Dubai, 15/02/2019

Verified European Experience with **VITAMIN D SUPPLEMENTATION IN INFANCY AND CHILDHOOD: WHY, WHO, WHEN and HOW?**

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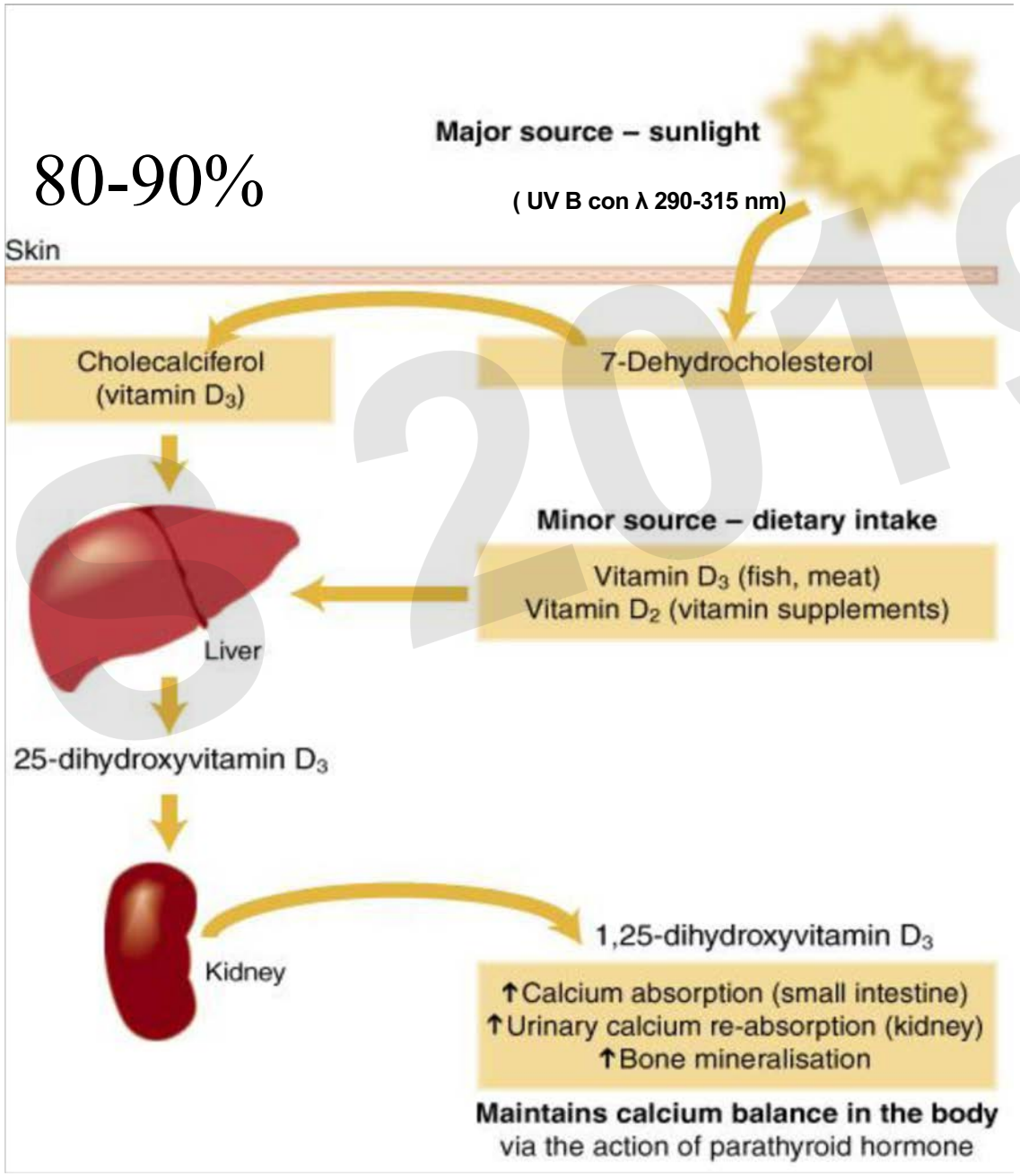
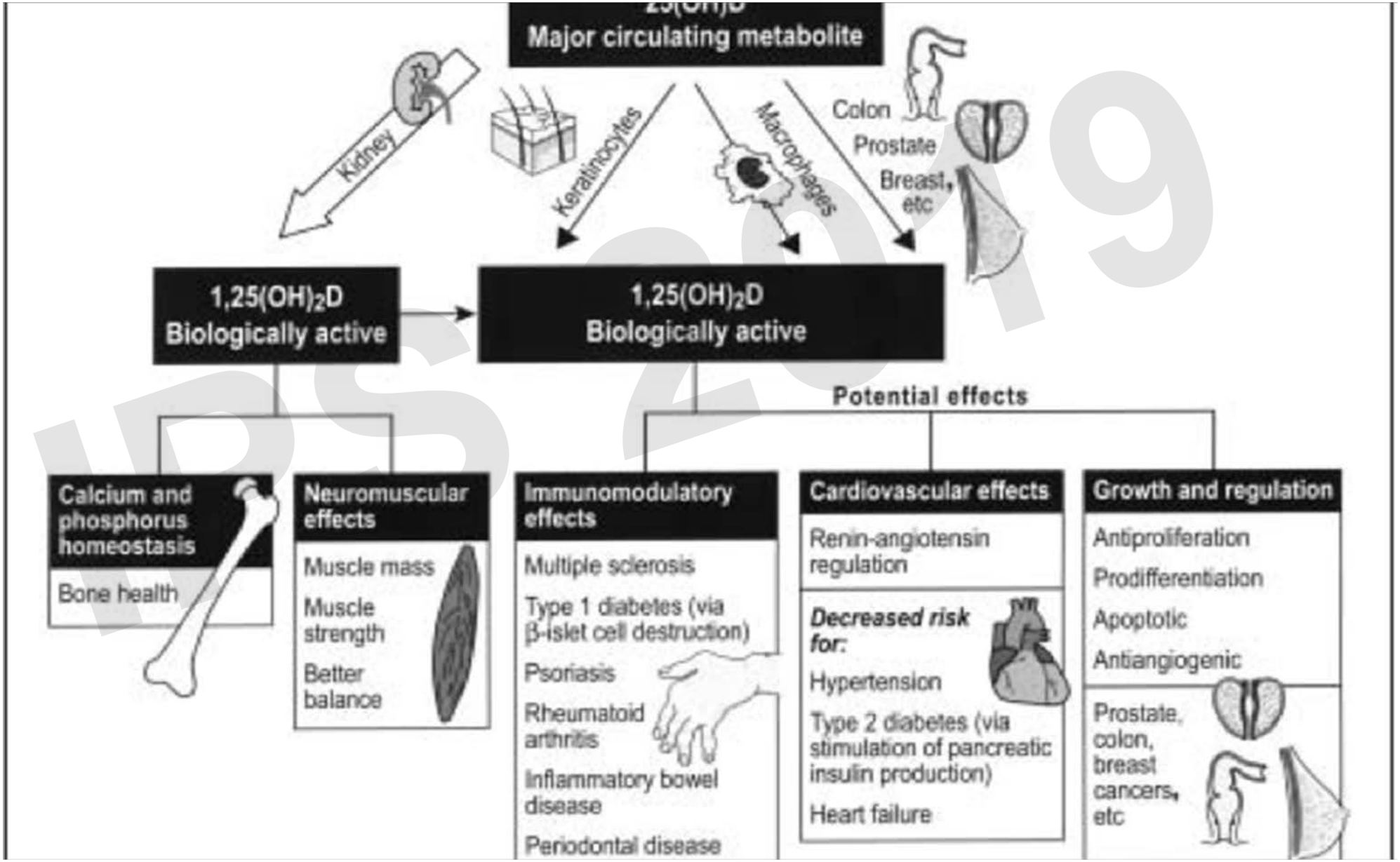
WHY?

VITAMIN D SYNTHESIS AND ACTIVATION



Skeletal and extra-skeletal functions due to ubiquitarious cell receptors



Immunological effects of Vitamin D

- Hypovitaminosis D associated with higher incidence and severity of airways infections and of asthmatic attacks
- Some studies show better outcome in children affected by tubercolosis and/or HIV infection on Vitamin D supplementation

Factors affecting skin photoconversion:

- Dark skin pigmentation
- Latitude
- Sun light exposure
- Environmental pollution
- Percentage of skin surface exposed
- Type of clothing
- Use of sunscreens

<u>Children more sensitive than adults due to:</u>

- Higher skin surface/body mass ratio
- Higher degree of synthesis

BUT…

In case of low sunlight exposure (e.g. fall and winter at given latitudes) skin photoconversion not sufficient to maintain adequate circulating vitamin D concentration (> 30 ng/ml)

THEREFORE…

Use of summer stores and/or need for exogen supplementation

VITAMIN D CONTENT IN MILKS AND DAIRY PRODUCTS

Food	I.U. Vit D/100g
Human milk	22
Infant Starting Formula	48-50
Follow-on Formula	40-80
Young child Formula	48-60
Goat's & Cow's milk	5-40
Yogurt	2.4
Butter	30

VITAMIN D CONTENT IN MILKS AND DAIRY PRODUCTS

Food	Vitamin D average content (IU)
Pork	40–50/100 g
Beef liver	40–50/100 g
Snapper (genus *Dentex dentex*), cod, gilthead (*Sparus auratus*), dogfish (*Mustelus mustelus*), sole, trout, salmon, herring	300–1500/100 g
Cod liver oil	400/5 ml
Egg yolk	20/100 g

Maternal preferences for vitamin D supplementation in breastfed infants

(Minnesota, USA)

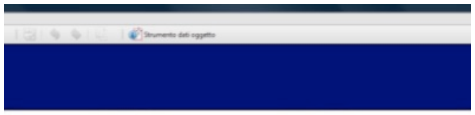


Table 2. Maternal Reasons for Not Supplementing Infants With Vitamin D

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)

CASE REPORT

A 4 month old, black and breastfed infant, came to our attention to be evaluated for…

seizures

-Generalized muscle hypertone

-eyes rolling back

-tonic-clonic seizures of the limbs

What to think?

What to ask?

CASE REPORT

Laboratory findings:

- Ca: 5,5 mg/dl
- Ca++: 2.65mg/dl
- P: 4.8 mg/dl
- Mg: 1.4mg/dl

I.V. Calcium gluconate continuous infusion was soos started and other investigations performed:

- Electrocardiography: prolonged QT interval
- PTH: 370 pg/ml (nv < 69 pg/ml)
- Vitamin D (25-OH): <7 ng/ml
- ALP: 1837 IU/L
- Urinary Ca excretion: 0.078 mg/Kg/die

CASE REPORT

Therapy:

Cholecalciferol: 2000 IU/day for 3 months

Calcium oral supplementation (50 mg/kg/day) for 2 weeks

At discharge (>10 days):

- Ca: 10,1 mg/dl
- Ca**: 4,97 mg/dl
- P: 5.0 mg/dl
- Mg: 2.1 mg/dl
- ALP: 1108 U/l

Left wrist Xray film

CONCLUSIONS

Hypocalcemic seizures

in a child suffering from nutritional rickets

(no vitamin D supplementation

during exclusive breastfeeding, dark skin, scarce sunlight exposure)

Male, 7yrs,6 mos

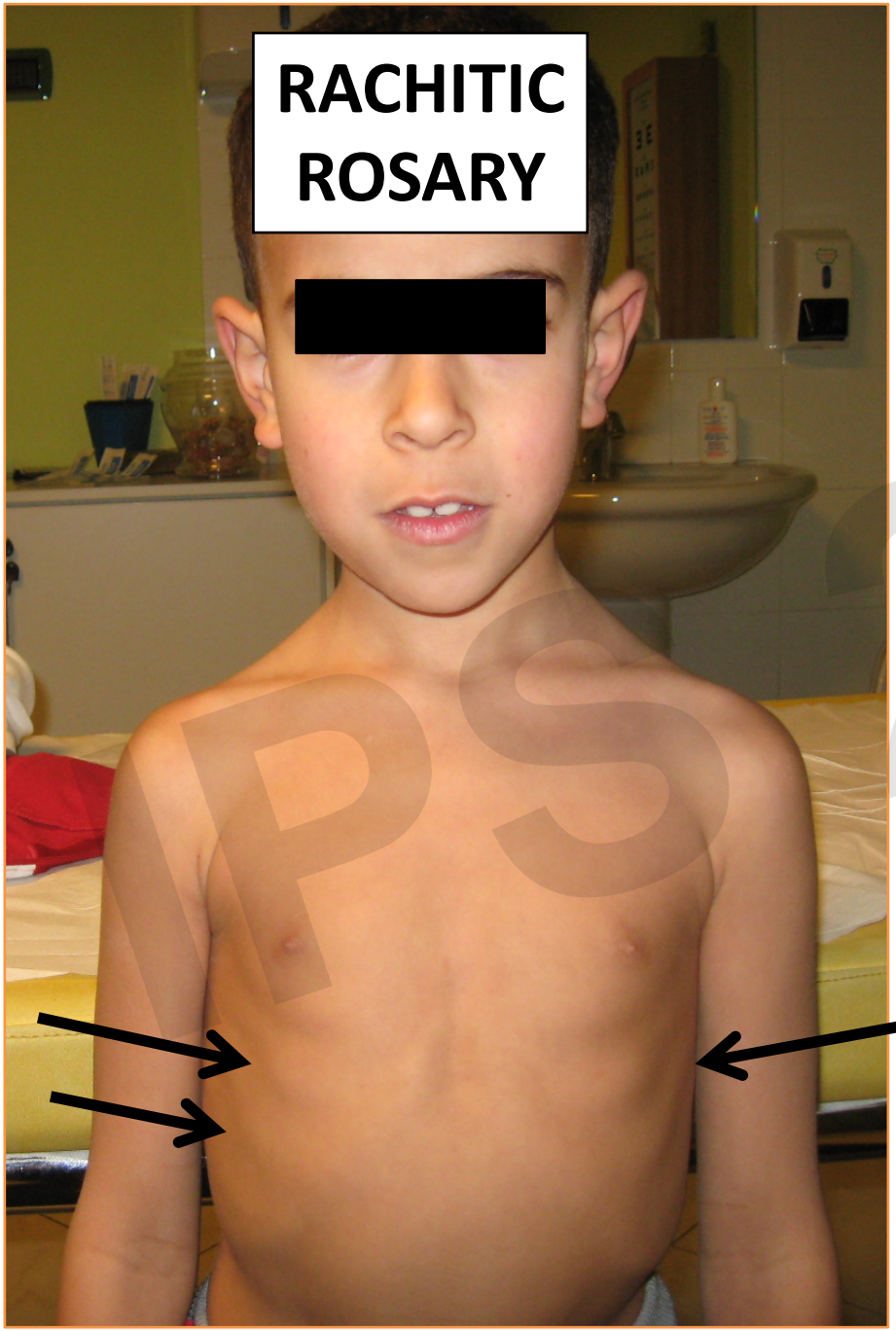
Referred to Pediatric Emergency Room for persisting fever

- Good general condition, no fever.
- Normal cardiac parameters.
- Normal respiratory parameters.
- Normal abdominal features.
- Pharyngitis.

DIAGNOSIS: VIRAL PHARYNGITIS

THERAPY: paracetamol (IN CASE OF FEVER)

BUT….



Laboratory findings

- 25(OH)D: 7 ng/ml (severe deficiency)
- Elevated ALP
- Secondary Hyperparathyroidism
- Still normal Ca and P values

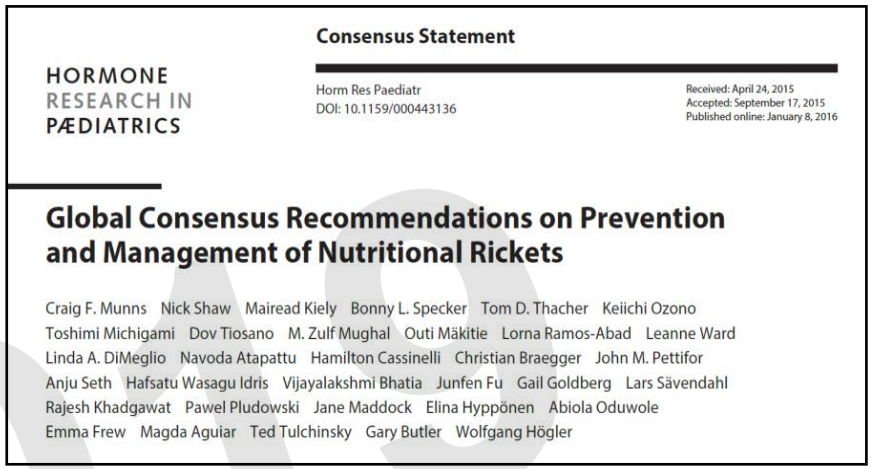
- The child was born in Italy
- Parents of Moroccan origin
- Prolonged exclusive breastfeeding
- No vitamin D prophylaxis

Diagnosis: Nutritional Rickets

- Cholecalciferol: 50.000 UI/week for 6 wks, then 600 IU/day
- Calcium carbonate: 500 mg/day for 2 wks

Table 1. Clinical features associated with NR

Osseous signs and symptoms
Swelling wrists and ankles
Delayed fontanelle closure (normally closed by the age of 2 years)
Delayed tooth eruption (no incisors by the age of 10 months, no molars by 18 months)
Leg deformity (genu varum, genu valgum, windswept deformity)
→ Rachitic rosary (enlarged costochondral joints – felt anteriorly, lateral to the nipple line)
Frontal bossing
Craniotabes (softening of skull bones, usually evident on palpation of cranial sutures in the first 3 months)
Bone pain, restlessness, and irritability
Radiographic features
Splaying, fraying, cupping, and coarse trabecular pattern of metaphyses
Widening of the growth plate
Osteopenia
Pelvic deformities including outlet narrowing (risk of obstructed labor and death)
Long-term deformities in keeping with clinical deformities
Minimal trauma fracture
Nonosseous features
Hypocalcemic seizure and tetany
Hypocalcemic dilated cardiomyopathy (heart failure, arrhythmia, cardiac arrest, death)
Failure to thrive and poor linear growth
Delayed gross motor development with muscle weakness
Raised intracranial pressure



Consensus Statement

HORMONE RESEARCH IN PÆDIATRICS

Horm Res Paediatr
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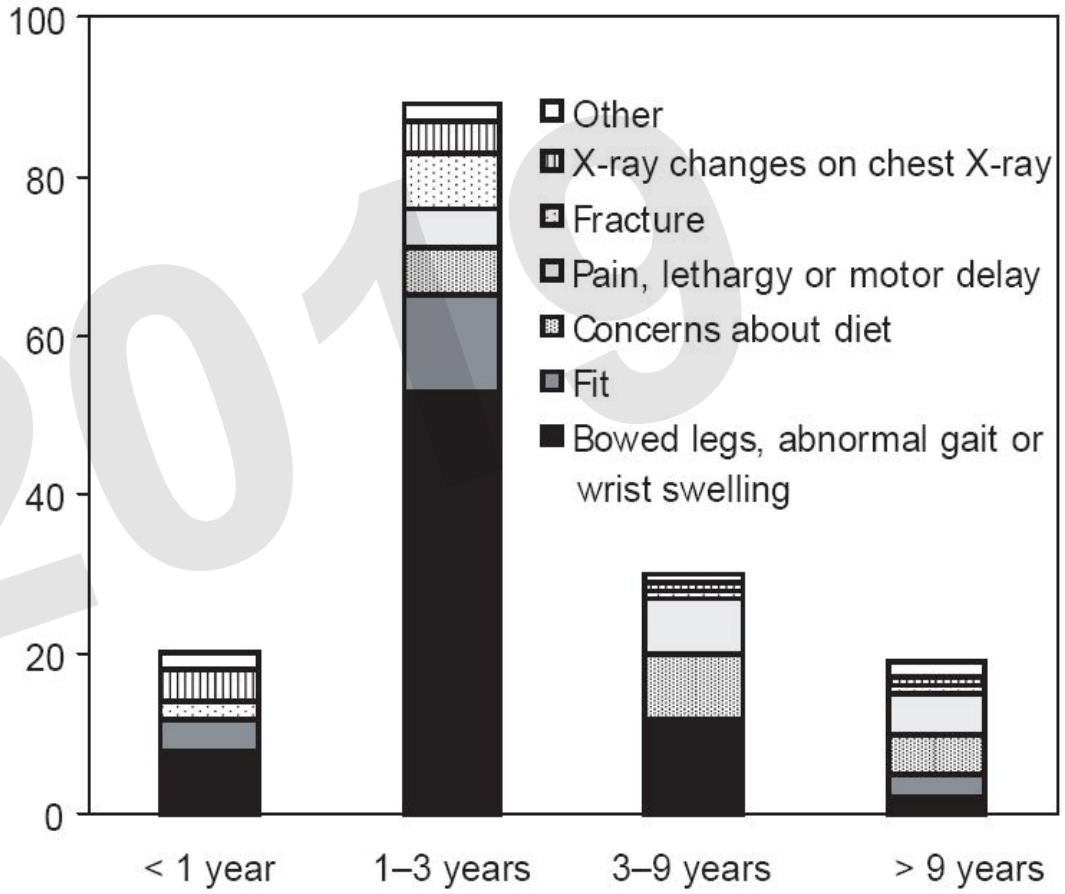
Global Consensus Recommendations on Prevention and Management of Nutritional Rickets

Craig F. Munns Nick Shaw Mairead Kiely Bonny L. Specker Tom D. Thacher Keiichi Ozono Toshimi Michigami Dov Tiosano M. Zulf Mughal Outi Mäkitie Lorna Ramos-Abad Leanne Ward Linda A. DiMeglio Navoda Atapattu Hamilton Cassinelli Christian Braegger John M. Pettifor Anju Seth Hafsatu Wasagu Idris Vijayalakshmi Bhatia Junfen Fu Gail Goldberg Lars Sävendahl Rajesh Khadgawat Pawel Pludowski Jane Maddock Elina Hyppönen Abiola Oduwole Emma Frew Magda Aguiar Ted Tulchinsky Gary Butler Wolfgang Högler

Clinical features of vitamin D deficiency during childhood and adolescence

- 160 cases of symptomatic vitamin D deficiency (Glasgow 2002-2008)
- Age range: 2 weeks - 14 years



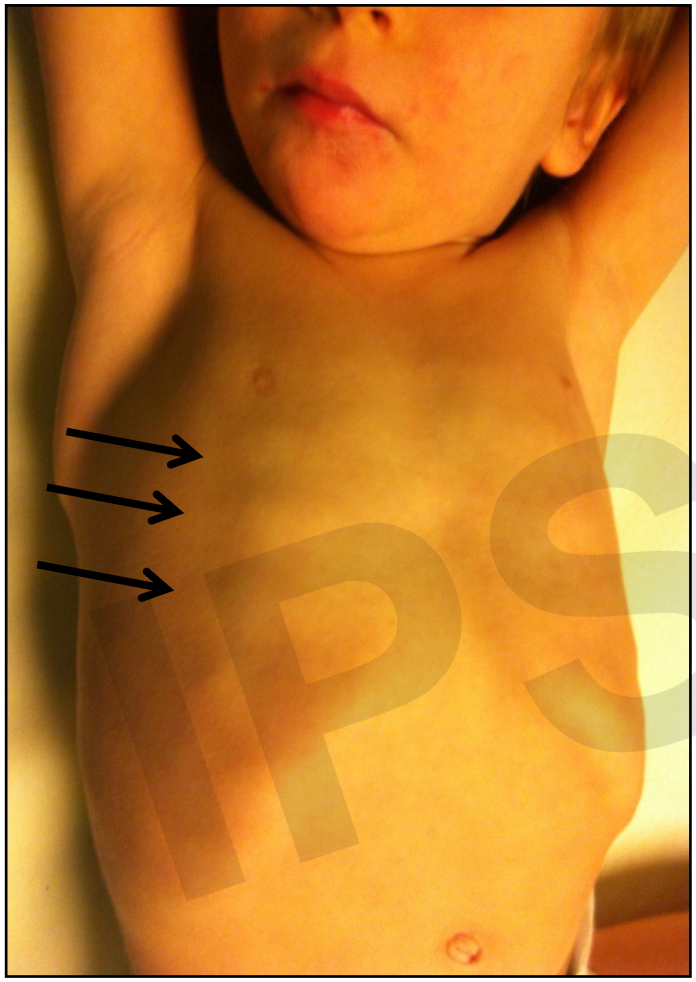
- *Older children with vitamin D deficiency present with vague symptoms such as pain and muscle weakness.*
- *Florid signs of rickets are rare in older children and adolescents.*

(Ahmed SF et al. Arch Dis Child 2010)

Take home messages

- **Nutritional Rickets may occur and develop also during childhood.**
- **The clinical features vary according to different age. In particular, bone signs may be milder in children compared to infants and toddlers.**
- **The signs of rachitic rosary should always be searched in children with multiple risk factors for hypovitaminosis D.**
- **Children with dark skin are at higher risk for nutritional rickets,**
- **BUT…**

ALSO ……male, 2 yrs, 6 mos, Italian



- March: Scarce sunlight exposure during the previous summer
- No vitamin D prophylaxis

To sum up:

• Human milk is the gold standard for infant nutrition, but its vitamin D content is low (average 22 IU/dl) and insufficient to meet infants' daily needs

• Infant Formulae can provide about 400 IU/day with 1 liter/day intake, which is not usually maintained after 6 mos of age, when solid foods are introduced.

• Vitamin D content is generally limited in most of the foods, except some fish species, which are seldom consumed by children.

• In Italy, for instance, vitamin D supplemented milk and yogurt are not frequently available nor used

• Therefore, vitamin D supplementation of milk and yogurt does not represent an ideal preventive strategy.

WHO
AND
WHEN?

Saggese et al. Italian Journal of Pediatrics (2018) 44:51
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]

Abstract

Vitamin D plays a pivotal role in the regulation of calcium-phosphorus metabolism, particularly during pediatric age when nutritional rickets and impaired bone mass acquisition may occur.
Besides its historical skeletal functions, in the last years it has been demonstrated that vitamin D directly or indirectly regulates up to 1250 genes, playing so-called extraskeletal actions. Indeed, recent data suggest a possible role of vitamin D in the pathogenesis of several pathological conditions, including infectious, allergic and autoimmune diseases. Thus, vitamin D deficiency may affect not only musculoskeletal health but also a potentially wide range of acute and chronic conditions. At present, the prevalence of vitamin D deficiency is high in Italian children and adolescents, and national recommendations on vitamin D supplementation during pediatric age are lacking. An expert panel of the Italian Society of Preventive and Social Pediatrics reviewed available literature focusing on randomized controlled trials of vitamin D supplementation to provide a practical approach to vitamin D supplementation for infants, children and adolescents.

Keywords: Vitamin D, Supplementation, Children, Adolescents, Deficiency, Hypovitaminosis D

Saggese et al. Italian Journal of Pediatrics (2018) 44:51
https://doi.org/10.1186/s13052-018-0488-7

Italian Journal of Pediatrics

DEFINITION OF VITAMIN D STATUS

Table 3 Cut-off points for the definition of vitamin D status based on circulating levels of 25(OH)D

	Severe deficiency	Deficiency	Insufficiency	Sufficiency
25(OH)D	< 10 ng/ml (< 25 nmol/l)	< 20 ng/ml (< 50 nmol/l)	20–29 ng/ml (50–74 nmol/l)	≥ 30 ng/ml (≥ 75 nmol/l)

Conversion factor: ng/ml = nmol/l*0.401; nmol/l = ng/ml*2.496

Society/Organization	Year	Severe deficiency	Deficiency	Insufficiency	Sufficiency/Adequacy
United Arab Emirates [27]	2016	–	< 20 ng/ml	20–29 ng/ml	≥ 30 ng/ml

Circulating Vitamin D status in Italian toddlers and children

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
Prodam [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 out of 2 children has hypovitaminosis D»

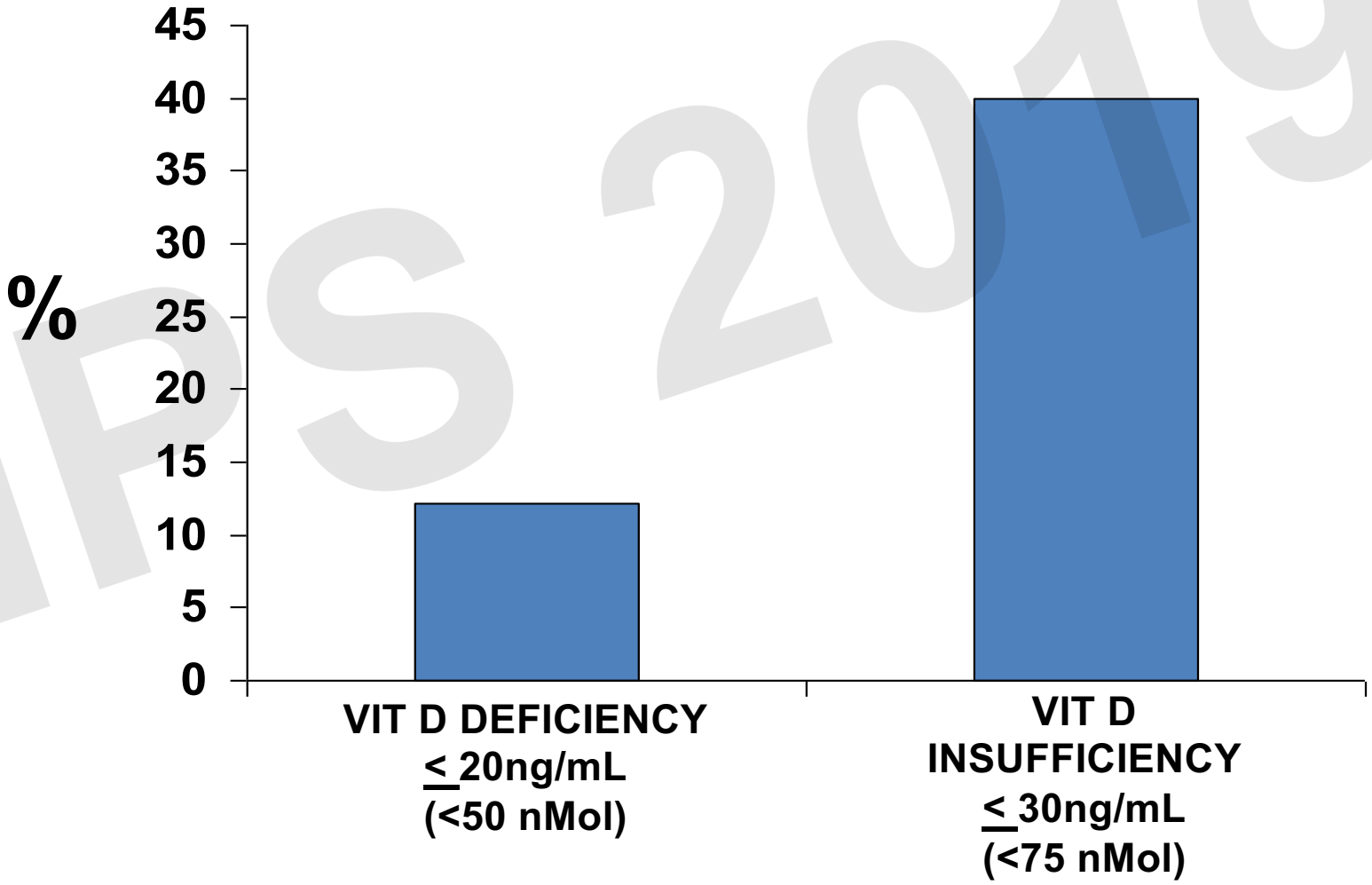
(Vierucci F et al. Il Medico Pediatra 2018)

Prevalence of Vitamin D Deficiency Among Healthy Infants and Toddlers

Catherine M. Gordon

Arch Pediatr Adolesc Med. 2008;162(6):505-512

380 children (8-24 mos)



International Journal of
Rheumatic Diseases
International Journal of Rheumatic Diseases 2011; 14: e22–e29

ORIGINAL ARTICLE

Knowledge, attitude and practice regarding vitamin D deficiency among female students in Saudi Arabia: a qualitative exploration

Floor T. E. CHRISTIE[1] and Linda MASON[2]

20–80% of apparently healthy individuals suffer from vitamin D deficiency.
In Saudi Arabia: 81% in an all female population, and 83% in a predominantly female sample of participants with low back pain.

Vitamin D deficiency associated with:
Rickets and osteomalacia
Different types of cancer,
Coronary heart disease,
Type 1 and 2 diabetesare
Multiple sclerosis
Rheumatoid arthritis
Hypertension
Alzheimer's

Conclusion:
Important barriers for the prevention of vitamin D deficiency in Saudi Arabia exist.

Governmental actions including increasing awareness of the importance of vitamin D and guidelines on how to obtain it are necessary.

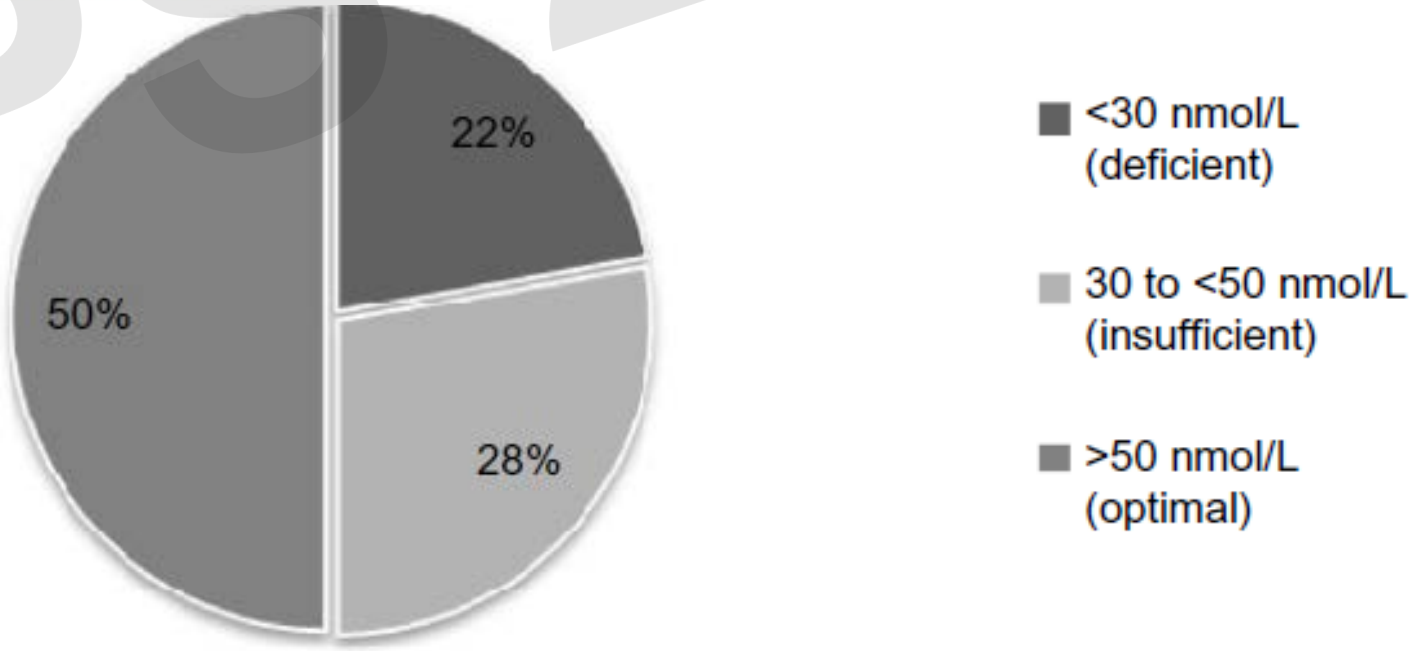
Creating areas where women, particularly those of lower socio-economic status, can enjoy sun exposure as well as fortifying more foods would go some way towards tackling this problem.

Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy Dovepress
Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy 2016:9 11–16
Open Access Full Text Article
ORIGINAL RESEARCH

Assessment of vitamin D levels in newly diagnosed children with type 1 diabetes mellitus comparing two methods of measurement: a facility's experience in the Middle Eastern country of Bahrain

Background: The number of children being diagnosed with type 1 diabetes mellitus (T1DM) is on the rise and has more than doubled in the past 10 years in Bahrain. Some studies have linked low vitamin D levels with an increased risk of diabetes. There are concerns regarding

Subjects: Eighteen children, aged 6–12 years, who received a confirmed diagnosis of T1DM in 2014 were chosen as subjects.



Acta Diabetol (2009) 46:183–189
DOI 10.1007/s00592-008-0071-6

ORIGINAL ARTICLE

High prevalence of vitamin D deficiency in type 1 diabetes mellitus and healthy children

Abdulbari Bener · Amer Alsaied · Mariam Al-Ali · Aisha Al-Kubaisi · Basma Basha · Amit Abraham · Gerardo Guiter · Marcellini Mian

Table 3 Type of feeding and vitamin D supplement with the breast milk in the studied diabetic and healthy subjects

Variables	Cases $n = 170$	Controls $n = 170$	P value
Type of feeding			
Breast feeding			
Never	6 (3.5)	3 (1.8)	
≤6 months	50 (29.4)	13 (7.6)	<0.001
> 6 months	114 (67.1)	154 (90.6)	
Duration of breastfed in months[a]	9.5 ± 6.0	11.8 ± 6.8	<0.001
Formula fed			
Never	53 (31.2)	41 (24.1)	
≤6 months	43 (25.3)	40 (23.5)	0.221
>6 months	74 (43.5)	89 (52.4)	
Duration of formula fed in months[a]	16.9 ± 9.9	17.1 ± 9.4	0.880
Any kind of Vitamin D supplements along with breast milk			
Yes	79 (46.5)	88 (51.8)	
No	91 (53.5)	82 (48.2)	0.329
Duration of vitamin D supplements used in months[a]	13.7 ± 7.9	11.7 ± 6.9	0.113

[a] Mean ± SD

Table 4 Clinical manifestations and diagnosed diseases in the studied diabetic and healthy subjects

Variables	Cases n =170	Controls n =170	P value
Clinical manifestations			
Fractures	34 (20.0)	19 (11.2)	0.025
Weakness	82 (48.2)	53 (31.2)	0.001
Gastro	56 (32.9)	33 (19.4)	0.005
Diagnosed diseases			
Rickets	20 (11.8)	18 (10.6)	0.731
Parathyroid	3 (1.8)	2 (1.2)	0.652
Vitamin D deficiency			
Vitamin D (ng/ml)[a] (median)	15.8 ± 9.2 (15)	18.5 ± 9.6 (17)	0.009
Optimum levels (30–80 ng/ml)	16 (9.4)	25 (14.7)	0.134
Vitamin D deficiency (<30 ng/ml)	154 (90.6)	145 (85.3)	

[a] Mean ± SD

Alyahya *BMC Pediatrics* (2017) 17:213
DOI 10.1186/s12887-017-0963-0

BMC Pediatrics

RESEARCH ARTICLE Open Access

Vitamin D levels in schoolchildren: a cross-sectional study in Kuwait

Khulood Othman Alyahya

Children, among other age groups, have demonstrated a moderate to high prevalence of vitamin D deficiency in the Middle East.
71.6% of 331 Saudi children (6–17 yrs): vitamin D levels <50 nmol/L
78.8% of 293 adolescent girls (11–18 yrs) in UAE: levels <27.5 nmol/L
61% of 11–16 year-old Qatari adolescents, 29% of 5–10 year old children, and 9.5% of children below 5-years: <75 nmol/L, among whom delayed milestones, fractures, rickets, and gastroenteritis were more common.

Methods: Kuwaiti schoolchildren were recruited and assessed for their serum vitamin D, 25(OH)D, parathyroid hormone (PTH) and adjusted serum calcium (adj-Ca). Anthropometric measurements and data on lifestyle and health status were recorded during an interview.

Table 3 Clinical mesurements of the schoolchildren

Measurement*	Total (*n* = 199)				Boys (*n* = 93)				Girls (*n* = 106)				*P*-value
	Median	IQR	Min	Max	Median	IQR	Min	Max	Median	IQR	Min	Max	
25(OH)D nmol/L	30.0	22.0–39.0	5.0	89.0	34.0	27.0–47.0	12.0	89.0	27.0	18.0–35.0	5.0	71.0	***0.001***
PTH pmol/L	4.70	3.80–5.90	1.90	20.70	4.20	3.55–5.40	1.90	9.00	5.20	4.08–6.33	2.00	20.70	***0.001***
Calcium mmol/L	2.47	2.39–2.52	1.43	2.71	2.45	2.36–2.53	2.09	2.70	2.47	2.40–2.52	1.43	2.71	*0.245*
Adj Calcium mmol/L	2.39	2.33–2.44	2.14	2.59	2.39	2.33–2.45	2.14	2.58	2.39	2.34–2.44	2.17	2.59	*0.749*

Iron and Vitamin D Deficiency in Healthy Young Children in Western Europe Despite Current Nutritional Recommendations

*Marjolijn D. Akkermans, †Judith M. van der Horst-Graat, †Simone R.B.M. Eussen, ‡Johannes B. van Goudoever, and *Frank Brus

JPGN • Volume 62, Number 4, April 2016

What Is Known

- Iron and vitamin D are common micronutrient deficiencies in young children worldwide.
- In Europe, strategies for the prevention of vitamin D deficiency exist but not for iron deficiency.
- Data on the prevalence of and risk factors for both deficiencies in the white population are scarce.

What Is New

- Iron and vitamin D deficiency are highly prevalent in white children in Western Europe.
- Compliance to vitamin D deficiency preventive strategies (eg, supplementation) is low.
- The use of cow's milk is associated with a higher prevalence of both deficiencies.

Children ages 12 to 36 months and with a stable health status

Nutrition details of the study population (n = 325)

Main type of milk intake during previous month		
Use of primarily cow's milk, %	143	44.0%
Use of >400 mL cow's milk per day, %	67	20.6%
Use of primarily formula, %	166	51.1%
Use of >400 mL formula per day, %	88	27.1%
Amount of milk per day, mL	515	SD 226
Supplements		
Use of supplements containing iron, %†	5	1.5%
Use of supplements containing vitamin D, %†	93	28.6%
Iron		
Iron intake from milk, mg/day‡	3.0	0.0–5.2
Iron intake from food, mg/day‡	4.4	2.8–6.1
Intake of haem iron from food, mg/day‡	0.2	0.1–0.3
Intake of nonhaem iron from food, mg/day‡	4.1	2.7–5.8
Iron intake below EAR of 3 mg/day, %	58	17.8%
Vitamin D		
Vitamin D intake from milk, µg/day‡	4.4	0.0–6.6
Vitamin D intake from food, µg/day‡	0.8	0.4–1.2
Vitamin D intake below EAR of 8 µg/day, %	194	59.7%

Table 5 Dietary reference values of vitamin D in infants, children, and adolescents as proposed by various Organizations and Societies

Organization/Society	Year	Country/Countries	Dietary reference value for vitamin D	0–12 months, IU/day	1–18 years, IU/day
European Food Safety Authority [26]	2016	Europe	AI	400 (7–11 months)	600 (1–17 years)
Scientific Advisory Committee on Nutrition [25]	2016	United Kingdom	Safe Intake (< 4 years)	340–400	400
			RNI (4–18 years)		
Nordic Nutrition Recommendations [16]	2012	Denmark, Finland, Iceland, Norway, Sweden, Faroe Islands, Greenland, Åland Islands	RI	400	400
German Nutrition Society [17]	2012	Germany, Austria, Switzerland	AI	400 (infants)	800[a] (children)
Health Council of the Netherlands [18]	2012	The Netherlands	AI	400	400
Italian Society of Nutrition [89]	2012	Italy	AI (< 12 months)	400 (6–12 months)	600
			PRI (1–18 years)		
Institute of Medicine [10]	2011	North America, Canada	AI (< 12 months)	400	600
			RDA (1–18 years)		
The Endocrine Society [11]	2011	Worldwide	Daily requirement[b]	400–1000	600–1000

AI Adequate Intake, the average observed daily level of intake by a population group of apparently healthy people that is assumed to be adequate
Safe Intake, a level or range of intakes considered to pose no risk of deficiency and below a level where there is a risk of undesirable effects
RNI Reference Nutrient Intake, the amount of a nutrient that is likely to meet the needs of 97.5% of the population
RI Recommended Intake, the amount of a nutrient that meets the known requirement and maintains good nutritional status among practically all (97–98%) healthy individuals in a particular life stage or gender group
PRI Population Reference Intake, the level of nutrient intake sufficient to satisfy the needs of almost all (97.5%) healthy subjects in one specific population group
RDA Recommended Dietary Allowance, the estimated intake capable of satisfying the needs of 97.5% of the population
[a]Adequate intake with missing endogenous synthesis of vitamin D
[b]Recommended requirements for subjects at risk of vitamin D deficiency

Recommended Daily Allowances of Vitamin D

< 1 year

400 IU

Adequate intake

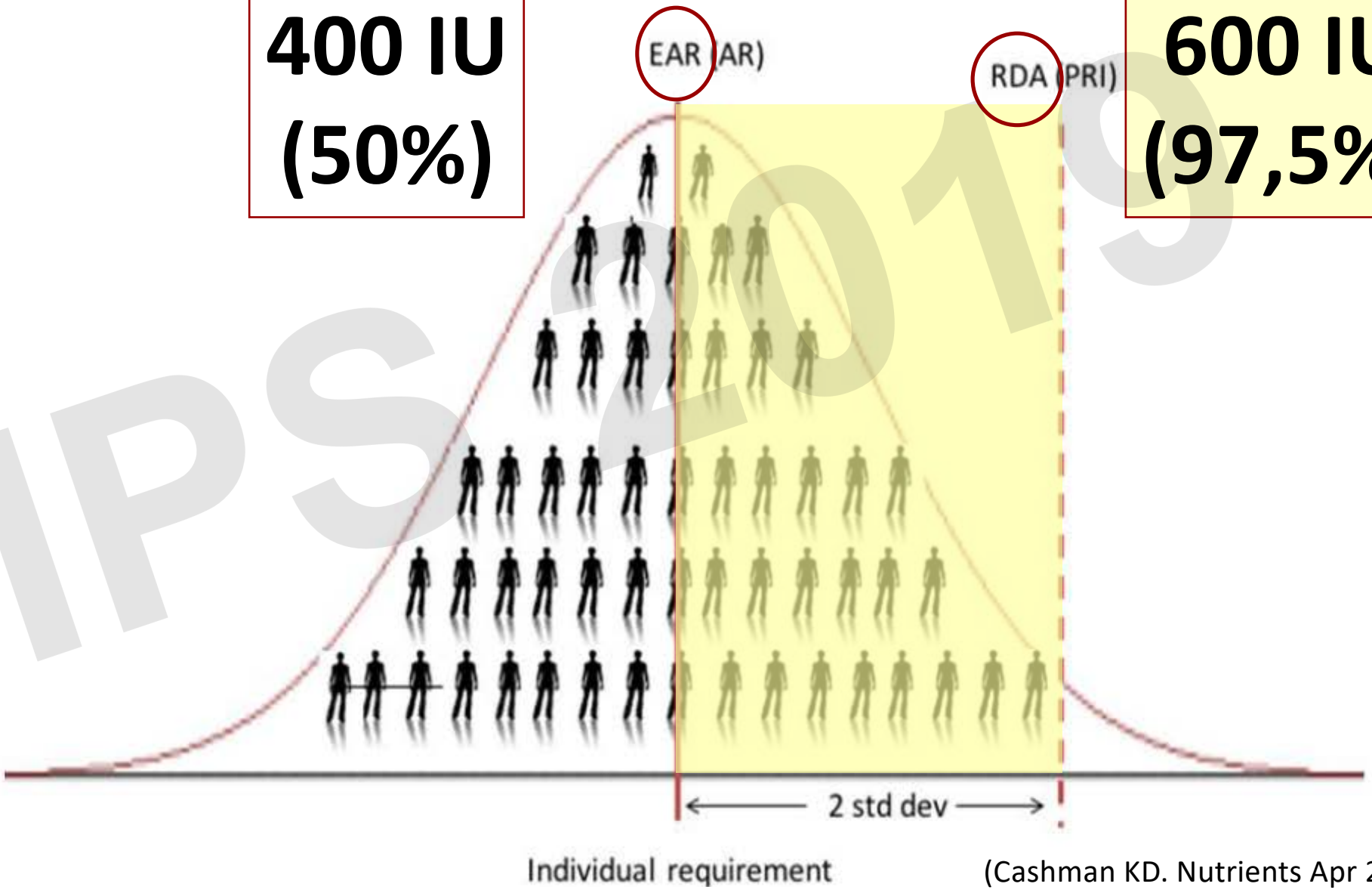
> 1 year

600 IU

Recommended Dietary Allowance (RDA)

Recommended Daily Allowances of Vitamin D

400 IU (50%)



600 IU (97,5%)

(Cashman KD. Nutrients Apr 2018)

Saggese et al. Italian Journal of Pediatrics (2018) 44:51
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

Vitamin D supplementation

0–12 months

- We recommend vitamin D supplementation in the first year of life to ensure an adequate vitamin D status and to prevent nutritional rickets.
- 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.
- Infants born at term without risk factors for vitamin D deficiency should receive 400 IU/day of vitamin D.
- In the presence of risk factors for vitamin D deficiency (Table 6) up to 1000 IU/day of vitamin D can be given.
- In the first year of life we recommend daily administration of vitamin D.

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Italian Journal of Pediatrics

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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

> 1 YEAR OF AGE

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

WHO

- 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).
- If 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.

HOW

- 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.

WHEN

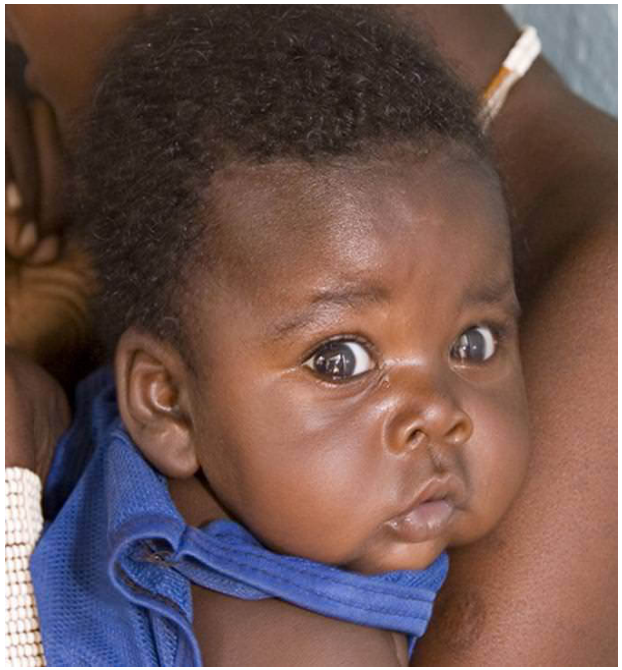


Table 6 Risk factors for vitamin D deficiency in the first year of life

- Non-Caucasian ethnicity with dark skin pigmentation
- Inadequate diets (i.e. vegan diet)
- Chronic kidney disease
- Hepatic failure and/or cholestasis
- Malabsorption syndromes (i.e. cystic fibrosis, inflammatory bowel diseases, celiac disease at diagnosis, etc.)
- Chronic therapies: anticonvulsants, systemic glucocorticoids, antiretroviral therapy, systemic antifungals (i.e. ketoconazole)
- Infants born from mothers with multiple risk factors for vitamin D deficiency, particularly in absence of vitamin D supplementation during pregnancy

Table 7 Risk factors for vitamin D deficiency between 1 and 18 years of age

- Non-Caucasian ethnicity with dark skin pigmentation
- Reduced sunlight exposure (due to lifestyle factors, chronic illness or hospitalization, complex disability, institutionalization, covering clothing for religious or cultural reasons) and/or constant use of sunscreens
- International adoption
- Obesity
- Inadequate diets (i.e. vegan diet)
- Chronic kidney disease
- Hepatic failure and/or cholestasis
- Malabsorption syndromes (i.e. cystic fibrosis, inflammatory bowel diseases, celiac disease at diagnosis, etc.)
- Chronic therapies: anticonvulsants, systemic glucocorticoids, antiretroviral therapy, systemic antifungals (i.e. ketoconazole)

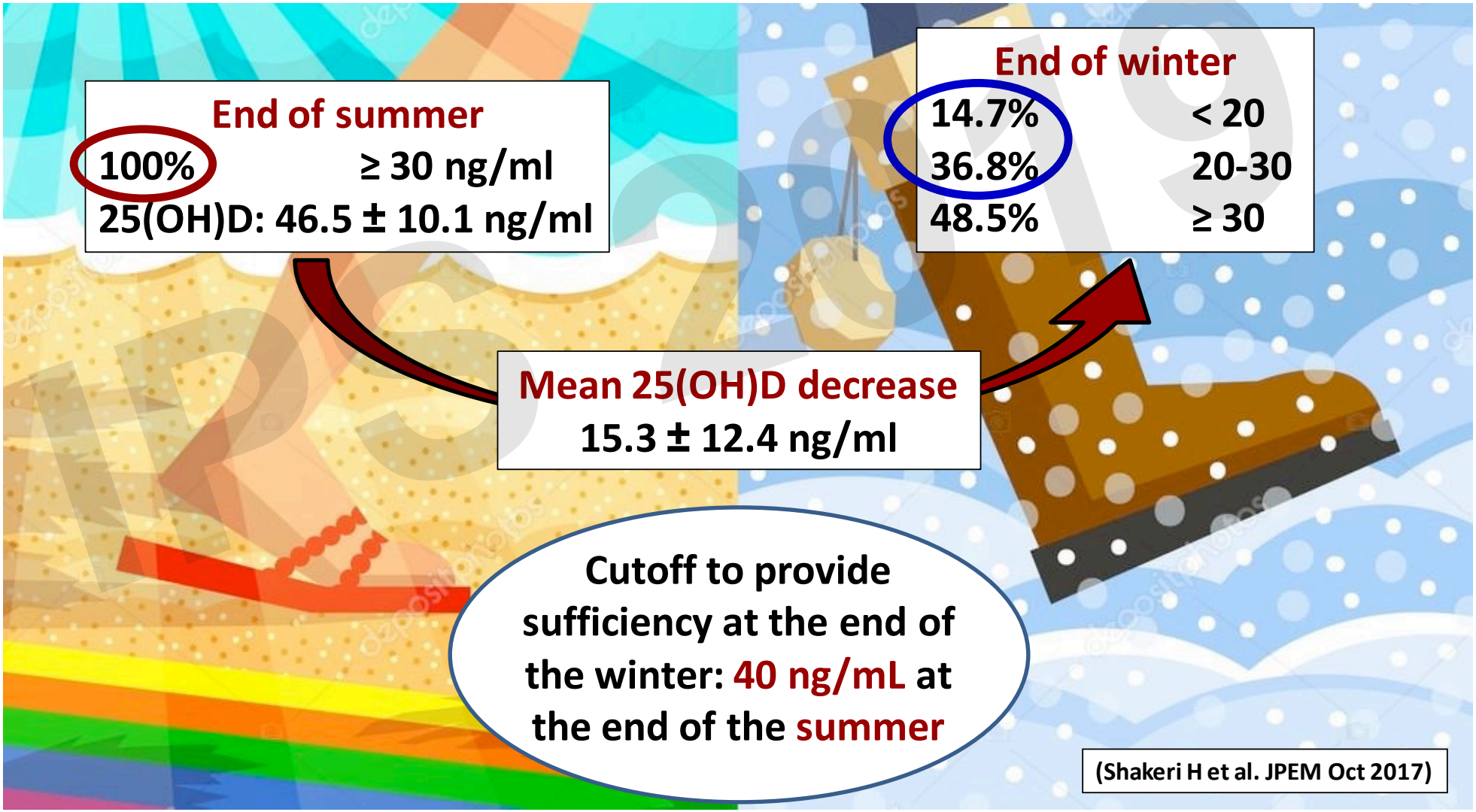
Presence of risk factors for hypovitaminosis D

0-12 mos: 400-1.000 IU/day

1-18 yrs: 600-1.000 IU/day

Obesity: 2-3 fold RDA for age

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)



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- People should consider taking a daily supplement containing 400 IU of vitamin D in autumn and winter.
- At risk people (little or no exposure to the sun, dark skin) should consider taking a supplement all year round.

From: Public Health England

Published: 21 July 2016

PHE is advising that 10 micrograms of vitamin D are needed daily to help keep healthy bones, teeth and muscles.

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Preterm infants

- We suggest for VLBW infants a vitamin D intake of 200–400 IU/day (including the amount administered through parenteral nutrition, fortified breast milk, or preterm infant formula).
- When VLBW infants reach a weight ≥ 1500 g and full enteral nutrition we suggest vitamin D supplementation at 400–800 IU/day.
- We recommend vitamin D supplementation at 400–800 IU/day for preterm infants with birth weight ≥ 1500 g.
- After a post-conceptional age of 40 weeks, recommendations for vitamin D supplementation are equal to those for healthy term infants.
- We recommend against routine 25(OH)D testing in preterm newborns.

Nutritional rickets

Treatment of nutritional rickets is based on the administration of vitamin D (2000 IU/day in patients aged less than 1 year, 3000–6000 IU/day in patients aged 1 to 12 years and 6000 IU/day in patients older than 12 years for a minimum of 3 months) and calcium (30–75 mg/kg/day of elemental calcium in 3 divided doses, starting at a higher dose and weaning down to the lower end of the range over 2–4 weeks).

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)

When circulating Vitamin D should be tested?

- Suspected symptomatic deficiency/nutritional rickets
- Suspected severe deficiency (multiple risk factors) needing treatment
- Suspected defect of Ca-P homeostasis (e.g. “osteoporosis”)
- Chronic diseases and/or drugs affecting vitamin D metabolism

Specific conditions (individualised approach)

- Severe asthma, steroid-resistant (prevention of exacerbations)
- Recurrent airways infections (prevention)
- Growing pains

+ Suspected severe vit. D deficiency

When testing is NOT indicated?

- In children “otherwise healthy”
- In children with scarce sunlight exposure
- In coloured children “otherwise healthy”
- In obese children “otherwise healthy”

Lifestyle

PROPHYLAXIS

Table 8 Indications for 25(OH)D evaluation (besides rickets) in children and adolescents as proposed by various Organizations and Societies

Organization/Society, year of publication	PES, 2008 [9]	ES, 2011 [11]	FCN, 2012 [15]	French Soc. of Pediatrics, 2012[a] [13]	Australia - New Zealand, 2013 [22]	Central Europe, 2013 [20]	SAHM, 2013 [21]	AAP, 2014 [23]	Arab Emirates, 2016 [27]	EAP, 2017 [30]
Frequent/low trauma fractures and/or low BMD	X	X	X			X	X	X[b]	X	
Calcium/phosphate metabolism abnormalities						X			X	
Immobilization/disabilities					X		X	X	X	
Dark skin pigmentation	X[c]	X[d]	X	X	X		X			X
Reduced sun exposure	X			X	X		X			X
Athletes (indoor sports)			X							
Children institutionalized									X	X
Constant use of sunscreens							X			
Obesity		X	X[e]	X	X		X		X	
Inadequate diets (e.g. vegan)				X			X			X
Elimination diets (e.g. cow/s milk allergy), eating disorders						X		X	X	
On anticonvulsants	X	X	X	X	X	X	X	X	X	X
On chronic glucocorticoids	X	X	X			X	X	X	X	
On HIV medications		X	X			X	X		X	
On antifungals (e.g. ketoconazole)		X	X			X			X	
On rifampicin				X	X					
Malabsorption syndromes	X	X	X	X	X	X	X	X	X	X
Chronic kidney disease		X	X	X	X	X	X	X	X	X
Nephrotic syndrome				X						
Hepatic failure and/or cholestasis		X	X	X	X	X	X		X	X
Granulomatous disorders (e.g. tuberculosis)		X	X			X			X	
Amenorrhea							X			
Cancer (different types)		X[f]				X		X	X	
Hepatitis C[g]						X			X	
Recurrent acute lower respiratory tract infections[g]						X			X	
Atopic dermatitis[g]						X			X	
Atopic Asthma[g]						X			X	
Autoimmune diseases[h]						X		X[i]	X	
Cardiovascular diseases (especially hypertension)						X			X	
Metabolic syndrome, type 2 diabetes										

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SAFE INTAKE

We endorsed as Tolerable Upper Intake Levels of vitamin D those proposed by EFSA in 2012 (1000 IU/day for infants; 2000 IU/day for children ages 1 to 10 years; 4000 IU/day for children and adolescents ages 11 to 17 years).

HOW?

nutrients

MDPI

Nutrients **2018**, *10*, 348; doi:10.3390/nu10030348

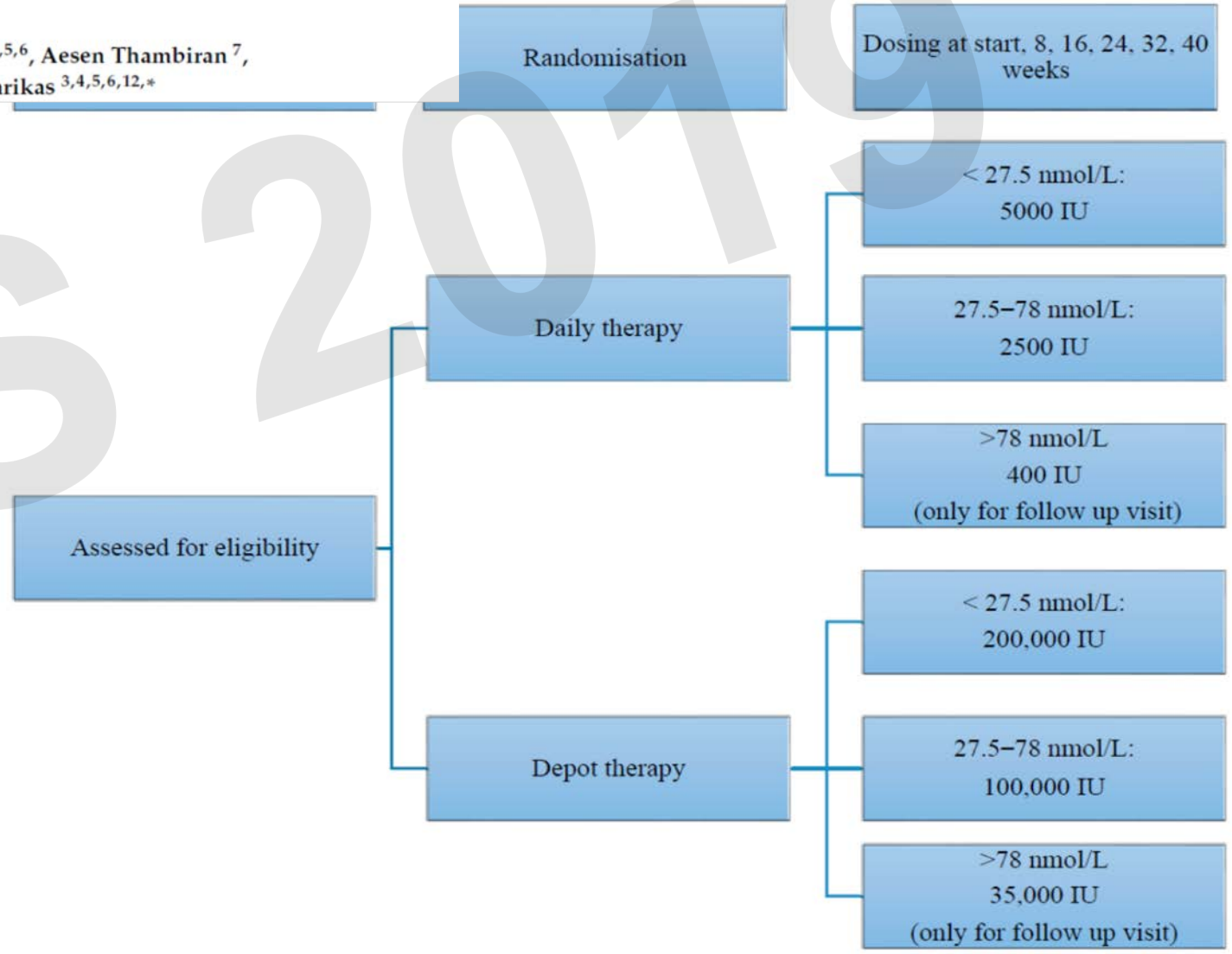
Article

Randomised Controlled Trial Comparing Daily Versus Depot Vitamin D3 Therapy in 0–16-Year-Old Newly Settled Refugees in Western Australia Over a Period of 40 Weeks

Ushma Wadia [1,2,†], Wayne Soon [3,†], Paola Chivers [4,5,6], Aesen Thambiran [7], David Burgner [8,9,10], Sarah Cherian [3,11] and Aris Siafarikas [3,4,5,6,12,*]

Newly settled refugees (n = 151; 5.5 mos- 16.0 yrs) with 25(OH)D levels less than 78 nmol/L were randomised to receive daily or depot vitamin D therapy with eight weekly interval follow up to 40 weeks.

Biochemical and clinical parameters were collected at each visit



Nutrients 2018, *10*, 348; doi:10.3390/nu10030348

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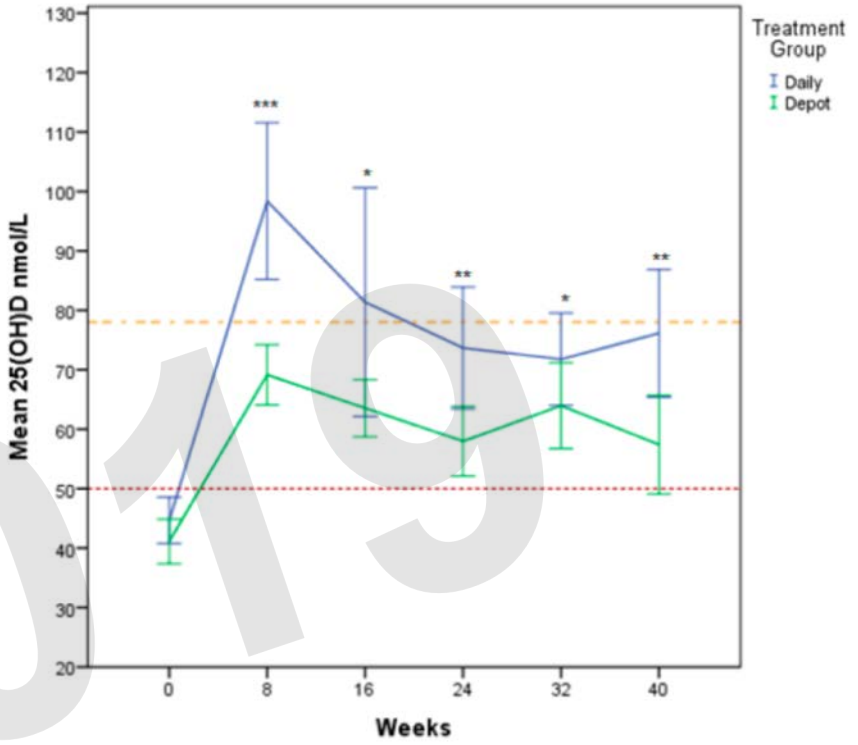
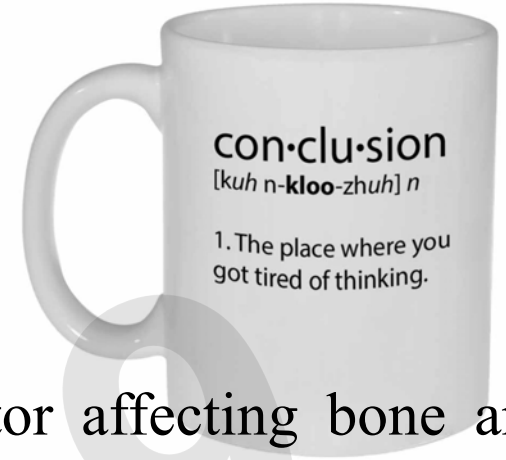


The daily treatment group had significantly higher 25(OH)D levels at each visit post baseline and a higher proportion of participants with levels above 50 nmol/L at all time points.

Time, treatment group, calcium and sun exposure score were significant predictors of 25(OH)D serum levels.

Depot vitamin D therapy is an alternative to daily treatment in this at-risk group of children and adolescents in whom treatment adherence is problematic.

Conclusions



Hypovitaminosis D is a relevant negative epigenetic factor affecting bone and global health in infancy and childhood

Nutritional rickets is still present all over the world, requiring adequate preventive strategies

The regular and universal Vitamin D supplementation starting from birth through the first year of life and thereafter tailored on the basis of type of feeding, lifestyle, latitude and concomitant risk factor, should be considered as an efficacious preventive strategy.

Any other strategy aimed at improving lifestyle and reducing obesity rates (i.e. to increase physical activity, to play outdoor, to increase sun light exposure, to support adequate dietary regimens), should be strongly supported.


PREVENTION
IS BETTER
THAN CURE

THANKS FOR YOUR ATTENTION

شكرا لاهتمامك