



Importanza della Vitamina D nella seconda e terza infanzia



XXX CONGRESSO NAZIONALE
SOCIETÀ ITALIANA DI PEDIATRIA
PREVENTIVA E SOCIALE

BAMBINI DI IERI, OGGI E DOMANI...
LA NOSTRA CARE, IL NOSTRO CUORE

TEATRO DI ORTIGIA • 7 - 10 GIUGNO 2018
SIRACUSA

Francesco Vierucci

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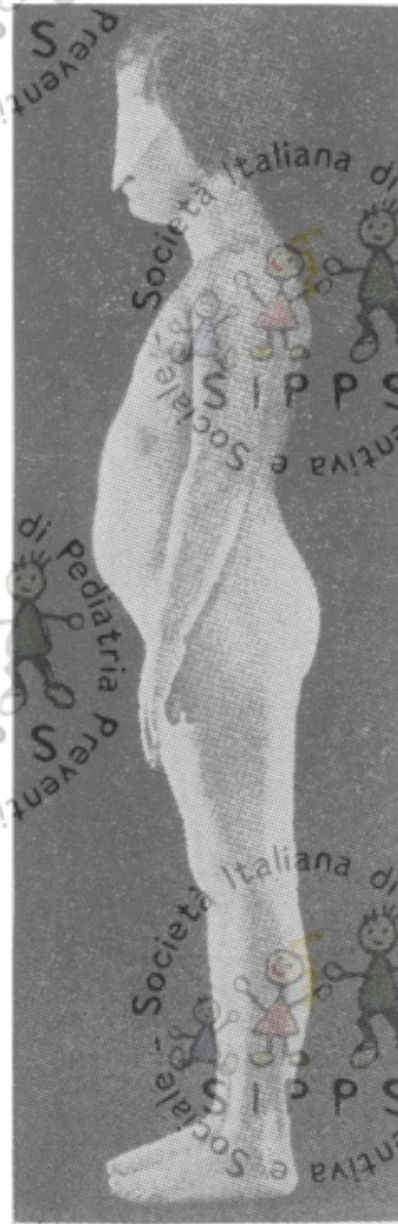
Number 7

Vitamin D in Child Health*

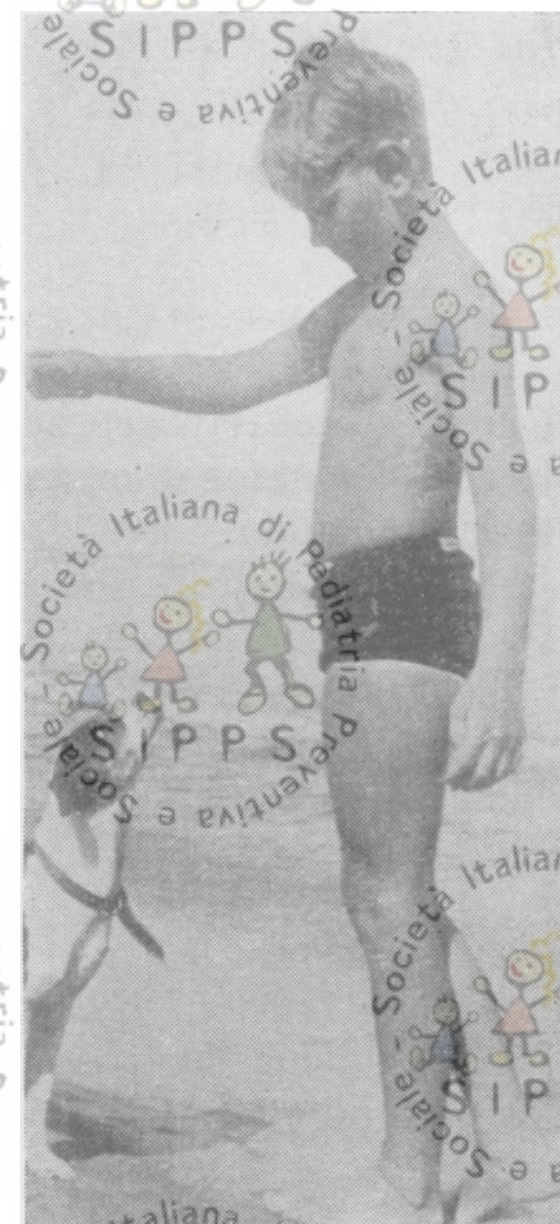
FRED O. TONNEY, M.D., F.A.P.H.A.

The influence of vitamin D upon the child's physical development is viewed from the standpoint of:

- growth,
- bone development,
- tooth development,
- posture,
- resistance to the infections.



A rachitic child in typical lax posture



A normal child with good muscle tonus



**Prima infanzia
(0-2 anni)**



**Seconda infanzia
(3-5 anni)**



**Terza infanzia
(6-11/12)**



Adolescenza





Vitamin D in pediatric age: Consensus SIP, SIPPS & FIMP



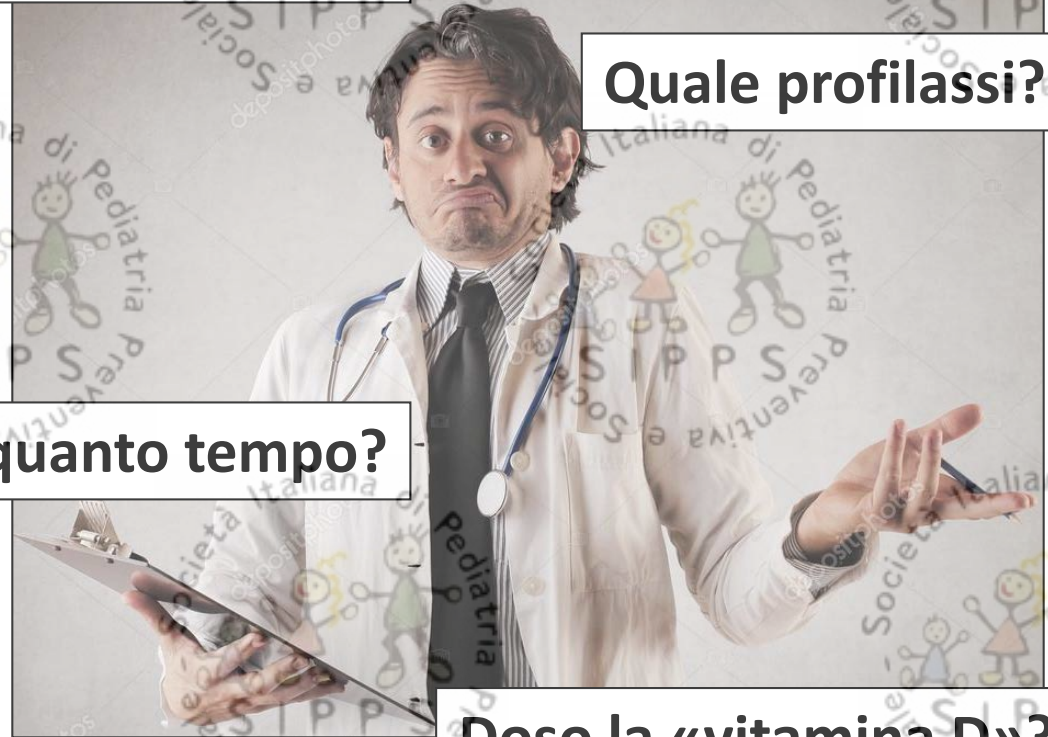
- We recommend vitamin D supplementation in **all newborns independently of the type of feeding.**
- Vitamin D supplementation should be started within the **first days of life** and continued **throughout the first year.**

E dopo il primo anno?

Profilassi?



Quale profilassi?



Per quanto tempo?

Doso la «vitamina D»?

Lo stato vitaminico D durante la seconda e la terza infanzia in Italia

Studio	Periodo di arruolamento	N.	Età (range)	Città/ Regione (latitudine)	Deficit, % [25(OH)D < 20 ng/ml]	Insuff., % [25(OH)D: 20-29 ng/ml]	Ipovit. D, % [25(OH)D < 30 ng/ml]
Vierucci ⁸	ott 2010- set 2012	283	2-11 anni	Pisa (43°N)	40,3	35,0	75,3
Franchi ⁹	gen 2010- dic 2012	1.148 (caucasici)	0-16 anni	Verona (45°N)	44,2	30,6	74,8
Ciresi ¹⁰	gen 2011- dic 2012	80*	4-16 anni	Sicilia (37°N)	40,0	35,0	75,0
Stagi ¹¹	set 2010- dic 2013	679	2-18 anni	Firenze (44°N)	58,7	30,0	88,7
Prodani ¹²	lug 2009- dic 2013	575°	6-18 anni	Novara (45°N)	46,1	37,6	83,7

* Bambini affetti da deficit di ormone della crescita; ° Soggetti con sovrappeso/obesità.

«1 bambino su 2 ha un deficit di vitamina D»

Chi è a rischio di deficit di vitamina D?

Elena, 4 anni



Fabio, 4 anni



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

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WHY IS IT
Important?



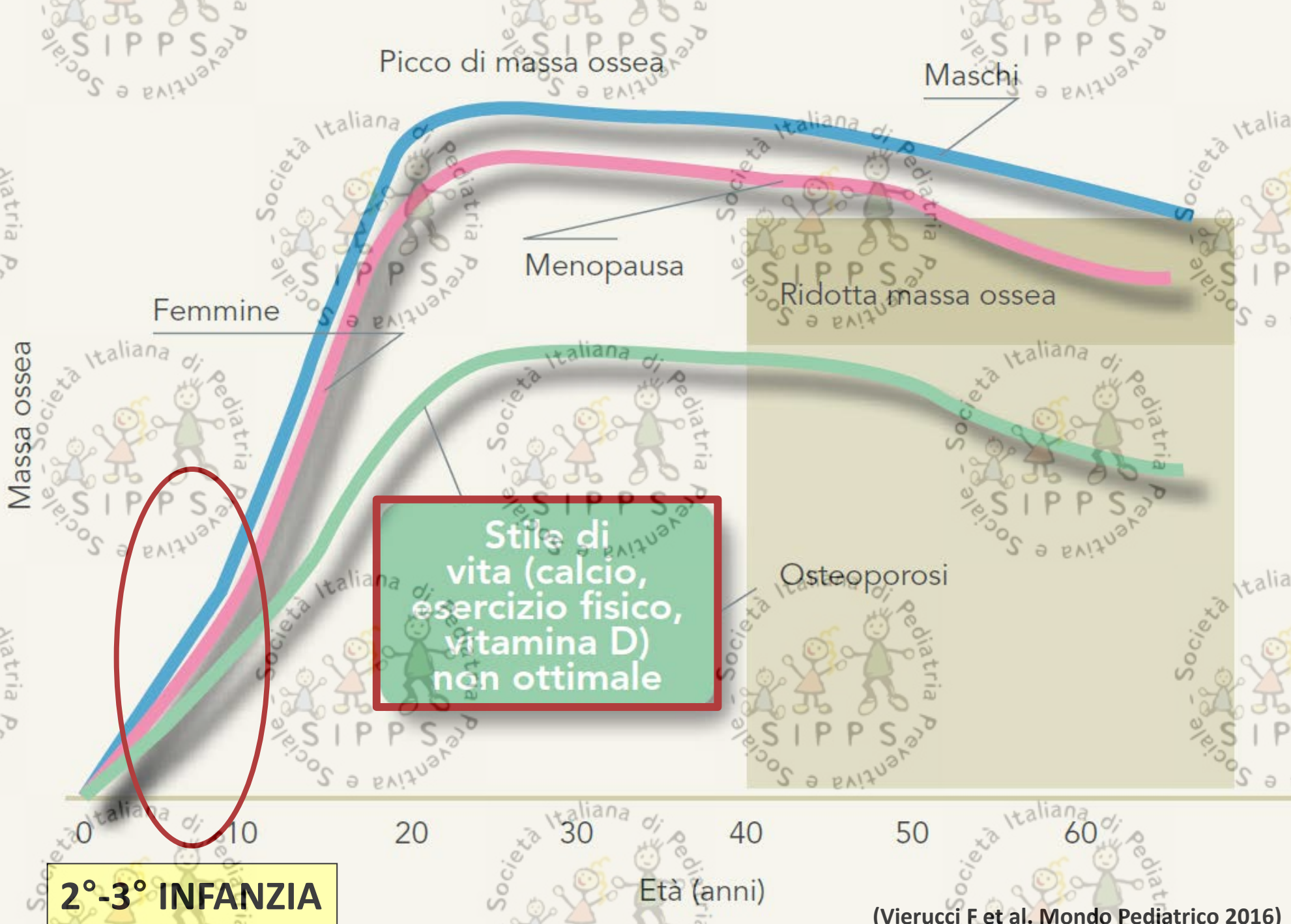
Caratteri sessuali

Peso

Statura



Massa ossea

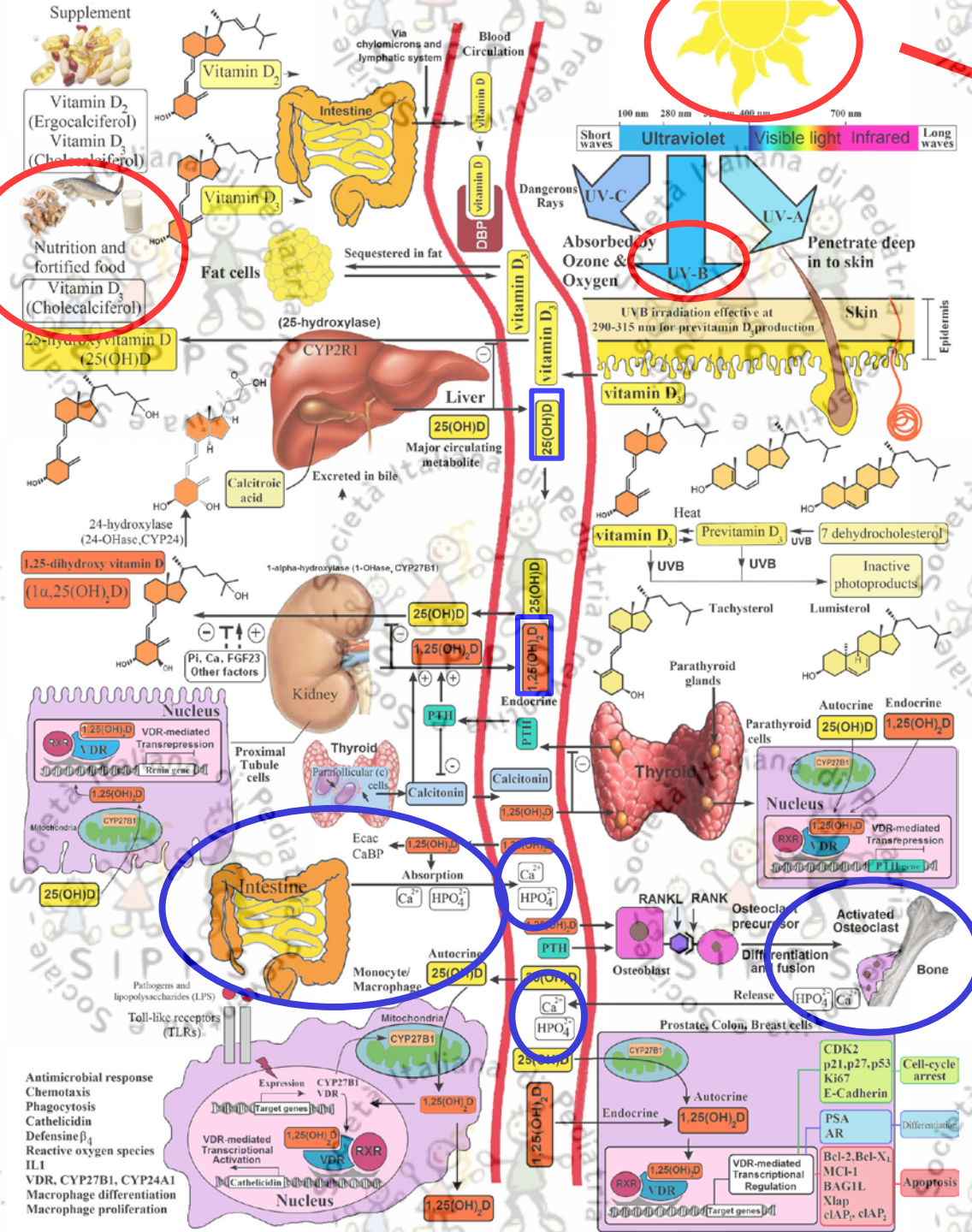


10%

90%

Calcio e fosforo

Calcio e fosforo



(Saggese G, Vierucci F, et al. Eur J Pediatr 2015)

Calcio

**Massa
ossea**

Vitamina D

**Massa
muscolare**

Esercizio fisico



The Spectrum of Vitamin D Deficiency



**FATTORI
DI RISCHIO**

**STATO
VITAMINICO D
SUFFICIENTE**

**DEFICIT VIT. D
ASINTOMATICO**

**DEFICIT VIT. D
ASINTOMATICO
CON IPERPTH**

RACHITISMO

**DEFICIT VIT. D
SINTOMATICO**

OSTEOMALACIA

PROFILASSI

M. M. (10 mesi): rachitismo con ipocalcemia

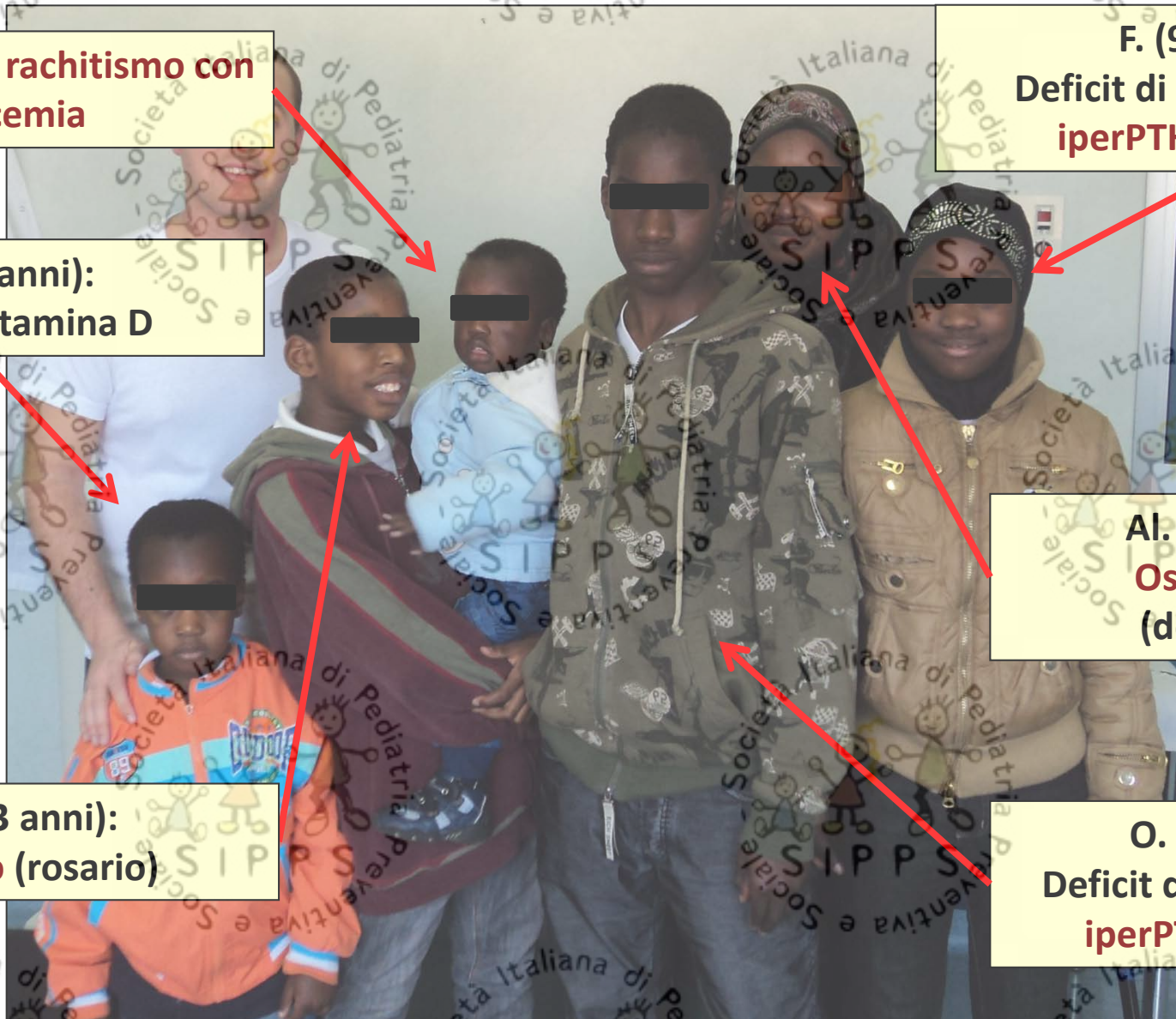
M. (4.5 anni): Deficit di vitamina D

F. (9.8 anni): Deficit di vitamina D con iperPTH secondario

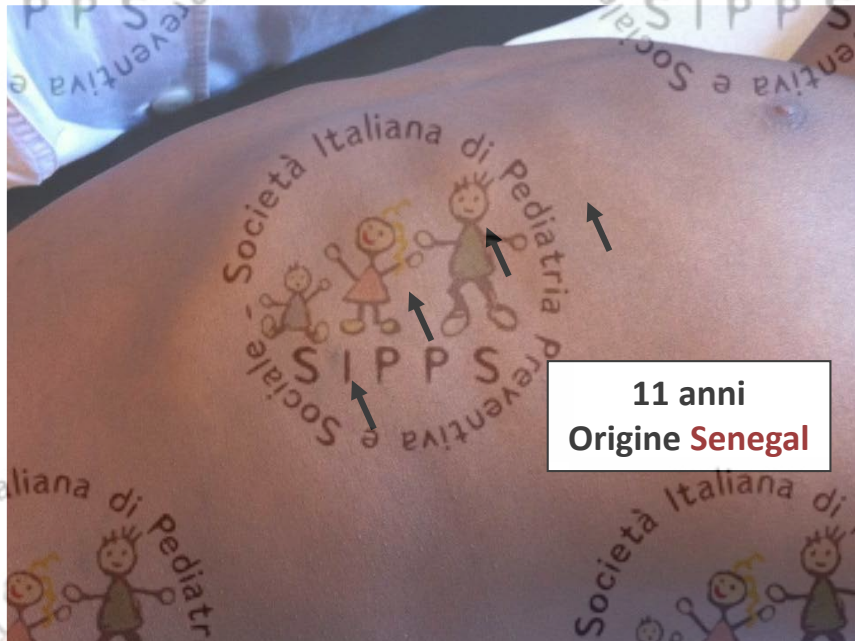
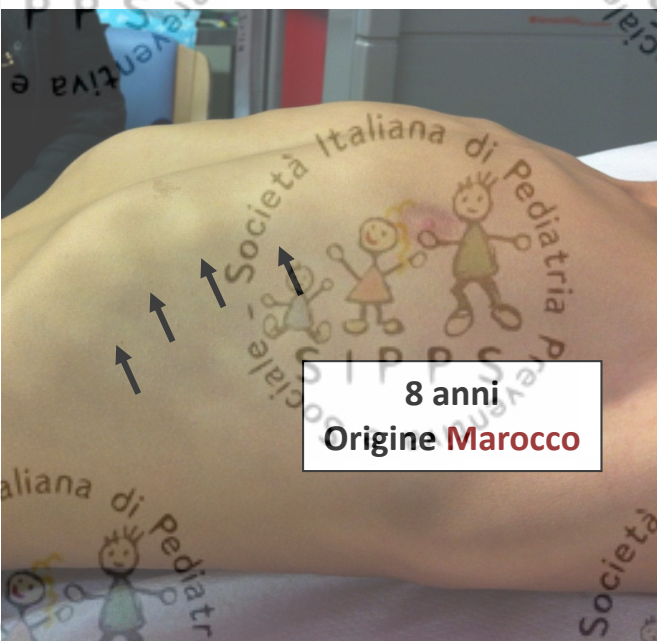
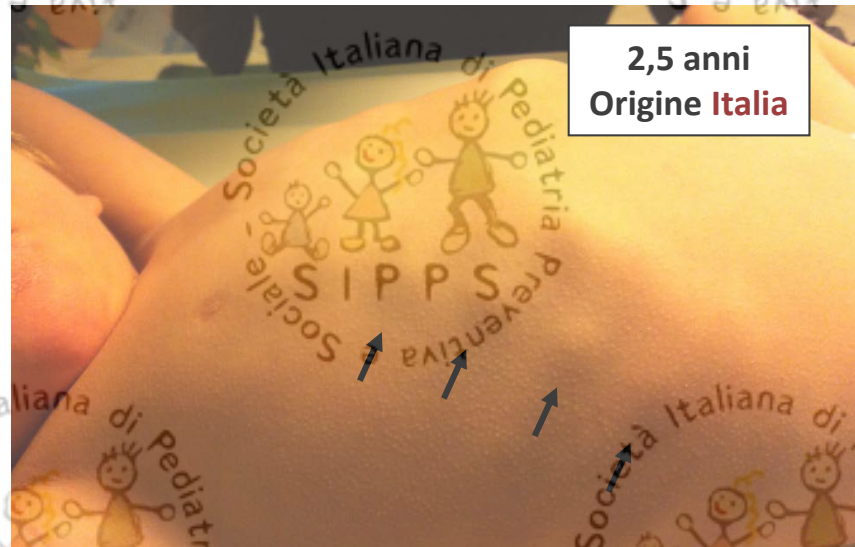
Al. (45.2 anni): Osteomalacia (dolori ossei)

Ab. (11.3 anni): Rachitismo (rosario)

O. (13.4 anni): Deficit di vitamina D con iperPTH secondario



Rachitismo carenziale: rosario



Fabbisogno giornaliero raccomandato di vit. D

Primo anno di vita

400 UI

Adequate intake

Dopo il primo anno di vita

Seconda infanzia

Terza infanzia

Adolescenza

600 UI

Recommended Dietary Allowance (RDA)

Fabbisogno giornaliero raccomandato di vit. D

**400 UI
(50%)**

EAR (AR)

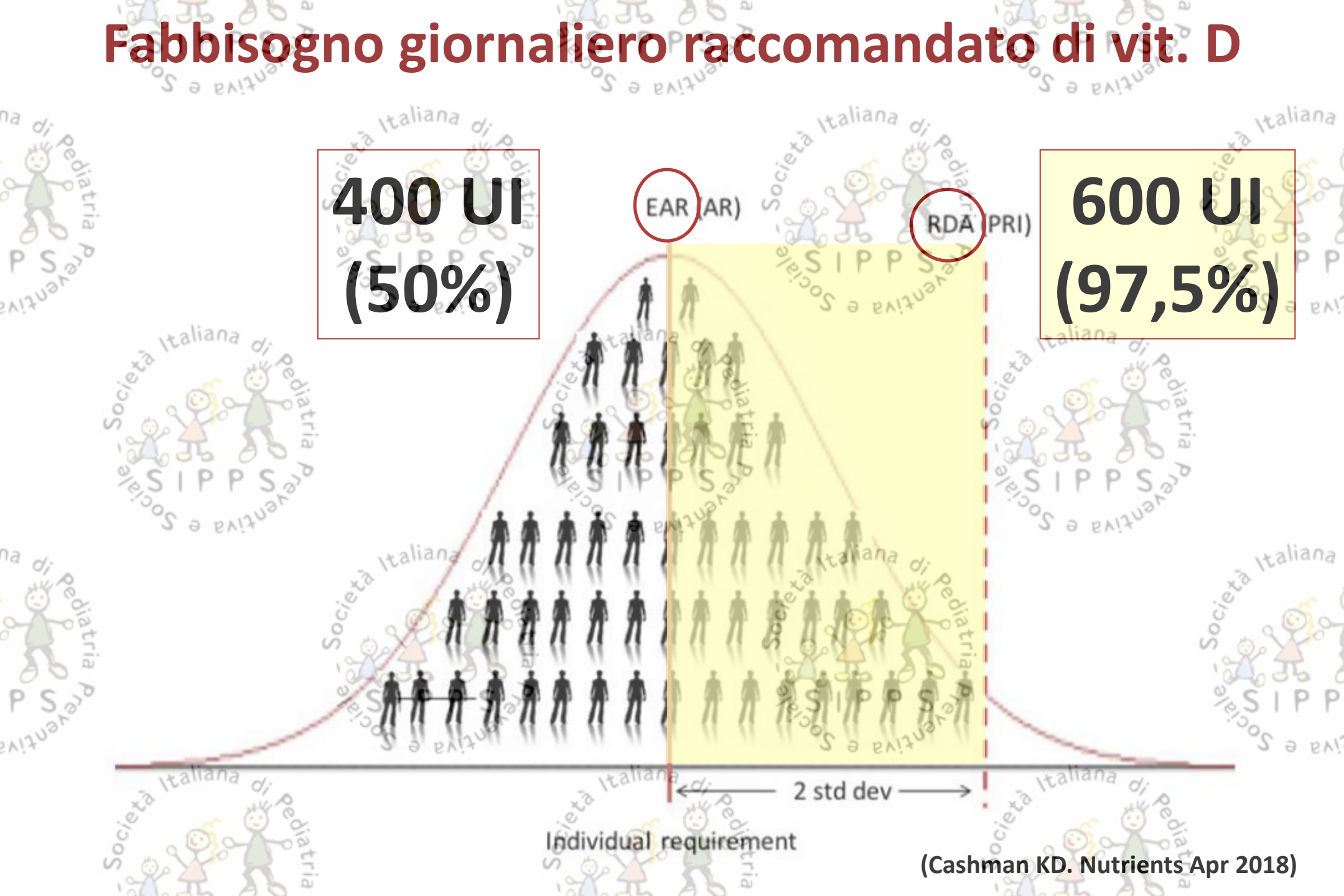
RDA (PRI)

**600 UI
(97,5%)**

2 std dev

Individual requirement

(Cashman KD. Nutrients Apr 2018)



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)

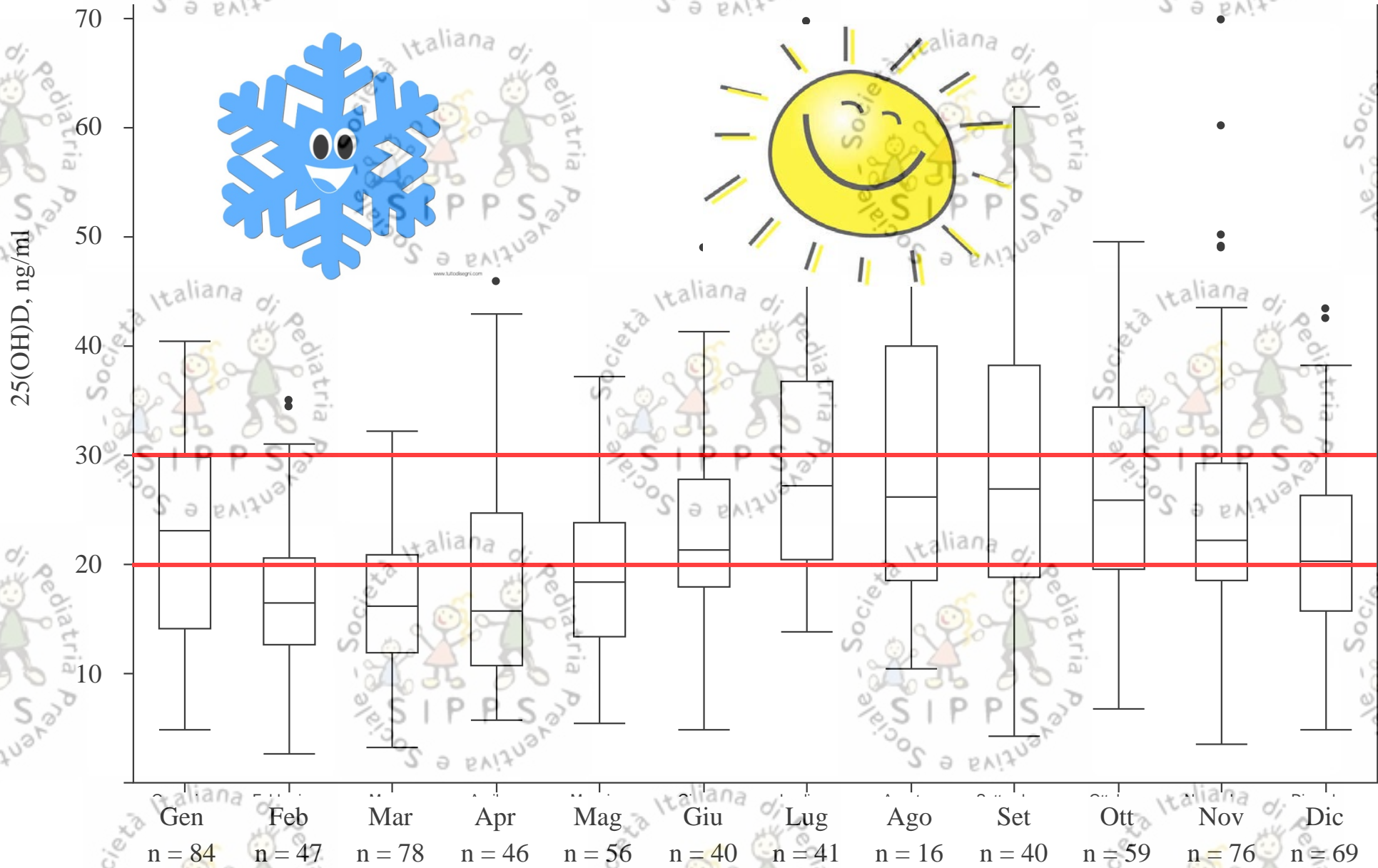


0-12 mesi: 400-1.000 UI/die

1-18 anni: 600-1.000 UI/die

Obesità: 2-3 volte i fabb. per età

Livelli mediани 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 ($p < 0,0001$)



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**

Italia ($47^{\circ}05'29''$ - $35^{\circ}29'26''$ N)



Bojnurd ($37^{\circ}28'N$)

Iran



Consensus SIPPS 2018: dopo il primo anno

A CHI

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

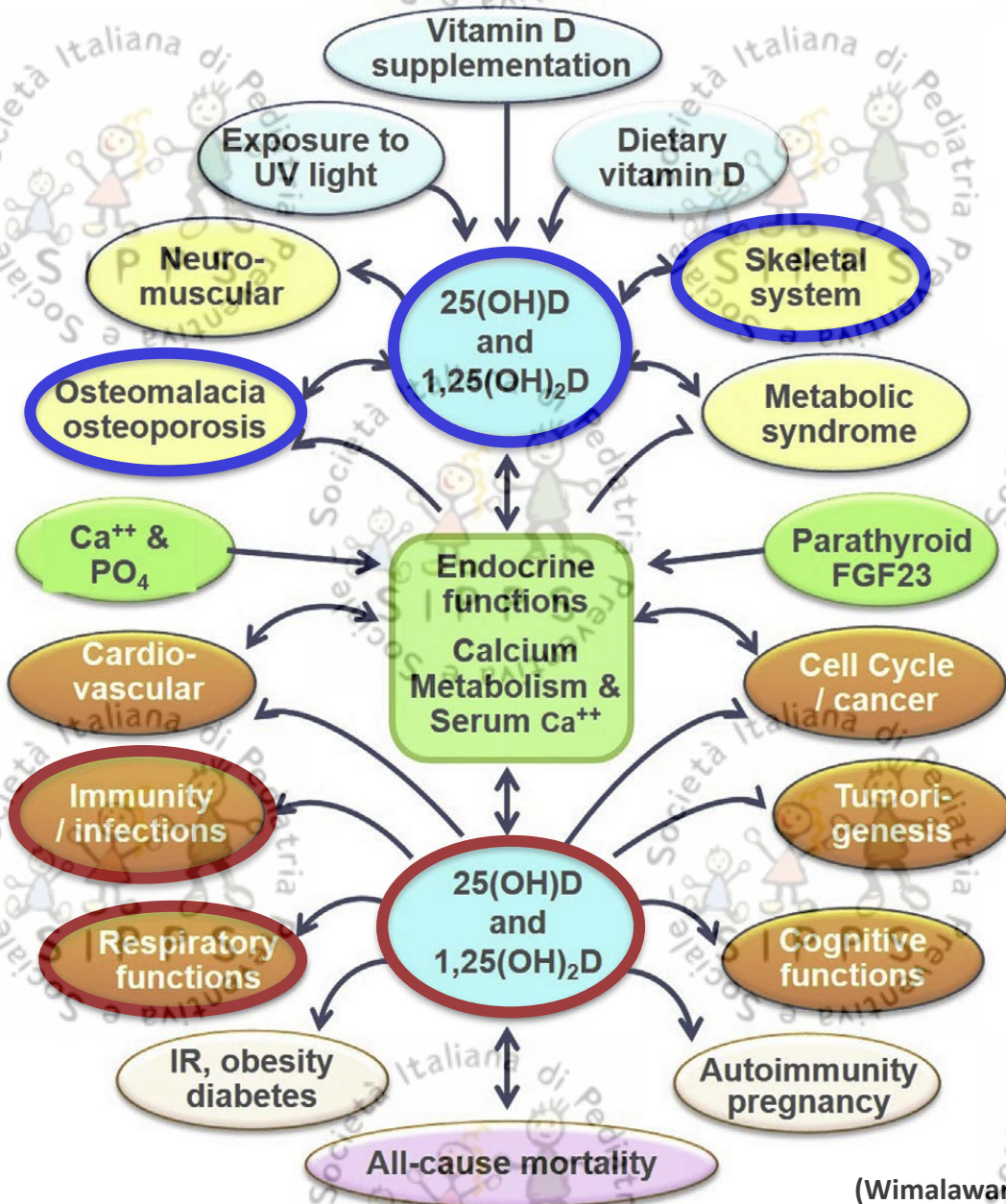
COME

- 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**.

PER QUANTO

- 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.

Non-musculoskeletal benefits of vitamin D

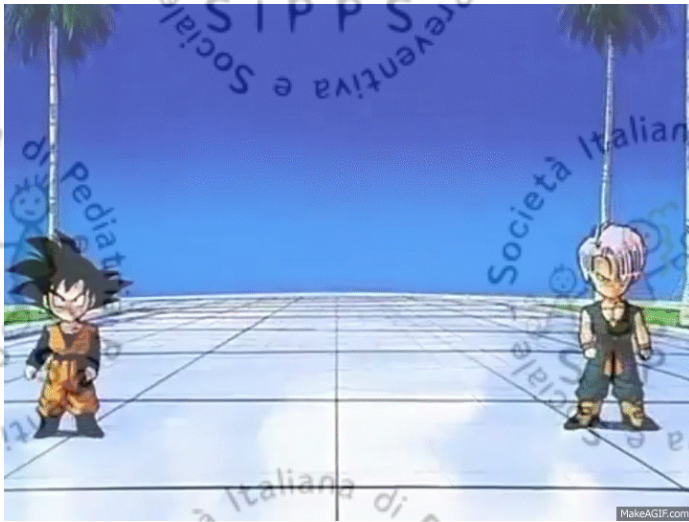




Vitamin D supplementation to prevent asthma exacerbations: a systematic review and meta-analysis of individual participant data (955 participants from 7 RCTs; 297 children from 5 RCTs)

	Number of participants; number of trials*	Event rate per participant-year (control group)	Event rate per participant-year (intervention group)	Adjusted incidence rate ratio (95% CI)†	p value	p _{interaction} ‡
Overall	955; 7	121/284.7 (0.43)	85/286.6 (0.30)	0.74 (0.56–0.97)	0.03	NA
Baseline 25(OH)D (nmol/L)						
<25 (< 10 ng/ml)	92; 3	14/33.0 (0.42)	6/32.2 (0.19)	0.33 (0.11–0.98)	0.046	0.25
≥25	764; 6	107/233.8 (0.46)	79/240.2 (0.33)	0.77 (0.58–1.03)	0.08	..

- Vit. D supplementation safely reduces the rate of asthma exacerbations requiring treatment with systemic corticosteroids.
- In view of the **low cost** of this intervention and the major economic burden associated with asthma exacerbations, vitamin D supplementation represents a **potentially cost-effective strategy** to reduce this important cause of morbidity and mortality.



Prenatal vitamin D supplementation reduces risk of asthma/recurrent wheeze in early childhood: A combined analysis of two randomized controlled trials

25% reduced risk of asthma/recurrent wheeze at **0-3yrs**:
Adjusted odds ratio = **0.74** (95% CI: 0.57-0.96), **p=0.02**

In **women** with **25(OH)D \geq 30 ng/ml** at study entry:
Adjusted odds ratio = **0.54** (95% CI: 0.33-0.88), **p=0.01**



(Wolsk HM et al. PLoS One 2017 Oct)

GRAVIDANZA



**PREVENZIONE
PRIMARIA**

**PREVENZIONE
ASMA NEL BAMBINO**

**STILE DI VITA,
PROFILASSI
CON VITAMINA D**



**BAMBINO CON
ASMA**



**PREVENZIONE
SECONDARIA**

**RIDUZIONE
ESACERBAZIONI
ASMATICHE**

Vitamin D supplementation to prevent acute respiratory tract infections: systematic review and meta-analysis of individual participant data



- 10,933 participants (0-95 yrs) from 25 7 RCTs
- 5,571 children < 1 yr; 1,079 aged 1.1-15.9 yrs



Table 2 | One step individual participant data meta-analysis, proportion of participants experiencing at least one acute respiratory tract infection (ARTI): overall and by subgroup

Variables	No of trials*	Proportion with ≥1 ARTI, control group (%)	Proportion with ≥1 ARTI, intervention group (%)	Adjusted odds ratio (95% CI)†	P value	P value for interaction
Overall	25	2204/5225 (42.2)	2303/5708 (40.3)	0.88 (0.81 to 0.96)	0.003	--
Baseline 25(OH)D (nmol/L):						
<25 (< 10 ng/ml)	14	137/249 (55.0)	117/289 (40.5)	0.58 (0.40 to 0.82)	0.002	0.01
≥25	19	1027/1639 (62.7)	1179/1995 (59.1)	0.89 (0.77 to 1.04)	0.15	
Dosing regimen type:						
Bolus dose ≥30 000 IU given	10	994/2786 (35.7)	1097/3014 (36.4)	0.97 (0.86 to 1.10)	0.67	0.05
Bolus dose not given	15	1210/2439 (49.6)	1206/2694 (44.8)	0.81 (0.72 to 0.91)	<0.001	

- Overall protective effect of vit. D supplementation against ARTI (NNT = 33).
- NNT = 20 in those receiving daily or weekly vitamin D without bolus doses.
- NNT = 4 in those with profound vitamin D deficiency (< 10 ng/ml).

Vitamin D and growing pains

Box Typical features of growing pains.⁶

- Pain in both legs
- Pain starts between the ages of 3 and 12 years
- Pain typically occurs at the end of the day or during the night
- There is no notable limitation of activity and no limping
- The typical distribution of the pain is anterior thigh, calf and posterior knee
- The pain is intermittent with some pain free days and nights
- Physical examination reveals no abnormalities with no evidence of orthopaedic disorder, swelling, erythema, tenderness, local trauma, infection or reduced range of motion
- The laboratory tests are within reference range with no objective findings, eg, erythrocyte sedimentation rate, radiograph and bone scan
- Pain persists at least 3 months
- There is no associated lack of well being



Clinical bottom line

- ▶ There is a high prevalence of hypovitaminosis D in children presenting with growing pains in Korea and Turkey when compared with the estimated population prevalence. (Grade C)
- ▶ No clear association or causal relationship has been demonstrated in the literature between low vitamin D levels and growing pains. However, it is possible that some children presenting with unexplained lower limb pain may have these symptoms secondary to low vitamin D levels. (Grade C)
- ▶ Vitamin D supplementation in those found to have low vitamin D levels may be associated with pain reduction in those suffering from growing pains. (Grade C)

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



Jan 2013-May 2017

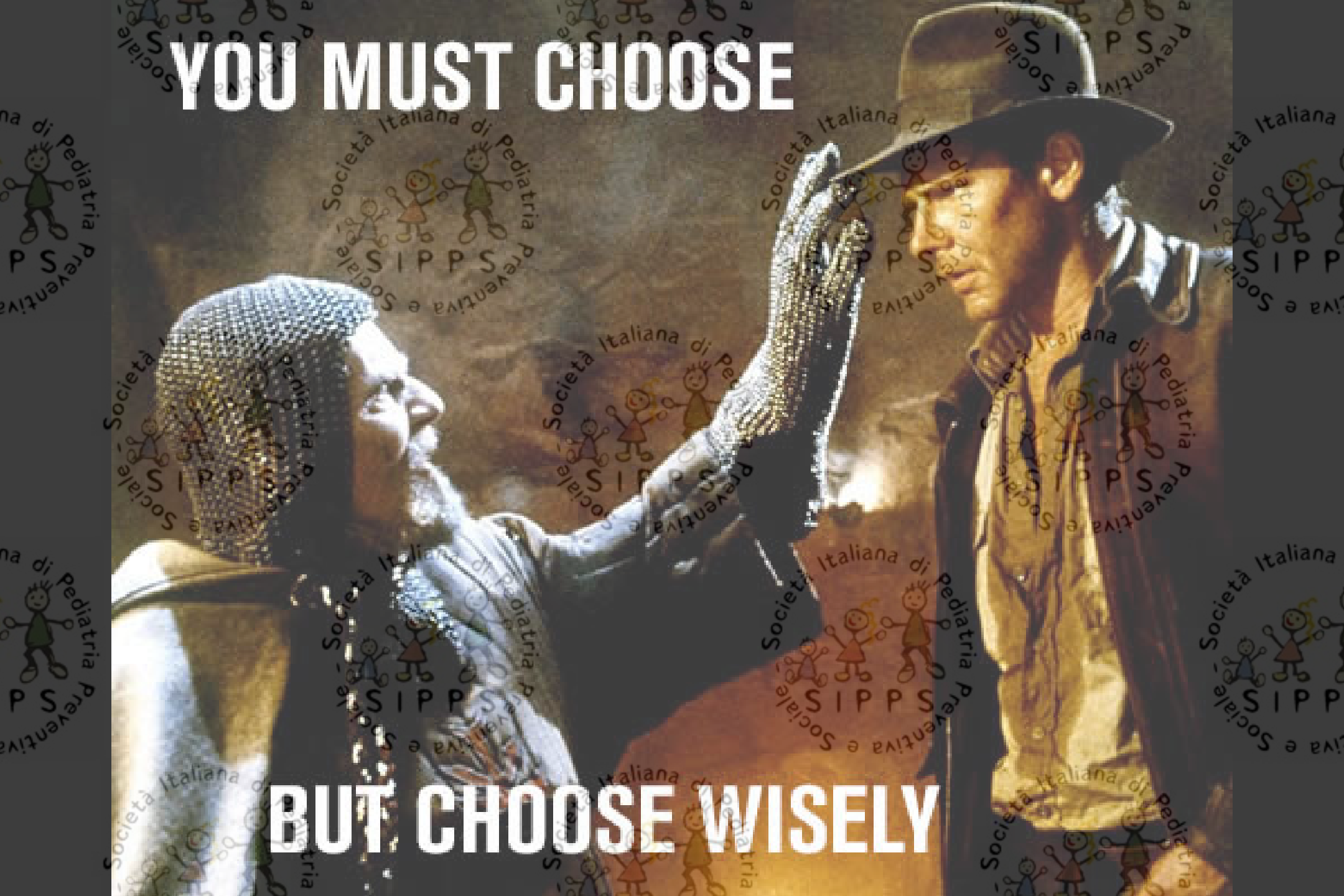
- **87** meta-analyses (**52** excluded as they contained less recent literature or were of suboptimal quality).
- **202** articles on trials that were not included in meta-analyses.

- **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)

YOU MUST CHOOSE

BUT CHOOSE WISELY



Choosing Wisely[®]

An initiative of the ABIM Foundation

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™



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.

(October 2, 2017)

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

- We recommend against routine 25(OH)D testing in children and adolescents. We suggest to measure serum 25(OH)D levels in presence of multiple risk factors for vitamin D deficiency. Vitamin D status should be monitored at least yearly in subjects that require supplementation during the whole year because affected from pathological conditions or receiving drugs affecting vitamin D metabolism

(May 8, 2018)

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, steroideo-resistente (prevenzione esacerbazioni)
- Infezioni respiratorie ricorrenti (prevenzione)
- Dolori di crescita



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

PREVENTION

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

THAN CORE

Grazie per l'attenzione

