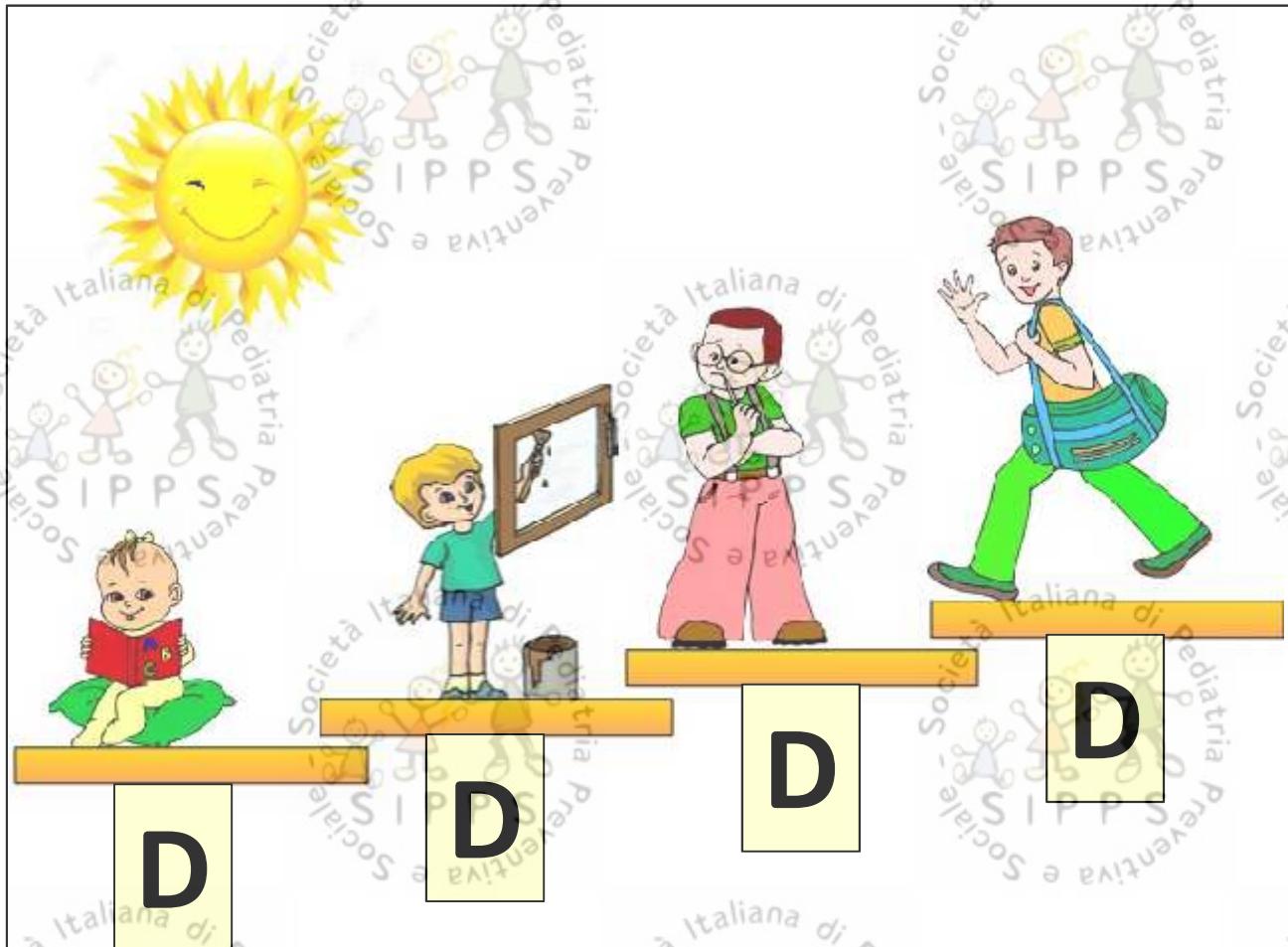


D-ventare grandi: la vitamina D nella seconda e terza infanzia



Francesco Vierucci

Skeletal and extraskeletal actions of vitamin D: current evidence and outstanding questions

ESSENTIAL POINTS

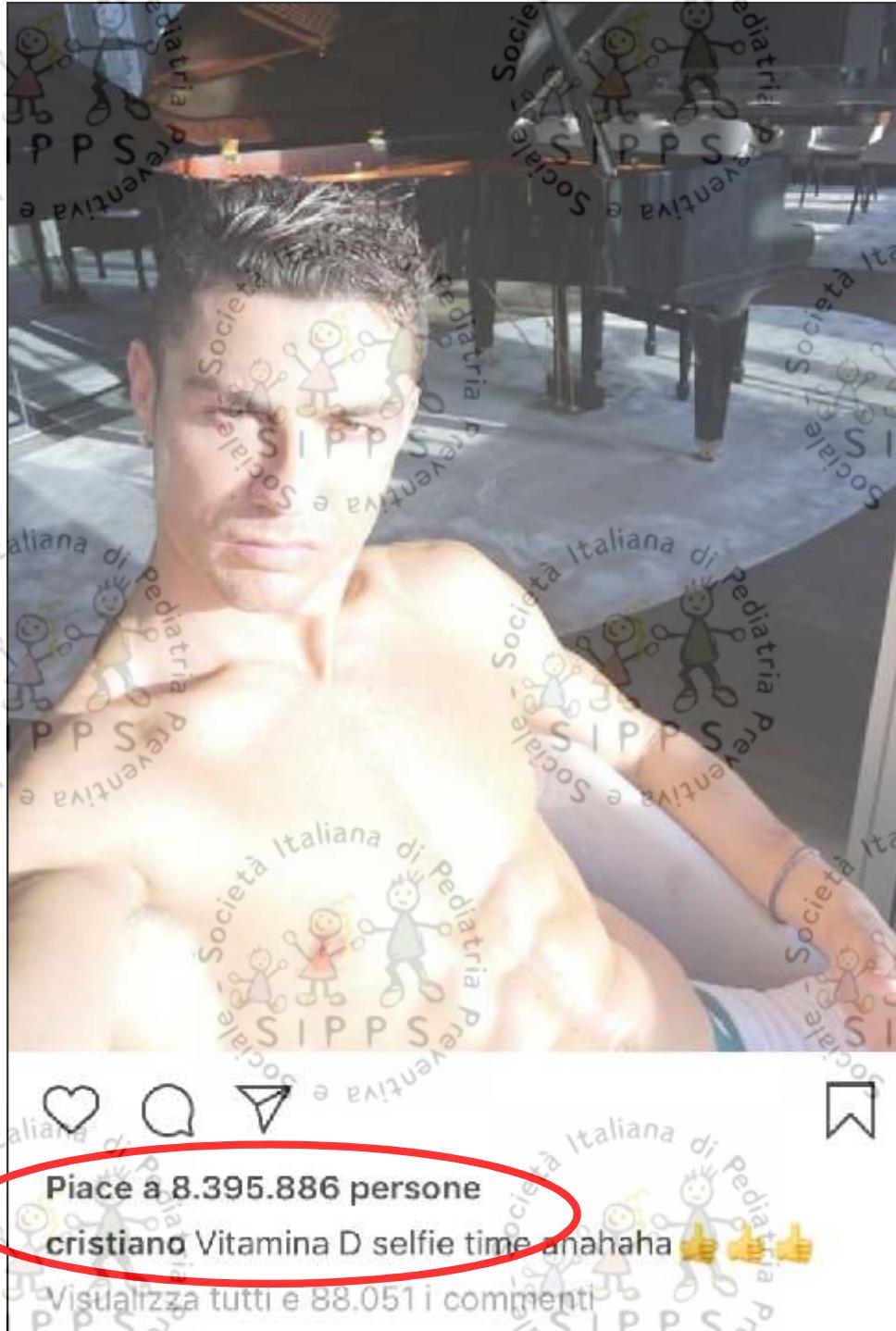
- Vitamin D prevents and cures nutritional rickets but implementation of an adequate intake is problematic in many countries or for subgroups of the world population.
 - The near universal distribution of the vitamin D receptor along with the large number of genes under its control in the human genome suggests a major role for vitamin D in the endocrine system.
 - Most animal tissues contain receptors for vitamin D.
- According to the National Institutes of Health ClinicalTrials.gov register, ~3000 RCTs dealing with vitamin D are still ongoing
- Addressed, in the past several years, a link between genetically lower 25-hydroxyvitamin D levels and skeletal or extraskeletal health outcomes; the best documented link so far is found between 25-hydroxyvitamin D levels and bone mineral content.
- Intervention studies for extraskeletal health effects are so far inconclusive, but the results of several ongoing randomized clinical trials may help to delineate these effects more clearly.

Il rachitismo
esiste ancora

La vit D controlla
il 3% del genoma

Azioni
scheletriche

Azioni extrascheletriche:
OS, MRS, RCTs



Booking.com

Soggiorno di 7 notti

Camere	Adulti	Bambini
1	2	0

Viaggi per lavoro?

Sì

No

Cerca

Tempo di tintarella

Fai il pieno di vitamina D in queste mete soleggiate

Barcellona, Spagna

Roma, Italia



Prima infanzia (0-2 anni)



Seconda infanzia (3-5 anni)



Terza infanzia (6-11/12)



Adolescenza

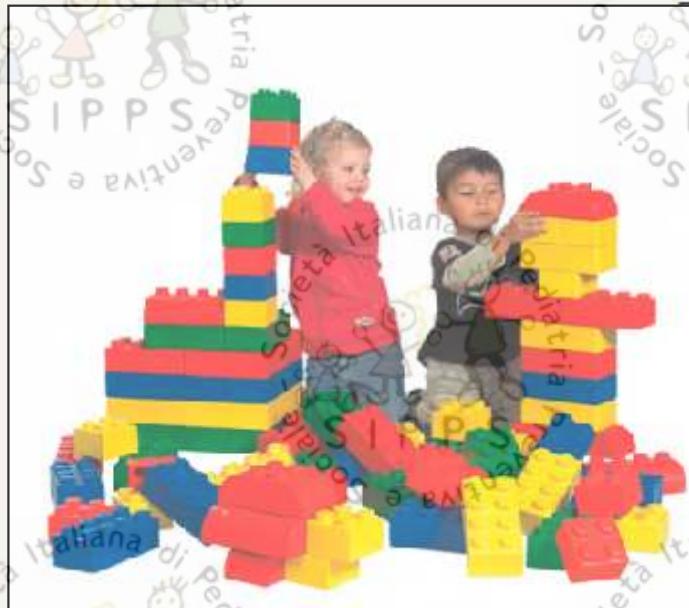
Caratteri sessuali

Statura

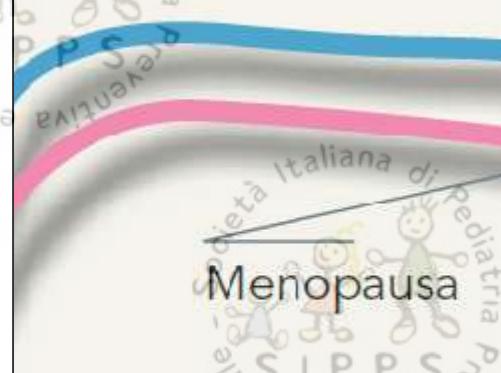


Peso

Massa ossea

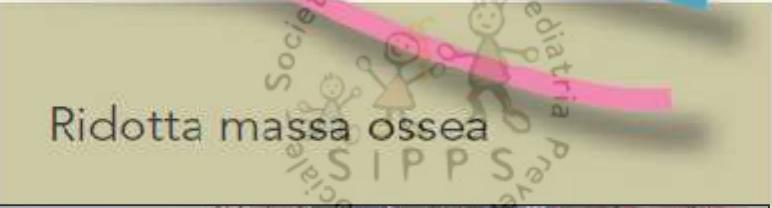


occo di massa ossea



Maschi

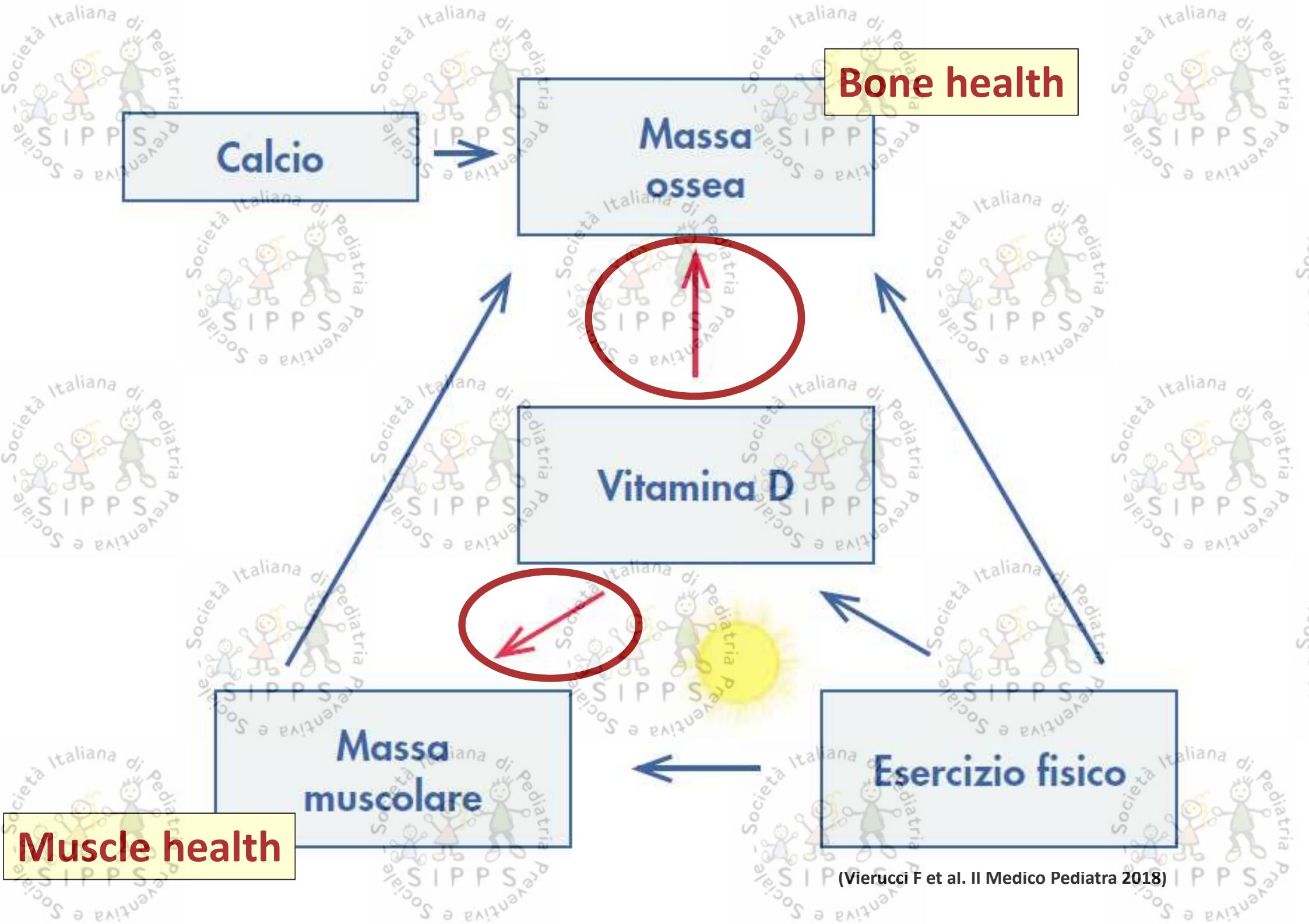
Menopausa

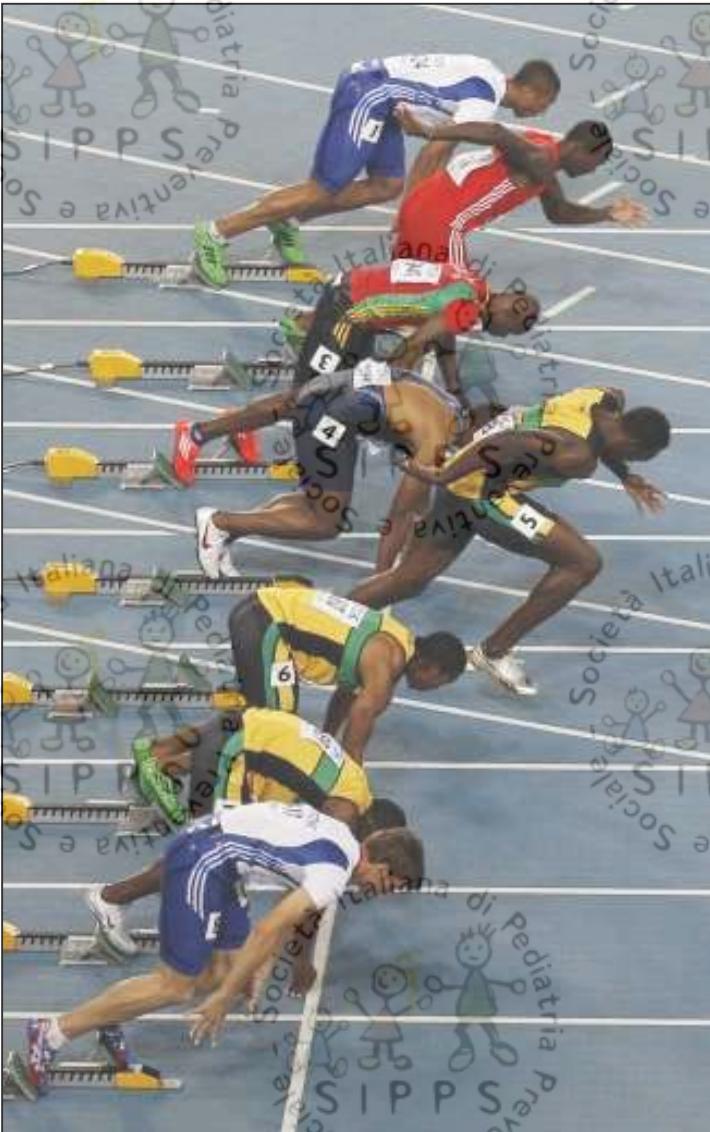


**Stile di
vita (calcio,
esercizio fisico,
vitamina D)
non ottimale**

Età (anni)

(Vierucci F et al. Mondo Pediatrico 2016)





We still don't know that our children need vitamin D daily: a study of parents' understanding of vitamin D requirements in children aged 0-2 years



"I don't remember being given any advice while pregnant or after birth. It wasn't until much later when it was brought up in a group that I became aware" (parent, interview 5)

"It was a checklist, one of the many things, no real explanation of why or benefits. In that environment, you just say okay" (parent 1, focus group 1)

Parents were generally not aware of the importance of vitamin D, dietary requirements including supplementation.

(Day et al. BMC Public Health 2019 Aug)

Fonti di vitamina D

Sources of Vitamin D

- What are the main sources of vitamin D?
- What are the main food sources of vitamin D?
- Can my child get enough vitamin D from sources other than supplements?
- Will my baby receive vitamin D through breast milk?
- Can my baby get enough vitamin D from going outside?
- What kinds of affordable meals can I prepare which contain vitamin D?

Importance of vitamin D

- Why is vitamin D important?
- What are the health benefits of vitamin D?
- What are the benefits of taking vitamin D supplements for me and my child?
- Why do we need vitamin D in our diets?
- What does vitamin D do to your body?
- Why is vitamin D important to take during pregnancy and breastfeeding?
- What are the risks of not getting enough vitamin D in the diet?
- What happens if you take too little or too much vitamin D?
- How much sunlight is needed to get enough vitamin D?

Vitamin D supplements for my baby/child

- Why do I need to give my baby/child a vitamin D supplement?
- When do I need to give a vitamin D supplement to my baby/child?
- Does my baby need vitamin D drops from birth when breastfeeding?
- Does my baby/child need vitamin D supplements when drinking formula milk?
- Does my baby/child need vitamin D supplements when drinking cow's milk?
- How much vitamin D does my baby/child need?
- How much vitamin D does my baby need when breastfeeding?
- How long do I need to give a vitamin D supplement to my baby/child for?
- How often should I give a vitamin D supplement to my baby/child?
- Which vitamin D supplement should I give to my baby/child?
- How do I give vitamin D supplements to my baby/child? E.g. during weaning?
- Are vitamin D supplements the only/best option for my baby?

Vitamin D supplements when breastfeeding or pregnant

- How much vitamin D do I need as a breastfeeding mother?
- How long should I take vitamin D for when breastfeeding?
- How often should I take a vitamin D supplement when pregnant and breastfeeding?
- Why do I need to take vitamin D when breastfeeding?
- Why does my milk not give my baby enough vitamin D?

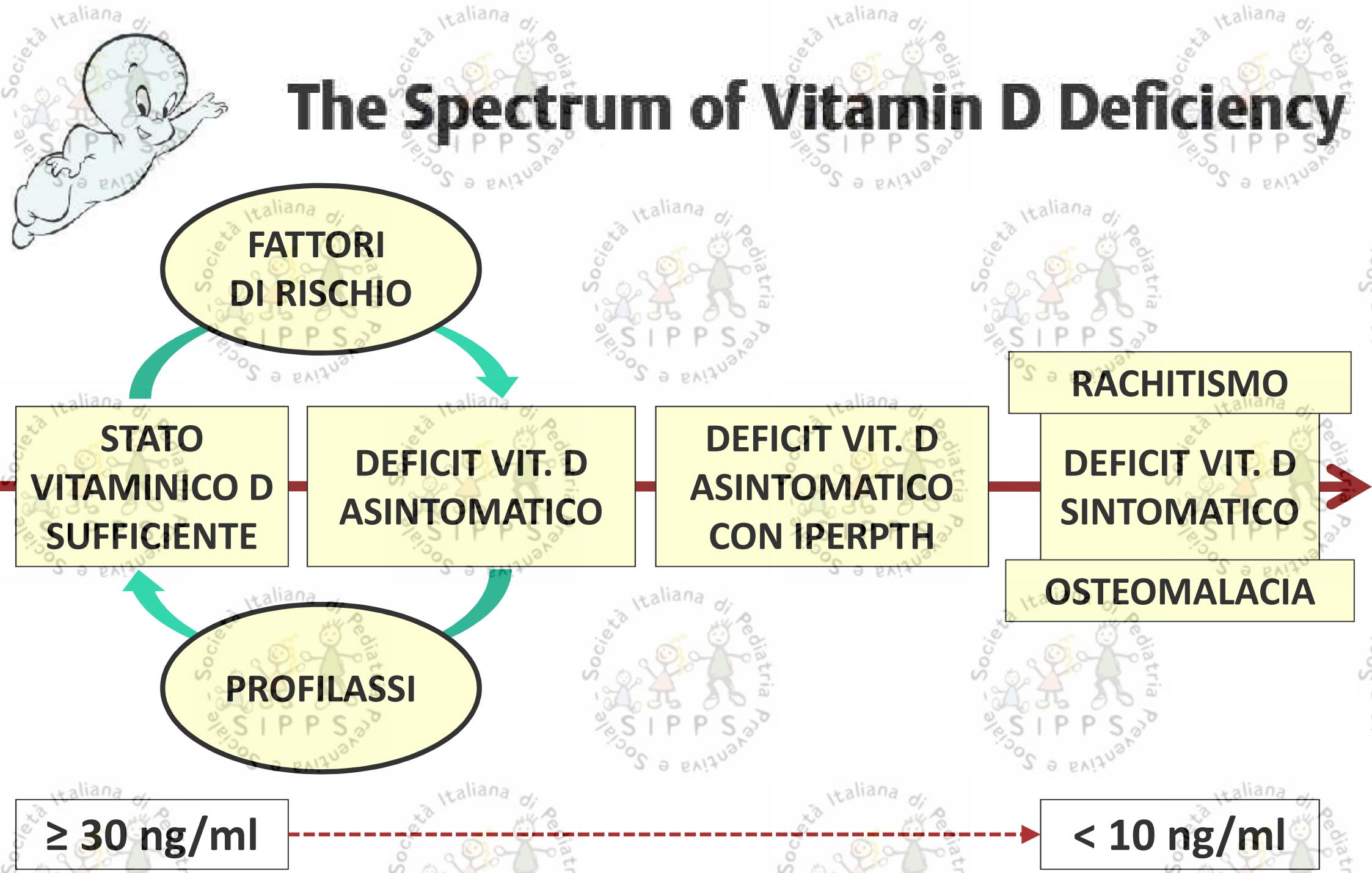
Importanza della vitamina D

Profilassi con vit. D per i bambini

Profilassi con vit. D in gravidanza/allatt.



The Spectrum of Vitamin D Deficiency





Lucca febbraio 2019

Rachid (16 mesi) - I infanzia

In data **03/02/19** febre. La mattina del **04/02** crisi generalizzata tonico clonica.

EGA venoso: pH 7.32; BE -6.0 mmol/l; glicemia 87 mg/dl; calcio ione 0.74 mmol/l.

Nato a **Lucca** il **23/09/2017**

Origine: **Marocco**

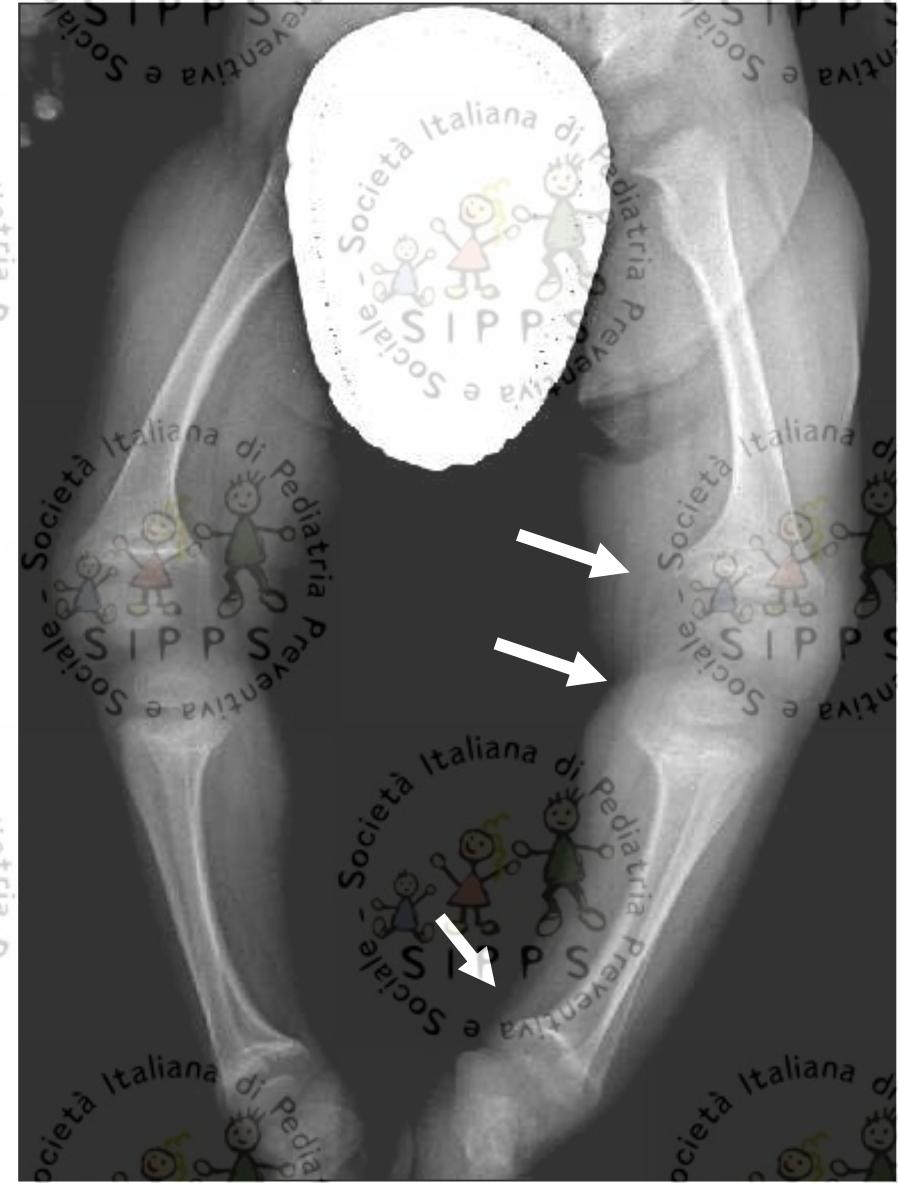
Allattamento al seno per **14 mesi**
(divorzamento regolare)

Fattori di rischio di deficit di vitamina D:

- scarsa esposizione solare,
- no profilassi con vitamina D (consigliata alla dimissione dal nido e dal curante, mai somministrata).

- **25(OH)D: < 4 ng/ml**
- **PTH: 110 pg/ml**
- **ALP: 918 U/l**
- **Fosforo: 3,81 mg/dl**
- **Calcio totale: 6,2 mg/dl**







Lucca febbraio 2019

Nour (3,5 anni) - II infanzia

Bambino con sindrome di **Down**.

Nato a **Lucca** il **08/10/2015**

Origine: **Marocco**

01/03/19: esami di follow-up

- **25(OH)D: < 4 ng/ml**
- **Calcio totale: 8,4 mg/dl**

Fattori di rischio di deficit di vitamina D:

- Scarsa (assente) esposizione solare,
- Profilassi con vitamina D durante il primo anno di vita (durata non precisata, sospetta scarsa compliance).
- N.B. **Scarsa compliance** con il pediatra di libera scelta.

- **PTH: 335 pg/ml**
- **ALP: 350 U/l**
- **Fosforo: 5,9 mg/dl**
- **Calcio ione: 1,05 mmol/l**





**Deficit grave
di vitamina D
($< 4 \text{ ng/ml}$)**

I INFANZIA

Segni ossei
evidenti

IperPTH

Ipocalcemia
sintomatica

II-III INFANZIA

Segni ossei
sfumati (assenti)

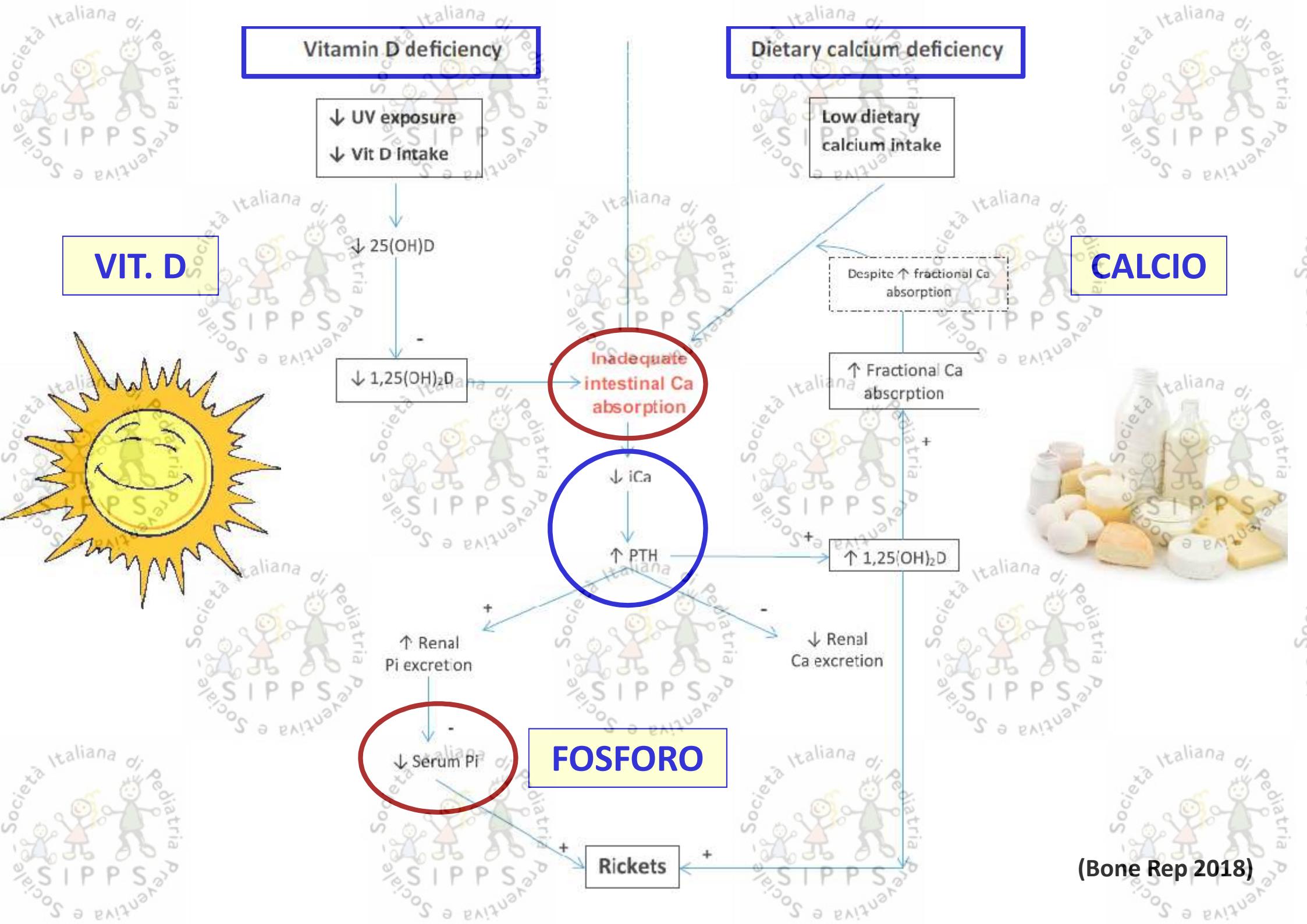
IperPTH

Ipocalcemia
latente

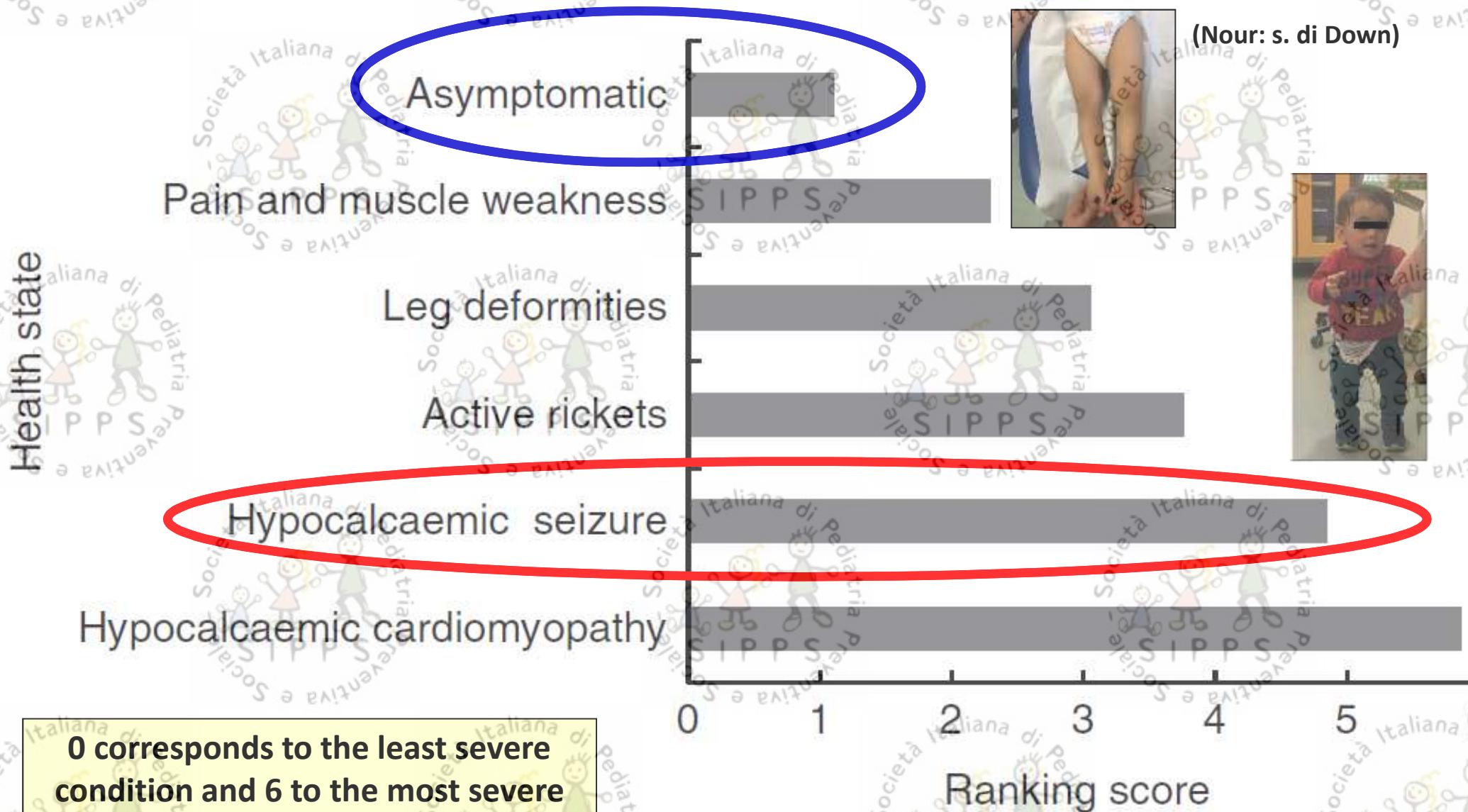
FATTORI DI RISCHIO

DIAGNOSI OCCASIONALE



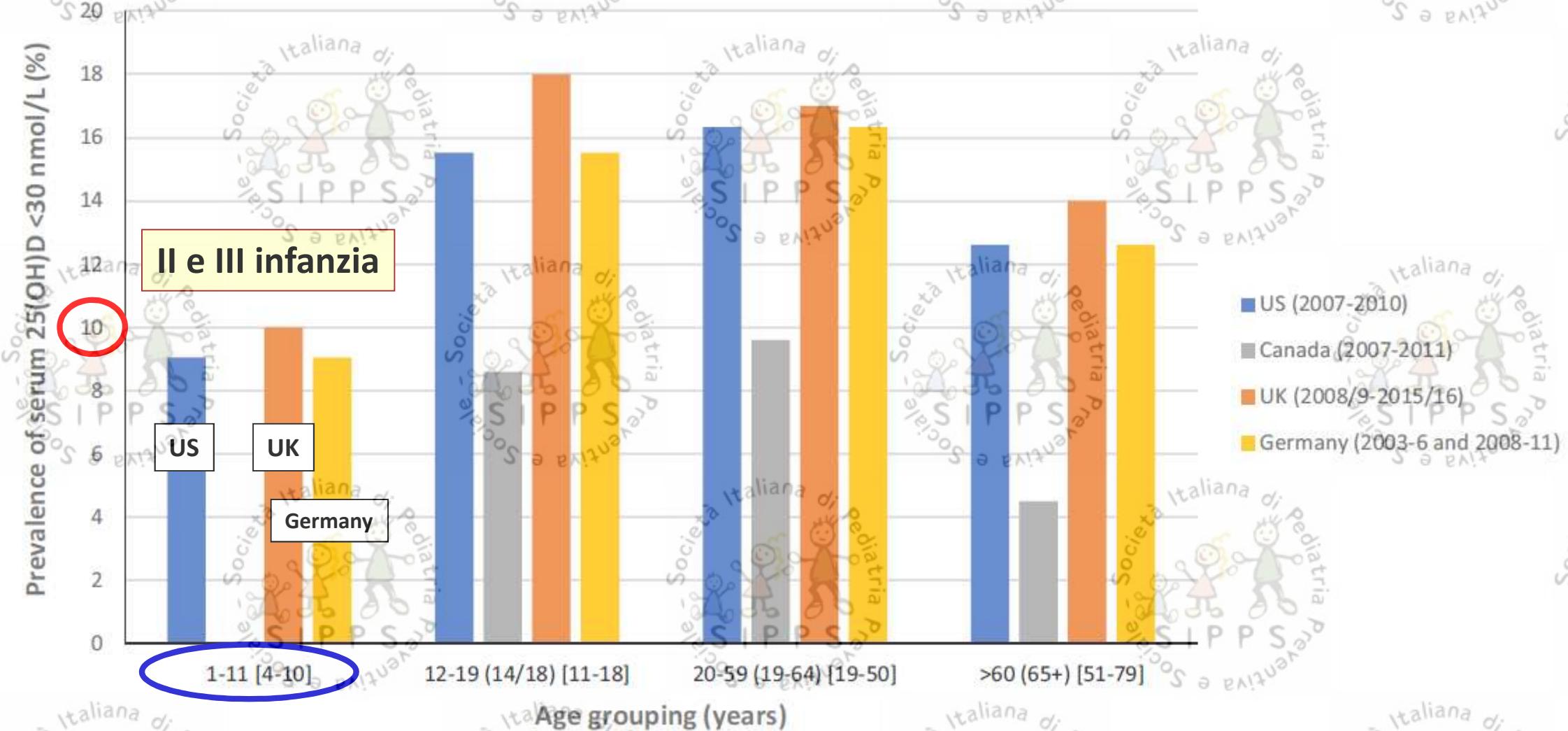


Micronutrient deficiencies and health-related quality of life: the case of children with vitamin D deficiency (38 Pediatric bone experts)



(Aguiar et al. Public Health Nutr 2019 Feb)

Prevalence of standardized serum 25(OH)D < 12 ng/ml in national surveys stratified by age grouping



Quasi 1 bambino su 10 e 1 adolescente su 5 hanno un deficit grave di vit. D

(Cashman. Calcified Tissue International 2019)

Laboratorio Analisi Ex ASL 2 Lucca (Provincia di Lucca, 391.228 abitanti)

Dosaggi vitamina D

Gen 2010-Ott 2018; range età 3 giorni-107 anni

Totale dosaggi:

n = 65.535

Prelievi basali:

n = 35.463 (~9:100 abitanti)
(19.673 no controllo)

Prelievi di controllo:

n = 30.072

Distribuzione prelievi per stagione

Autunno	17.386	26%
Inverno	14.307	22%
Primavera	18.196	28%
Estate	15.646	24%

Distribuzione prelievi per fasce di età

< 18 anni	1.966	3%
18-30 anni	2.267	4%
30-50 anni	11.724	18%
50-70 anni	24.401	37%
70-90 anni	23.612	36%
≥ 90 anni	1.205	2%

Distribuzione prelievi per anno

2010	1.840	3%
2011	3.179	5%
2012	4.047	6%
2013	5.316	8%
2014	7.505	11%
2015	9.084	14%
2016	10.428	16%
2017	12.563	19%
2018 (ott)	11.573	18%

Distribuzione prelievi per sesso

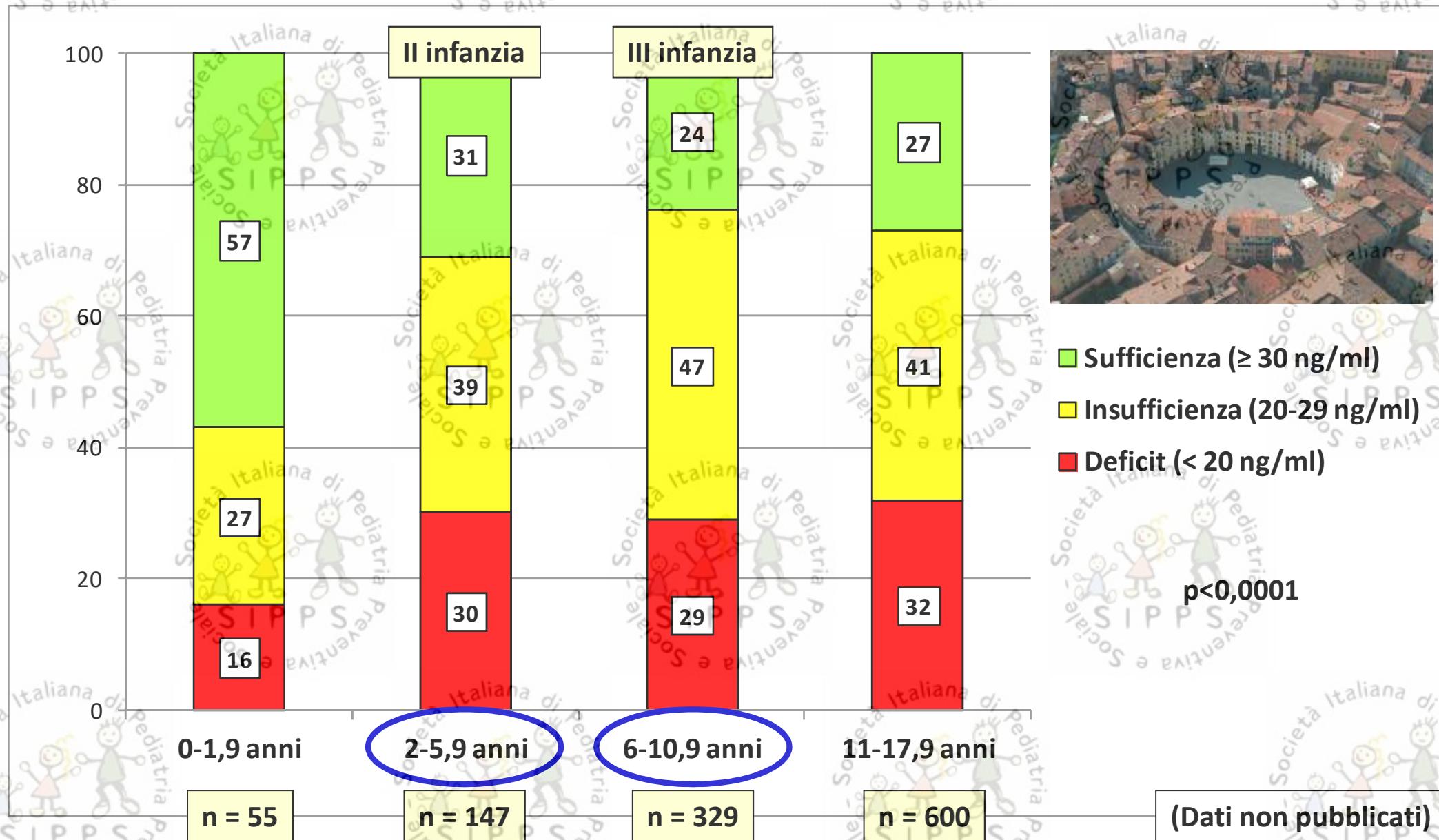
Maschi	15.078	23%
Femmine	50.457	77%

(Dati non pubblicati)

Laboratorio Analisi Ex ASL 2 Lucca

Stato vitaminico D (dosaggi basali)

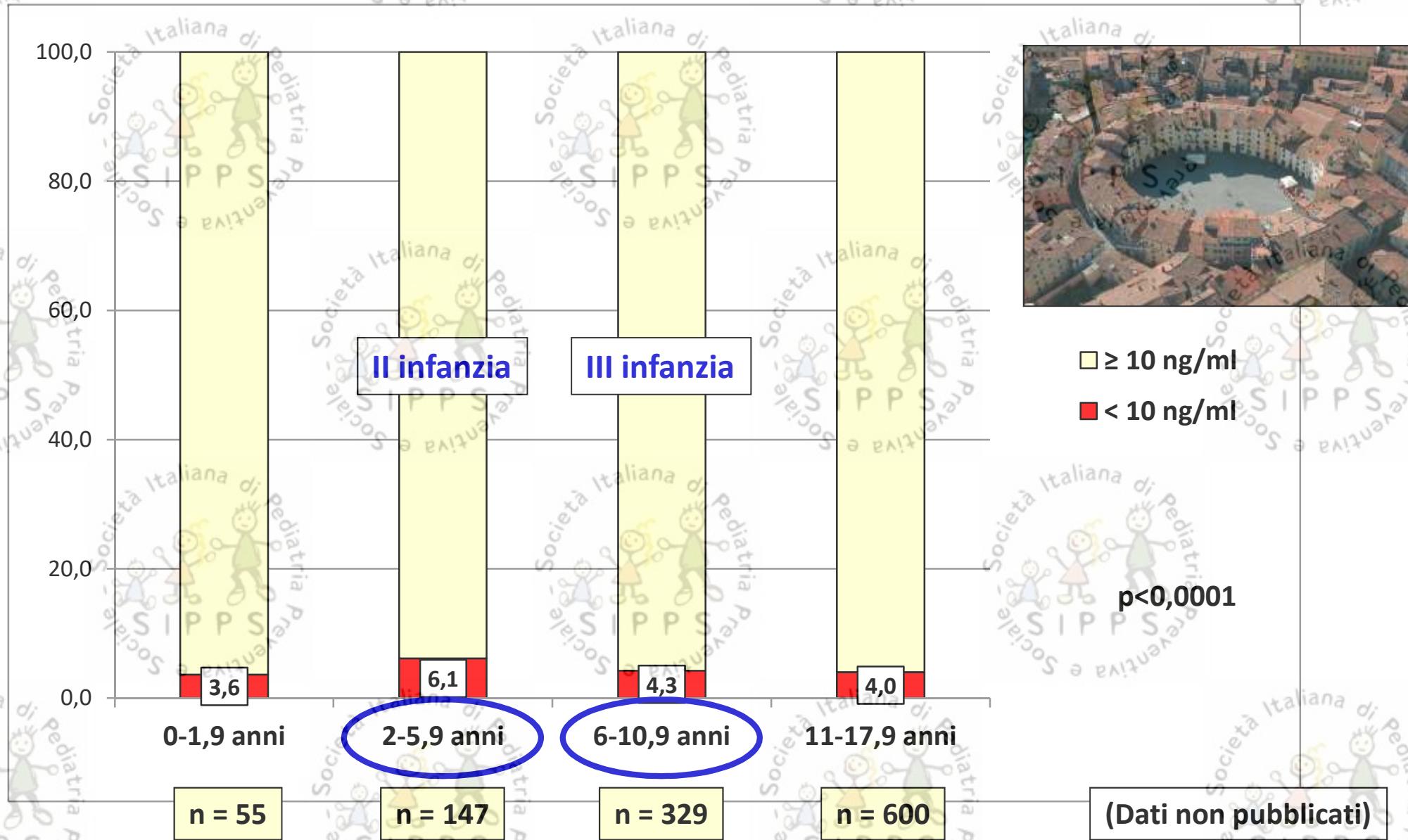
Gen 2010-Ott 2018; n= 1.131 (0-17,9 anni)



Laboratorio Analisi Ex ASL 2 Lucca

Prevalenza deficit grave [$25(\text{OH})\text{D} < 10 \text{ ng/ml}$] (dosaggi basali)

Gen 2010-Ott 2018; n= 1.131 (0-17,9 anni)



Vitamin D and Your Child

How can my child get vitamin D?

Exposure to direct sunlight

Sunlight converts a chemical in the skin to an active form of vitamin D.

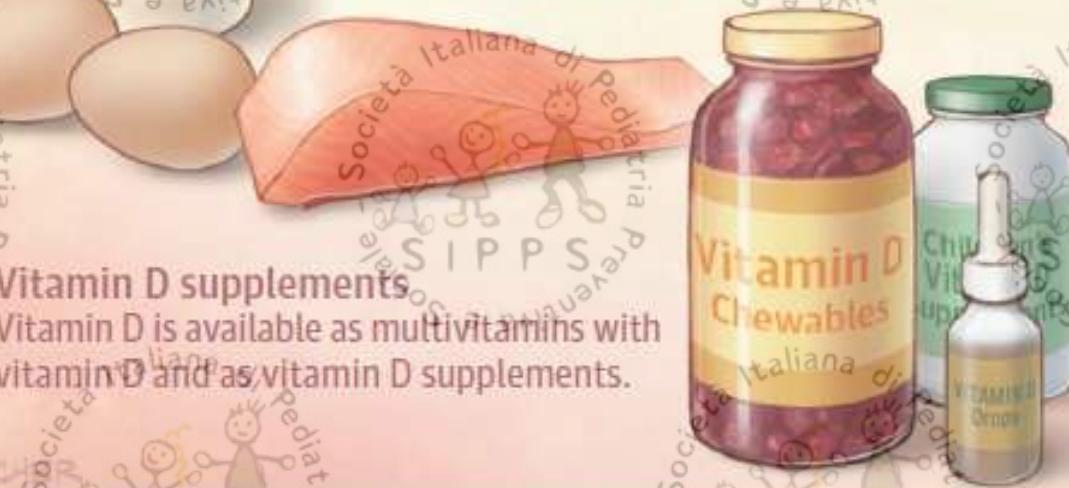


Dietary sources

Fatty fishes and vitamin D-fortified foods, such as dairy products and cereals, are sources of vitamin D. Eggs also have a small amount of vitamin D.

Vitamin D supplements

Vitamin D is available as multivitamins with vitamin D and as vitamin D supplements.



(JAMA Pediatrics 2018 Jul)

Sunscreen photoprotection and vitamin D status

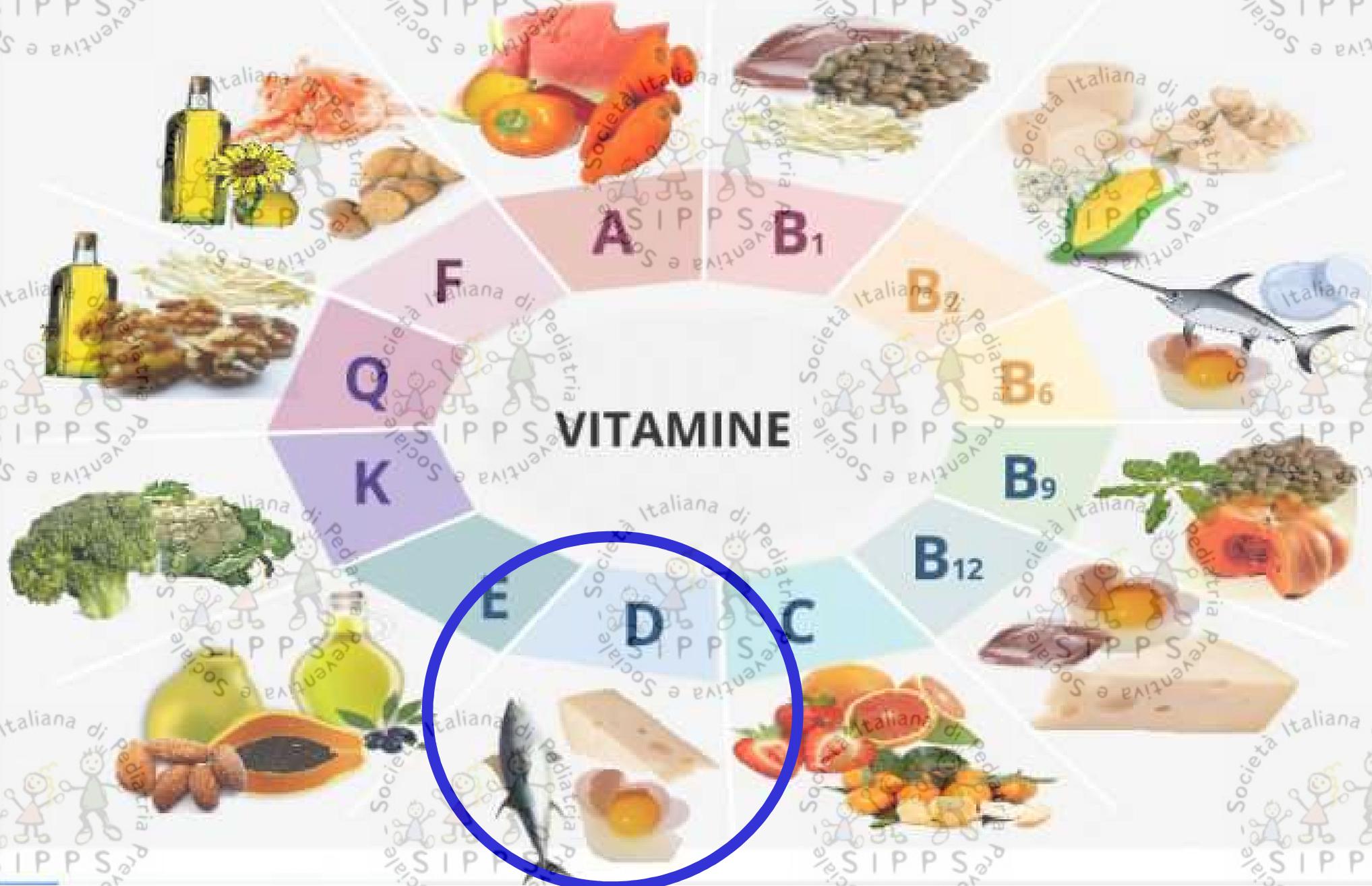
(International panel of 13 experts in endocrinology, dermatology, photobiology, epidemiology and biological anthropology)

- Judicious use of daily broad-spectrum sunscreens (with high UVA protection) will not compromise vitamin D status in healthy people.
- Vitamin D screening and supplementation should be restricted to those at risk of hypovitaminosis, such as patients with photosensitivity disorders, who require rigorous photoprotection.



(Passeron et al. Br J Dermatol 2019 May)

Vitamine contenute negli alimenti





Childhood Dietary Intake in Italy. The Epidemiological "MY FOOD DIARY" Survey

443 Italian children (6.4 - 131 months), through a three-day food record

1-4 anni
144 UI/die

Table 9. Daily dietary intake of minerals and vitamin D in infants/children aged 1 ≤ years < 4 ($n = 148$) [†].

Variable	Mean (SD)	Median (25th-75th Centile)	Min-Max	Reference Values ^a
Calcium (mg/day)	613.1 (237.6)	606.6 (430.8-780.4)	187.2-1277.7	450 (AR); 600 (PRI)
Vitamin D (mcg/day)	3.6 (5.0)	1.3 (0.8-3.8)	0.2-23.9	10 (AR); 15 (PRI); 65 (UL)

AI, adequate intake; AR, average requirement; PRI, population reference intake; UL, tolerable upper intake level.

^a According to [16]. [†] As calculated from ingested food. No data were available about the intake of minerals and vitamins from other sources, such as supplements, medicines, or others.

II infanzia
4-7 anni
56 UI/die

Table 10. Daily dietary intake of minerals and vitamin D in children aged 4 ≤ years < 7 ($n = 134$) [†].

Variable	Mean (SD)	Median (25th-75th Centile)	Min-max	Reference Values ^a
Calcium (mg/day)	495.4 (188.8)	477.5 (379.0-613.8)	133.6-1126.4	700 (AR); 900 (PRI)
Vitamin D (mcg/day)	1.4 (1.4)	1.1 (0.7-1.7)	0.3-10.6	10 (AR); 15(PRI); 75 (UL)

III infanzia
7-11 anni
52 UI/die

Table 11. Daily dietary intake of minerals and vitamin D in children aged 7 ≤ years < 11 ($n = 95$) [†].

Variable	Mean (SD)	Median (25th-75th Centile)	Min-Max	Reference Values ^a
Calcium (mg/day)	459.4 (180.5)	433.2(326.6-589.5)	126.2-964.4	900 (AR); 1100 (PRI)
Vitamin D (mcg/day)	1.3 (1.0)	1.0 (0.7-1.4)	0.2-5.7	10 (AR); 15 (PRI); 75(UL)



nutrients

Review

A Review of Mushrooms as a Potential Source of Dietary Vitamin D

When commonly consumed mushroom species are exposed to a source of **UV radiation** (sunlight or UV lamp), they can generate nutritionally relevant amounts of vit. D₂ ($> 400 \text{ IU}/100 \text{ g}$)

(Cardwell G et al. Nutrients 2018)



Kyoto 19/09/19: 26°C





Consensus SIPPS-SIP 2018: dopo il primo anno

- We recommend vitamin D supplementation in children and adolescents with **risk factors for vitamin D deficiency**.

A CHI

- We recommend **daily vitamin D supplementation** ranging from **600** IU/day (i.e. in presence of reduced sun exposure) up to **1000** IU/day (i.e. in presence of multiple risk factors for vitamin D deficiency).
- In cases of poor compliance, supplementation with **intermittent dosing** (**weekly or monthly** doses for a cumulative monthly dose of **18000-30000 IU** of vitamin D) can be considered, starting from children aged **5-6 years** and particularly during **adolescence**.

COME

- We suggest vitamin D supplementation **from the end of fall to the beginning of spring** (**Nov-Apr**) in children and adolescents with **reduced sun exposure** during summer.
- We suggest **continuous** vitamin D supplementation in cases of **permanent risk factors for vitamin D deficiency**.

PER QUANTO

Effect of vitamin D3 seasonal supplementation with 1500 IU/day in north Italian children

- Padova (45°N)
- N = 203 children (age 2-15 years)
- November 2010 - January 2015
- Group A (n = 82): 1,500 IU vitamin D3/day from November to April
- Group B (n = 121): no supplementation



(Mazzoleni et al. Italian Journal of Pediatrics 2019)

Table 5 Mean serum levels of 25-OH-D (ng/ml) per month

	n	Total	Groups		T-test P
			A. Suppl.	B. No suppl.	
01. January	29	29	14	15	0.009*
			Mean	21.6	26.6 16.9
02. February	24	24	11	13	0.007*
			Mean	27.8	36.0 20.8
03. March	16	16	8	8	0.014*
			Mean	25.5	36.5 14.5
04. April	16	16	7	14	0.046*
			Mean	18.6	30.5 16.9
05. May	23	23	8	15	0.861
			Mean	24.8	25.4 24.5
06. June	21	21	10	11	0.096
			Mean	23.8	28.6 19.4
07. July	16	16	9	7	0.627
			Mean	29.4	30.7 27.9
08. August	12	12	7	5	0.574
			Mean	36.8	38.4 34.6
09. September	10	10	3	7	0.295
			Mean	30.4	36.0 28.0
10. October	10	10	4	6	0.049*
			Mean	29.2	38.3 23.2
11. November	12	12	3	9	0.476
			Mean	26.0	35.0 23.0
12. December	14	14	3	11	0.228
			Mean	26.3	32.7 24.5

n = number of children in each group

*below P significance level



Vitamin D supplementation after the second year of life: joint position of the Committee on Nutrition, German Society for Pediatric and Adolescent Medicine, and the German Society for Pediatric Endocrinology and Diabetology

- Desirable total vit. D intake for children older than 1 year, adolescents, and adults is **600-800 IU/day**.
- Untargeted **testing** of vit. D concentrations in healthy children without risk factors for deficiency is not recommended.
- Groups at **high risk of vit. D deficiency** include children and adolescents with certain chronic diseases and risk factors. In these cases, vit. D **supplementation (500-1000 IU/day)** may be useful, especially in the winter months.

Table 2 Pediatric populations at increased risk for vitamin D deficiency

- Exclusively breastfed infants without vitamin D prophylaxis
- Infants, children, and adolescents with:
 - Malabsorption or maldigestion disorders (e.g., celiac disease, Crohn's disease, cystic fibrosis)
 - Chronic inflammatory diseases (e.g., inflammatory bowel disease)
 - Chronic kidney disease
 - Chronic liver disease
- On permanent medication with substances that affect calcium or vitamin D metabolism (e.g., antiepileptic drugs, antiviral medication, fungicides, or high dose glucocorticoid therapy which inhibits intestinal calcium absorption and stimulates tubular calcium excretion)
- With very low sun exposure, for example, chronically immobilized children and adolescents
- With a migrant background (through the influence of pigmentation, nutrition, and sun exposure)

Serum 25OHD concentration < 20 ng/ml does not constitute an indication for supplementation unless there are additional risk factors.

(Reinehr et al. Mol Cell Pediatr 2019 May)

Quando dosare la vitamina D?

- Sospetto deficit sintomatico/**rachitismo** carenziale
- Sospetto deficit **grave** di vit. D (fattori di rischio multipli) tale da richiedere trattamento
- Sospetta patologia del metabolismo **calcio-fosforo** (es. “osteoporosi”)
- Patologie **croniche** e/o **farmaci** interferenti con il metabolismo della vit. D

Casi particolari (da individualizzare)

- Asma grave, steroido-resistente (prevenzione esacerbazioni)
- Infezioni respiratorie ricorrenti (prevenzione)



**Sospetto
deficit
di vit. D**

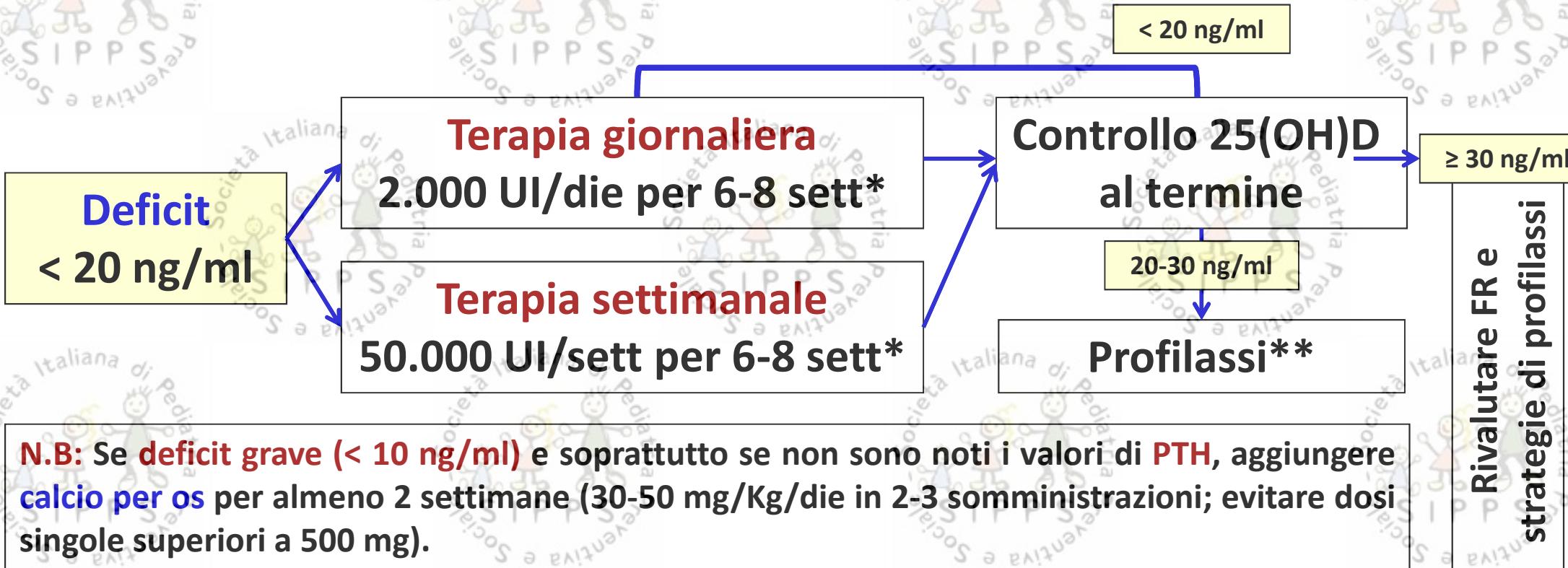
Quando NON dosare la vitamina D?

- Nel bambino “altrimenti sano”
- Nel bambino con scarsa esposizione alla luce solare
- Nel bambino di colore “altrimenti sano”
- Nel bambino obeso “altrimenti sano”

Stile di vita

PROFILASSI

E se ho dosato la vitamina D?



*8 settimane negli adolescenti

**durata da valutare in base alla stagione (almeno 1-2 mesi)

Somministrazione giornaliera o intermittente?

Giornaliera

- Più studi disponibili
- Obbligatoria nel primo anno di vita
- Minor rischio di «errore»
- Livelli circolanti di 25(OH)D più «stabili»
- Minor dose totale richiesta
- Promozione azioni extrascheletriche?

Intermittente

- Settimanale-bisettimanale-mensile
- Scarsa compliance con somm. giornaliera
- Dopo il 5°-6° anno di vita
- Non somministrare boli > 300.000 UI
- Considerare l'attivazione di vie enzimatiche «di protezione»

Trattamento deficit

TABLE 3 Treatment of Vitamin D Deficiency

Age	Preparation and Dose ^a	
Infants, 0–12 mo	Vitamin D ₂ or D ₃ 50 000 IU weekly for 6 wk Followed by a maintenance dose of 400–1000 IU daily	or Vitamin D ₂ or D ₃ 2000 IU daily for 6 wk
Children and adolescents, 1–18 y	Vitamin D ₂ or D ₃ 50 000 IU weekly for 6–8 wk Followed by a maintenance dose of 600–1000 IU daily	or Vitamin D ₂ or D ₃ 2000 IU daily for 6–8 wk

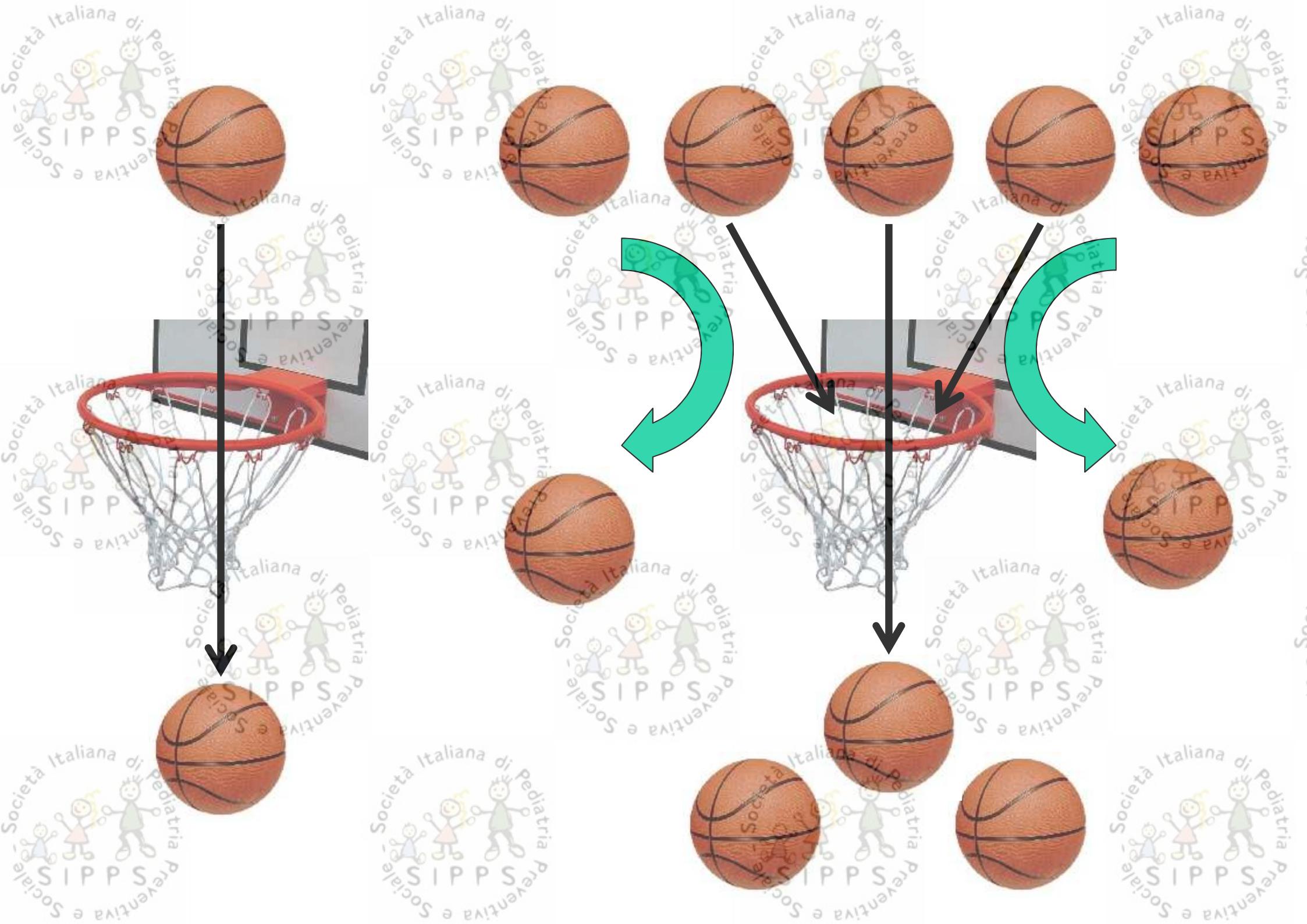
Vitamin D₂, ergocalciferol; vitamin D₃, cholecalciferol.

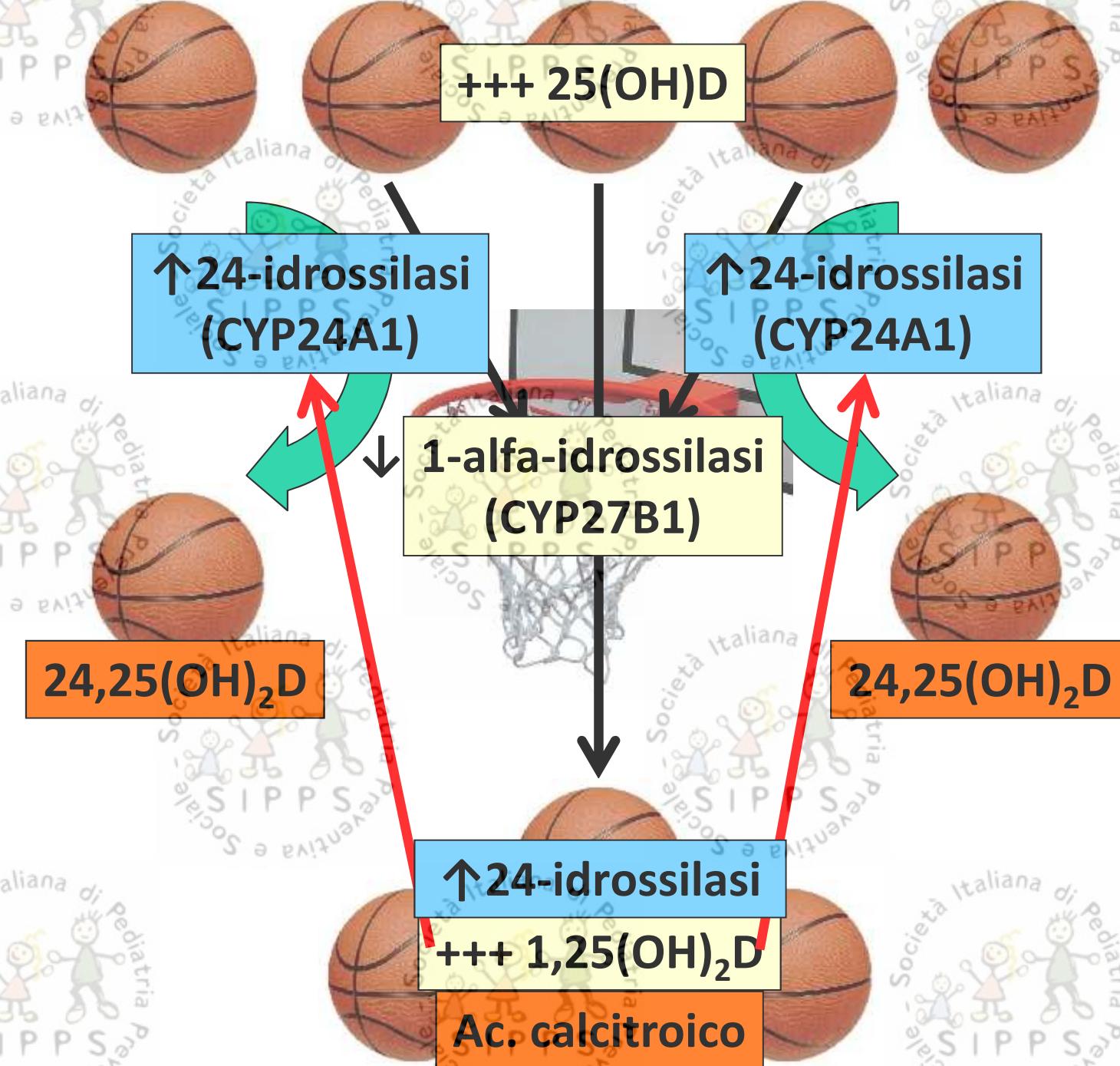
^a Vitamin D₂ may be more potent than vitamin D₃.

300.000 UI/6 sett vs. 84.000 UI/6 sett.

(Golden et al.
Pediatrics 2014)

400.000 UI/8 sett vs. 112.000 UI/8 sett.



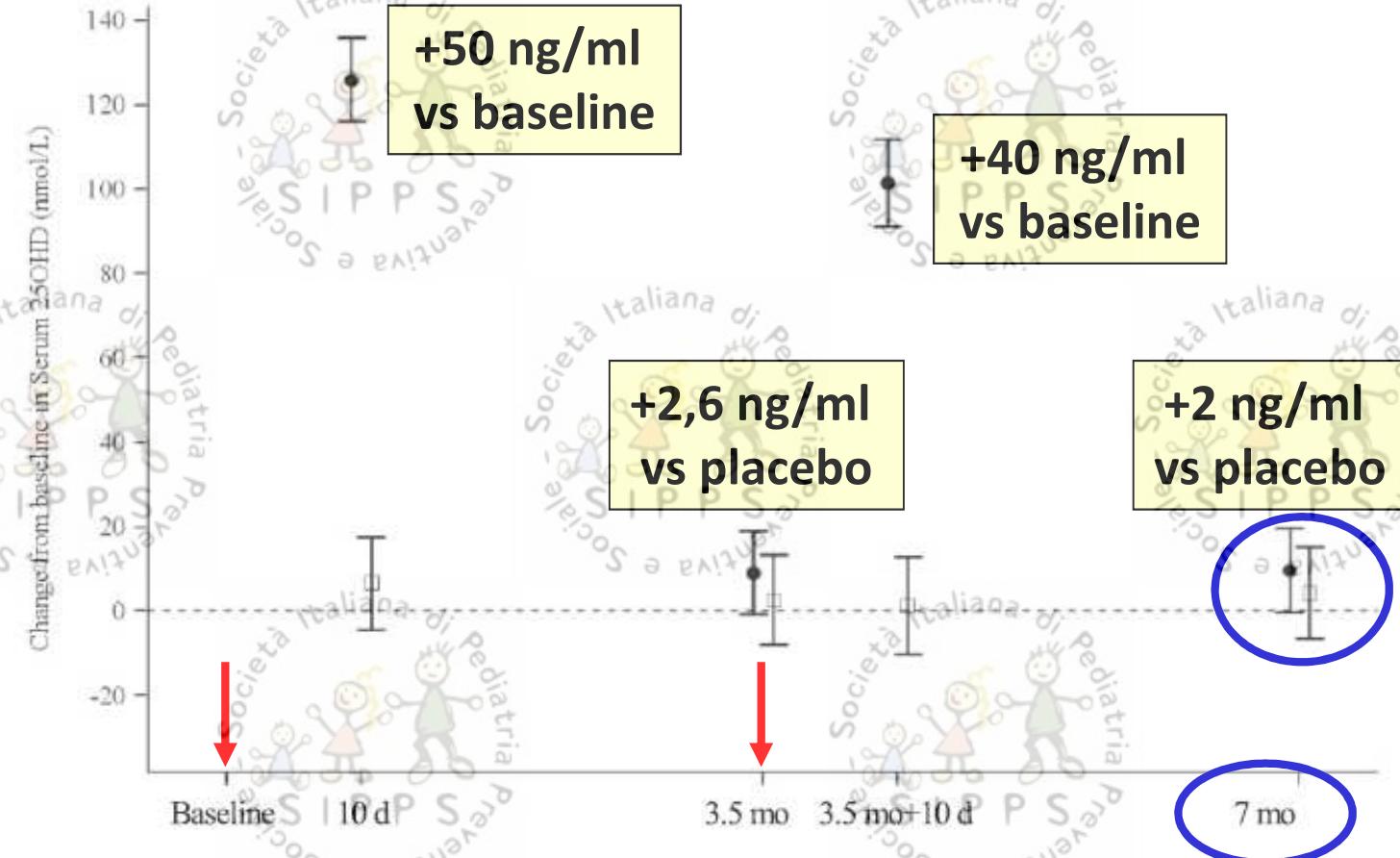


Impact of two oral doses of 100,000 IU of vitamin D3 in preschoolers with viral induced asthma

(Age 1-5 years; n = 47; intervention = 22; 100,000 IU in fall and in winter)

Baseline 25OHD < 30 ng/ml:

- Vit. D group: 68%
- Placebo group: 54%
- (nessuno < 10 ng/ml)



Two oral boluses of 100,000 IU vitamin rapidly raises serum 25OHD. However, it is sufficient to maintain $25\text{OHD} \geq 30 \text{ ng/ml}$ throughout 7 months in only slightly more than half of participants (56% vit. D vs 36% placebo).

(Ducharme et al. Trials 2019 Feb)

Azioni extrascheletriche della vitamina D

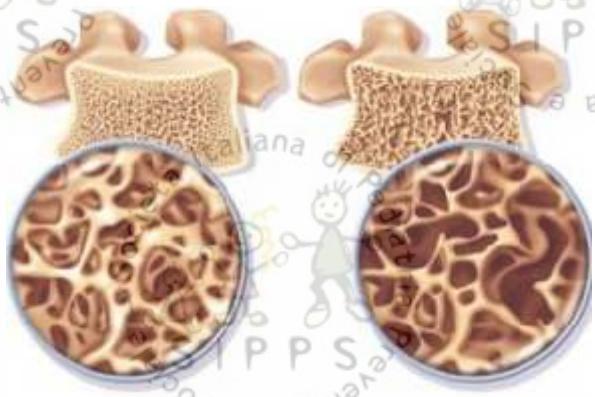
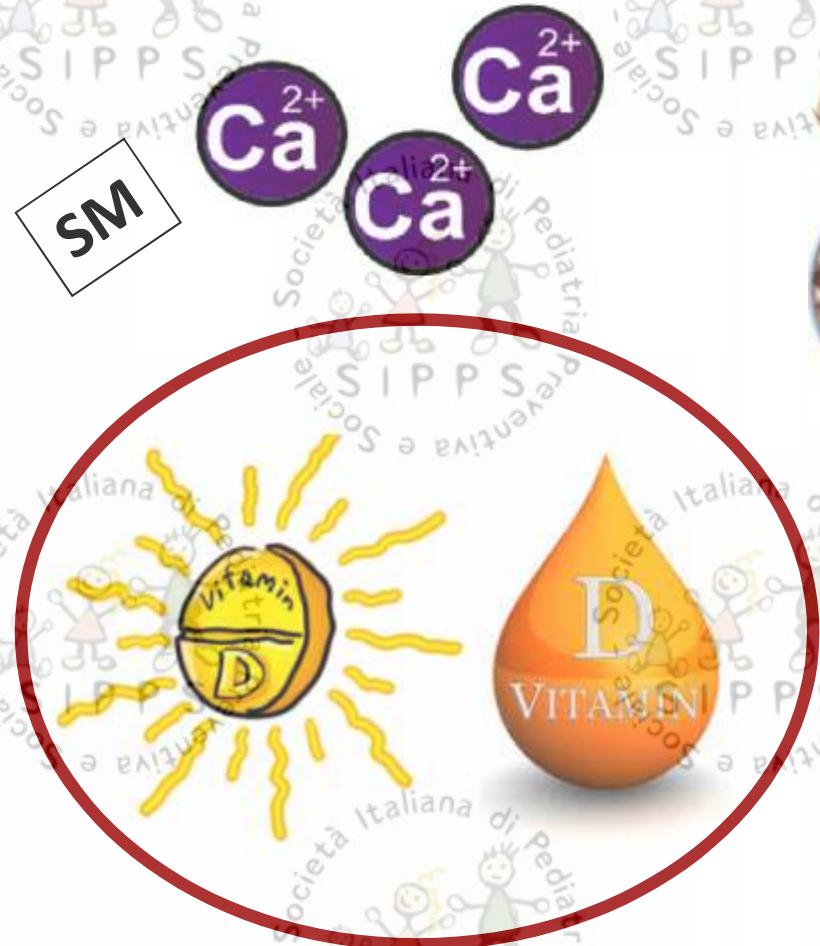
Diabete



MICI



Sindrome metab.



Cancro

Evaluation of vitamin D levels and response to therapy of childhood migraine (Turkey; age 7-18 years; n = 92, intervention = 42)

Vit. D group: 2000 IU/day for 2 months, then 600-1000 IU/day for 6 months.

If hypocalcemia or iperPTH levels: **calcium** supplementation (30-75 mg/kg/day)

Table 5. Migraine frequency, duration, VAS score, and PedMIDAS score after vitamin D treatment in group 1 patients.

Variable	Before Treatment	After Treatment	p *
25-OH vit D level, ng/mL	9.4 (4.2–20)	34.6 (16.3–45)	<0.001
Migraine duration, hours/day	10.8 (1–72)	2.5 (0–12)	<0.001
Migraine frequency, number of attacks/month	11.8 (1–30)	4.5 (0–15)	<0.001
Migraine severity, VAS score	6.7 (3–10)	3.6 (3–6)	<0.001
PedMIDAS, score	21.4 (1–83)	5.6 (0–30)	<0.001

Values are median (range). PedMIDAS: Pediatric Migraine Disability Assessment, VAS: Visual Analog Scale.

* Wilcoxon test was used.

Vitamin D therapy (supplemented with calcium) produced favorable effects on pediatric patients. Thus, vitamin D supplementation can help improve the quality of life of pediatric patients suffering from migraine.

Vitamina D & asma

(Wolk H et al. PLoS One 2017)

(Li W et al. J Asthma 2018)

GRAVIDANZA



Meta-analyses

PREVENZIONE PRIMARIA

PREVENZIONE ASMA NEL BAMBINO

STILE DI VITA, PROFILASSI CON VITAMINA D



SOGGETTO ASMATICO

PREVENZIONE SECONDARIA

RIDUZIONE ESACERBAZIONI ASMATICHE

(Jolliffe DA et al. Lancet Respir Med 2017)

Vitamin D for secondary prevention of acute wheeze attacks in preschool and school-age children

II e III infanzia

- **Preschool age** children with a history of wheeze attacks and $25(\text{OH})\text{D} < 30 \text{ ng/ml}$ are at increased risk and frequency of future acute **wheeze**.
- No consistent association between low vitamin D status and risk of acute wheeze is reported in **school-age** children.
- Seven RCTs with relatively small sample sizes (30–430) and variable **quality** showed inconsistent results regarding the effect of oral vit. D supplementation during childhood on the risk of asthma attacks, asthma symptom control, inhaled corticosteroid requirements, spirometry and healthcare attendances for wheeze.

There is **conflicting evidence** for the use of vitamin D supplementation as adjuvant therapy for the secondary prevention of acute wheeze in **school-age** children with asthma, and **limited evidence** for the use of vitamin D to reduce risk of wheezing attacks in **preschool** children.

META-ANALISI

Vitamin D Deficiency and Effects of Vitamin D Supplementation on Disease Severity in Patients with Atopic Dermatitis: A Systematic Review and Meta-Analysis in Adults and Children

(Hattangdi-Haridas et al. Nutrients 2019 Aug)

Dermatite atopica (supplement.)

Supplementation with around **1600 IU/daily** results in a clinically meaningful AD **severity reduction.**

Importance of vitamin D in acute and critically ill children with subgroup analyses of sepsis and respiratory tract infections: a systematic review and meta-analysis

(Cariolou et al. BMJ Open 2019 May)

Bambino critico (associazione)

25(OH)D deficiency in acute and critically ill **children** is high and associated with increased **mortality.**

Small-study effects, reverse causation and other biases may have confounded results.

Sepsi (associazione)

The association between vitamin D deficiency/lower 25(OH)D levels and **sepsis** was significant in **children** and **neonates.**

Further studies are required to confirm the results by considering more confounders.

Meta-analyses

Association between vitamin D status and sepsis in children: A meta-analysis of observational studies

(Xiao et al. Clin Nutr 2019 Aug)

Randomized controlled trial of vitamin D supplementation in children with autism spectrum disorder

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Pathology, Aswan, Egypt; ⁴Norway; ⁵Department of Clinical Medicine, Mö i Rana, Norway; ⁶University of Exeter, Exeter, UK; ⁷Departamento de Zoología, Facultad de Ciencias Naturales y Oceanográficas, Universidad de Concepción, Concepción, Chile; ¹⁰Department of Pediatrics, Qena Faculty of Medicine, South Valley University, Qena, Egypt; ¹¹Department of Pharmaceutics and Industrial Pharmacy, Alazhar University, Assiut, Egypt

Background: Autism spectrum disorder (ASD) is a frequent developmental disorder characterized by pervasive deficits in social interaction, impairment in verbal and nonverbal communication, and stereotyped patterns of interests and activities. It has been previously reported that there is vitamin D deficiency in autistic children; however, there is a lack of randomized controlled trials of vitamin D supplementation in ASD children. **Methods:** This study is a double-blinded, randomized clinical trial (RCT) that was conducted on 109 children with ASD (85 boys and 24 girls; aged 3–10 years). The aim of this study was to assess the effects of vitamin D supplementation on the core symptoms of autism in children. ASD patients were randomized to receive vitamin D3 or placebo for 4 months. The serum levels of 25-hydroxycholecalciferol (25(OH)D) were measured at the beginning and at the end of the study. The autism severity and social maturity of the children were assessed by the Childhood Autism Rating Scale (CARS), Aberrant Behavior Checklist (ABC), Social Responsiveness Scale (SRS), and the Autism Treatment Evaluation Checklist (ATEC). Trial registration number: UMIN-CTR Study Design: trial number: UMIN000020281. **Results:** Supplementation of vitamin D was well tolerated by the ASD children. The daily doses used in the therapy group was 300 IU vitamin D3/kg/day, not to exceed 5,000 IU/day. The autism symptoms of the children improved significantly, following 4-month vitamin D3 supplementation, but not in the placebo group. This study demonstrates the efficacy and tolerability of high doses of vitamin D3 in children with ASD. **Conclusions:** This study is the first

- This study is the first double-blinded RCT proving the efficacy of vit. D3 in ASD patients.
- Oral vit. D supplementation may safely improve signs and symptoms of ASD.

Retraction: Randomized controlled trial of vitamin D supplementation in children with autism spectrum disorder

K. Saad, A. Abdel-Rahman, Y. Elserogy, A. Al-Atram, A. El-Houfey, H. Othman, G. Bjørklund, F. Jia, M. Urbina, M. Abo-Elela, F. Ahmad, A. Abd El-Baseer, A. Ahmed, and A. Abdel-Salam

<https://doi.org/10.1111/jcpp.12652>

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The above article, published in print in the Jan 2018 issue of the Journal of Child Psychology & Psychiatry and online in Wiley Online Library (wileyonlinelibrary.com), has been retracted by the JCPP Editor-in-Chief, Edmund Bourque-Barke, and John Wiley & Sons.

Following a series of communications from readers highlighting concerns about the paper (now published on the journal website), the journal editors requested that the authors send them the raw data from the trial. In response the authors informed the editors that i) the electronic data base had been lost following a computer outage and ii) that they could send only 95 out of 120 hard-copy participant data sheets as one site had closed and was no longer contactable. The substantial data loss in and of itself posed a serious difficulty in verifying the correctness of the data presented in the paper. The JCPP then analysed the data from the 95 cases itself. A number of significant discrepancies emerged between the re-analysis and the findings reported in the paper both in terms of means and standard deviations of key outcome variables across the trial. These involved very substantial differences that we judged to be extremely unlikely to have arisen due to variations in composition of the original and re-analysed samples. We also discovered previously unidentified/reported problems with missing data and recording irregularities regarding changes in treatment regimen and subject identifiers.

As a result of these issues the Editors no longer have confidence in the findings reported in the original paper. Based on all these matters combined and following published guidance from the Committee on Publishing Ethics (COPE) and Wiley's Best Practice Guidelines on Publishing Ethics, we have decided that the only course of action available to us is to retract the paper.

RETRACTION
2019 Jun

"the electronic data base
had been lost following a
computer outage"



Vitamin D and Your Child

Vitamin D is essential for building and maintaining healthy bones. While many know that calcium is a primary component of bone growth and development, not everyone knows that calcium can only be absorbed by your body when vitamin D is present.

- While **daily multivitamins are not recommended as necessary for children**, supplementing with **vitamin D may be helpful for those not getting their daily vitamin D allowance through **foods** or who have limited sun exposure.**
- If you are unsure if your child is getting enough vitamin D, **talk with your pediatrician.**

Grazie per l'attenzione

La Digue (Seychelles)