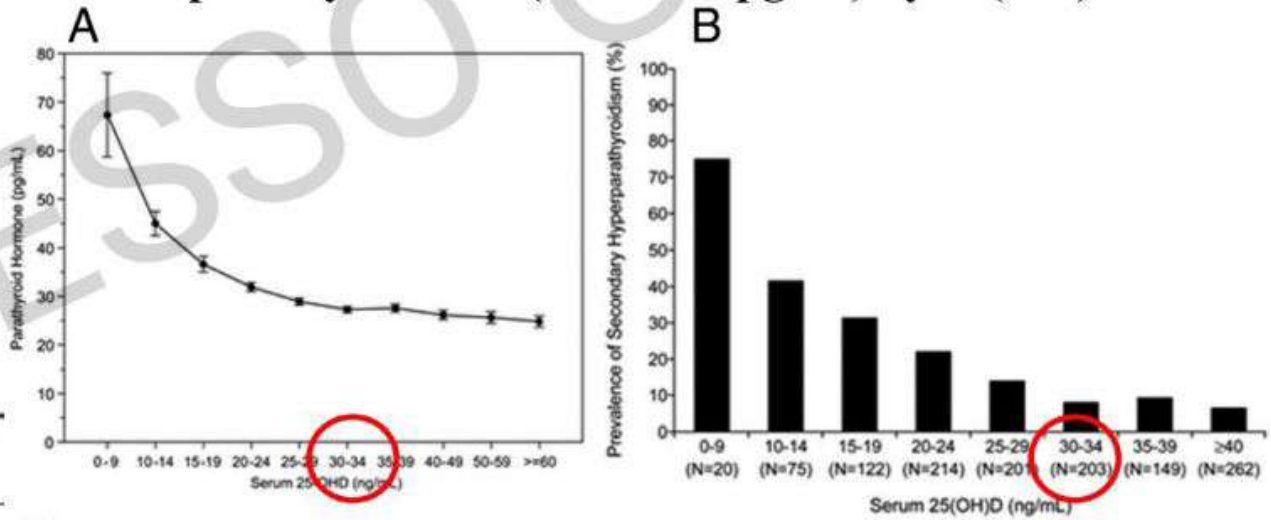
Identification of optimal 25(OH)D values according to iPTH levels

Relationship between 25[OH]D and PTH



Lips P. et al. 2010

A. **PTH values began to increase with 25(OH)D concentrations less than 29.8 ng/ml.**
B. **B. Percent of subjects with secondary hyper-parathyroidism (PTH <40 pg/ml) by 25(OH)D level.**



Holick et al, 2012

National Institutes of Health
Office of Dietary Supplements

Vitamin D

Fact Sheet for Health Professionals

Table 1: Serum 25-Hydroxyvitamin D [25(OH)D] Concentrations and Health [1]

nmol/L*	ng/mL*	Health status
<30	<12	Associated with vitamin D deficiency, which can lead to rickets in infants and children and osteomalacia in adults
30 to <50	12 to <20	Generally considered inadequate for bone and overall health in healthy individuals
≥50	≥20	Generally considered adequate for bone and overall health in healthy individuals
>125	>50	Linked to potential adverse effects, particularly at >150 nmol/L (>60 ng/mL)

Institute of Medicine, Food and Nutrition Board. Dietary Reference Intakes for Calcium and Vitamin D. Washington, DC: National Academy Press, 2010.

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Review

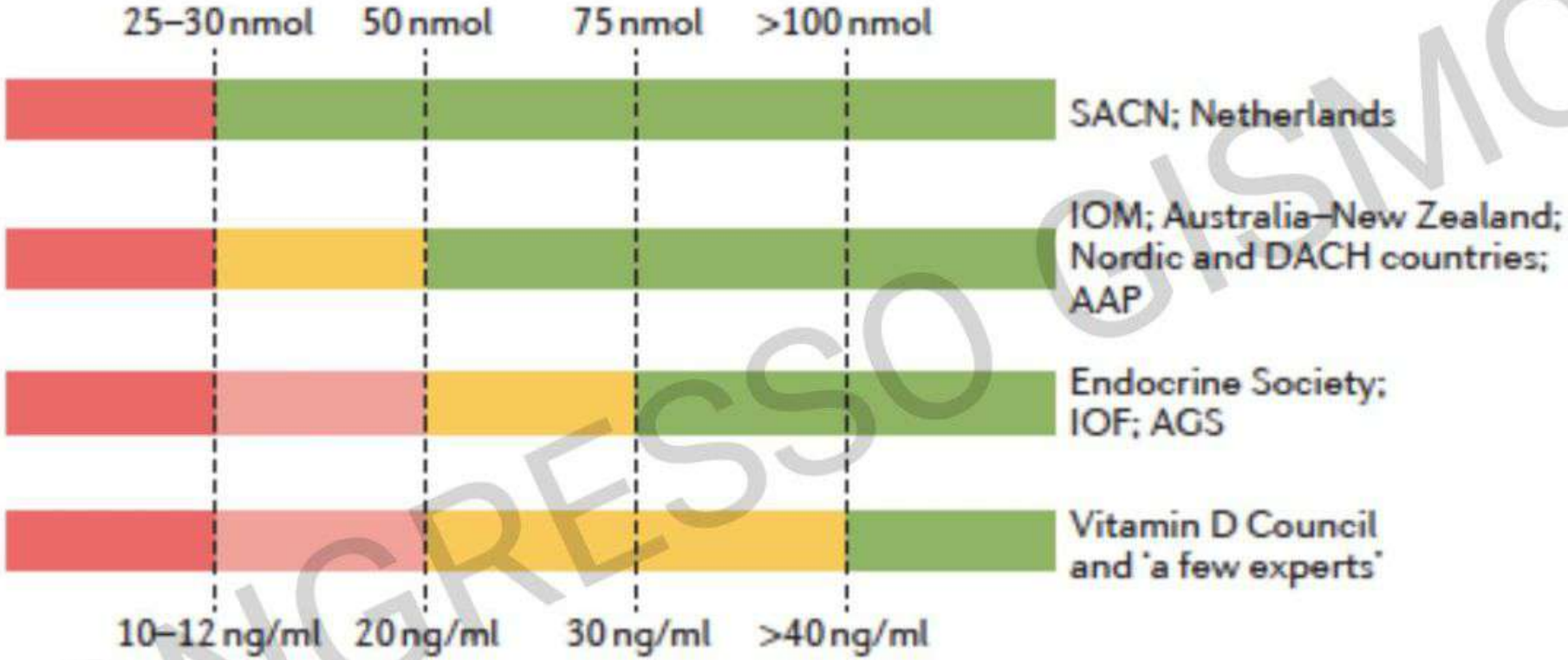
Definition, Assessment, and Management of Vitamin D Inadequacy: Suggestions, Recommendations, and Warnings from the Italian Society for Osteoporosis, Mineral Metabolism and Bone Diseases (SIOMMMS)

Definition of Vitamin D Status

	Deficiency *	Insufficiency *	Optimal * Optimum *
GENERAL POPULATION	<10 ng/mL	<20 ng/mL	**20–50 ng/mL**
POPULATION AT RISK ** OR ON TREATMENT WITH *BONE MODIFYING AGENTS*	<10 ng/mL	<30 ng/mL	**30–50 ng/mL**

* Reported cut-off values should be considered with a margin of variability of +/−10%, considering the analytical variability of the 25(OH)D dosage. Moreover, due to the seasonal variability of 25(OH)D levels, a dosage performed at the end of winter/early spring should be particularly considered. A serum value of <10 ng/mL (25 nmol/L) is associated with rickets and osteomalacia, if long lasting. From ng/mL to nmol/L: ng/mL × 2.5.
** The population at risk of hypovitaminosis is shown in Table 2.

Recommendations for interpreting serum levels of 25OHD

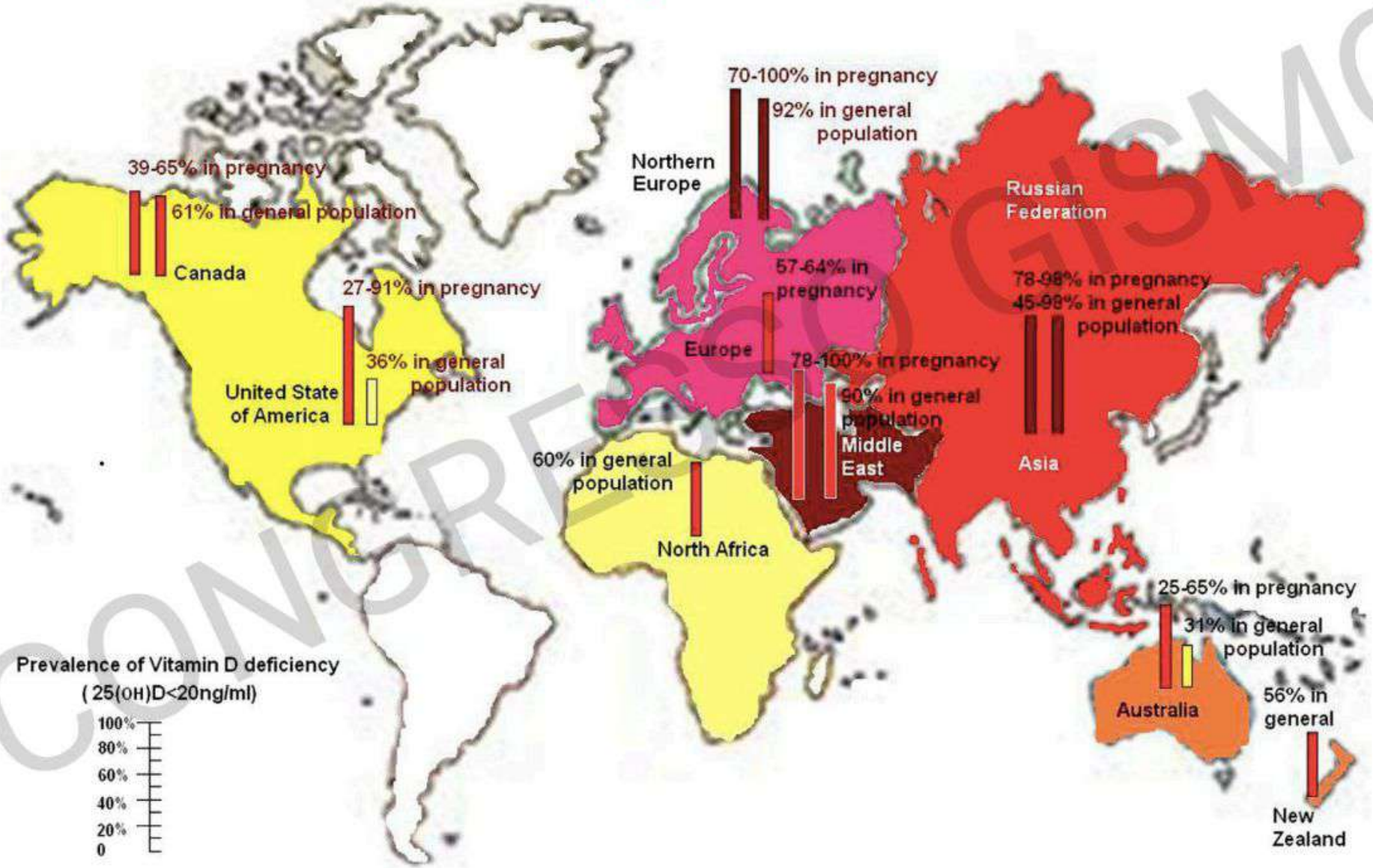


Colour code: red denotes a state of severe deficiency (danger) that has to be corrected without exception; orange denotes a state of mild deficiency, in which intervention is desirable; green denotes a state of sufficient supply that does not benefit from additional supplementation

AAP, American Academy of Pediatrics; AGS, American Geriatrics Society; DACH, Deutschland (Germany), Austria and Confoederatio Helvetica (Switzerland); IOF, International Osteoporosis Foundation; IOM, Institute of Medicine; SACN, Scientific Advisory Committee on Nutrition.

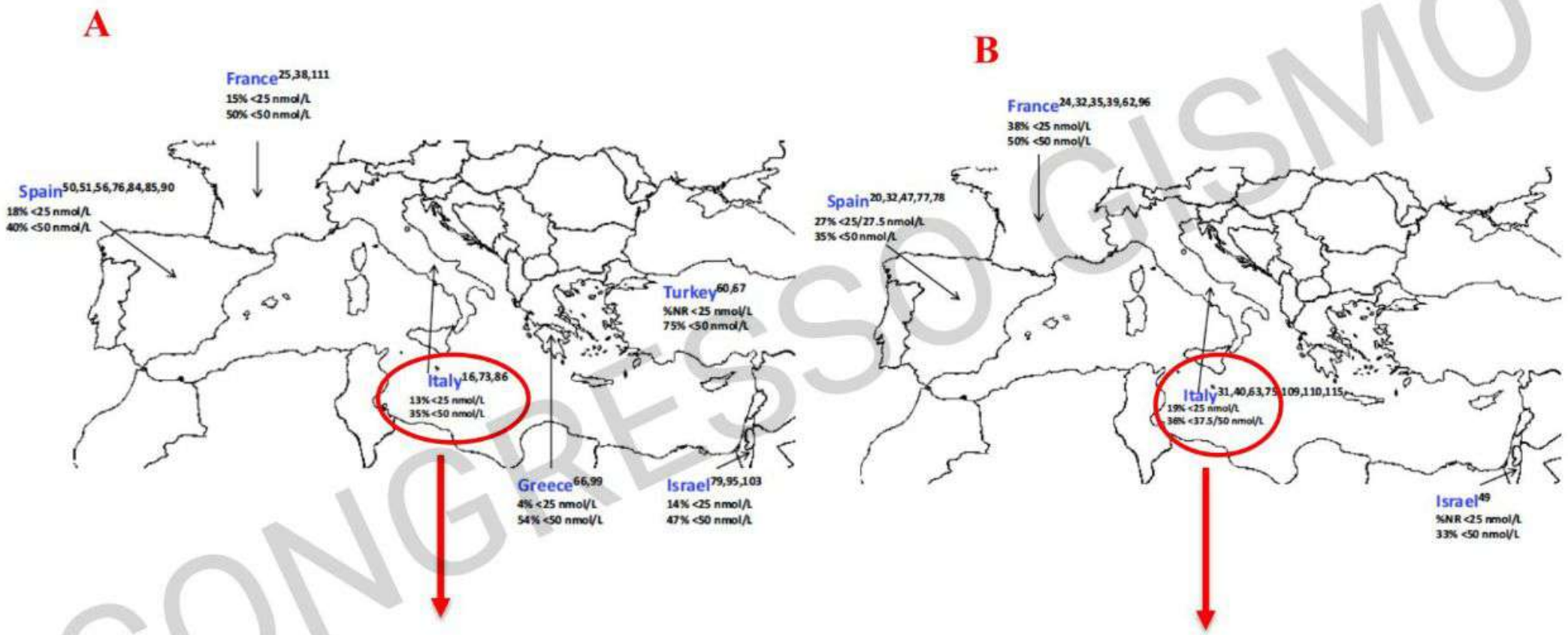
Bouillon R. et al. 2017

Reported incidence of vitamin D deficiency defined as a 25OHD level below 20 ng/ml around the globe in pregnant women and general population.



Holick M. 2013

The prevalence of circulating 25(OH)D concentration below 25 and 50 nmol/L in studies of adults (A) and of the elderly, including postmenopausal women (B), from Southern European (and east Mediterranean) countries.



13% <25 nmol/L (10 ng/ml)
35% <50 nmol/L (22 ng/ml)

19% <25 nmol/L (10 ng/ml)
36% <37.5/50 nmol/L (15/22 ng/ml)

One nmol/L is equal to 0.4 ng/mL.

Manios Y. et al. Eur J Nutr 2018

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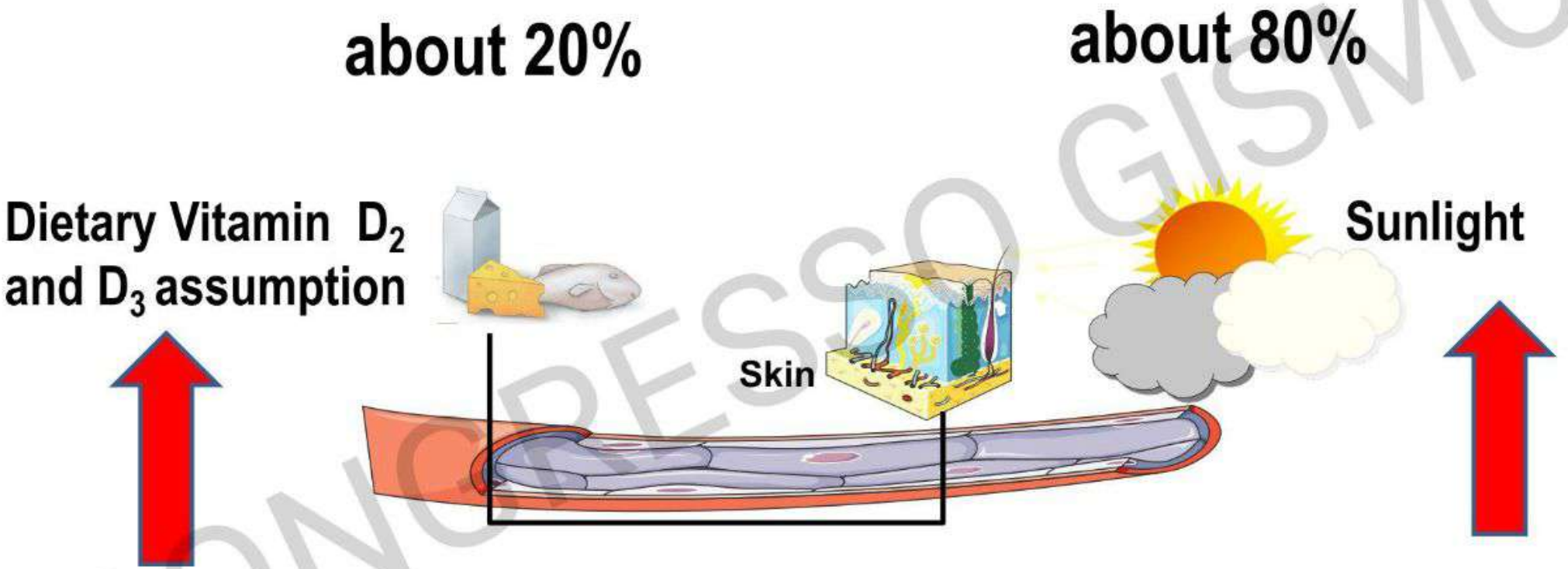
Review

Definition, Assessment, and Management of Vitamin D Inadequacy: Suggestions, Recommendations, and Warnings from the Italian Society for Osteoporosis, Mineral Metabolism and Bone Diseases (SIOMMMS)

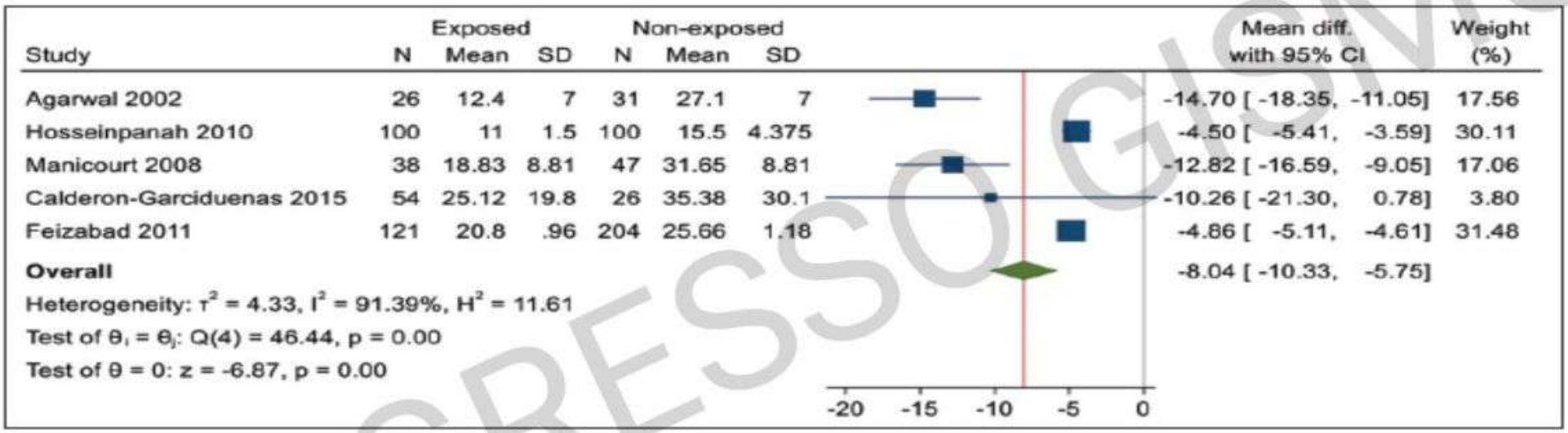
Population/condition at risk of hyvitaminosis D

- Old people (≥75 years)
- Institutionalized subjects or conditions associated with inadequate solar exposure
- Obesity
- Pregnancy and breast-feeding
- Metabolic bone diseases and other skeletal disorders
- Vegan diet
- Anorexia nervosa
- Chronic renal failure
- Cancer (in particular breast, prostate, and colon)
- Type 2 diabetes mellitus
- Intestinal malabsorption and bariatric surgery
- Drugs that interfere with the absorption or hepatic metabolism of vitamin D (antiepileptics, glucocorticoids, antiviral AIDS, antifungal agents, cholestyramine)
- Cystic fibrosis

Vitamin D sources



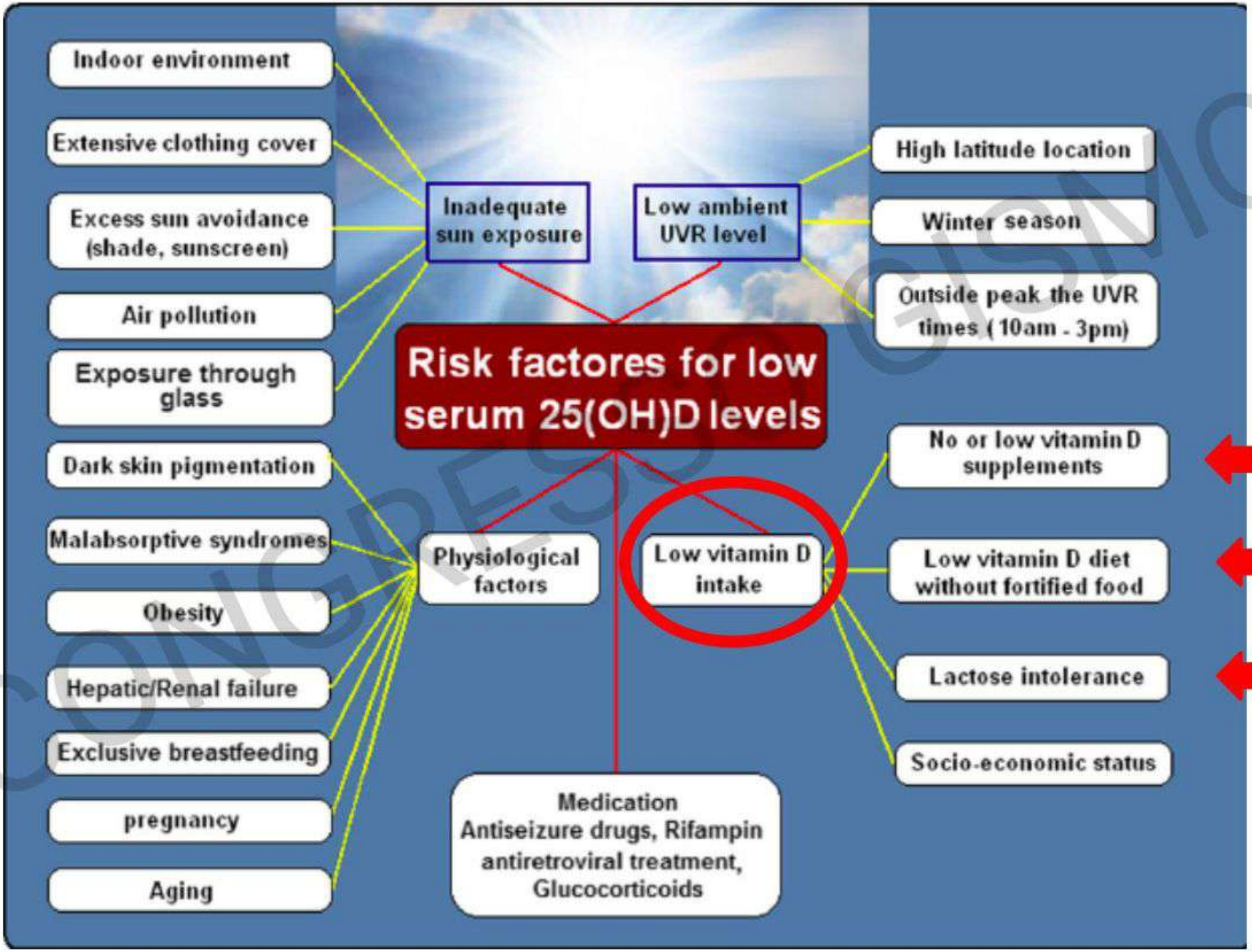
Relationship between Air Pollution and Serum Vitamin D Levels: A Systematic Review and Meta-Analysis



Exposure to air pollution was associated with lower vitamin D levels (pooled mean difference (MD) = -8.04, 95% confidence interval (CI): -10.34, -5.75). Consequently, the occurrence of vitamin D deficiency could be linked to air pollution.

Golastani B. Adv Biomed Res 2024;13:96.

Risk factors of hypovitaminosis

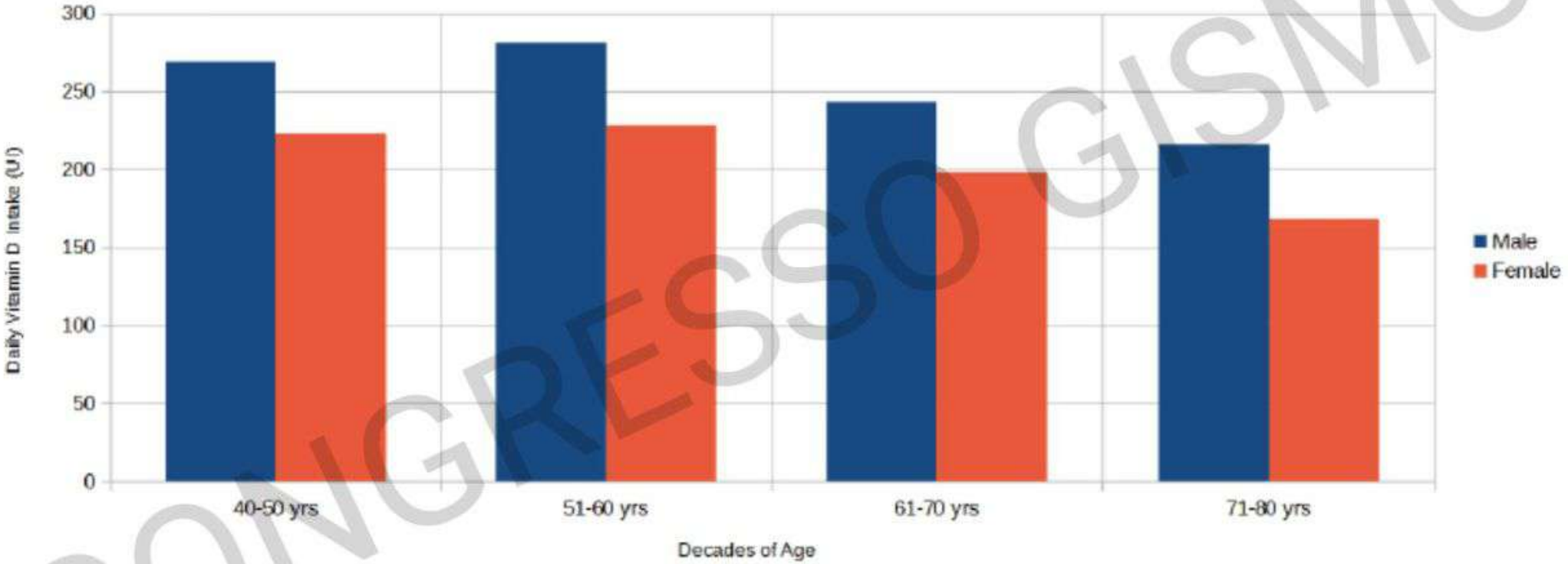


What causes vitamin D deficiency?

You can become deficient in vitamin D for different reasons:

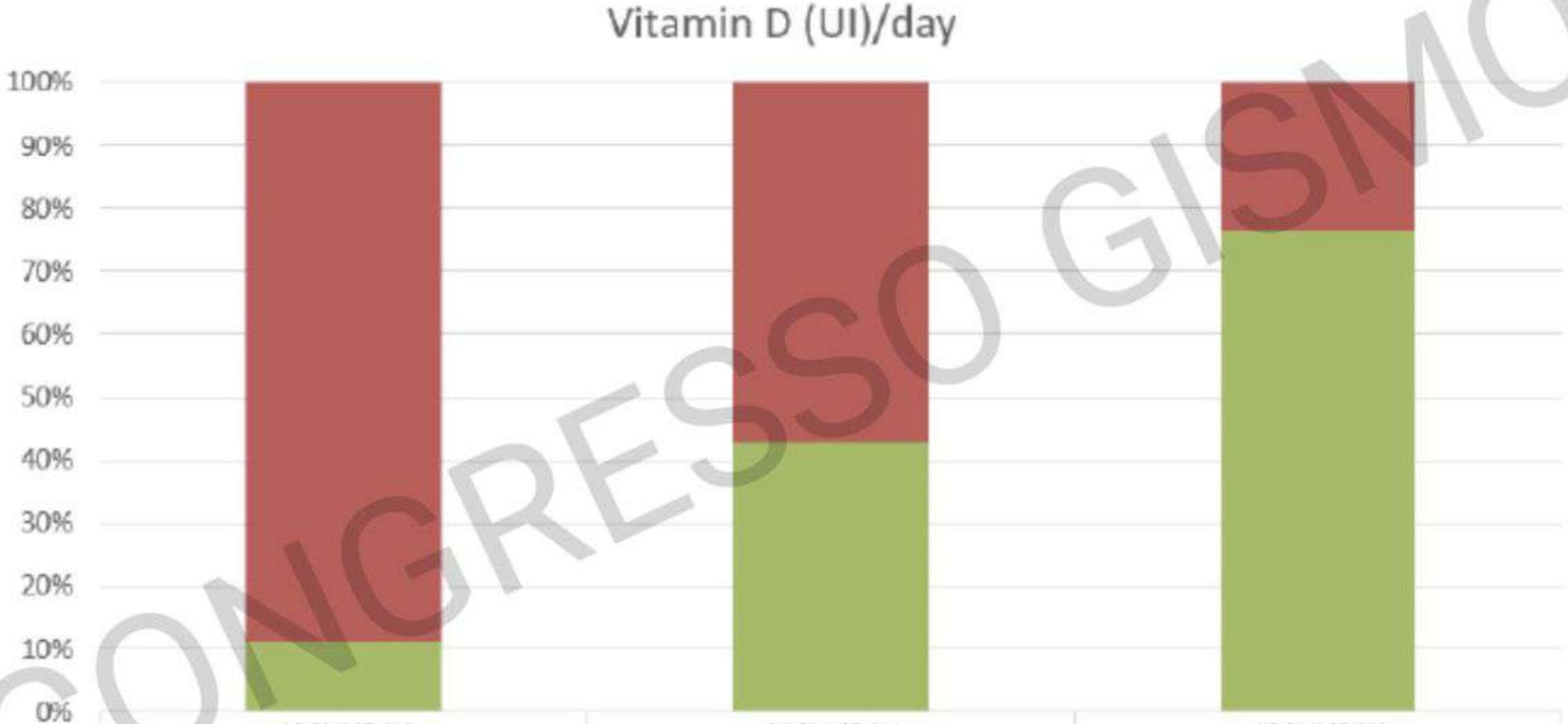
- You don't get enough vitamin D in your diet
- You don't absorb enough vitamin D from food (a malabsorption problem)
- You don't get enough exposure to sunlight
- Your liver or kidneys cannot convert vitamin D to its active form in the body
- You take medicines that interfere with your body's ability to convert or absorb vitamin D

Daily intake of vitamin D in males and females according to age



Nutrients 2024, 16, 4194.

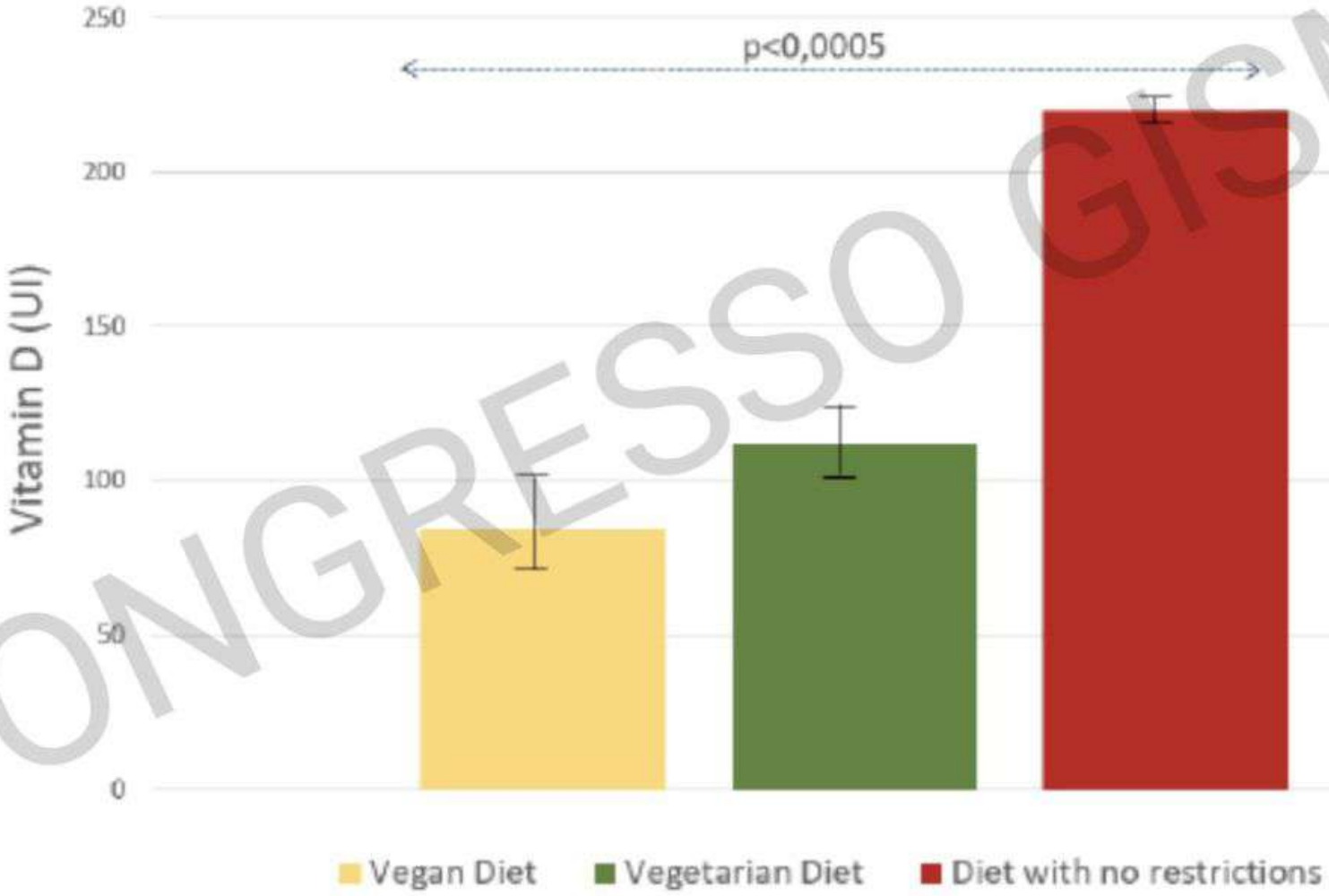
Percentage of subjects reaching 2.5 µg (100 IU), 5.0 µg (200 IU) or 10.0 µg (400 IU) daily intake of vitamin D



	400UI/DAY	200UI/DAY	100UI/DAY
NO	88,70%	57,20%	23,60%
YES	11,30%	42,80%	76,40%

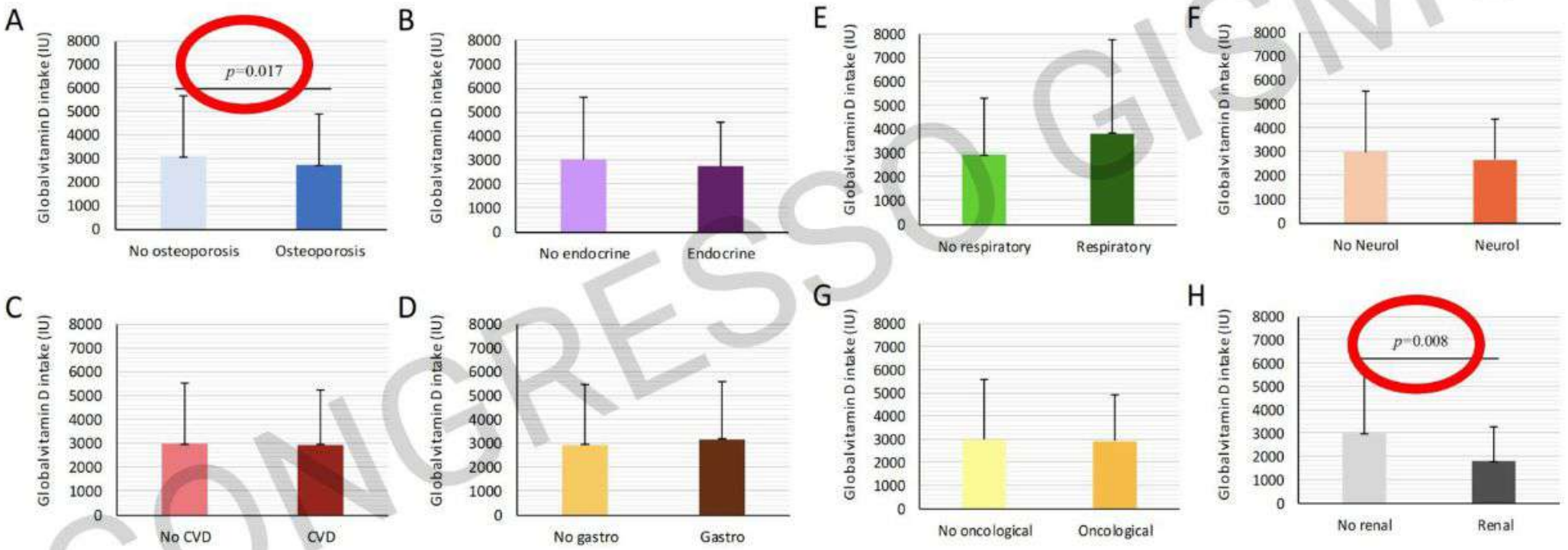
Nutrients 2024, 16, 4194.

Mean daily vitamin D intake in vegan, vegetarian and no-restriction diets



Nutrients 2024, 16, 4194.

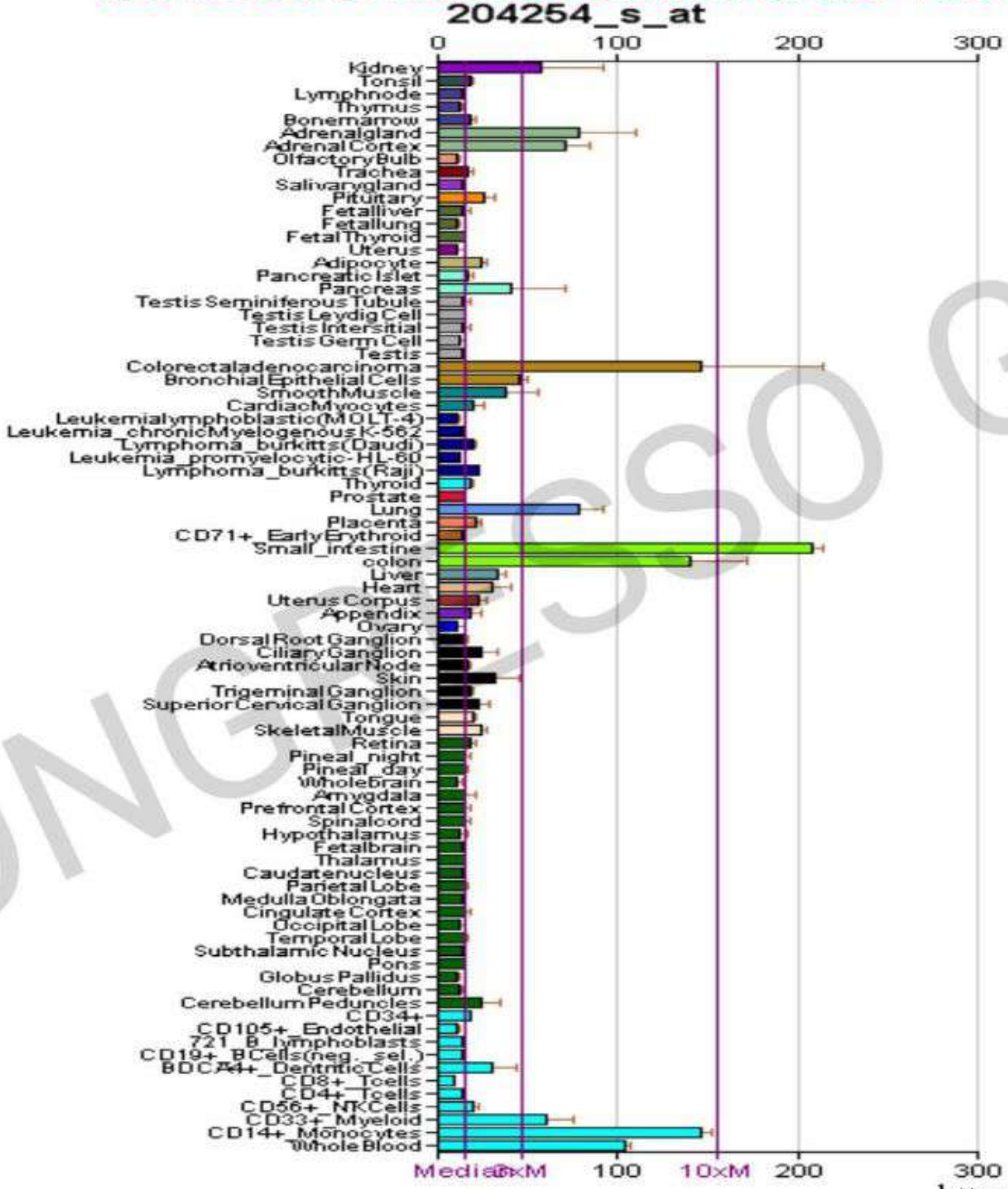
Mean global vitamin D intake in patients with and without specific pathological conditions.



Daily intake in most patient groups averaged around 200 IU/day or less. Patients with osteoporosis, and renal disorders had significantly lower intake than in healthy individuals (p=0.017 and p<0.008, respectively).

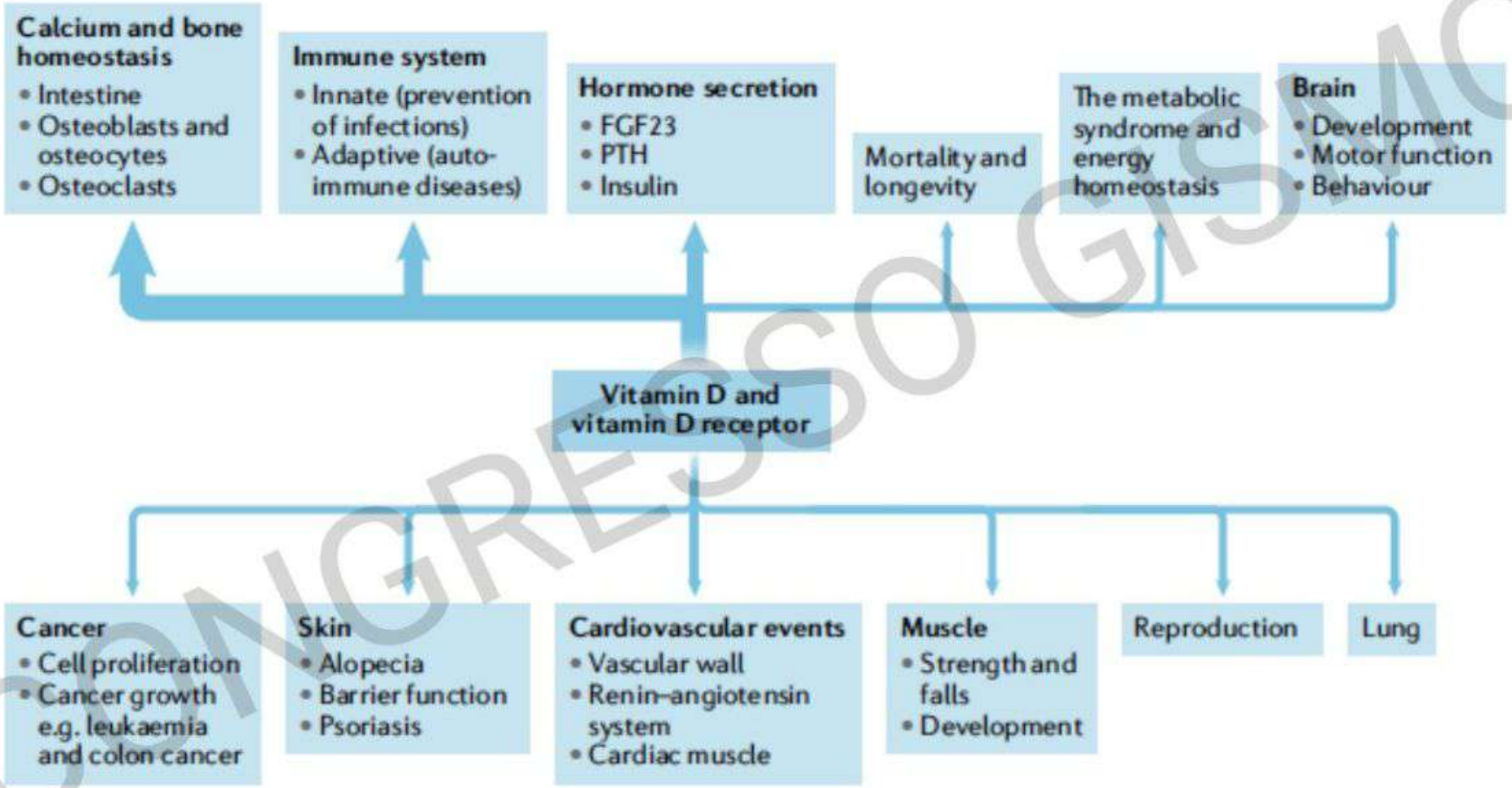
N uti R. et al.Front. Nutr. 12:1672798. doi: 10.3389/fnut.2025.

Many in vitro and in vivo studies have demonstrated that 1,25(OH)2D is able to regulate a very large number of genes; about 3% of the human genome is under the direct or indirect control of the VDR system



http://biogps.gnf.org/updated october 2010

The many plausible target tissues and effects of the vitamin D



Bouillon R. et al. 2022

Vitamin D deficiency – Hypovitaminosis D

Clinical outcome

- **Rickets in children**
- **Osteomalacia, often with myopathy (asthenia)**
- **Low bone density, secondary hyperparatiroidism, osteoporosis**

Bone pain, muscle weakness or aches, deformed bones, fragility fractures

- **Cancer ?**
- **Cardiovascular events ?**
- **Lung function and respiratory effects ?**
- **Autoimmune diseases ?**
- **Diabetes ?**
- **Mortality ?**

Consequences of Vitamin D Inadequacy

↓25-OH-D

↓ Intestinal calcium absorptionn

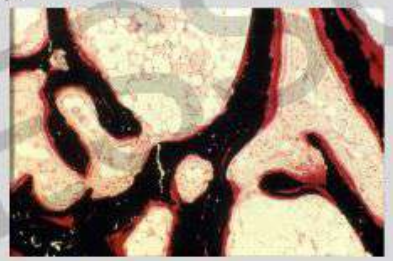
↓ Serum calcium

Deficiency

Insufficiecy

↓1,25 $(OH)_2$ D

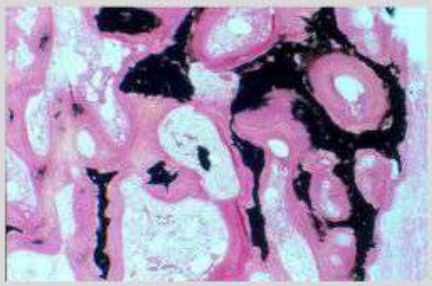
↑ Parathyroid Hormone

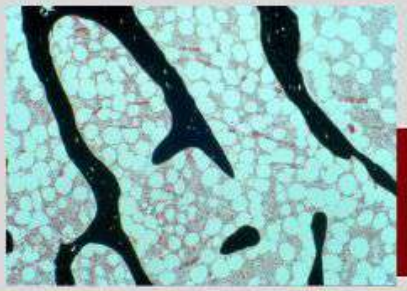


↓Matrix Mineralizationin

Osteoporomalacia?

↑ Bone Turnover





Osteoidosis Osteomalacia

Osteopenia Osteoporosis

Overview of the large vitamin D supplementation clinical trials 2017–2020

Study	Country	Number of patients	Age (years, mean ± SD)	Ethnicity[a] (% white ethnicity)	Serum 25OHD (ng/ml)		Duration of follow-up (years)	Intervention (vitamin D vs placebo)	Primary outcome(s)
					Baseline	Final[b]			
VITAL[c]	USA	25,874	67 ± 7	71	30.8 ± 10	42 ± 10	5.3	2,000 IU per day	Cancer and cardiovascular disease
ViDA	New Zealand	5,110	66 ± 8	83	26.5 ± 9[d]	54 ± 16	3.3	One dose of 200,000 IU and 100,000 IU per month	Cardiovascular events and mortality
D2d	USA	2,423	60 ± 10	67	28.0 ± 10.2	54 ± 15	2.5	4,000 IU per day	T2DM
DO-HEALTH	Europe	2,157	74.9 ± 4.4	NM	22.4 ± 8.4	37.6 ± 11.3	3	2,000 IU per day[e]	Six health outcomes[f]
Calgary	Canada	373	62 ± 4	94	31 ± 8	80 ± 16[g]	3	400, 4,000 or 10,000 IU per day	BMD

Bouillon R et al. 2022

Key points

- Vitamin D and calcium supplementation can cure nutritional rickets and can modestly decrease the risk of major fractures in older adults with poor vitamin D status or calcium intake.

- Large supplementation trials recruiting vitamin D-replete adults (serum 25OHD concentration >50 nmol/l) have demonstrated no effects on the incidence of cancer, cardiovascular events or type 2 diabetes mellitus and no benefits in terms of bone density and the risk of falls.

- Post-hoc analysis of large supplementation trials has suggested that supplementation of individuals with vitamin D deficiency modestly delays age-related bone loss and progression to T2DM, and improves lung function.