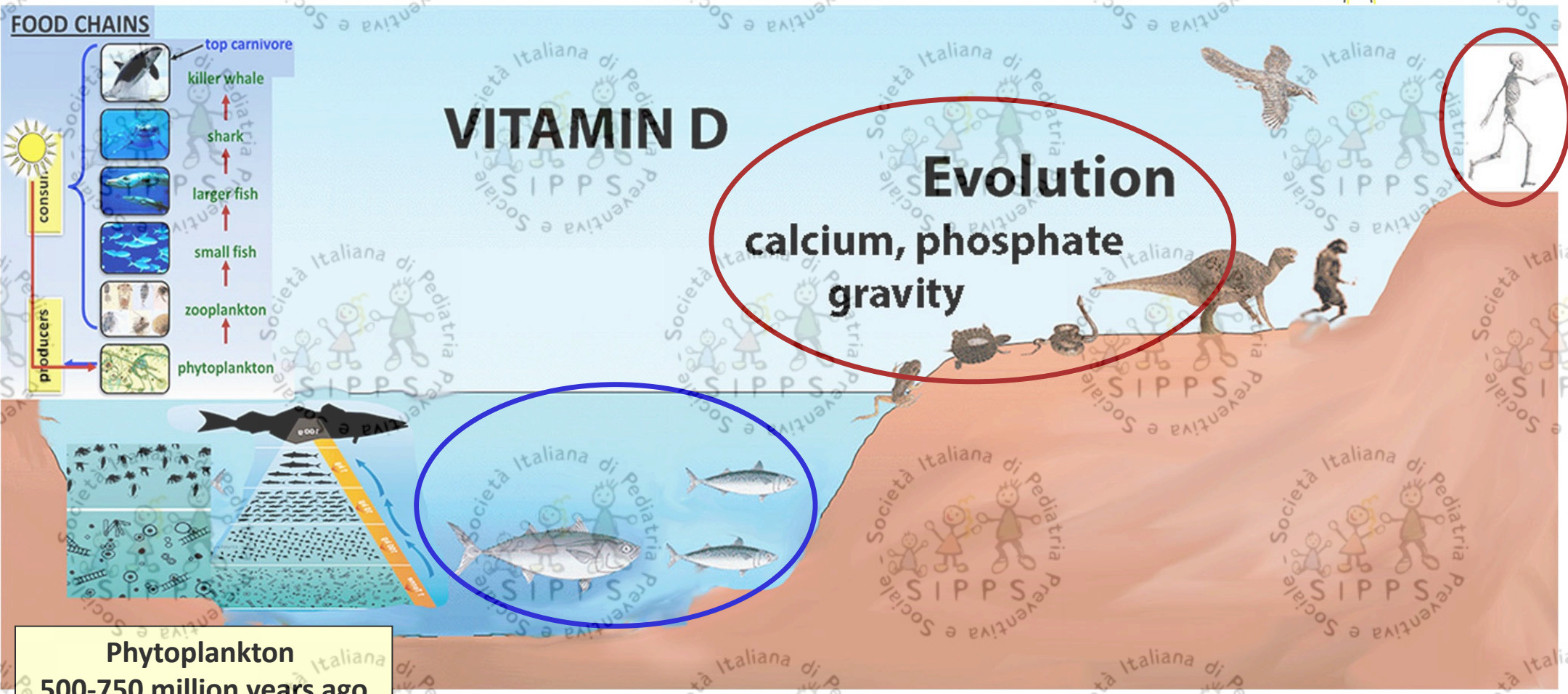
Vitamina D

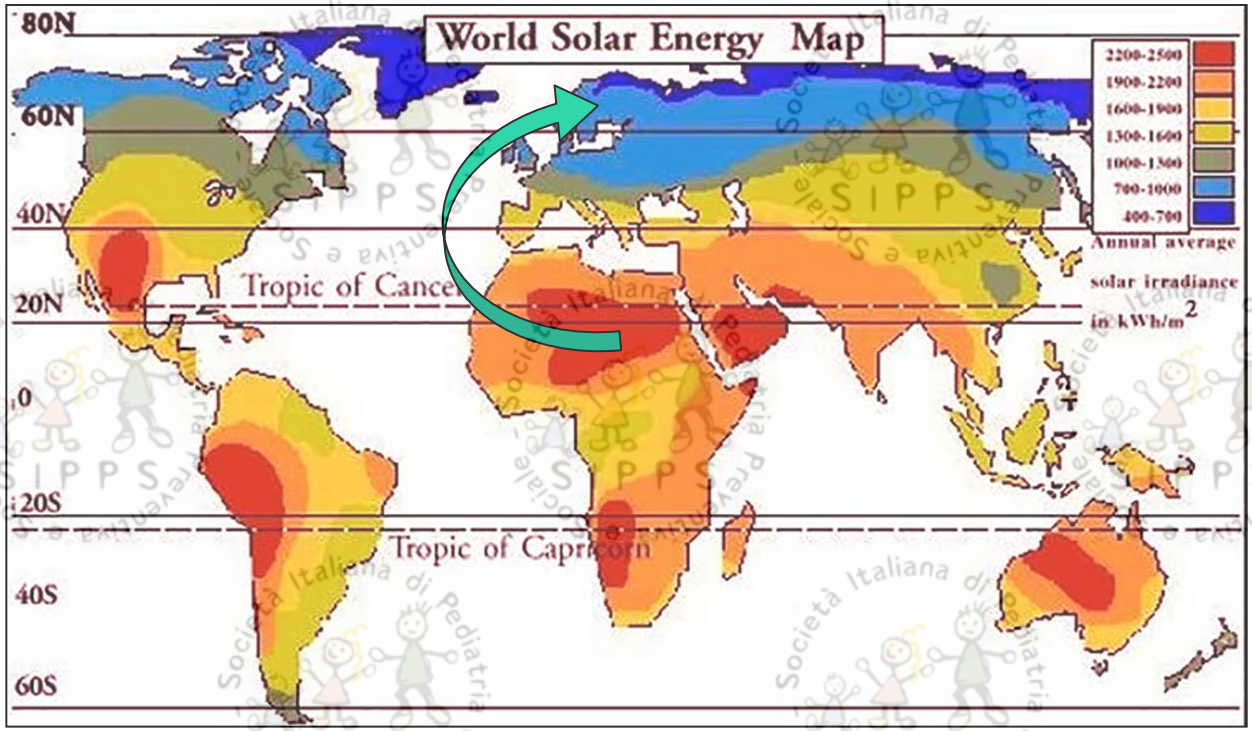
Francesco Vierucci

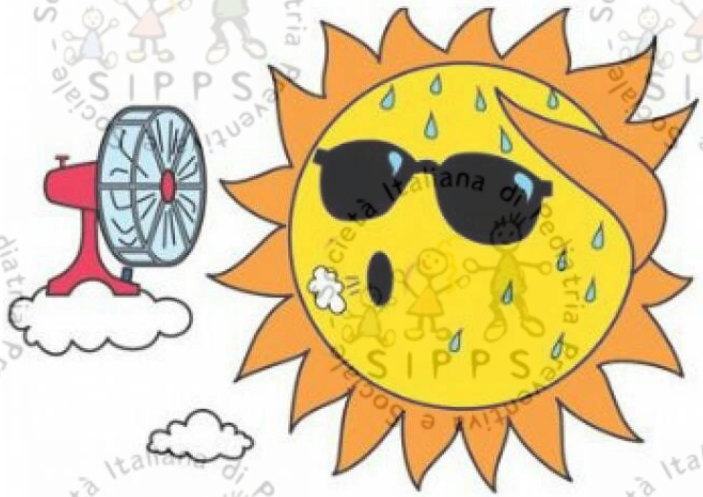
The vitamin D story

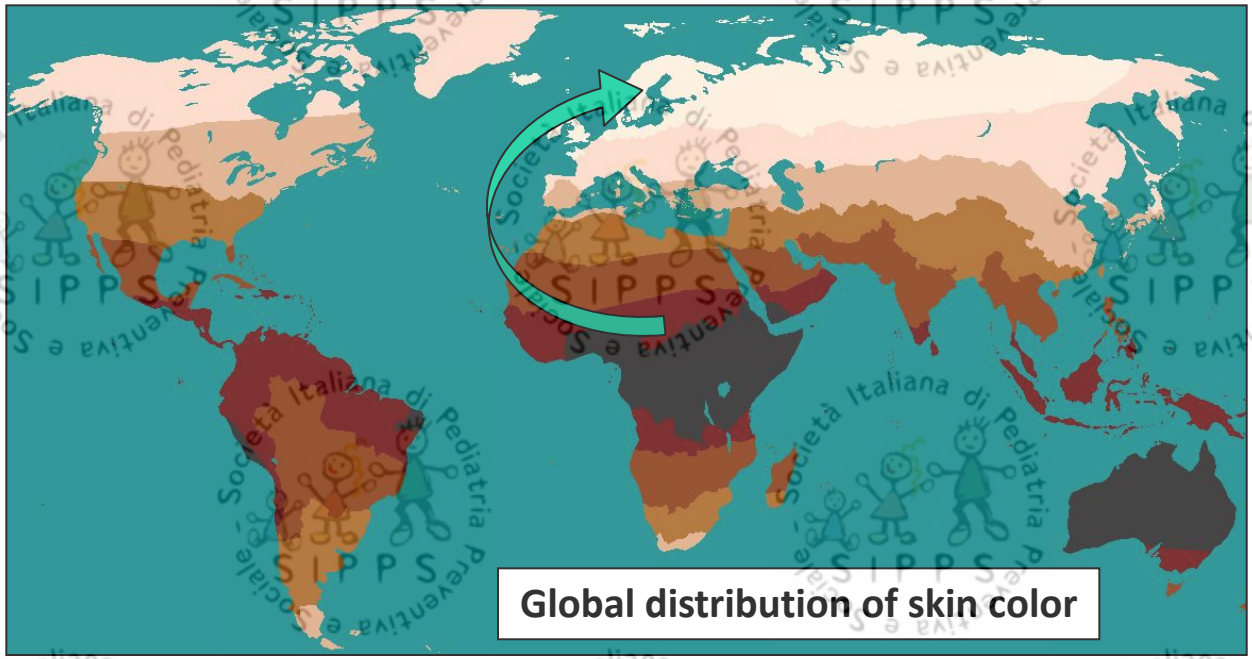


Phytoplankton
500-750 million years ago
(to protect DNA from UVB)

(Hernigou P et al. Int Orthop Mar 2018)







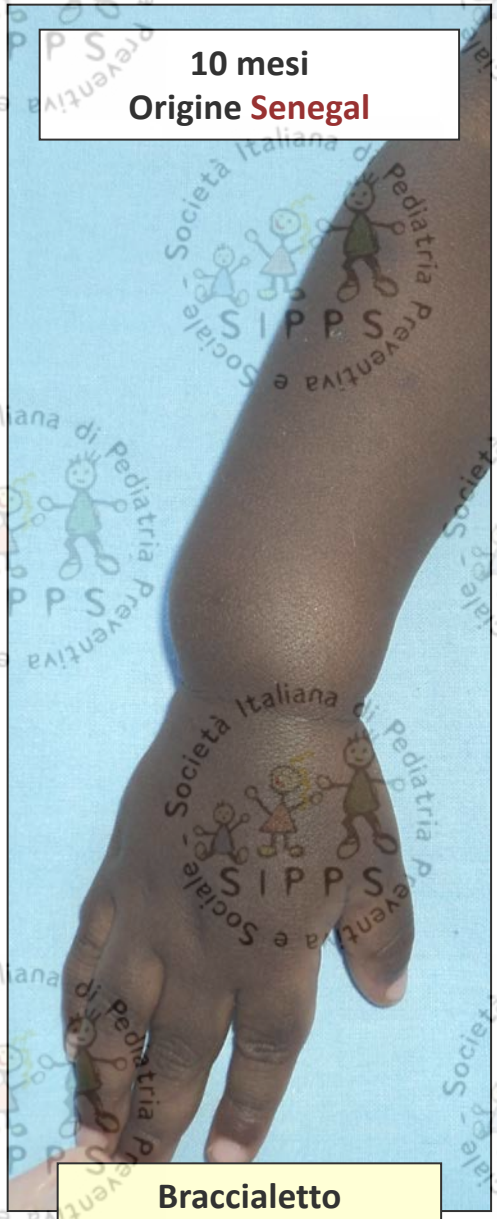
(Hernigou P et al. Int Orthop Mar 2018)

Il rachitismo carenziale

Rosario rachitico

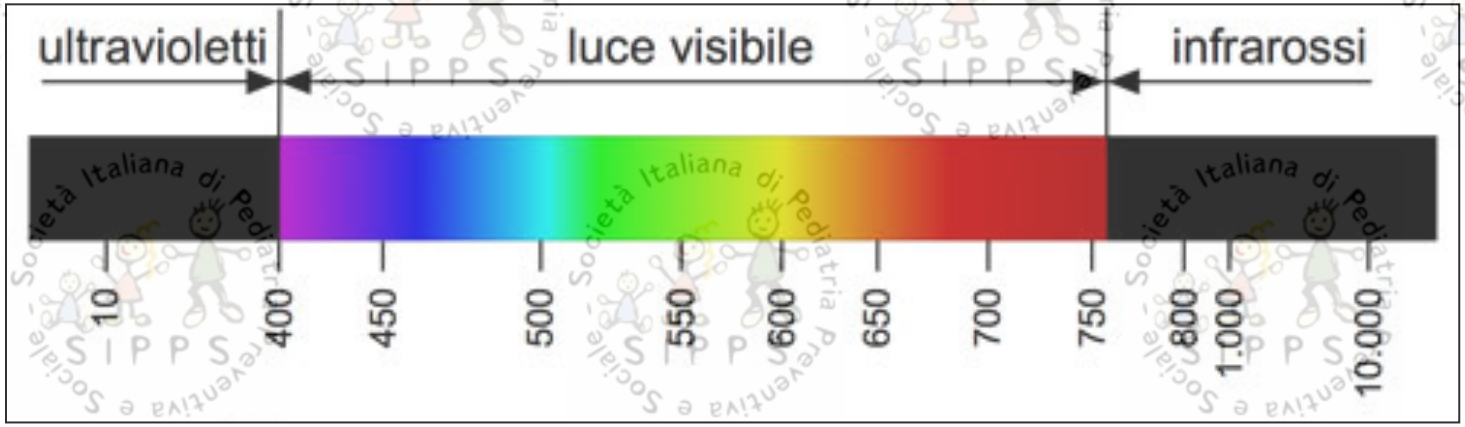
Caviglia rachitica

Rosario rachitico, valgismo



Braccialetto rachitico

The Spectrum of Vitamin D Deficiency



STATO VITAMINICO D SUFFICIENTE → **DEFICIT VIT. D ASINTOMATICO** → **DEFICIT VIT. D ASINTOMATICO CON IPERPTH** → **DEFICIT VIT. D SINTOMATICO**

RACHITISMO

OSTEOMALACIA

(Vierucci F et al. Exp Clin Endocrinol Diabetes Jul 2017)

DEFINIZIONE DELLO STATO VITAMINICO D

- Deficit grave: < 10 ng/ml
- Deficit: < 20 ng/ml
- Insufficienza: 20-29 ng/ml
- Sufficienza: ≥ 30 ng/ml

Ipovitaminosi D: < 30 ng/ml

https://doi.org/10.1186/s13052-018-0488-7

Italian Journal of Pediatrics

REVIEW

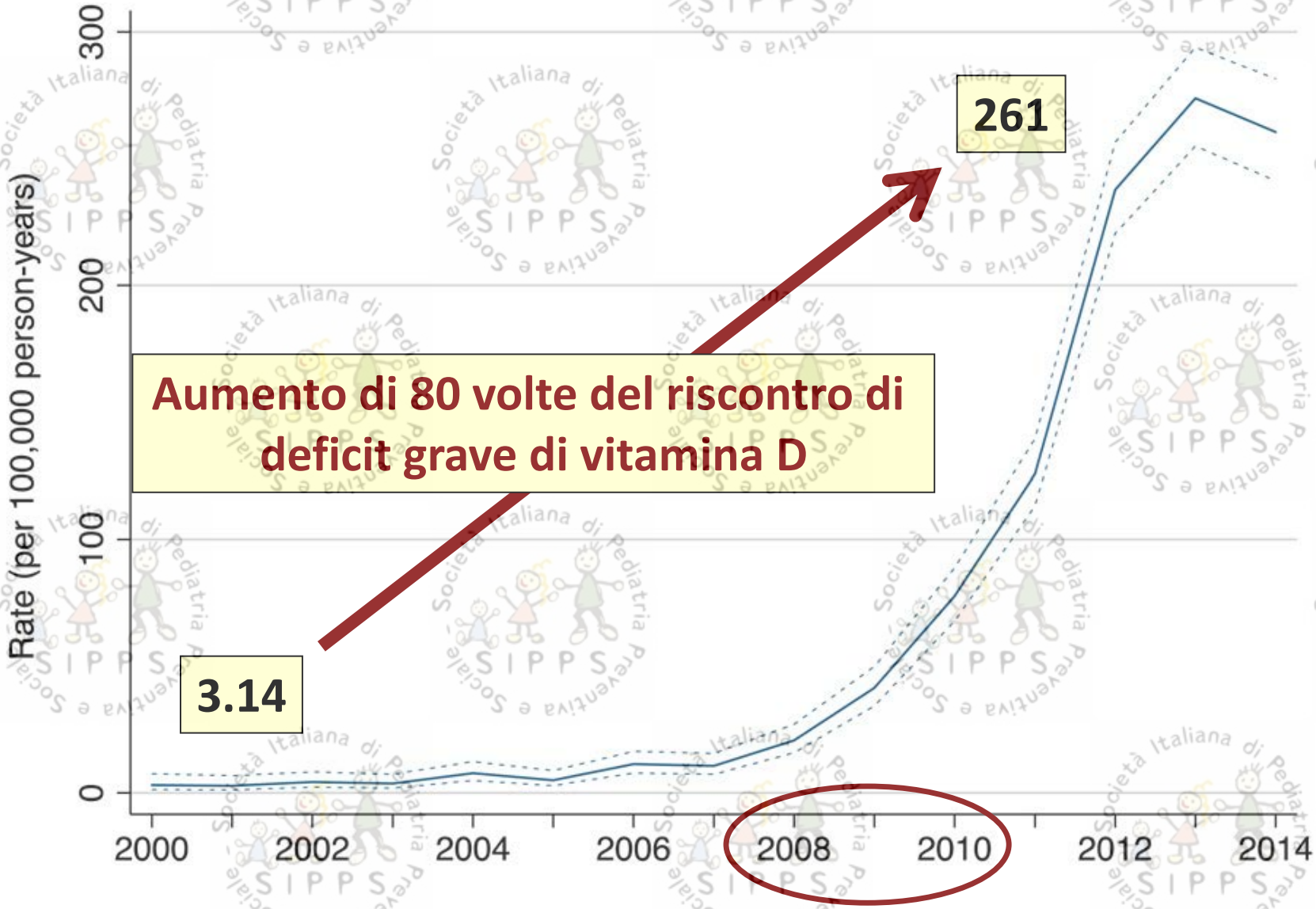
Open Access

Vitamin D in pediatric age: consensus of the Italian pediatric society and the Italian Society of Preventive and Social Pediatrics, jointly with the Italian Federation of Pediatricians

Giuseppe Saggese[1†], Francesco Vierucci[2*†], Flavia Prodam[3], Fabio Cardinale[4], Irene Cetin[5], Elena Chiappini[6], Gian Luigi de' Angelis[7], Maddalena Massari[5], Emanuele Miraglia Del Giudice[8], Michele Miraglia Del Giudice[8], Diego Peroni[1], Luigi Terracciano[9], Rino Agostiniani[10], Domenico Careddu[11], Daniele Giovanni Ghiglioni[12], Gianni Bona[13], Giuseppe Di Mauro[14] and Giovanni Corsello[15]

Trends in the diagnosis of vitamin D deficiency [25(OH)D < 10 ng/ml]

(England; The Health Improvement Network database; n = 711,788; 0-17 yrs)

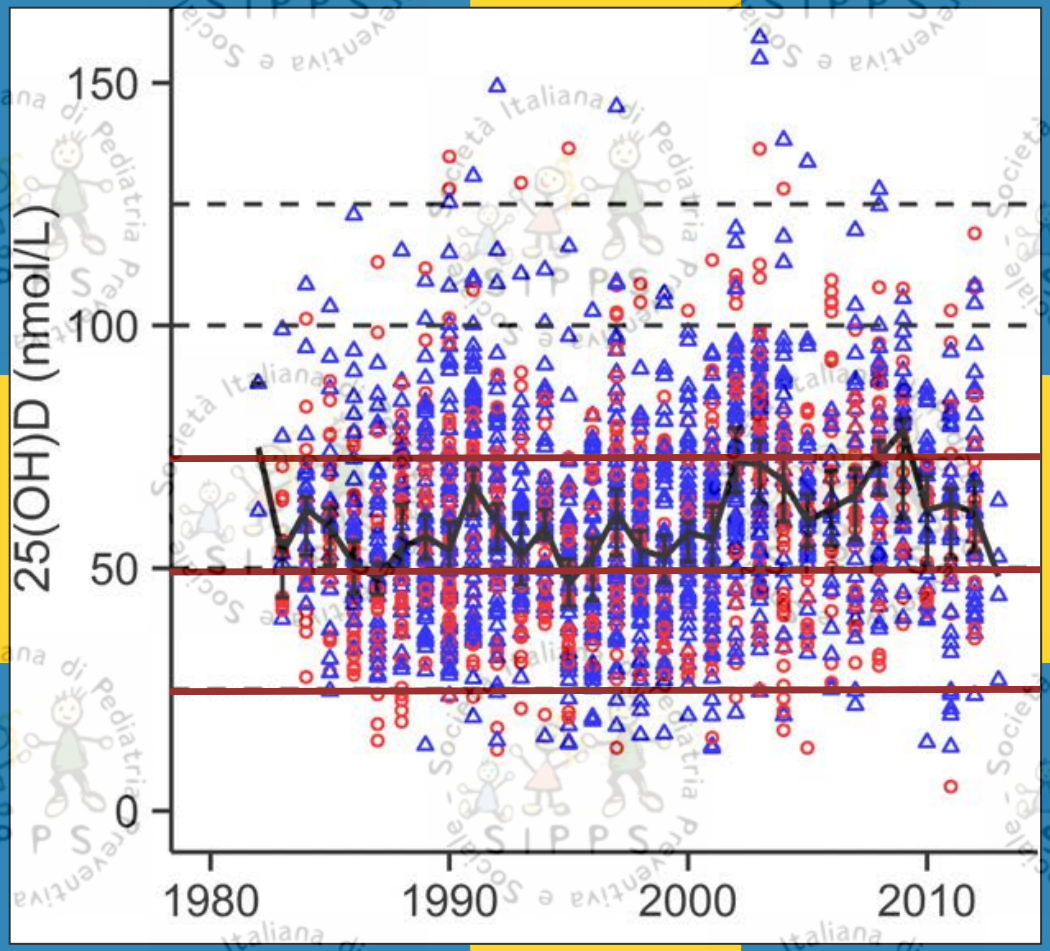


Aumento di 80 volte del riscontro di deficit grave di vitamina D

(Basatemur E et al. Pediatrics Mar 2017)

Vitamin D status in children over three decades (1982-2013)

(2,048 Swedish children; age 1-18 years)



30 ng/ml

20 ng/ml

10 ng/ml

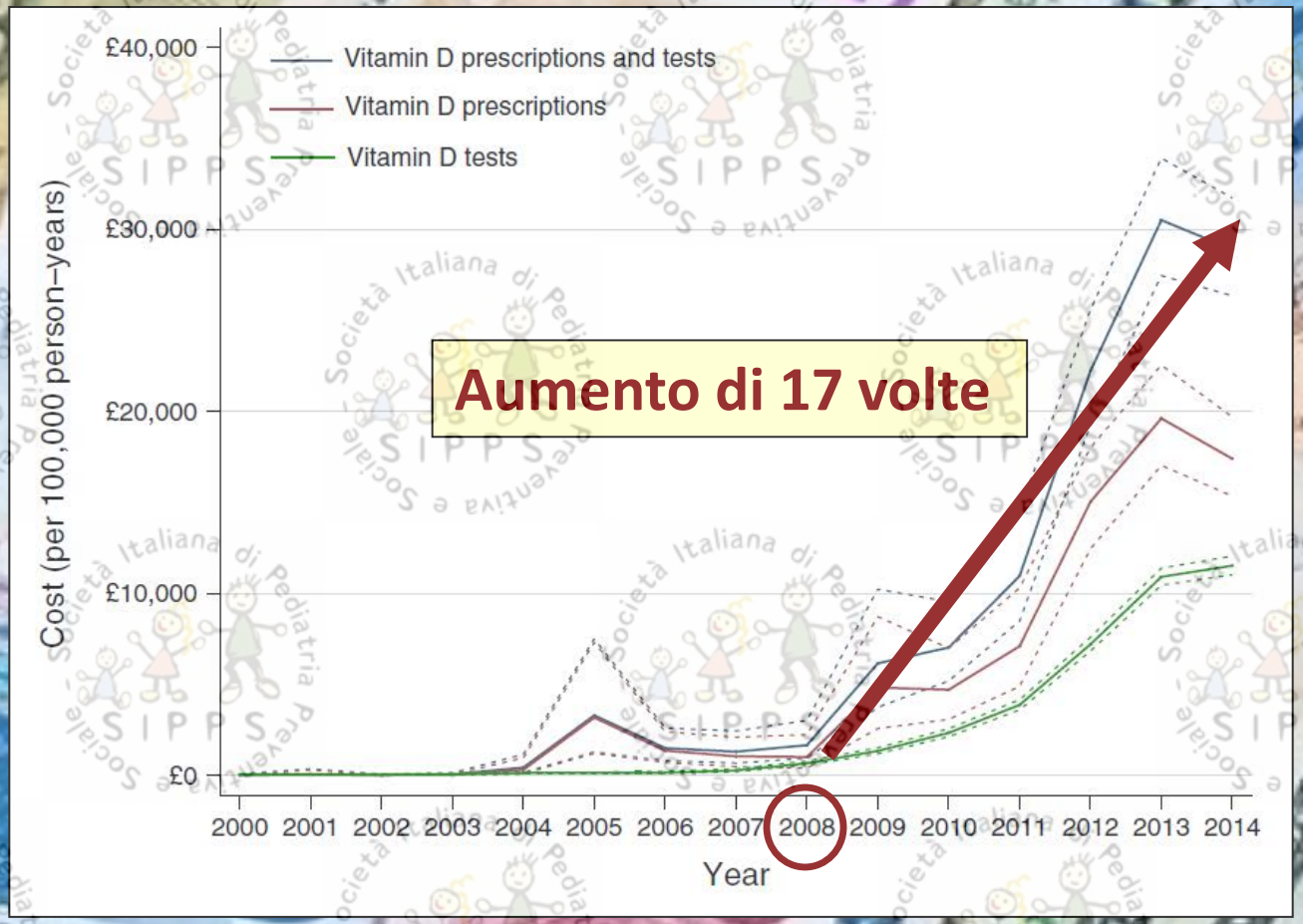
Year	25(OH)D (nmol/L) Median
1982	75.0
1983	53.2
1984	62.2
1985	58.4
1986	50.8
1987	47.9
1988	54.2
1989	56.6
1990	53.7
1991	67.3
1992	59.2
1993	52.4
1994	58.6
1995	46.8
1996	52.5
1997	61.4
1998	53.8
1999	52.3
2000	57.4
2001	56.1
2002	71.9
2003	71.4
2004	68.0
2005	59.7
2006	62.3
2007	65.0
2008	72.8
2009	78.6
2010	62.0
2011	63.3
2012	61.4
2013	48.4

No trend for decreased vitamin D levels over time was found in this population.

(Andersson B et al. Bone Reports 2016)

Costs of vit. D testing and prescribing among children in primary care

(England, The Health Improvement Network database, n=722.525, age: 0-17 yrs)



- Combined costs increased from £ 1647 (€ 1.880) per 100,000 person-years in 2008 to £ 28,913 (€ 33.000) per 100,000 person-years in 2014.
- Estimated total cost of vit. D prescriptions and tests for children in primary care at the national level in 2014: £ 4.31 million (€ 4.919.820) [test 25(OH)D: € 1.929.117]

(Basatemur E et al. Eur J Pediatr Oct 2017)

Fattori di rischio di deficit di vitamina D

- RIDOTTA ESPOSIZIONE SOLARE E/O USO COSTANTE DI FILTRI SOLARI
- SOGGETTI DI ETNIA NON CAUCASICA CON ELEVATA PIGMENTAZIONE CUTANEA
- OBESITÀ
- BAMBINI NEL PRIMO ANNO DI VITA NATI DA MADRI CON FATTORI DI RISCHIO DI DEFICIT DI VITAMINA D DURANTE LA GRAVIDANZA NON SOTTOPOSTE A PROFILASSI CON VITAMINA D
- INSUFFICIENZA EPATICA CRONICA
- INSUFFICIENZA RENALE CRONICA
- MALASSORBIMENTO (AD ESEMPIO FIBROSI CISTICA, MALATTIE INFIAMMATORIE CRONICHE INTESTINALI, CELIACHIA ALLA DIAGNOSI, ETC.)
- TERAPIE CRONICHE: ANTIEPILETTICI (FENOBARBITAL, FENITOINA), CORTICOSTEROIDI PER VIA SISTEMICA, FARMACI ANTIRETROVIRALI, ANTIMICOTICI PER VIA SISTEMICA (KETOCONAZOLO)
- FRATTURE RICORRENTI O CONDIZIONI ASSOCIATE A RIDOTTA DENSITÀ MINERALE OSSEA
- IMMOBILIZZAZIONE (PARALISI CEREBRALE, MALATTIE NEUROMUSCOLARI)
- MALATTIE GRANULOMATOSE (AD ESEMPIO TUBERCOLOSI)

0-12 mesi: 400-1.000 UI/die

1-18 anni: 600-1.000 UI/die

Obesità: 2-3 volte i fabb. per età

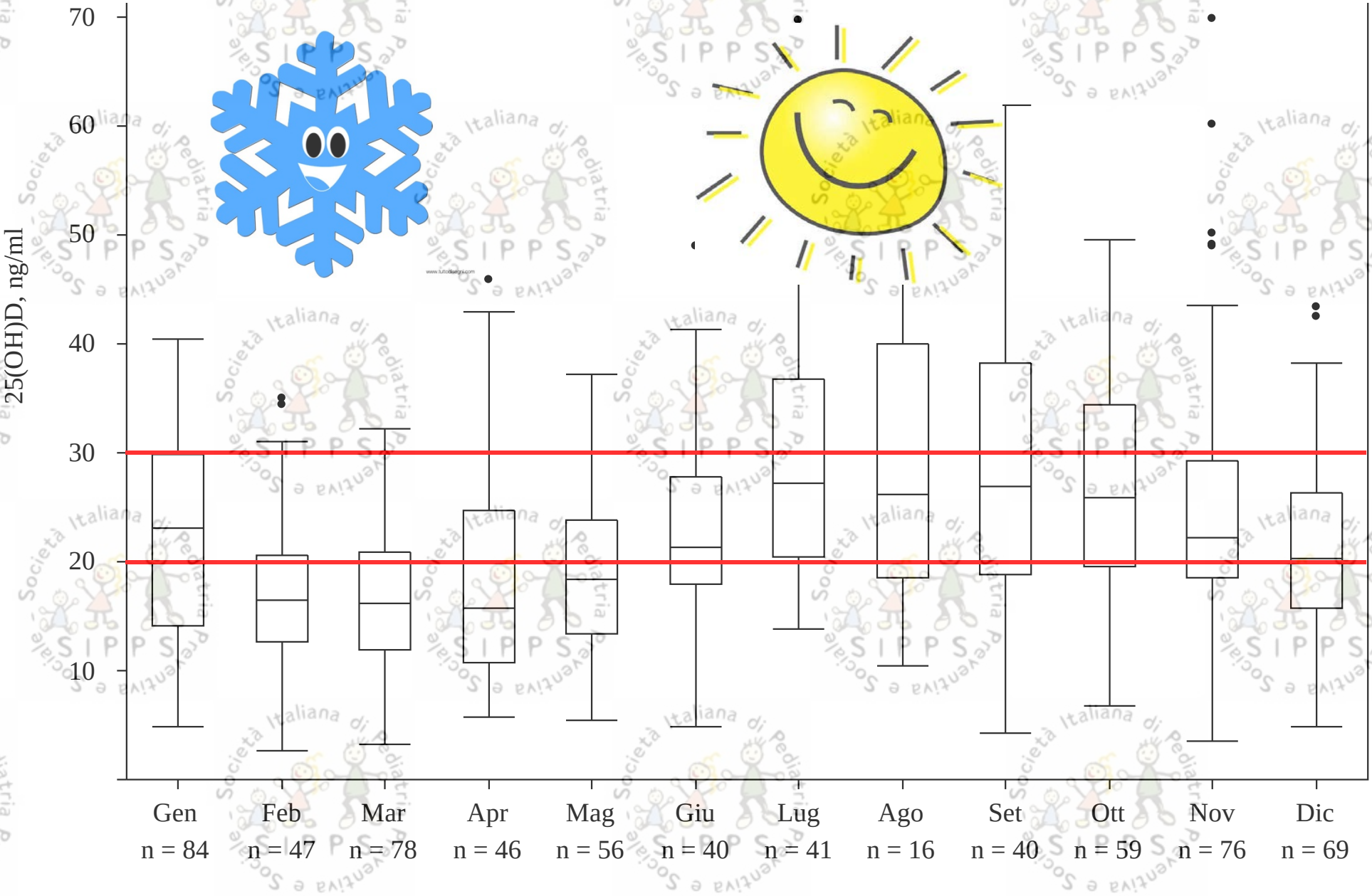

PIETRO VALSECCHI PRESENTA
CHECCO ZALONE
SOLE A CATINELLE
DAL 31 OTTOBRE AL CINEMA
taodue film
LIBERO. SOLEACATINELLE.LIBERO.IT


BELLA THORNE
PATRICK SCHWARZENEGGER
IL SOLE A MEZZANOTTE
MIDNIGHT SUN
È tutta la vita che aspetto di vedere l'alba...


DIANE LANE
SOTTO IL SOLE DELLA TOSCANA
DVD VIDEO


I CLASSICI
NAPOLI, sole mio!
MAURIZIO ARENA - LORELLA DE LUCA - TINA PICA
con VIRGILIO RIENTO - CLELIA MATANIA - ENZO TURCO - M. TERESA VIANELLO
e la partecipazione di TITINA DE FILIPPO
Regia: GIORGIO SIMONELLI
Produzione FLORA FILM - VARIETY FILM
DYALI-SCOPE

Livelli mediani di 25(OH)D nei diversi mesi dell'anno valutati trasversalmente in 692 bambini e adolescenti toscani (età 2-21 anni) non sottoposti a profilassi con vitamina D (p < 0,0001)



(Vierucci F et al. Eur J Pediatr 2013)

Do sufficient vitamin D levels at the end of summer in children and adolescents provide an assurance of vitamin D sufficiency at the end of winter?

(Iran; Longitudinal study; n = 68; 7-18 years; summer 2011-winter 2012)

End of summer

100%	≥ 30 ng/ml

25(OH)D: 46.5 ± 10.1 ng/ml

End of winter

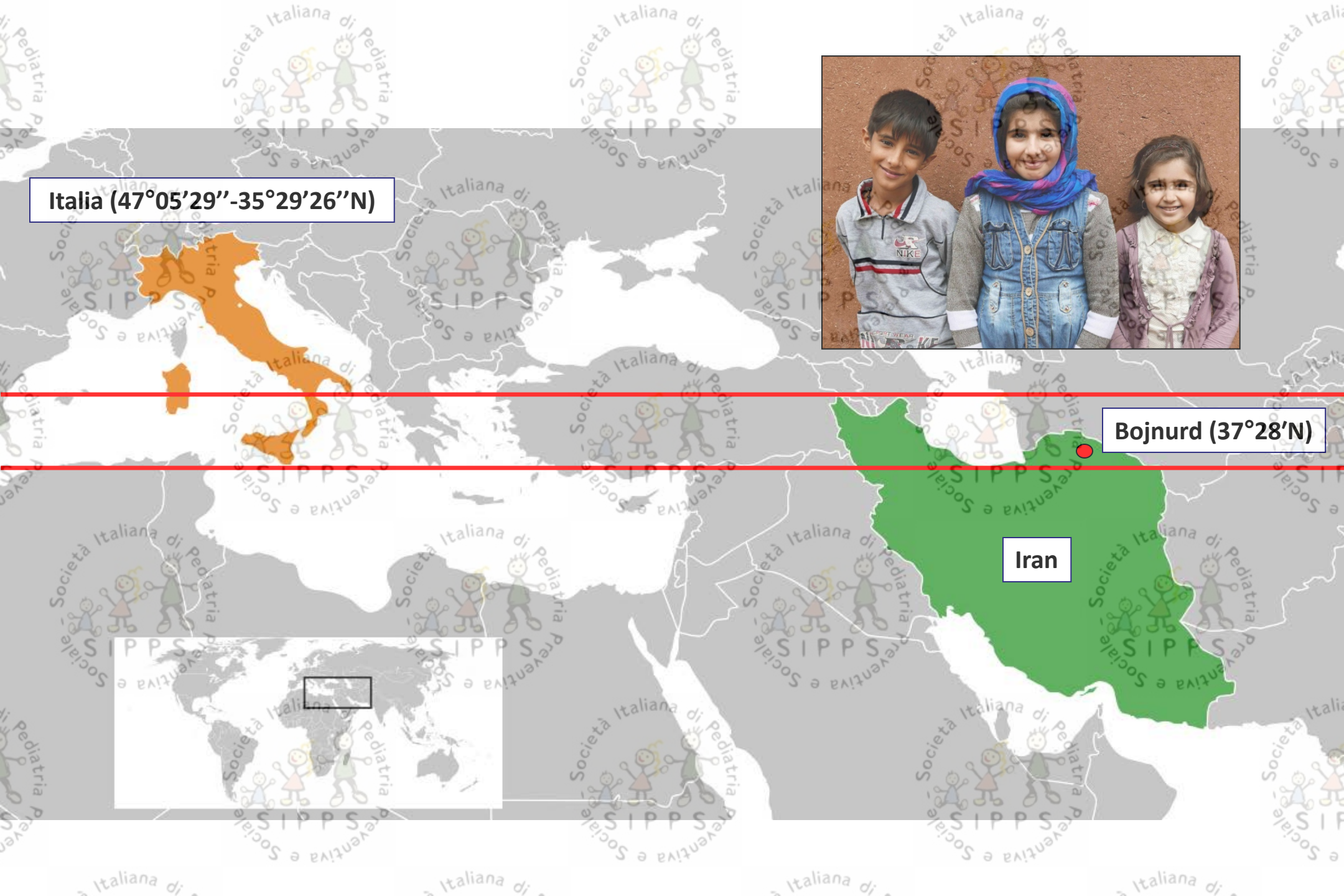
14.7%	< 20
36.8%	20-30
48.5%	≥ 30

Mean 25(OH)D decrease

15.3 ± 12.4 ng/ml

Cutoff to provide sufficiency at the end of the winter: 40 ng/mL at the end of the summer

(Shakeri H et al. JPEM Oct 2017)

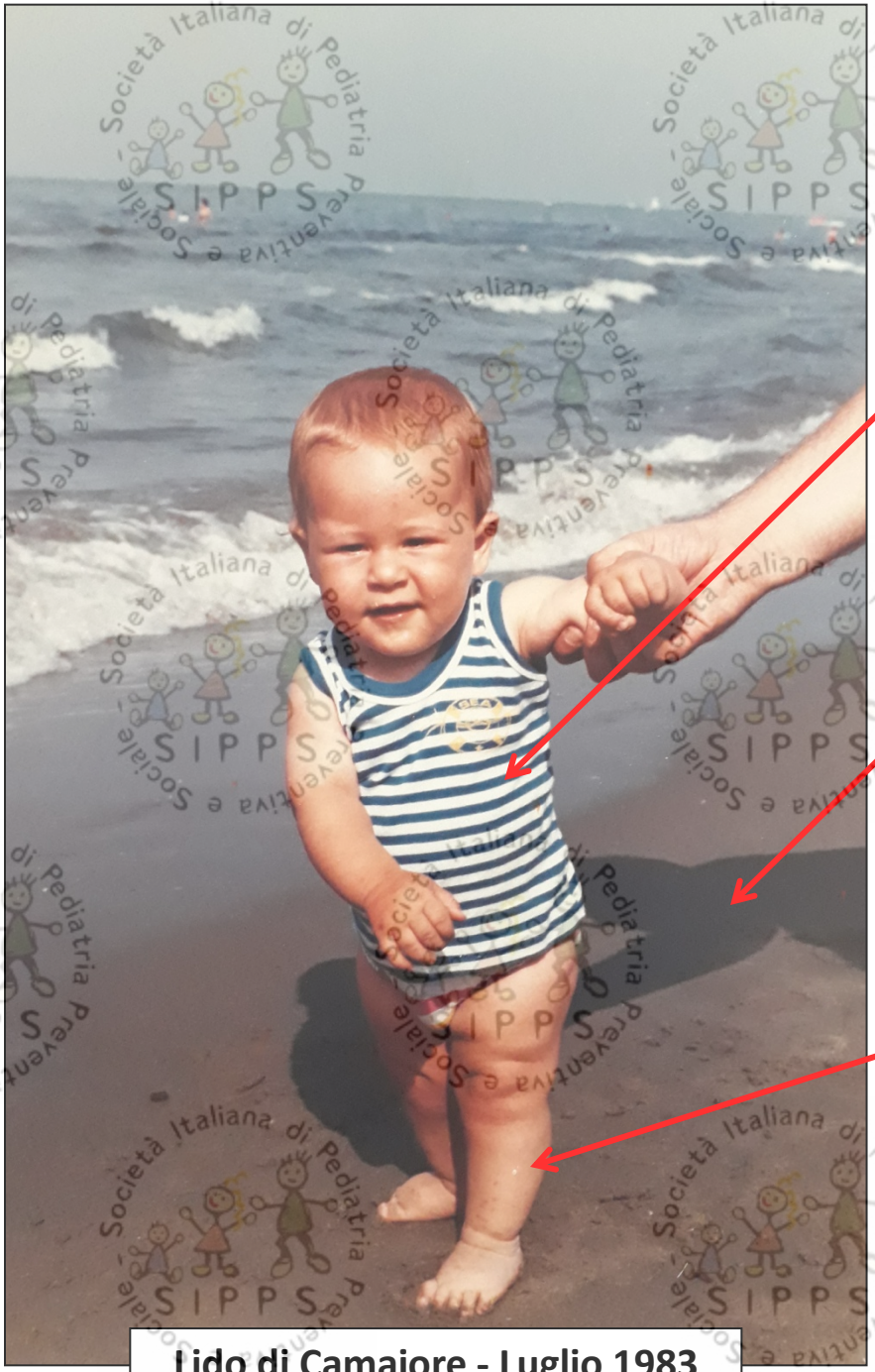

Italia (47°05’29’’-35°29’26’’N)
Bojnurd (37°28’N)
Iran

Vitamin D status in Italian children and adolescents

Study	Period of enrolment	n	Age (range)	City/Region (Latitude)	Deficiency, % [< 20 ng/ml]	Insufficiency, % [20-29.9 ng/ml]	Factors for associated with serum 25(OH)D levels
Marrone G *et al.*	July 2009-June 2010	93	2-220 months	Udine (**46**°N)	54.8	*	Ethnicity, BMI, **seasonality**
Vierucci F *et al.*	Oct 2010-Sept 2012	652	2.0-21.0 years	Pisa (**43**°N)	45.9	33.9	Age, **seasonality**, ethnicity, BMI, sun exposure, sunscreen use
Franchi B *et al.*	Jan 2010-Dec 2012	1,374	0-16 years	Verona (**45**°N)	Caucasian 44.2 Not Caucasian 44.8-69.2	Caucasian 30.6 Not Caucasian 16.0-31.1	Age, **seasonality**, ethnicity, gestational age, birth weight, BMI
Ciresi A *et al.*	Jan 2011- Dec 2012	80#	4.3-16.0 years	Sicily (**37**°N)	40.0	35.0	**Seasonality**
Stagi S *et al.*	Sept 2010-Dec 2013	679	2.1-17.9 years	Florence (**44**°N)	58.7	30.0	Age, **seasonality**, BMI, sun exposure, sunscreen use
Vierucci F *et al.*	Oct 2010-Sept 2012	427	10.0-21.0 years	Pisa (**43**°N)	49.9	32.3	Age, **seasonality**, BMI, ethnicity, sun exposure, sunscreen use
Cadario F *et al.*	Apr 2012-Mar 2013	533	1-3 days	Novara (**45**°N)	85.4	12.5	**Season of birth**, ethnicity, maternal supplementation
Prodam F *et al.*	July 2009-Dec 2013	575	6-18 years	Novara (**45**°N)	46.1	37.6	Age, BMI, waist circumference, **seasonality**, UVR, sun exposure

* data not reported

\# children affected by growth hormone deficiency



Lido di Camaiore - Luglio 1983

Esporre le estremità

Evitare le ore centrali della giornata

Filtri solari (prevenzione eritema solare)

Con Calcio + Vit B_2 B_{12} D_2

con calcio, fosforo, vit. D e K

VALORI MEDI PER 100 ML	
ENERGIA	
kJ	175
kcal	41
GRASSI	1,0 g
di cui acidi grassi saturi	0,7 g
CARBOIDRATI	4,9 g
di cui zuccheri	4,9 g
FIBRE	0,0 g
PROTEINE	3,2 g
VITAMINE	
Vitamina D	1 µg
MINERALI	
Calcio	160 mg
Fosforo	115 mg
Sodio	0,13 g

Dichiarazione Nutrizionale per 100g		
Energia	374 kJ 88 kcal	
Grassi	0,9	g
di cui:		
acidi grassi saturi		
acidi grassi monoinsatu		
acidi grassi polinsaturi		
Carboidrati		
di cui: zuccheri	16	g
Fibre	0,7	g
Proteine	2,7	g
Sale	0,13	g
Calcio	120 (*)	mg
Riboflavina (Vit B_2)	0,21 (*)	mg
Vitamina B_{12}	0,38 (*)	µg
Vitamina D	1,5 (**)	µg

(*) 15%-(**) 30% dell'Assunzione di Riferimento Giornaliera

1 budino (115 gr): 69 UI vit. D2

1 bicchiere di latte (200 ml): 80 UI vit. D

- Si raccomanda la profilassi con vitamina D in tutti i bambini indipendentemente dal tipo di allattamento (400 UI/die in assenza di fattori di rischio) per tutto il primo anno di vita.
- Oltre il primo anno di vita si raccomanda di sottoporre a profilassi con vitamina D (600-1.000 UI/die) bambini e adolescenti con fattori di rischio di deficit.

HORMONE RESEARCH IN PÆDIATRICS

Consensus Statement

Horm Res Paediatr
DOI: 10.1159/000443136

Received: April 24, 2015
Accepted: September 17, 2015
Published online: January 8, 2016

Global Consensus Recommendations on Prevention and Management of Nutritional Rickets

The consensus group represented 11 international scientific organizations (33 participants)

- 400 IU/day (10 µg) is adequate to prevent rickets and is recommended for all infants from birth to 12 months of age, independently of their mode of feeding (1 ⊕ ⊕ ⊕).
- Children at high risk of vitamin D deficiency are candidates for preventative vitamin D supplementation beyond 12 months of age (1 ⊕ ⊕ ⊕).

Maternal preferences for vitamin D supplementation in breastfed infants

(Minnesota, USA)

Table 2. Maternal Reasons for Not Supplementing Infants With Vitamin D

Themes	Quotes
Lack of knowledge about supplementation	"I didn't know I should"
	"Too young – will start soon"
	"Never even knew vitamin D supplementation was needed"
Assumption that fortified milk provides infant with needed vitamin D	"I gave vitamin D supplement when she was breast milk-fed, provider told us to discontinue when formula started"
	"My baby went to exclusive soy formula at 2 months old, which has vitamin D supplement"
	"Baby formula has all that is needed and recommended"
	"Stopped giving it when I stopped nursing and started to give formula"
Assumption that breast milk provides infant with needed nutrition	"Find it hard to believe the whole population is so deficient in Vitamin D, especially in breast milk"
	"I feel like my breast milk was designed by God to give my baby what she needs. Babies have been fine and healthy without Vitamin D supplementation for generations"
Inconvenience/ Dislike	"It causes her to spit up"
	"I forget to because she doesn't take it well and doesn't seem to like the taste"

(Umaretiya PJ et al. Ann Fam Med 2017)

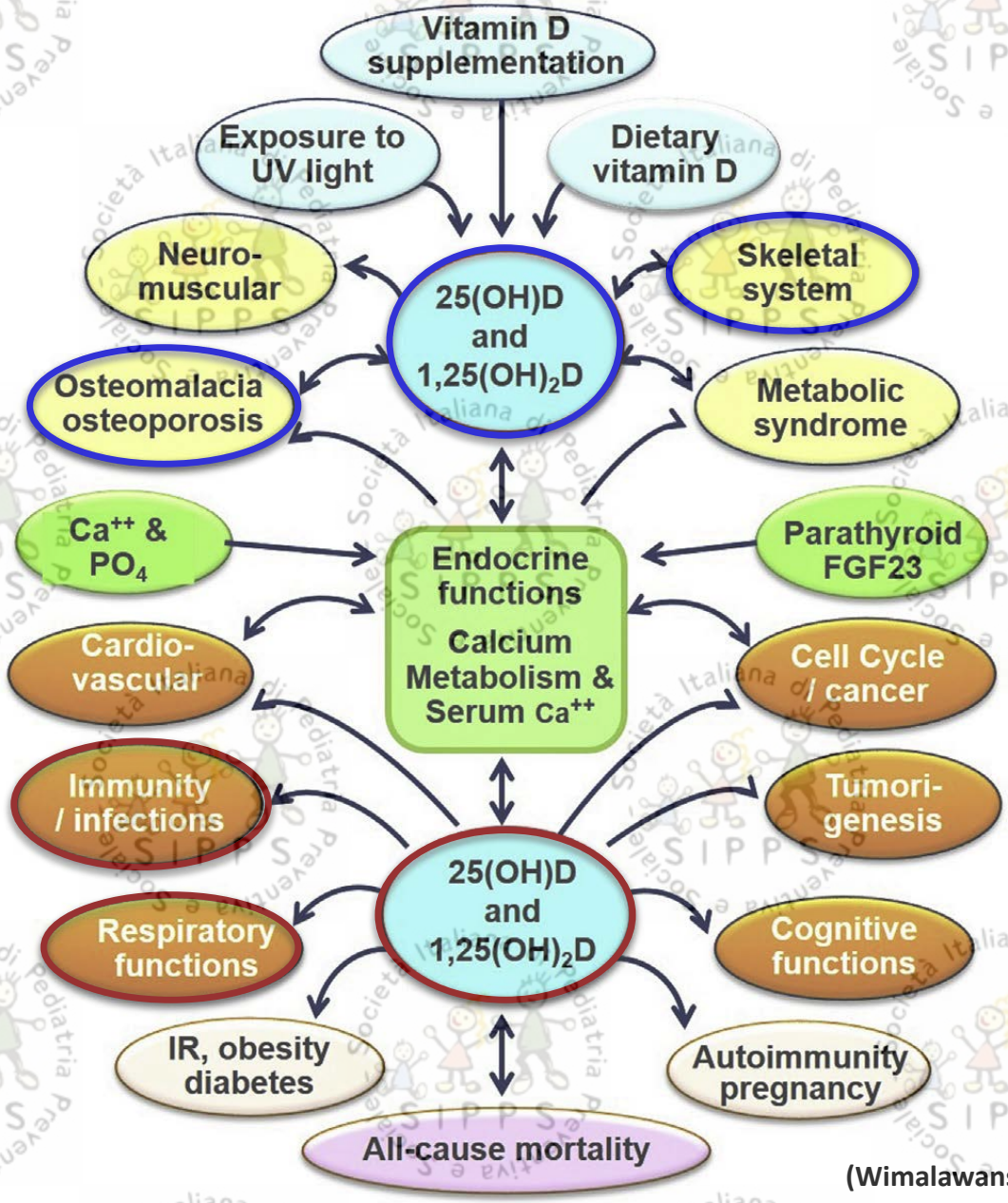
Vit. D and the breastfeeding infant: Family Medicine Clinicians' knowledge

(Oct 2013, Minnesota, USA)

Question (multiple responses were accepted)	Total (*N* = 56)
Why do you NOT recommend vitamin D?[a]	**N=4 (7.1%)**
Not enough time in the visit	6 (10.7)
Insufficient evidence of benefit	6 (10.7)
Breastfed infants can get vitamin D from other sources	6 (10.7)
May result in mothers choosing formula	5 (8.9)
I am not aware of AAP or IOM recommendations.	3 (5.4)
Because I didn't supplement my own child(ren)	3 (5.4)
Because parents are resistant to recommendation	2 (3.6)

(Oberhelman SS et al. J Hum Lact May 2018)

Non-musculoskeletal benefits of vitamin D



(Wimalawansa SJ. J Steroid Biochem Mol Biol 2016)

THE LANCET
Diabetes & Endocrinology

	Meta-analyses suggest risk reduction with vitamin D?	
	All participants	Stronger† effect in people with low 25(OH)D
All-cause mortality in community and home-dwelling adults, and elderly people	Yes	No
Mortality of critically ill patients	ND	ND
Occurrence of cardiovascular diseases	No	No
Cardiovascular mortality	No	No
Occurrence of cancerous diseases and other neoplasms	No	No
All cancer mortality	Yes	ND
Metabolism disorders		
Adiposity	No	No
Glucose metabolism disorders	No	No
Infectious diseases		
Acute respiratory tract infections of children and adults	Yes	Yes
Acute respiratory infections in children after vitamin D supplementation during pregnancy	ND	ND
Pneumonia in children	No	ND
Tuberculosis	No	ND
Prevention of common infectious episodes	ND	ND
Prevention of exacerbations in patients with COPD	ND	ND
Allergic conditions		
Asthma exacerbations in children and adults	Yes	ND
Wheezing in children after vitamin D supplementation during pregnancy	Yes	ND
Dermatitis	ND	ND
Daily activity	No	Uncertain
Multiple sclerosis	No	ND
Quality of life	ND	ND
Pain	No	ND
Depression	No	No
Rheumatic conditions	No	ND
Crohn's disease	ND	ND
Serum biomarkers of inflammation	No	ND
Health status and mortality of low birthweight children	ND	ND
Pregnancy-related conditions‡ and vitamin D supplementation during pregnancy	Uncertain	ND
Perinatal conditions§ and vitamin D supplementation during pregnancy	Uncertain	ND

ND=no meta-analysis or trial of acceptable quality was available. 25(OH)D=25-hydroxyvitamin D. COPD=chronic obstructive

Jan 2013-May 2017

- 87 meta-analyses (52 excluded as they contained less recent literature or were of suboptimal quality).
- 202 articles on trials that were not included in meta-analyses.

- Good quality meta-analyses based on large numbers of trials of acceptable quality already exist.
- The research community should encourage the sharing and pooling of patient-level data to allow better subgroup analyses and more robust conclusions.

(Autier P et al. Lancet Diabetes Endocrinol 2017 Oct)

Research

The hobbit — an unexpected deficiency

Vit. D score (0-4): sun exposure score (0-3) + diet vit. D score (0-1)

Inhabitants	Good	Victorious	Vitamin D score
Hobbits	Yes	Yes	4
Dwarves	Yes	Yes	3
Beorn	Yes	Yes	3
Men	Yes	Yes	4
High elves	Yes	Yes	4
Wood elves	Yes	Yes	2
Eagles	Yes	Yes	3
Smaug the dragon	No	No	0
Trolls	No	No	0
Goblins	No	No	0
Gollum	No	No	1

The mean vit. D score was higher among the victorious (3.4± 0.5) than the non-victorious (0.2 ± 0.4) ($p<0.001$)

(MJA 2013; 199: 805–6)

Battaglia di Pelusio (525 a.C.)

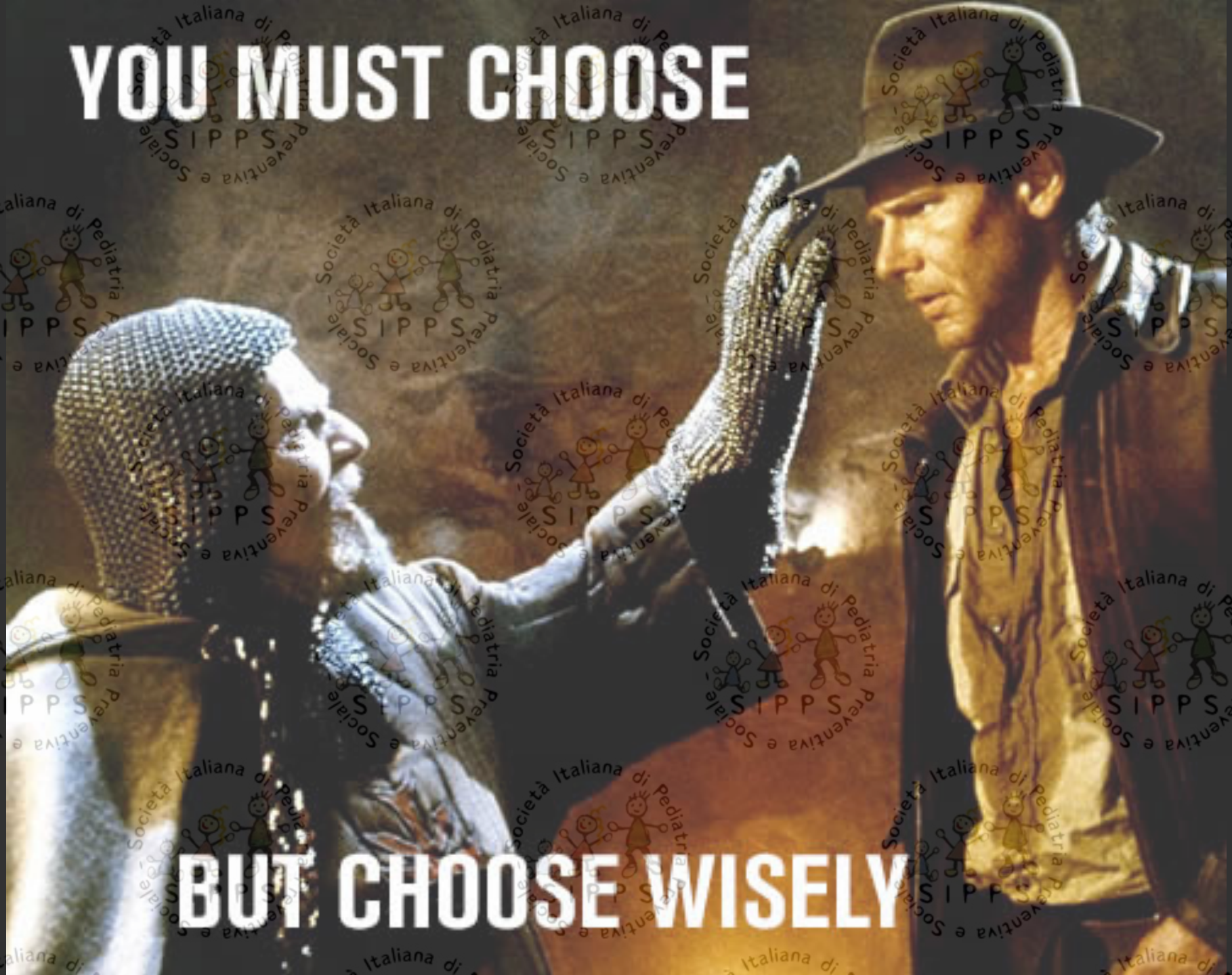
Guerrieri Egiziani

Erodoto (484-425 A.C.)

Guerrieri Persiani

- Presso il luogo della battaglia sorgevano due tumuli per i caduti di entrambe le parti.
- Il cranio degli Egizi era molto più resistente di quello dei Persiani in quanto, spiega Erodoto, questi ultimi erano soliti coprire il capo con la tiara fin da piccoli.

(Hernigou P et al. Int Orthop Mar 2018)


YOU MUST CHOOSE
BUT CHOOSE WISELY

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An initiative of the ABIM Foundation

American Academy of Pediatrics

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Section on Endocrinology

Five Things Physicians and Patients Should Question

Avoid ordering Vitamin D concentrations routinely in otherwise healthy children, including children who are overweight or obese.

Although a 25-hydroxyvitamin D concentration, reflecting both vitamin D synthesis and intake, is the correct screening lab to monitor for vitamin D deficiency, current evidence is not sufficient to suggest that screening in otherwise healthy including children who are overweight or obese is necessary or safe.

(Released October 2, 2017)

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).
- Dermatite atopica grave non responsiva a tp convenzionale (score).

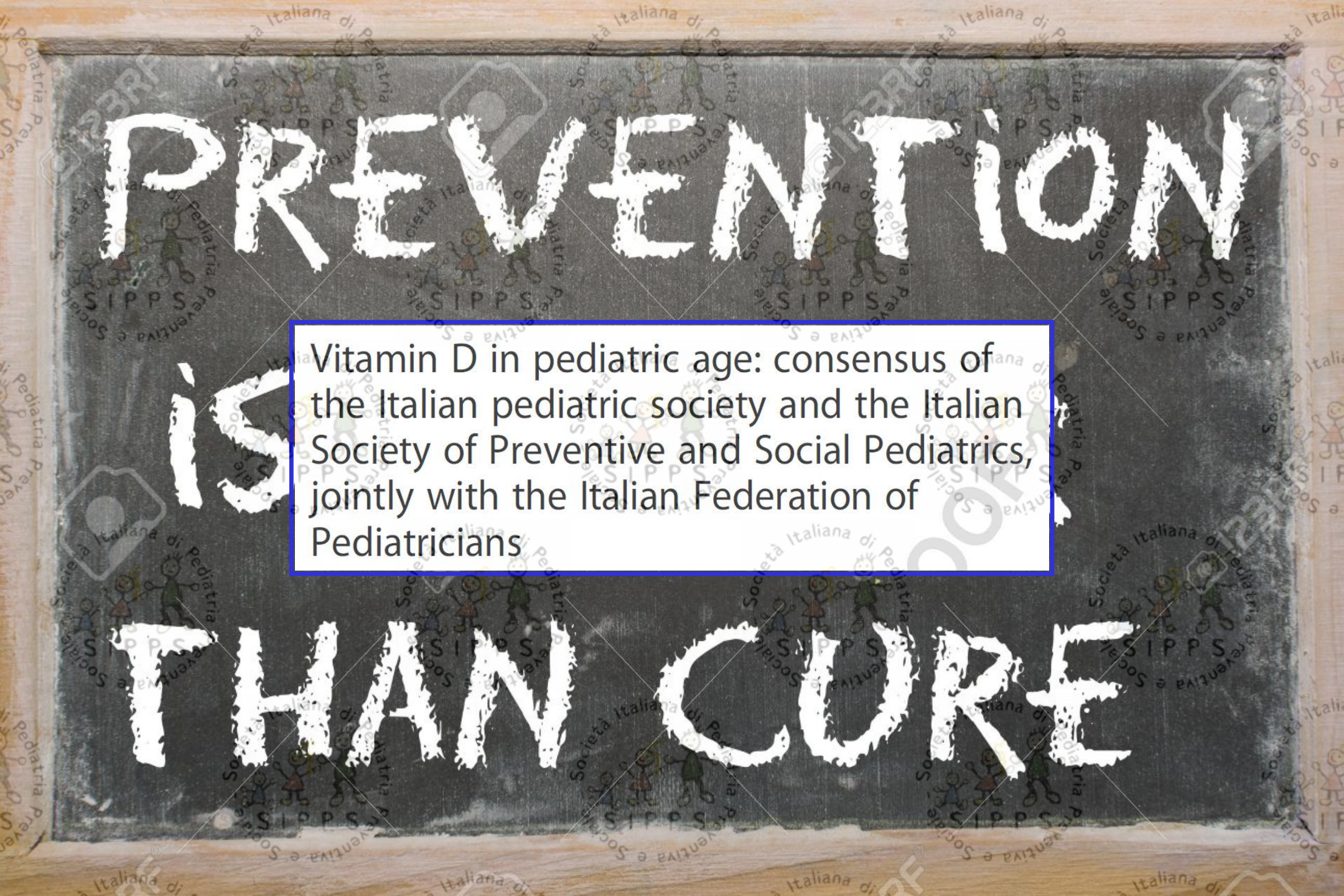
+ Sospetto deficit grave di vit. D

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



Vitamin D in pediatric age: consensus of the Italian pediatric society and the Italian Society of Preventive and Social Pediatrics, jointly with the Italian Federation of Pediatricians


Grazie per l'attenzione