

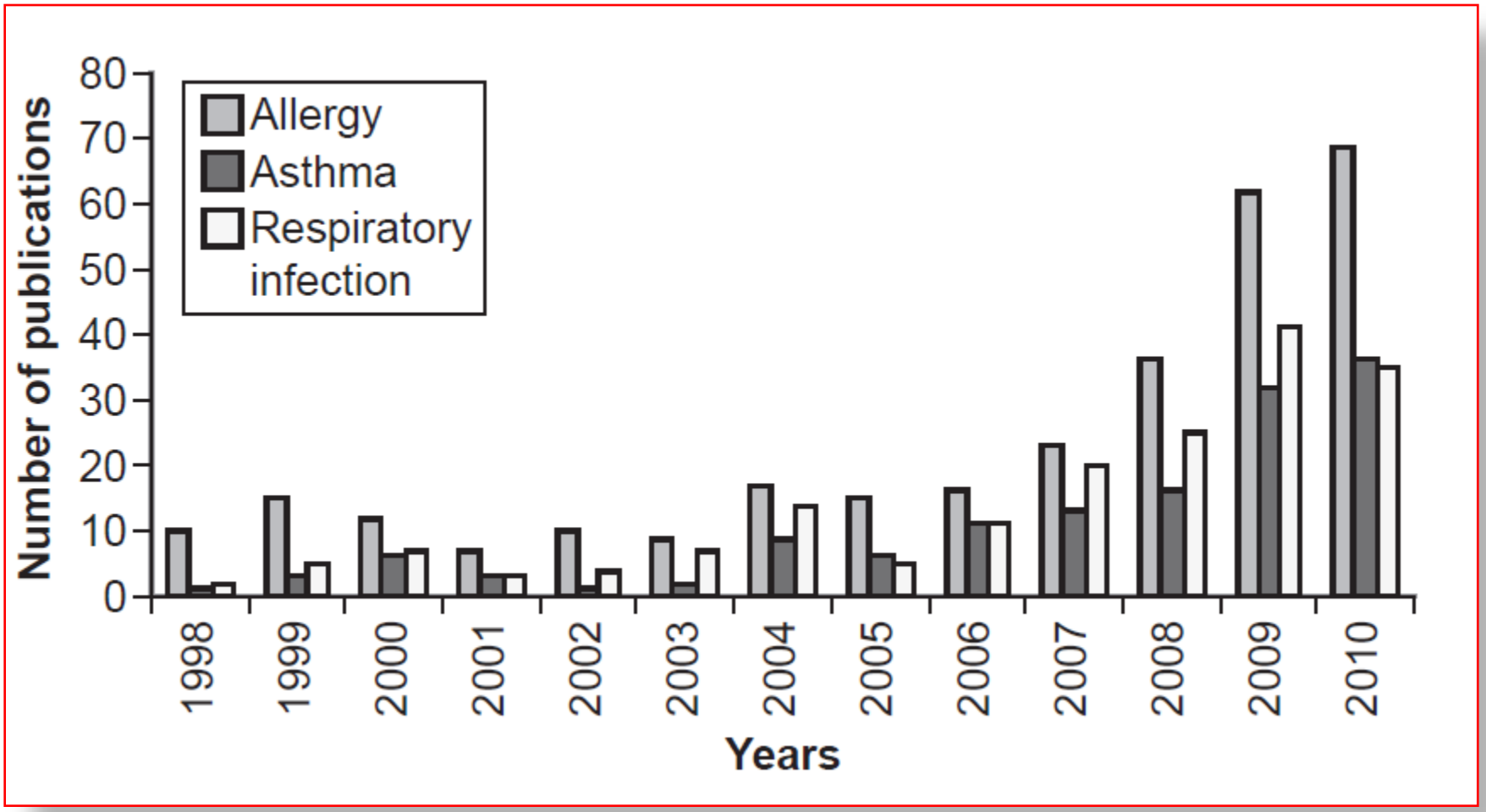
Novità in ALLERGOLOGIA ed IMMUNOLOGIA PEDIATRICA

Benevento, 18-19 maggio 2012

Vitamina D, atopia e asma

Giuseppe Pingitore
Allergologia, ASL Roma D

Vitamina D e allergia:
l'argomento è "caldo"



La vitamina D

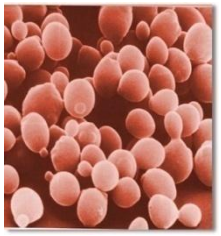


Produzione di Vitamina D

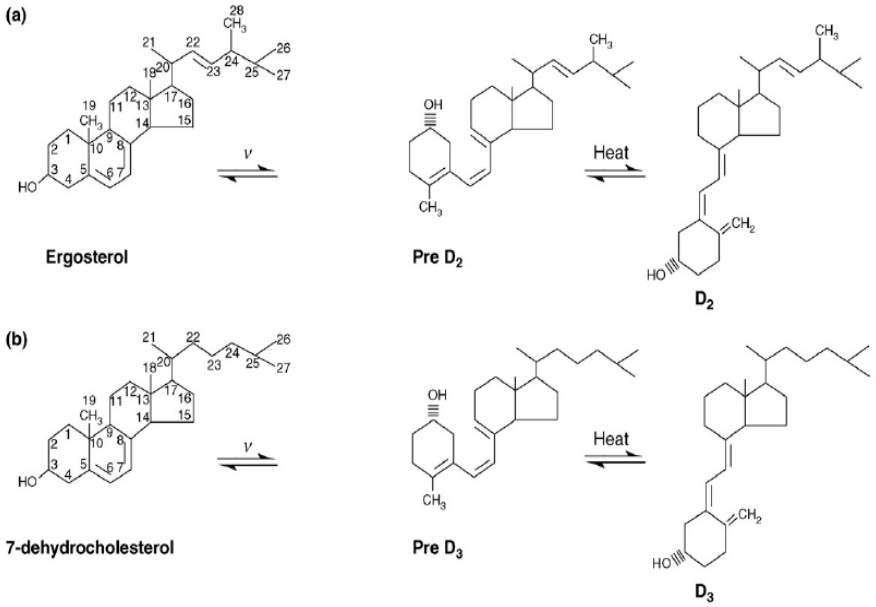
Esistono 2 forme di vitamina D: vitamina D2 (ergocalciferolo) e vitamina D3 (colecalciferolo)

Ergocalciferolo è prodotta in una varietà di piante e lieviti sotto l'influenza delle radiazioni ultraviolette (UVR),

Colecalciferolo, è prodotta nella pelle anche essa per azione delle UVR.





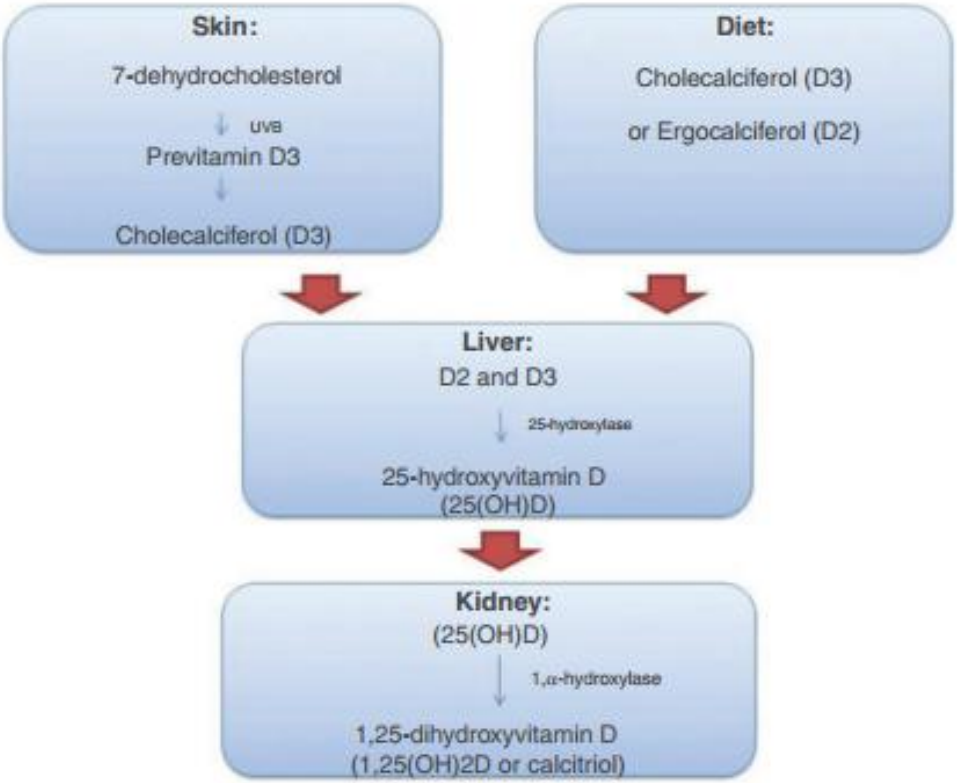




Metabolismo della vitamina D

90%





10%



Produzione di vitamina D a Boston (latitudine 42 = Roma)

L'esposizione alla luce solare per **5-15 minuti** (tra le 10:00 e le 15:00) durante la **primavera**, **l'estate**, e in **autunno** garantisce alle persone di pelle bianca adeguati livelli di vitamina D.



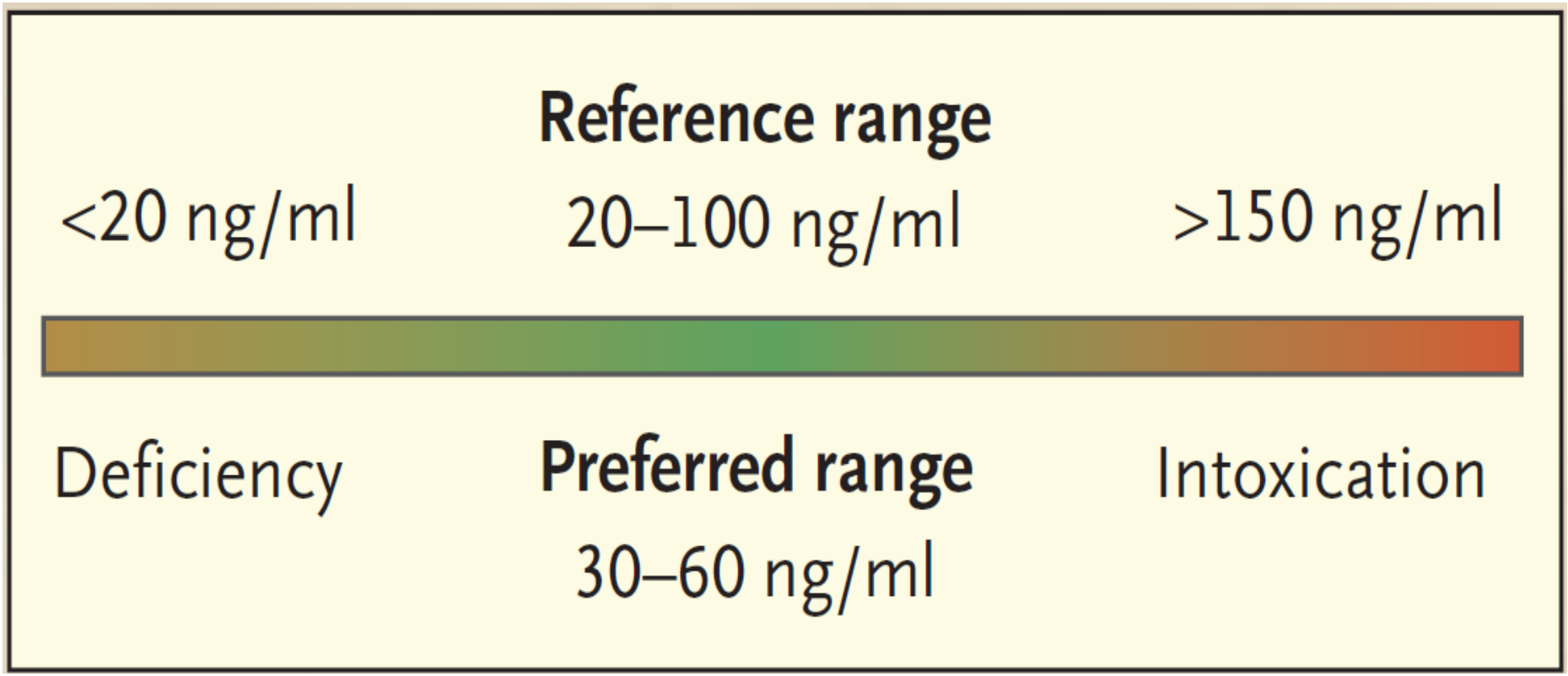
Le persone di pelle scura necessitano di una esposizione da **5 a 10 volte più lunga**.

Inoltre, coloro che vivono sopra al **35 parallelo di latitudine** non riescono a produrre adeguate quantità di D_3 durante **l'inverno.**



Rovner, Arch Pediatr Adolesc Med. 2008;162(6):513-519

Vitamin D Deficiency



La variabile più affidabile per determinare lo stato di nutrizione per la vitamina D è il livello di **25(OH)D** nel plasma.

Holick MF. NEJM 2007;357:266-81

Vitamin D insufficiency

TABLE. **Classification of Vitamin D Status by 25(OH)D Concentration**[a,b]

25(OH)D concentration	Classification
≤10 ng/mL	Deficient
11-20 ng/mL	Insufficient
>20 ng/mL	Optimal

[a] 25(OH)D = 25-hydroxyvitamin D.
[b] To convert from ng/mL to nmol/L, multiply by 2.496.

30 ng/mL

25(OH)D

- **Misura i livelli di Vitamina D**
- **Emivita di 3 settimane**
- **Rappresenta i depositi totali di vitamina D**

Tracher TD et al. Mayo Clin Proc. 2011; 86(1):50-60

Assessing the vitamin D status of the US population

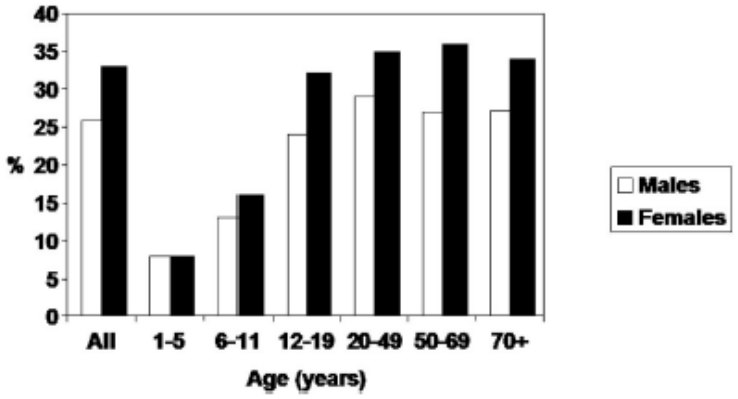
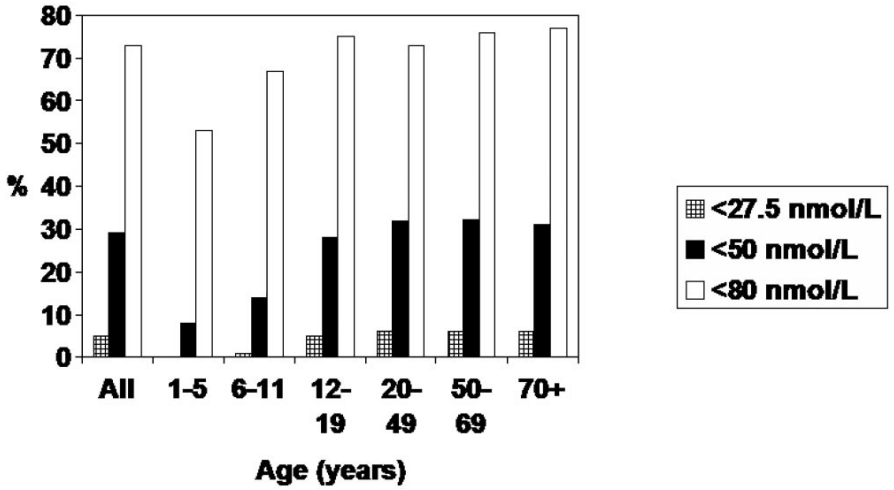
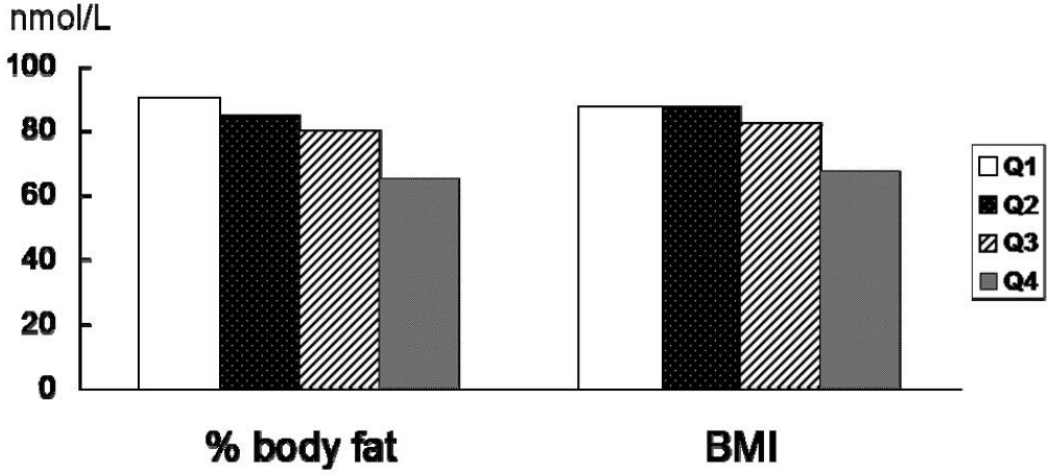


FIGURE 2. Prevalence (as a percentage of the group) of a serum 25-hydroxyvitamin D concentration <50 nmol/L for men (□) and women (■) from the National Health and Nutrition Examination Survey (NHANES) 2000–2004. Data for ages 1–5 y are available from NHANES 2003–2004 only.

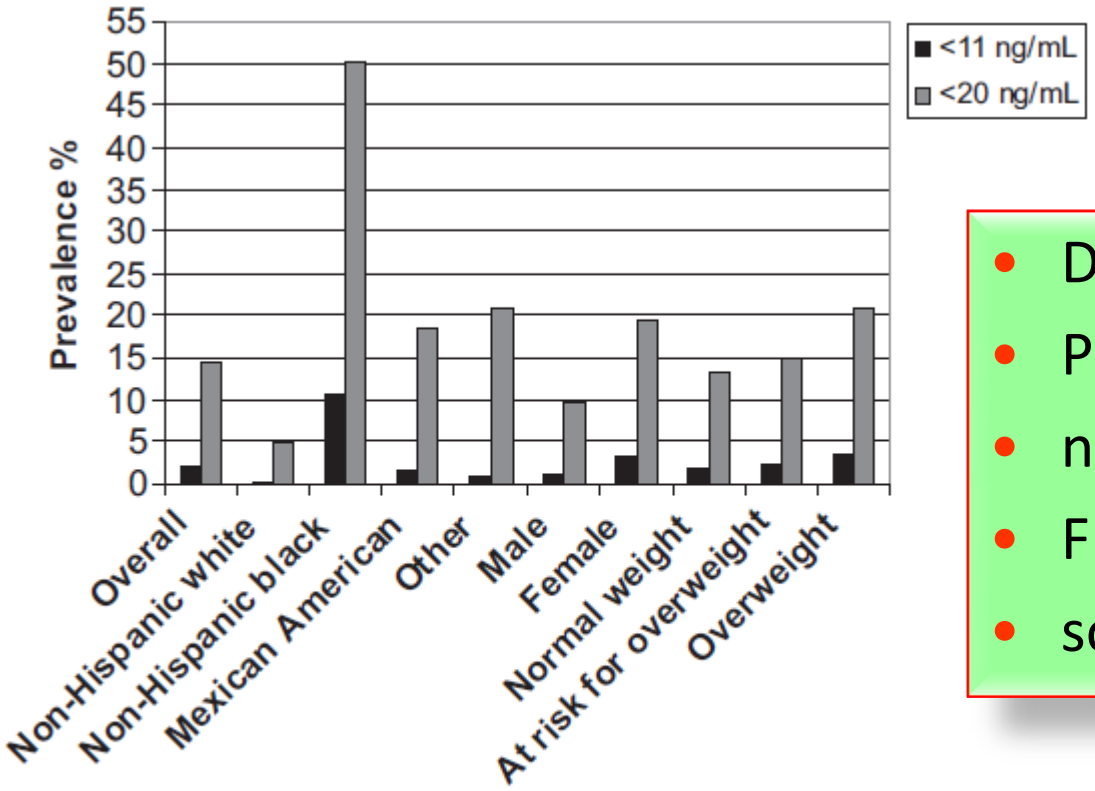


- NAHNES 1988-1994
- Non-Hispanic white women
- Age: 20-49 y
- Bioelectrical impedance



Yetley EA. Am J Clin Nutr 2008;88(suppl):558S– 64S

Implications of a New Definition of Vitamin D Deficiency in a Multiracial US Adolescent Population: The National Health and Nutrition Examination Survey (NHANES III)

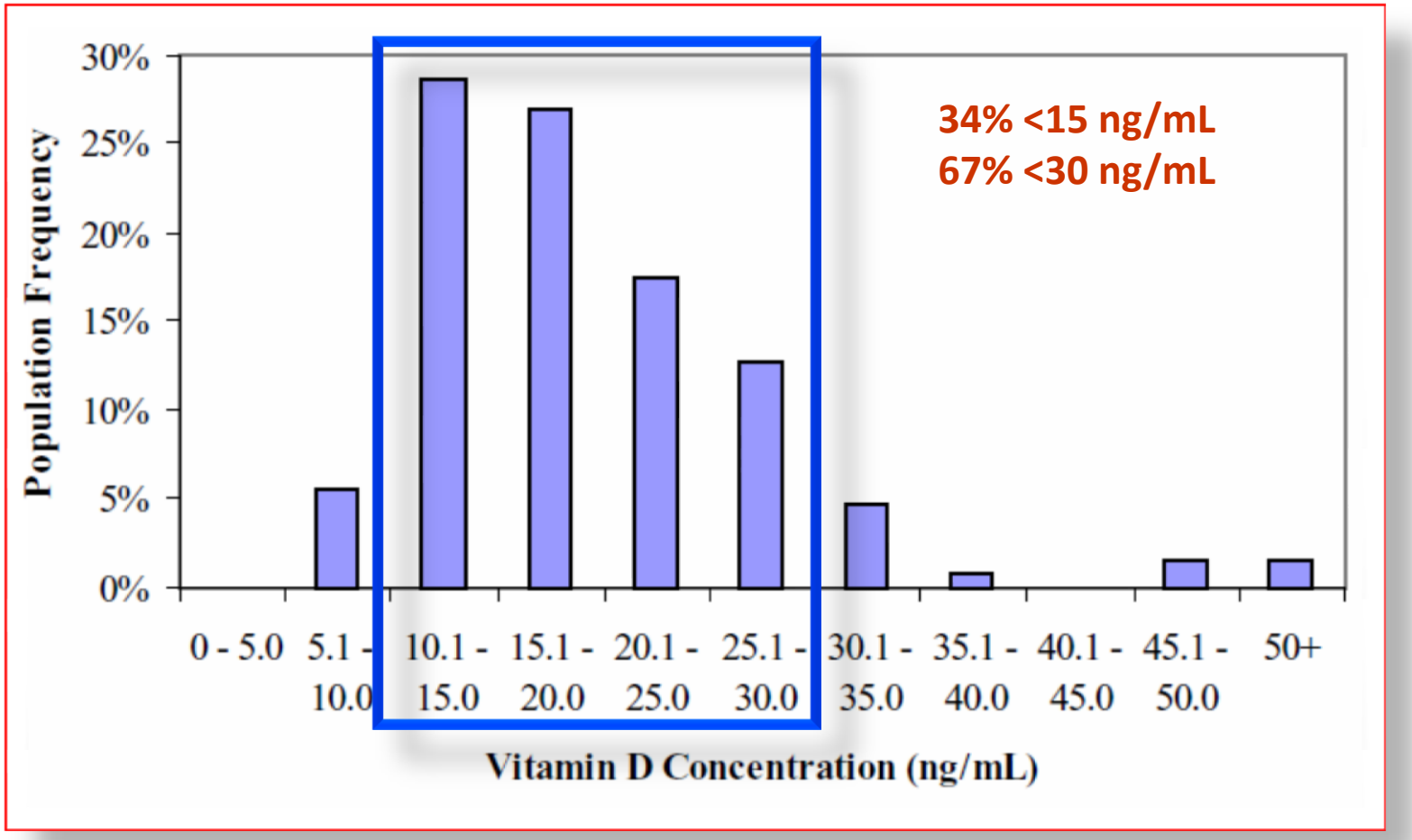


- Deficit: <11 ng ➔ <20 ng
- Prevalenza: 2% ➔ 14%
- neri > bianchi (20 volte)
- F > M (2 volte)
- sovrappeso > normopeso

FIGURE 1
Weighted prevalence of vitamin D deficiency: current (<11 ng/mL) versus recommended (<20 ng/mL) levels according to race/ethnicity, gender, and weight.

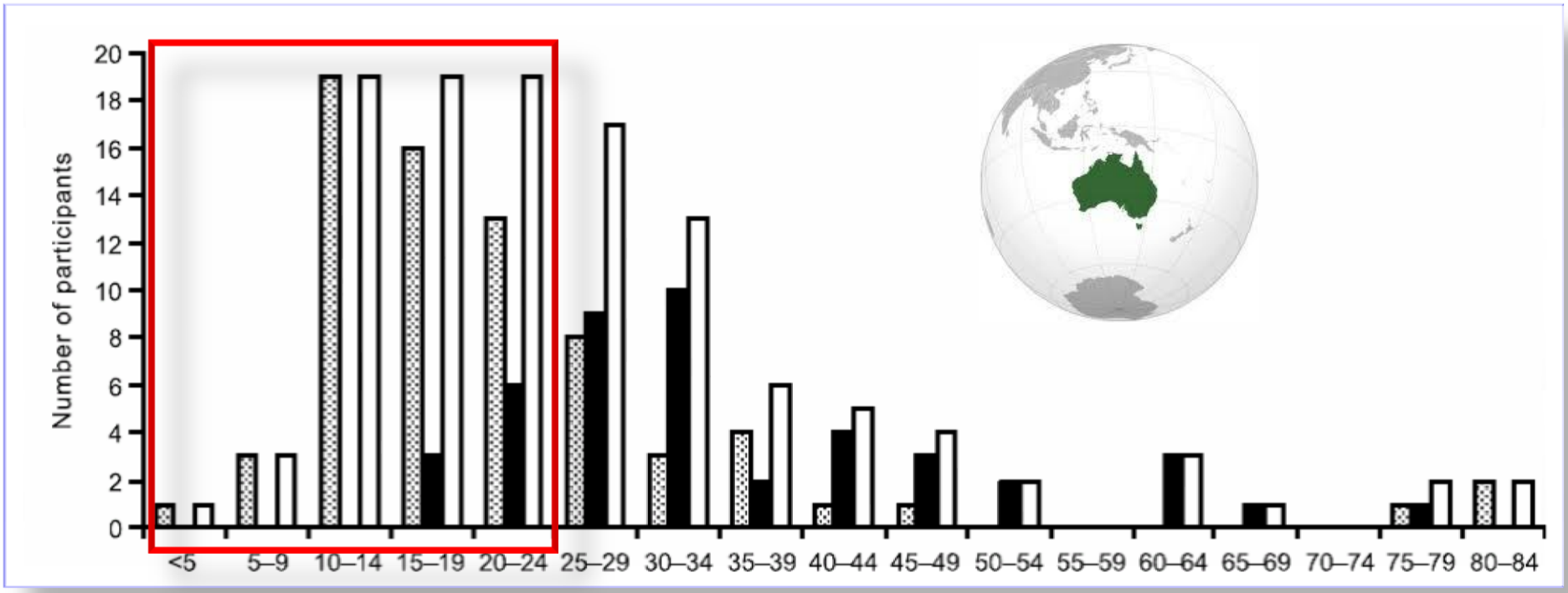
Saintonge S et al. Pediatrics 2009;123;797

Hypovitaminosis D in normal, apparently healthy urban European population



MacFarlane GD et al. J Steroid Biochem Mol Biol. 2004;89-90(1-5):621-2

Vitamin D deficiency is common and unrecognized among recently arrived adult immigrants from The Horn of Africa



Bassi livelli di Vitamina D (< 25 nmol/ml) trovati nel 53% dei patienti (74% femmine, 20% maschi)

Skull SA et al. Intern Med J. 2003 Jan-Feb;33(1-2):47-51

Hypovitaminosis D in developing countries: prevalence, risk factors and outcomes



- Hypovitaminosis D is a widespread disorder in developing countries, regardless of their latitude
- The disorder is highly prevalent in China, Mongolia, Sub-Saharan Africa, the Middle East and Latin America, especially in children, the elderly and women

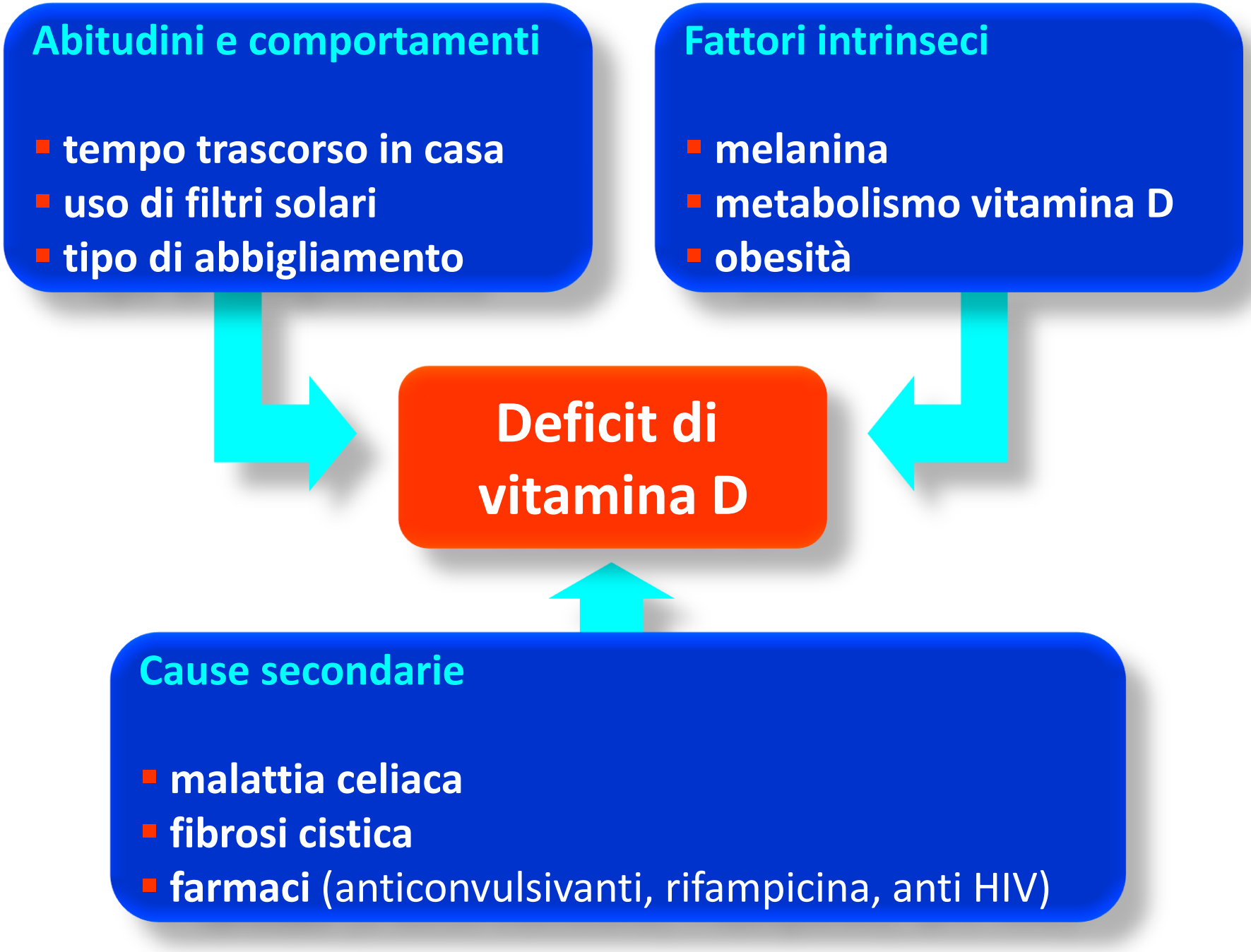
Arabi, A. et al. Nat. Rev. Endocrinol 2010;6, 550–561

High prevalence of vitamin D deficiency in pregnant non-Western women in The Hague, Netherlands

- Alta prevalenza di deficit di vitamina D nelle donne gravide (XII sett.)
- > 50% delle donne non-occidentali (pelle scura)
- 8% delle donne occidentali (pelle chiara)
- Definizione di deficit < 25 nmol/L (10 ng/mL)
- **Oggi in Olanda (e non solo) si parla di deficit per valori di < 80 nmol/L (32 ng/mL)**



van der Meer IM et al. Am J Clin Nutr 2006;84:350 –3


Abitudini e comportamenti
tempo trascorso in casa
uso di filtri solari
tipo di abbigliamento
Fattori intrinseci
melanina
metabolismo vitamina D
obesità
Deficit di vitamina D
Cause secondarie
malattia celiaca
fibrosi cistica
farmaci (anticonvulsivanti, rifampicina, anti HIV)

Prevalence and predictors of low vitamin D concentrations in urban Canadian toddlers

- 91 bb 2 anni
- Prevalenza di bassi livelli di vit.D
- Rapporto con ridotto consumo di latte vaccino e aumento del BMI
- 32% < 50 nmol/L (20 ng/mL)
- 82% < 75 nmol/L (30 ng/mL)

TABLE 3
Logistic regression model for low vitamin D concentration (lower than 50 nmol/L)

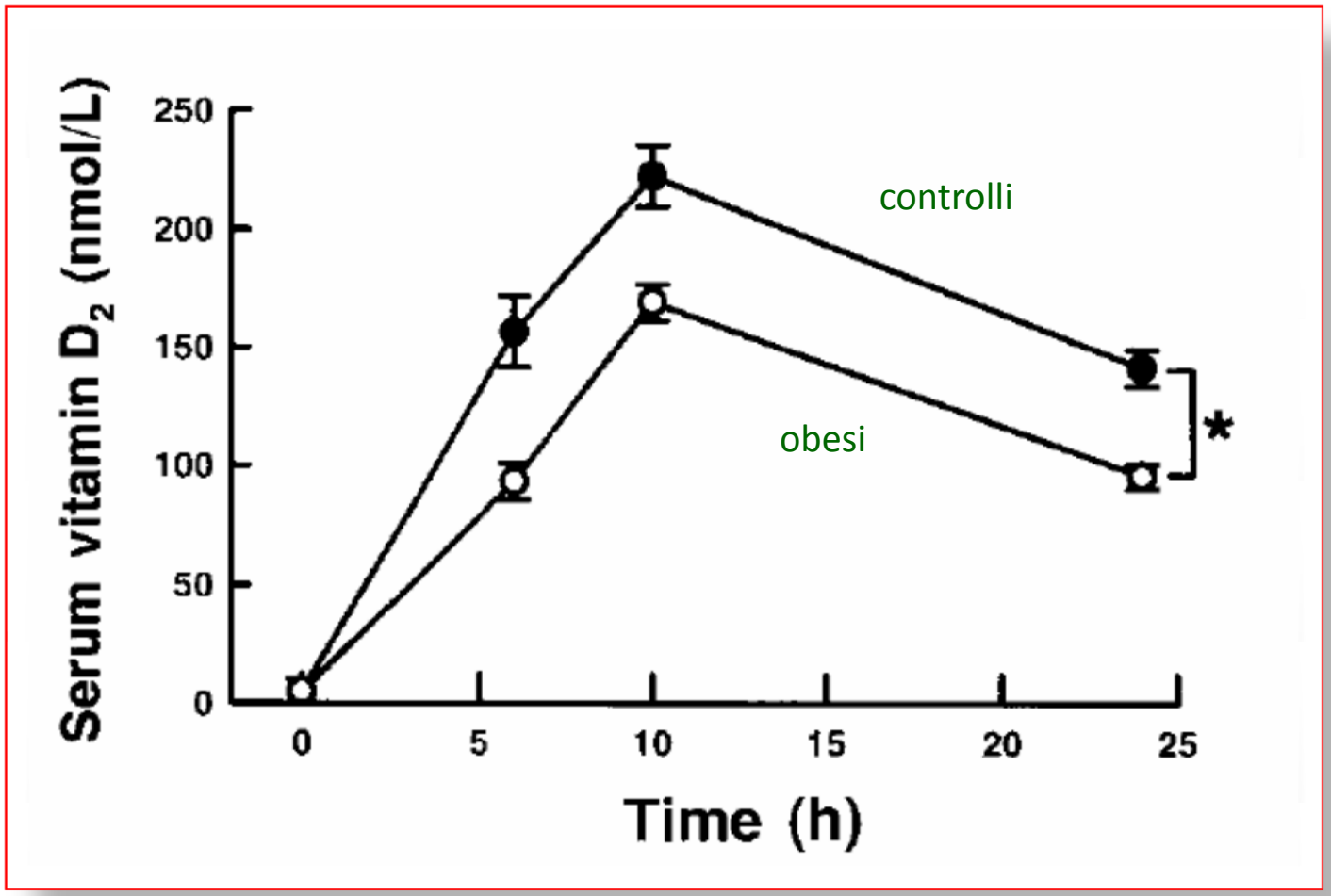
Characteristic	OR* (95% CI)	P
Cow's milk intake (per 250 mL cup daily)	0.44 (0.2–0.96)	0.04
Body mass index 14–15 kg/m^2	2.6 (0.8–8.3)	0.07†
Body mass index 17–18 kg/m^2	1.2 (0.6–2.6)	

**OR represents the increase in odds per unit predictor; †P value includes two degrees of freedom (body mass index 14 kg/m^2 to 15 kg/m^2, and 17 kg/m^2 to 18 kg/m^2)*

Latte vaccino fortificato con aggiunta di 100IU di vit D in 250ml

Maguire JL et al. Paediatr Child Health 2011;16(2):e11-e15.

Decreased bioavailability of vitamin D in obesity



Wortsman J et al. Am J Clin Nutr. 2000 Sep;72(3):690-3

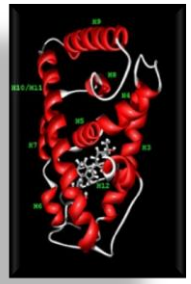


Vitamina D

Rachitismo



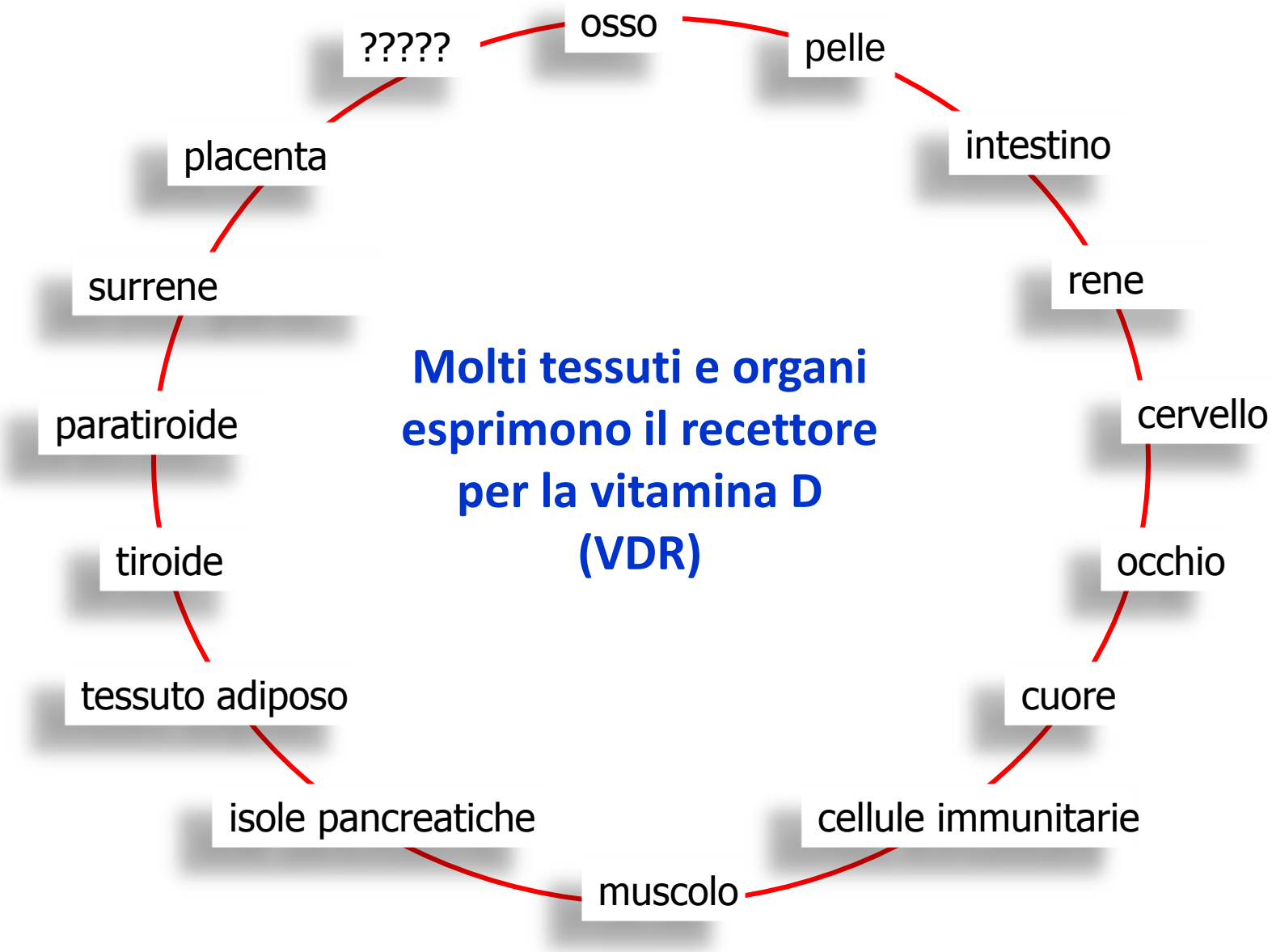
Funzioni Multiple della Vitamina D



Il **recettore della vitamina D** (VDR), che si trova nel nucleo e che media la maggior parte se non tutte le funzioni del suo ligando 1,25 diidrossivitamina D [1,25(OH)2D] o calcitriolo, è **presente in quasi tutti i tessuti del corpo**.

Inoltre, molti di questi tessuti contengono anche l'enzima, CYP27B1, il quale converte il principale metabolita circolante della vitamina D, 25 idrossivitamina D(25OHD), a 1,25(OH)2D.

Pertanto, è molto probabile che la **vitamina D svolga la sua azione non solo sui classici tessuti che regolano l'omeostasi del calcio** (ossa, intestino, rene) ma anche su altri tessuti.



Baeke, Curr Opin Pharmacol 2010;10:482

Vitamina D e…

sistema immunitario

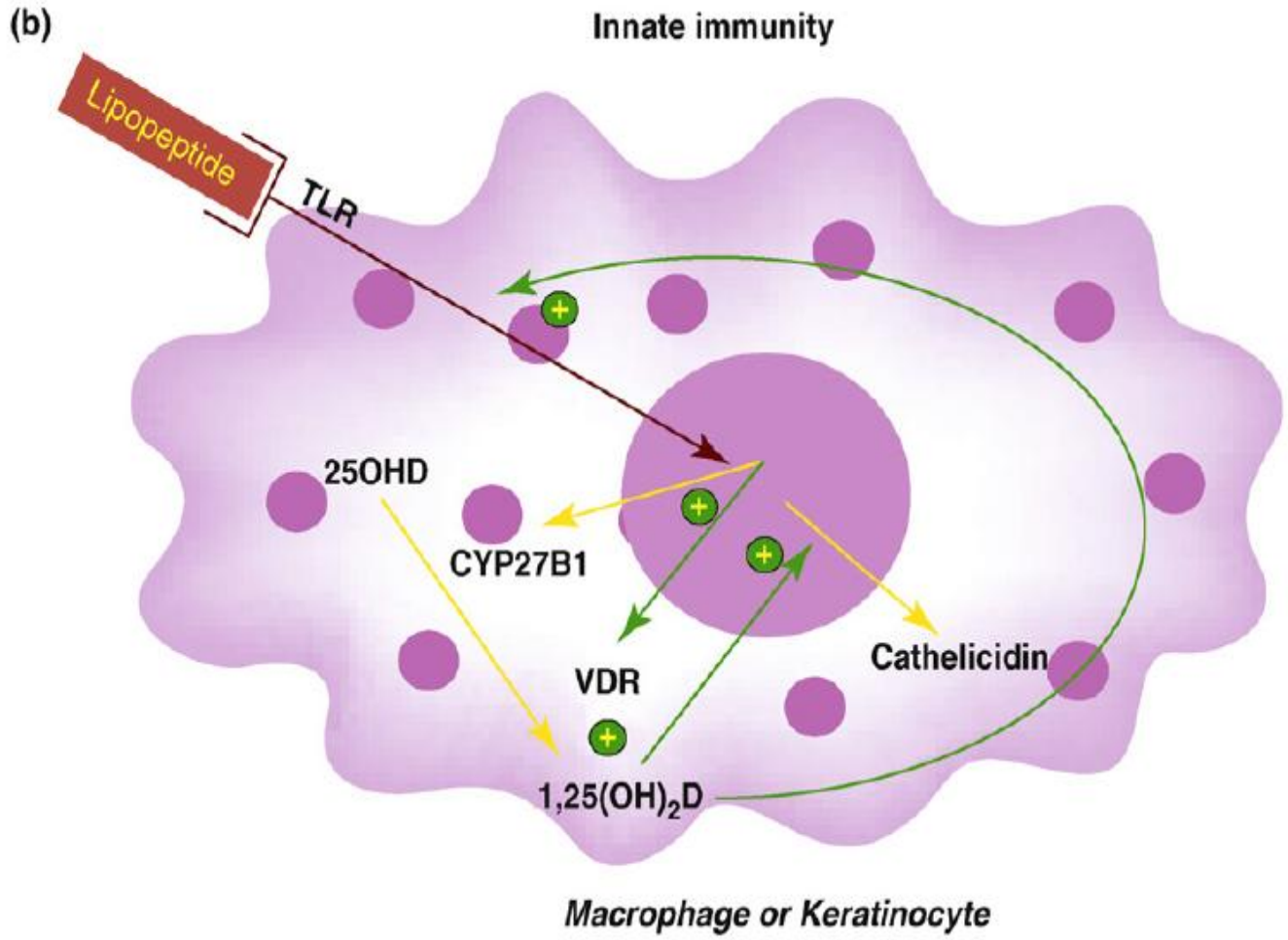
infezioni respiratorie

asma

allergie

considerazioni terapeutiche

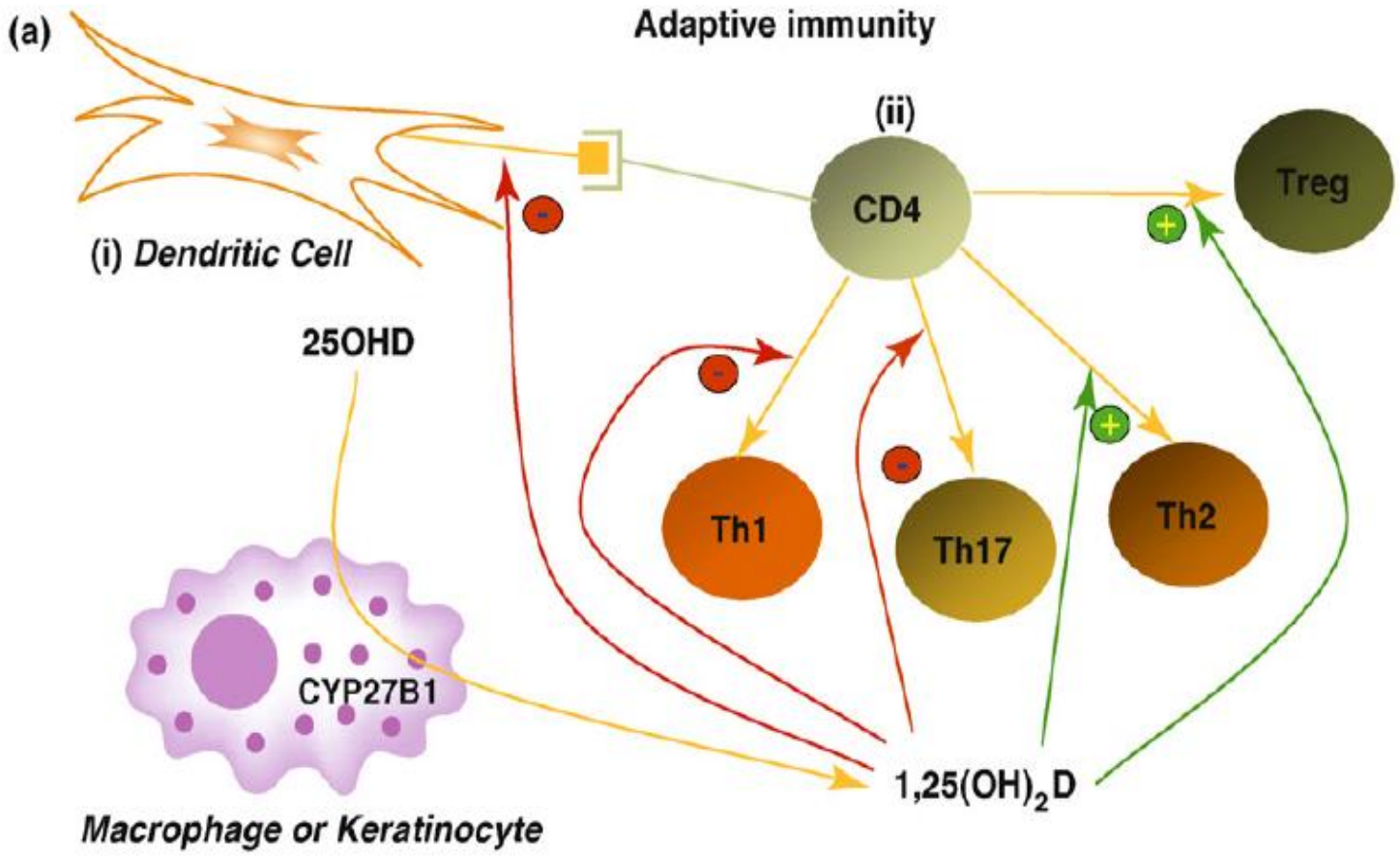
Nonclassic Actions of Vitamin D



1,25(OH)2D legata al suo recettore favorisce la sintesi di **peptidi antimicrobici** come la **catelicidina** capaci di distruggere gli agenti infettivi

Bikle D. J Clin Endocrinol Metab 2009; 94: 26–34

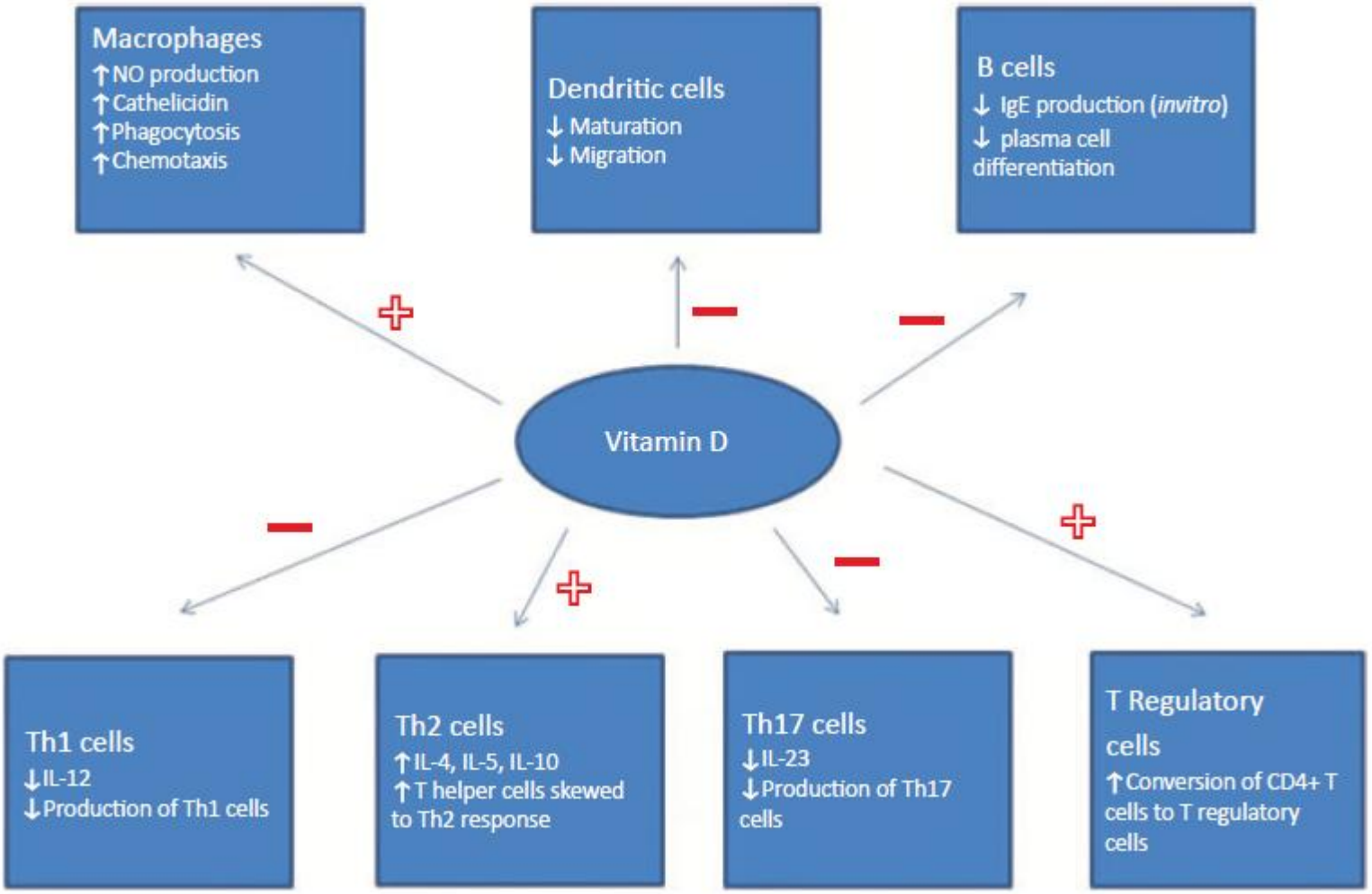
Nonclassic Actions of Vitamin D



La cellula dendritica stimola la cellula CD4 a differenziarsi in uno dei quattro differenti tipi di cellule T helper (Th). 1,25(OH)2D riduce la capacità di presentare l'antigene e influenza il processo **inibendo lo sviluppo di Th1 eTh17**, e **promuovendo quello di Th2 eTreg**

Bikle D. J Clin Endocrinol Metab 2009; 94: 26–34

The role of vitamin D in the immunopathogenesis of allergic skin diseases



Benson AA et al. Allergy 2012;67:296-301

Vitamina D e…

sistema immunitario

infezioni respiratorie

asma

allergie

considerazioni terapeutiche









RACHITISMO E MALATTIE INFETTIVE

I BAMBINI CHE VANNO AL MARE SI AMMALANO DI MENO

Low serum vitamin D levels and tuberculosis: a systematic review and meta-analysis

Table 4 Effect sizes of low serum vitamin D in tuberculosis patients and controls

Study or sub-category	Cases N	Control N	Effect Size (SE)	Effect Size (random) 95% CI	Weight %	Effect Size (random) 95% CI
Davies, UK	40	40	0.8600 (0.2300)		16.69	0.86 [0.41, 1.31]
Grange, Indonesia	40	38	0.1800 (0.2300)		16.69	0.18 [−0.27, 0.63]
Davies, Kenya	15	15	1.0400 (0.3900)		8.34	1.04 [0.28, 1.80]
Davies, Thailand	51	51	0.9600 (0.2100)		18.31	0.96 [0.55, 1.37]
Chan, Hong Kong	24	24	0.3300 (0.3000)		12.14	0.33 [−0.26, 0.92]
Wilkinson, UK	103	42	0.5900 (0.2300)		16.69	0.59 [0.14, 1.04]
Sasidharan, India	35	16	0.9400 (0.3200)		11.13	0.94 [0.31, 1.57]
Total (95% CI)	308	226			100.00	0.68 [0.43, 0.93]

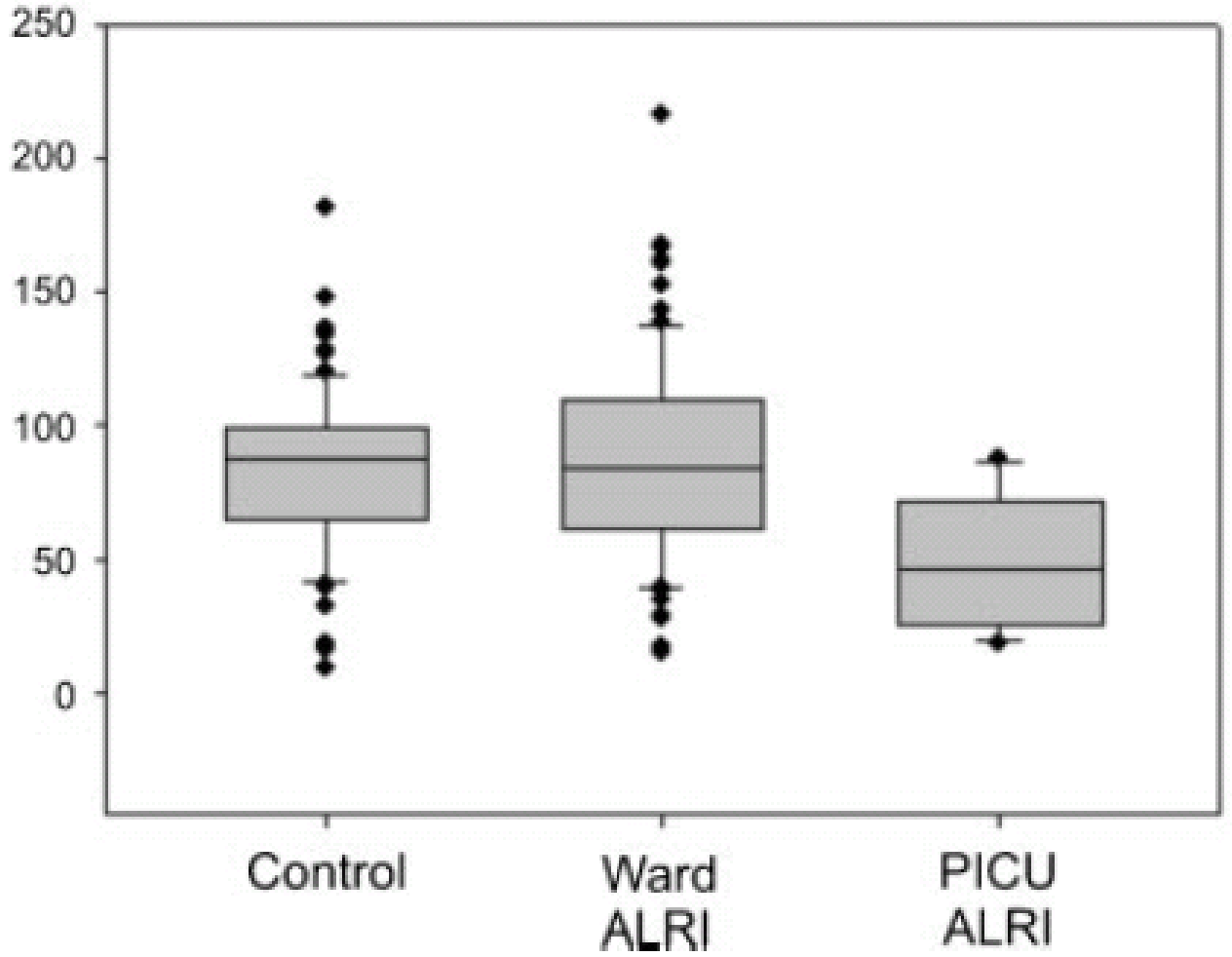
Test for heterogeneity: $Chi^2 = 10.14$, $df = 6$ ($P = 0.12$), $I^2 = 40.8\%$

Test for overall effect: $Z = 5.28$ ($P < 0.00001$)

- **Probabilità del 70% circa che gli individui sani abbiano valori di vitamina D più alti dei soggetti affetti da tubercolosi**

Nnoaham KE et al. International Journal of Epidemiology 2008;37:113–119

Vitamin D deficiency in young children with severe acute lower respiratory infection



ALRI

Acute Lower Respiratory Infection

PICU

Pediatric Intensive Care Unit

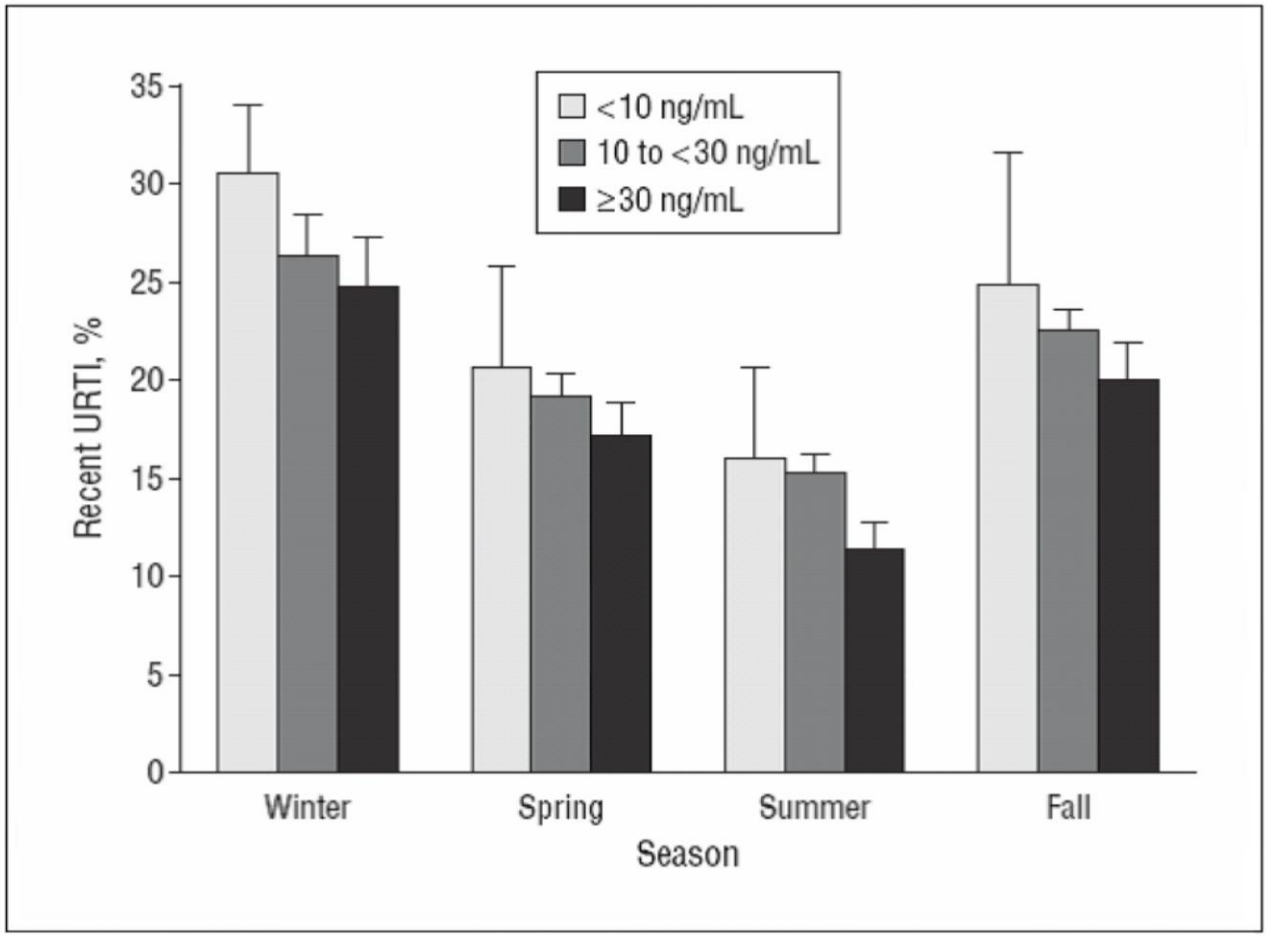
McNally JD et al. Pediatr Pulmonol. 2009 Oct;44(10):981-8

Association between serum 25-hydroxyvitamin D level and upper respiratory tract infection in the Third National Health and Nutrition Examination Survey (1988-1994)

18883 partec.
12 y and older

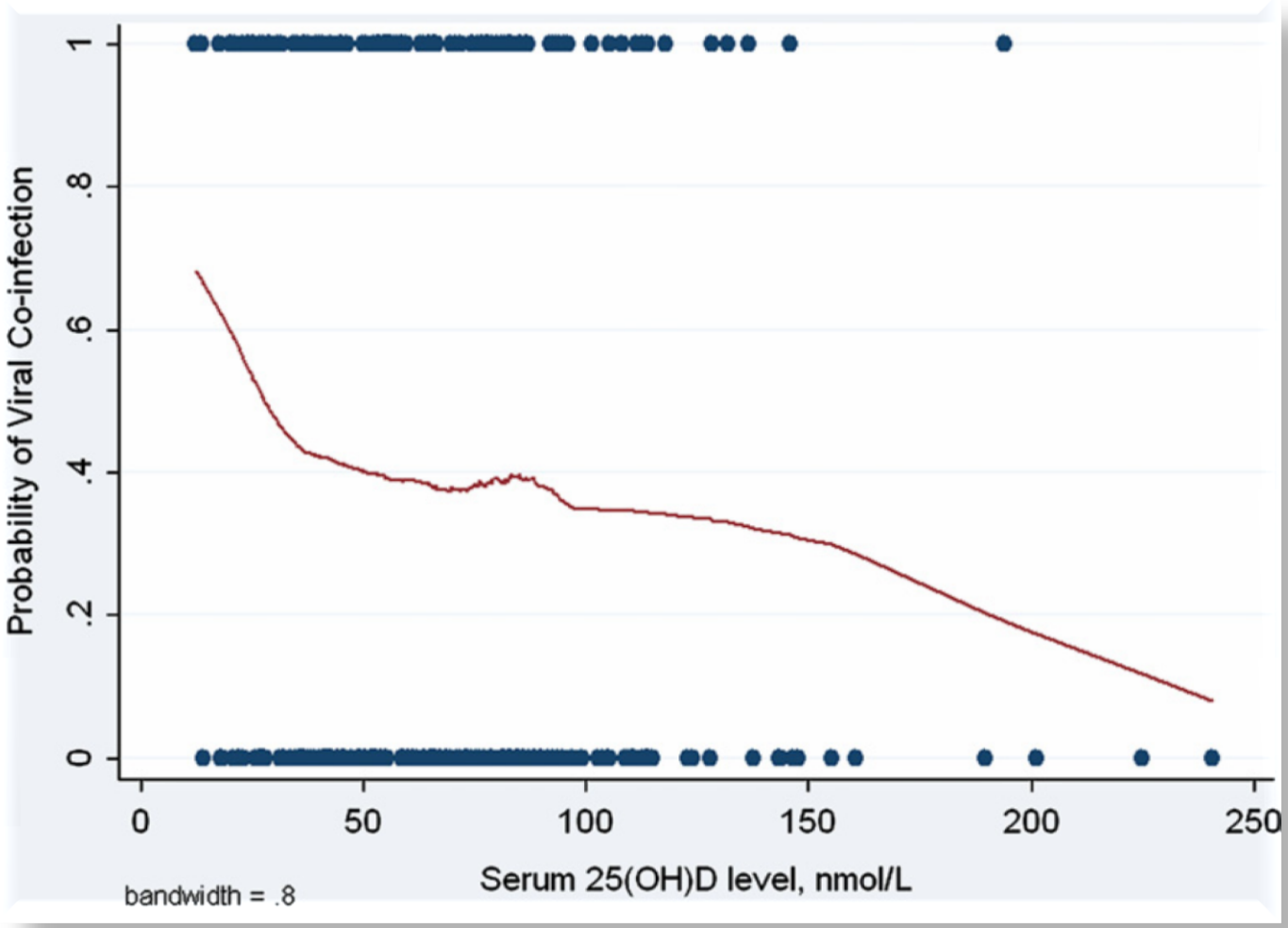
25(OH)D invers. associated with recent URTI





Ginde AA et al. Arch Intern Med. 2009 Feb 23;169(4):384-90.

Low serum 25-hydroxyvitamin D levels are associated with increased risk of viral coinfections in wheezing children

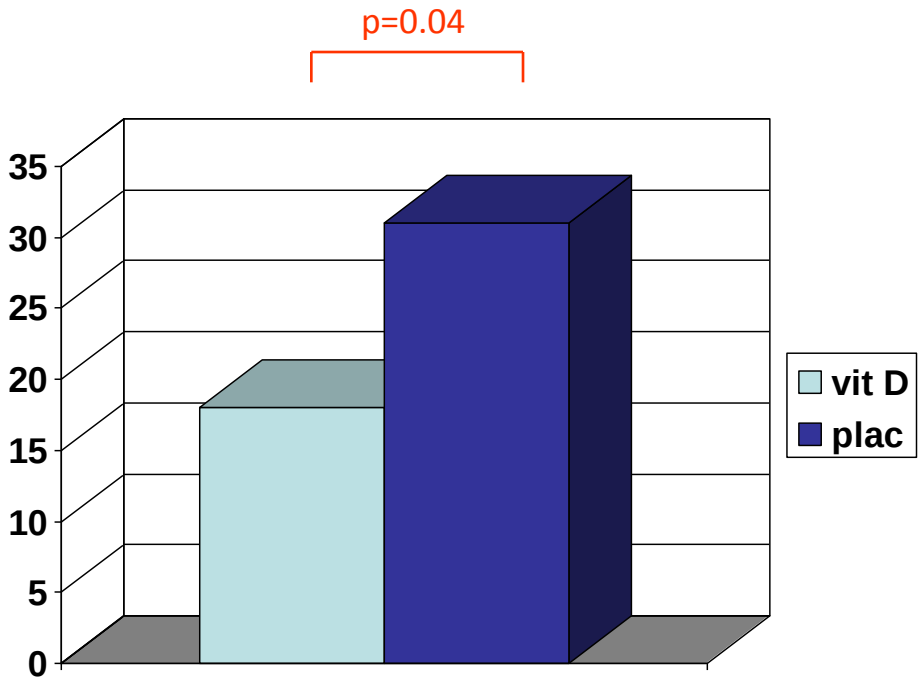




Jartti T et al. J Allergy Clin Immunol. 2010 Nov;126(5):1074-6, 1076.e1-4

Randomized trial of vitamin D supplementation to prevent seasonal influenza A in schoolchildren

- Studio RCT
- Effetti della supplementazione di vit.D **sull'incidenza di influenza** in età scolare
- 1200 UI/die vit.D o placebo (dic.2008-mar.2009)
- 18/167 (10.8%) vs 31/167 (18.6%)
- **RR=0.58**; 95%CI 0.34-0.99
- Attacchi di asma (outcome secondario): **RR=0.17** (p=0.006)



Urashima M et al. Am J Clin Nutr. 2010 May;91(5):1255-60

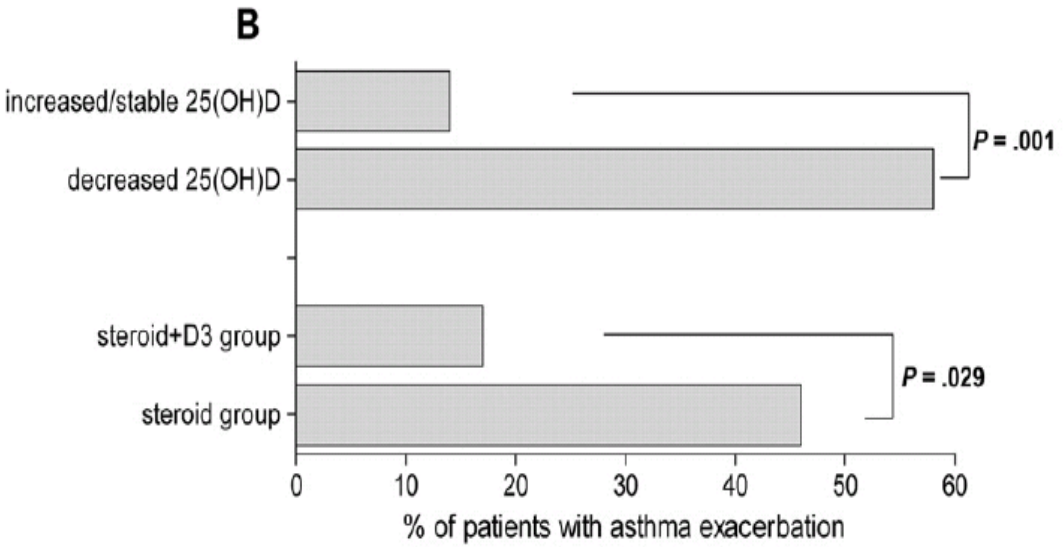
Vitamin D supplementation in children may prevent asthma exacerbation triggered by acute respiratory infection

- 48 bb (5-18y)
- Asma e DPT+
- RCT a gruppi paralleli
- Budesonide +/- vitamina D
- Durata 6 mesi
- Score sintomi/farmaci (ATAQ)

- Nei bb con **↓ vit D3** dopo il 6 m il rischio di accessi asmatici è **8 volte più elevato** (OR 8.6)

✓ Meno accessi nel gruppo BUD+D3

✓ N.accessi correla con livelli vit.D



Majak P et al. J Allergy Clin Immunol. 2011 May;127(5):1294-6

Vitamina D e…

sistema immunitario

infezioni respiratorie

asma

allergie

considerazioni terapeutiche

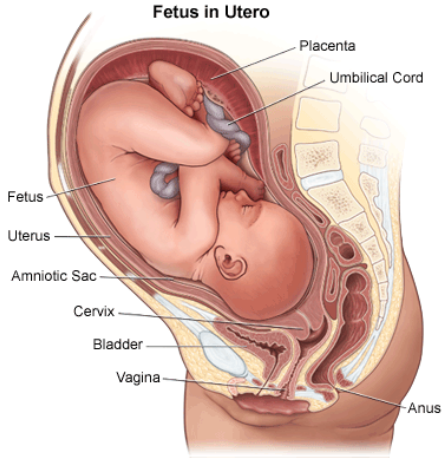
MATERNAL INTAKE OF VITAMIN D DURING PREGNANCY AND RISK OF RECURRENT WHEEZE IN CHILDREN AT 3 Y OF AGE

Camargo, Am J Clin Nutr 2007; 85: 788

MATERNAL VITAMIN D INTAKE DURING PREGNANCY AND EARLY CHILDHOOD WHEEZING (5 yrs)

Devereux, Am J Clin Nutr 2007; 85: 853

Rischio di asma



"using data from the two birth cohorts with maternal vitamin D assessment, we estimate that the ***population attributable risk for asthma incidence*** *caused by vitamin D deficiency in pregnancy is about* ***40%*** *of all cases."* *Weiss JACI 2007;120:1031*

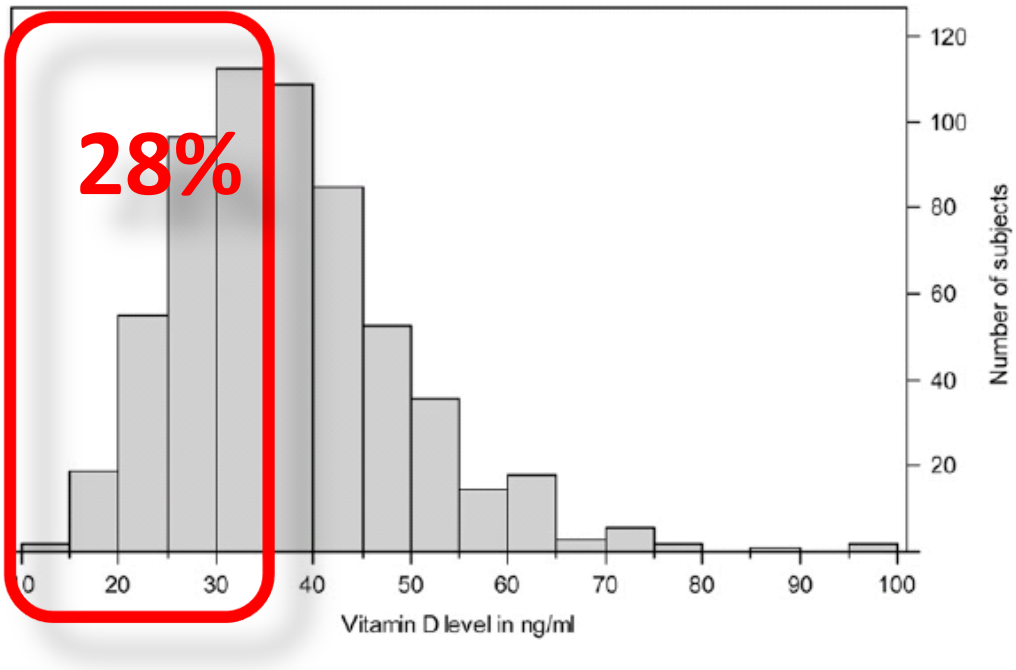
Serum Vitamin D Levels and Markers of Severity of Childhood Asthma in Costa Rica



- 616 bb con asma
- 175 (28%) <30ng/mL vit D

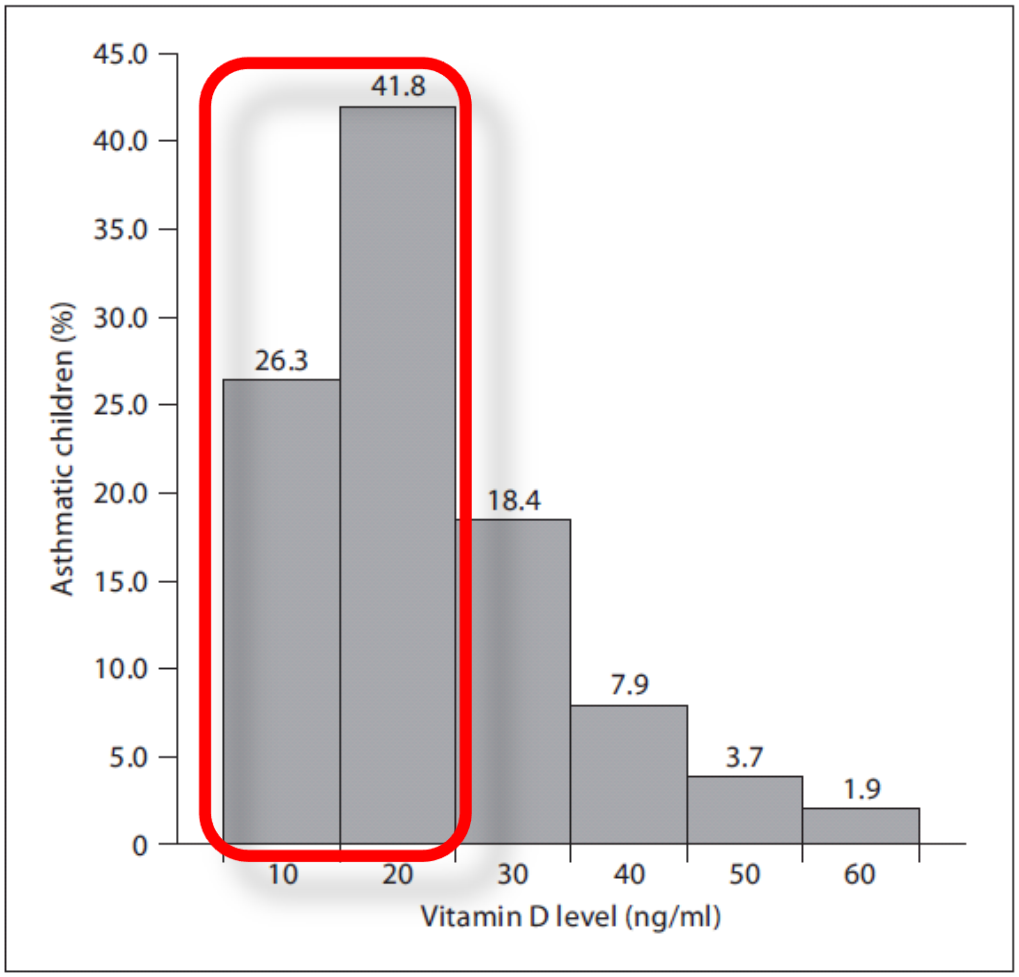
- ↓ vit D ↑ IgE, eosinofili

- ↑ vit D ↓ ospedalizz.
- ↑ vit D ↓ consumo CSI
- ↑ vit D ↓ BHR (PC_{20})



Brehm JM et al.Am J Respir Crit Care Med 2009;179:765–771

Vitamin D Deficiency as a Strong Predictor of Asthma in Children



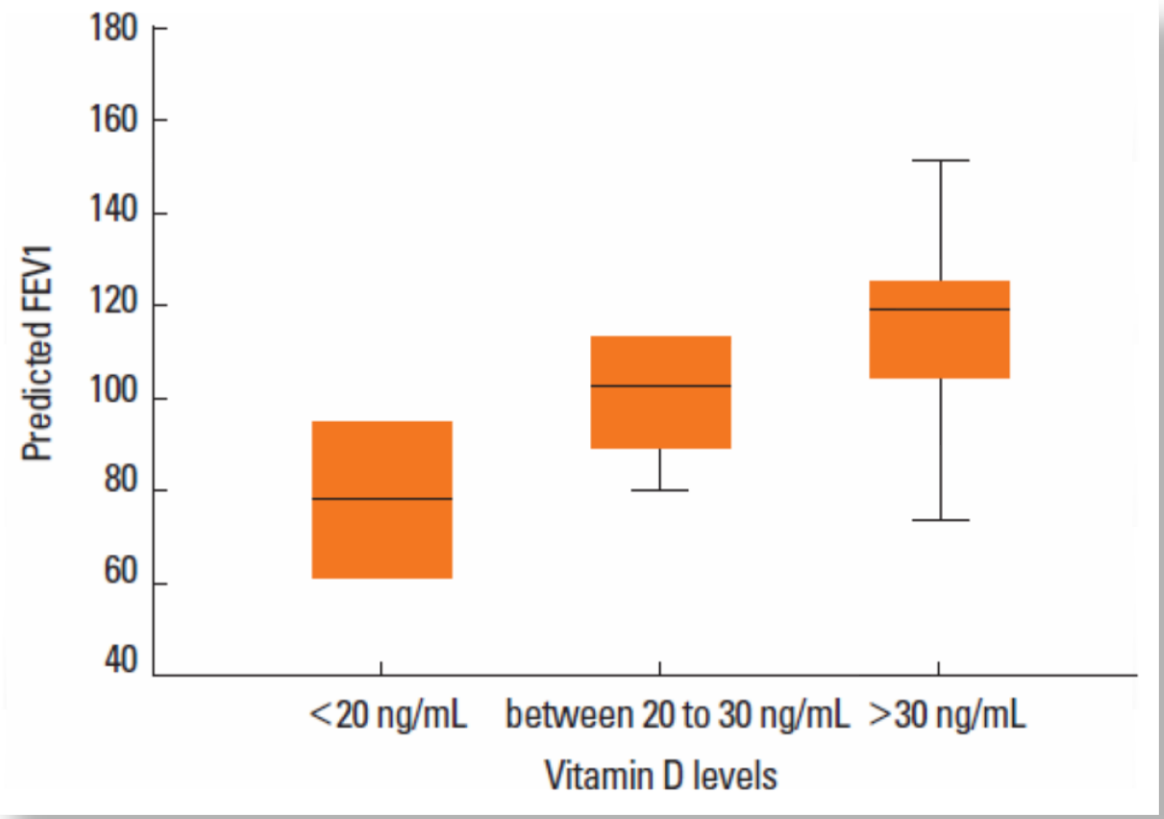
- ✓ 483 asma, 483 controlli
- ✓ Età < 16 aa
- ✓ Deficit: < 20 ng/mL
- ✓ 68% degli asmatici
- ✓ 36% dei controlli

Bener A et al. Int Arch Allergy Immunol 2012;157:168–175

The Relationship Between Serum 25 Hydroxy Vitamin D Levels and Asthma in Children

- Cross-sectional
- 50 asma e 50 sani
- Età: 6-18 anni
- Livelli 25(OH)D

- Correlazione tra livelli vit D e
  - PFR
  - eosinofili

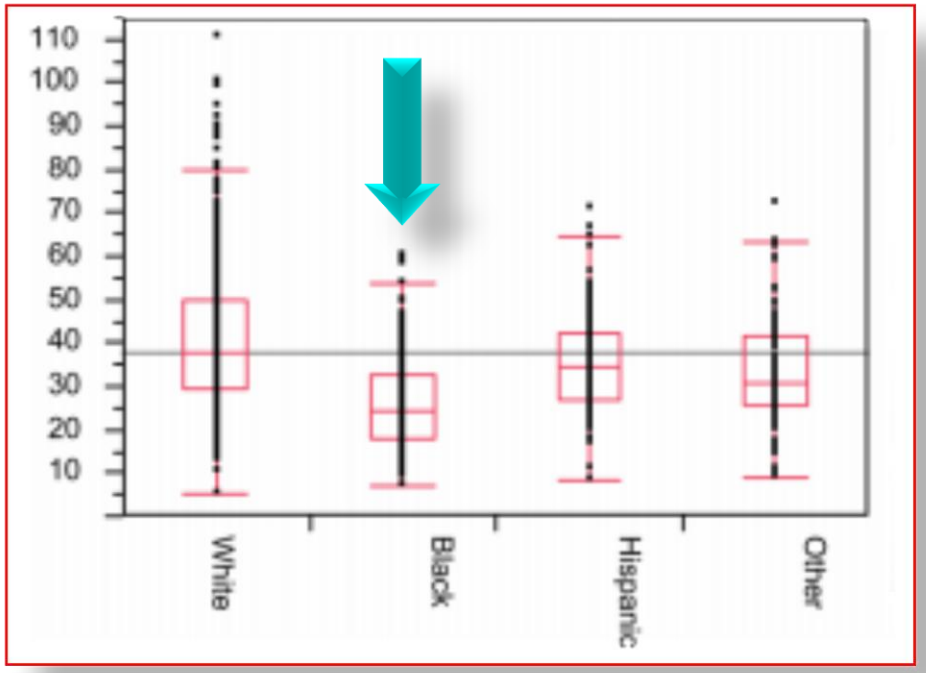


Alyasin S et al. Allergy Asthma Immunol Res. 2011 October;3(4):251-255

Serum Vitamin D Levels and Severe Asthma Exacerbations in the Childhood Asthma Management Program Study

- ✓ 1024 bb con asma lieve-moderato
- ✓ Budesonide, nedocromile o placebo (+ beta-2 al bisogno)
- ✓ Rapporto tra livelli di vitamina D (basale) e rischio di ospedalizzazione o accesso in PS per asma (4 aa)
- ✓ 35% dei bb valori di 25(OH)D <30 nl/mL
- ✓ OR per asma acuto = 1.5





Brehm JM et al. J Allergy Clin Immunol. 2010 July ; 126(1): 52–58.e5.

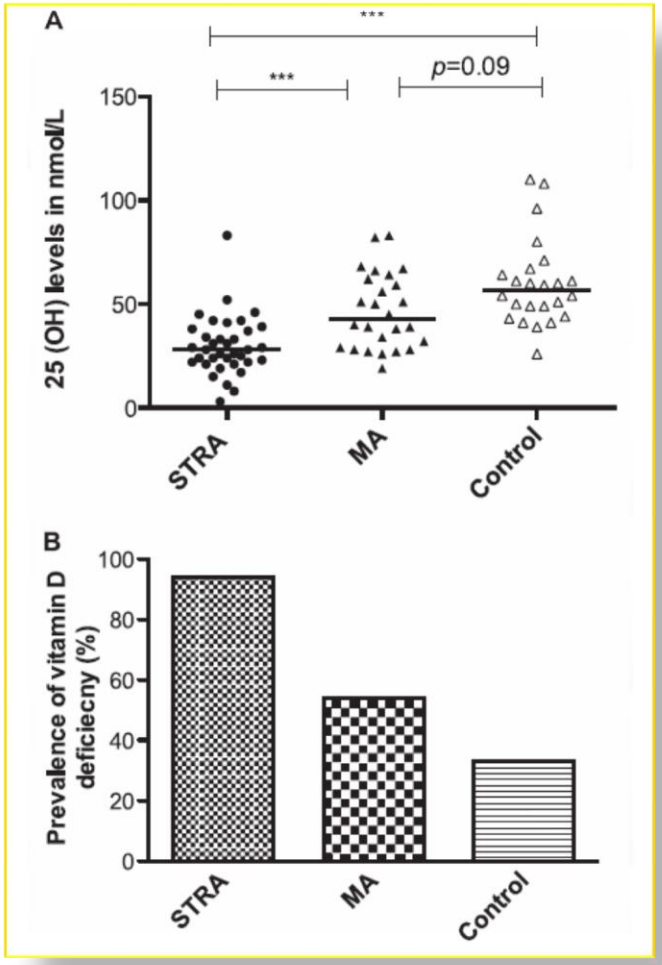
Decreased serum vitamin D levels in children with asthma are associated with increased corticosteroid use

TABLE IV. Univariate analysis of serum VitD levels and medication use

Medication used, sample size (n = 100)	VitD level,† median (IQR)	*P* value*
ICS (n = 60)	ICS: 29 (21-36) No ICS: 35 (26-42)	.0475
Oral CS (n = 14)	Oral CS: 25 (18-30) No oral CS: 32 (25-40)	.02
TCS (n = 69)	TCS: 31 (23-40) No TCS: 31 (24-38)	.98
LTRA (n = 42)	LTRA: 29 (25-37) No LTRA: 32 (23-41)	.50
LABA (n = 29)	LABA: 25 (19-31) No LABA: 34 (27-42)	.0007
MVI (n = 6)	MVI: 40 (27-53) No MVI: 31 (23-39)	.12
Total steroid dose (mg)‡ (n = 64)	$\rho = -0.32$§	.001

Searing DA et al. J Allergy Clin Immunol 2010;125:995-1000

Relationship between serum vitamin D, disease severity and airway remodeling in children with asthma



- 36 STRA = Severe Therapy Resistant Asthma
- 26 MA = Moderate Asthma
- 24 Controlli

✓ ↓ vit D ↓ VEF1, ↓ FVC, ↓ ACT

✓ ↓ vit D ↑ esacerbazioni

✓ ↓ vit D ↑ consumo di CSI

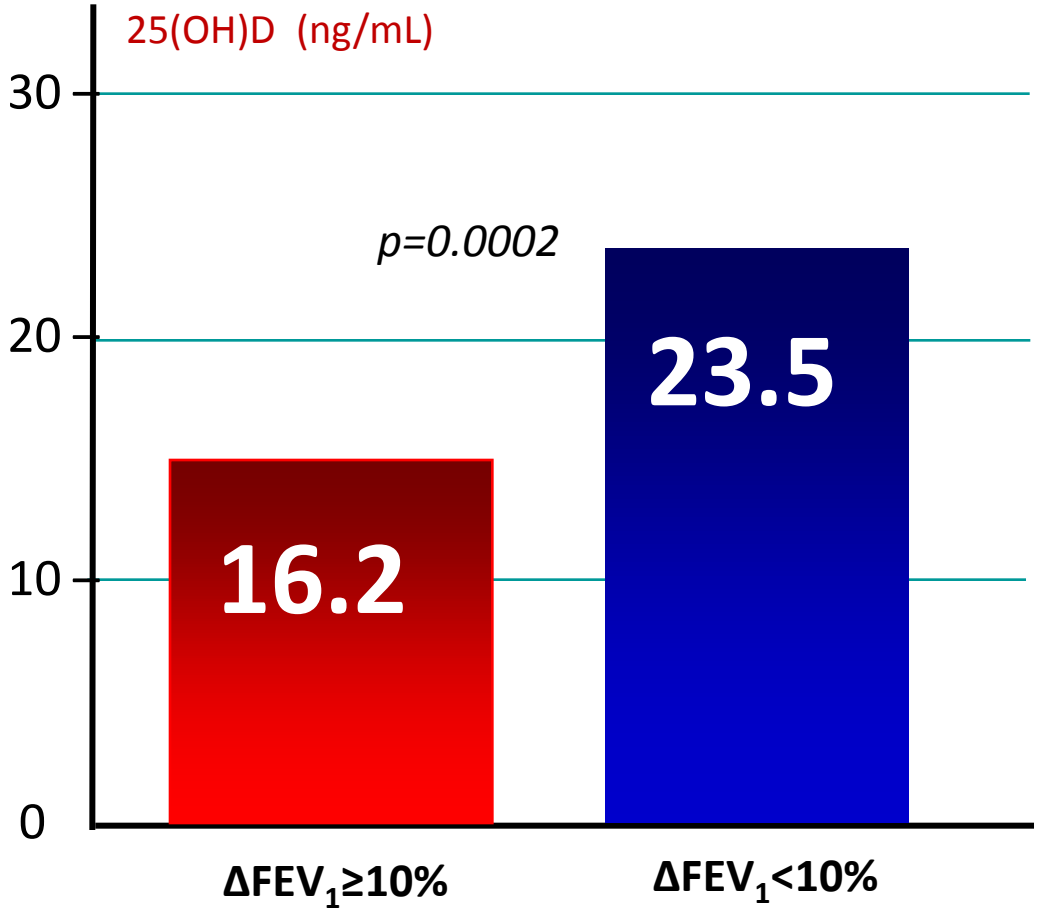
✓ ↓ vit D ↑ ASM (Airway Smooth Muscle mass)

Gupta A et al. Am J Respir Crit Care Med. 2011 Dec 15;184(12):1342-9

Vitamin D Serum Levels and Lung Function and Exercise Induced Bronchoconstriction In Children With Intermittent Asthma

- ✓ 45 bambini con asma intermittente
- ✓ 25-hydroxyvitamin D basale, FVC, FEV_1
- ✓ ΔFEV_1 dopo un test da sforzo standardizzato





Chinellato I et al. Eur Respir J. 2011 Jun;37(6):1366-70

Vitamina D e…

sistema immunitario

infezioni respiratorie

asma

allergie

considerazioni terapeutiche

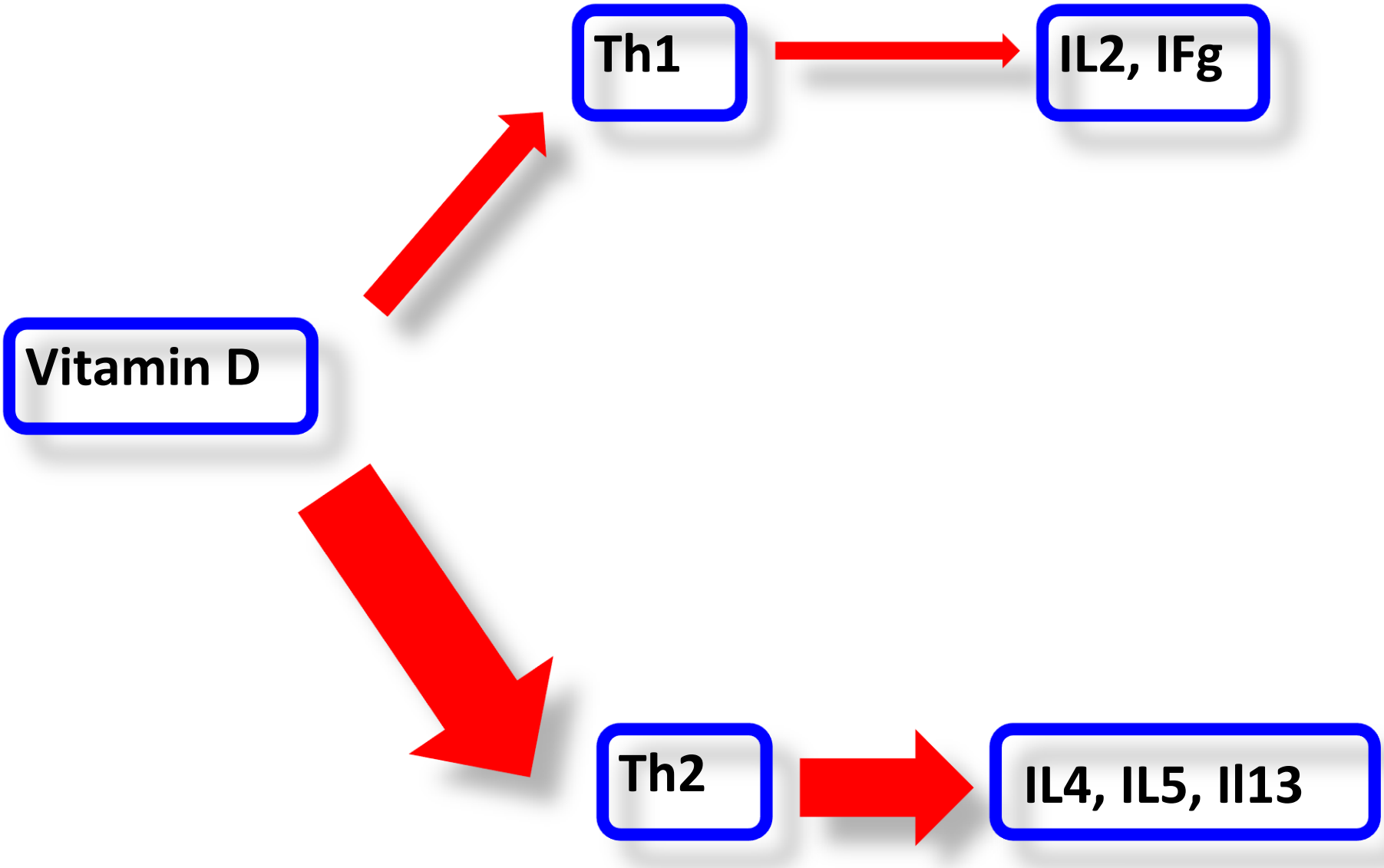
Una voce fuori dal coro



The vitamin D slant on allergy

- *"It eradicated rickets that had been endemic at the beginning of the last century"*
- *"Calcitriol suppresses dendritic cell maturation and consecutive Th1 cell development mainly by blocking the IL-12 signal. Such a delayed Th1 maturation has been independently implicated in allergy and finally led to the* ***hypothesis that allergy development may be a delayed side effect of early rickets prophylaxis****"*

Wjst M. Pediatr Allergy Immunol 2006: 17: 477–483


Th1
IL2, IFg
Vitamin D
Th2
IL4, IL5, Il13

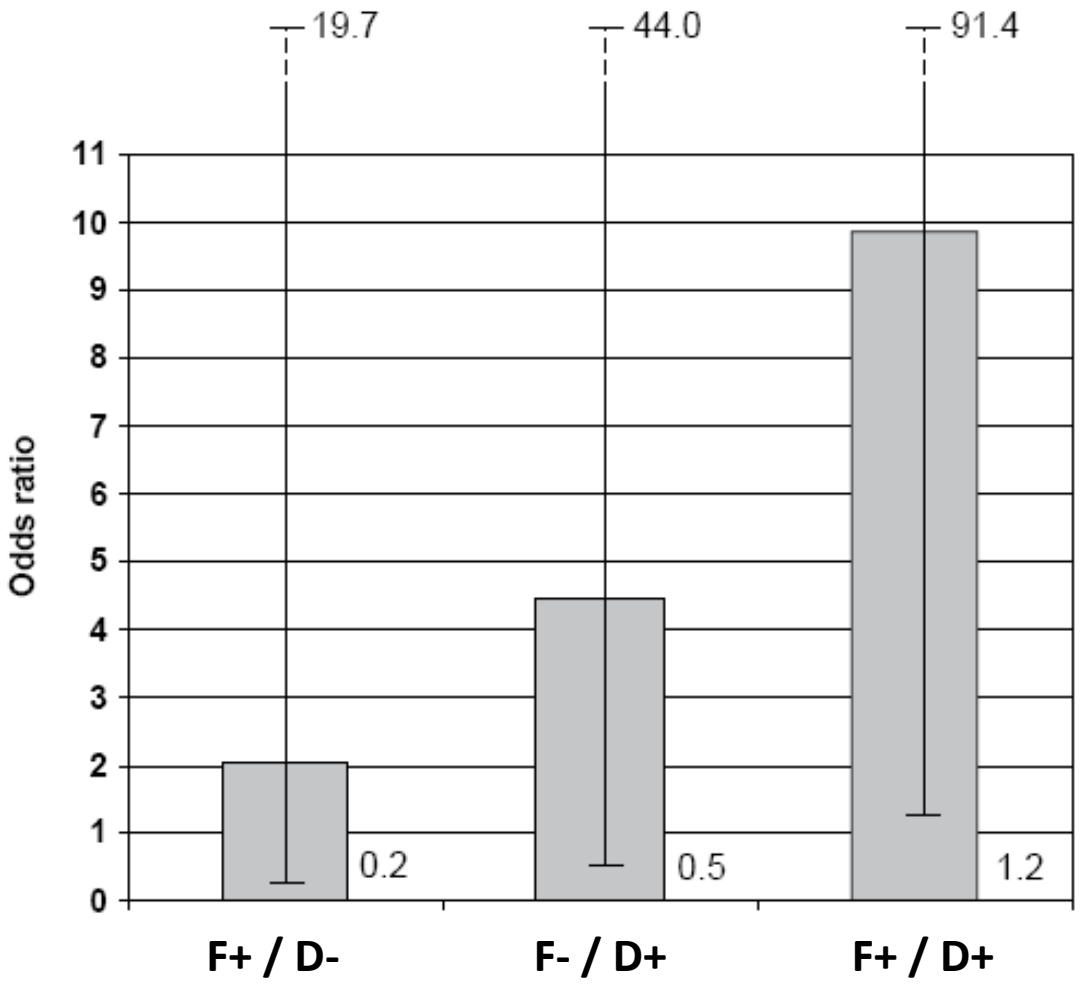
Infant vitamin d supplementation and allergic conditions in adulthood: northern Finland birth cohort 1966

- ✓ 6.007 partecipanti
- ✓ Prevalenza di atopia e rinite allergica più elevata in coloro che ricevevano supplementazioni di vitamina D (OR: 1.46 e 1.66 rispettivamente)
- ✓ Simile associazione osservata per asma (OR: 1.35)
- ✓ Questa associazione persisteva dopo aggiustamento per i fattori comportamentali e sociali

Hypponen E et al. Ann. N.Y. Acad. Sci. 1037: 84–95 (2004)

Does Vitamin D Intake During Infancy Promote the Development of Atopic Allergy?

RR Dermatite Atopica



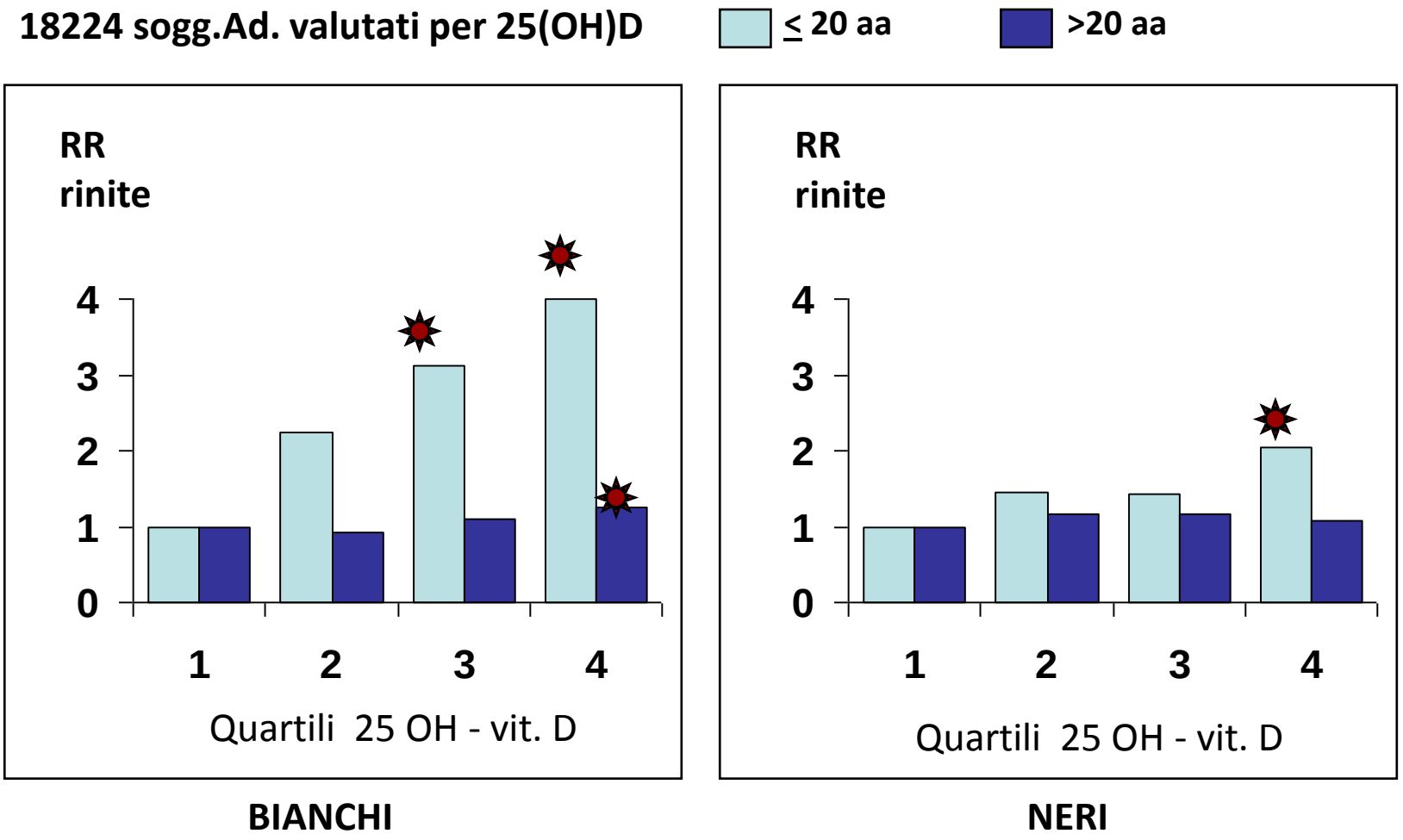
Intake *nel 1 anno*
Valutazione *fino al 6 aa*

F = familiarità
D = introito vitamina D

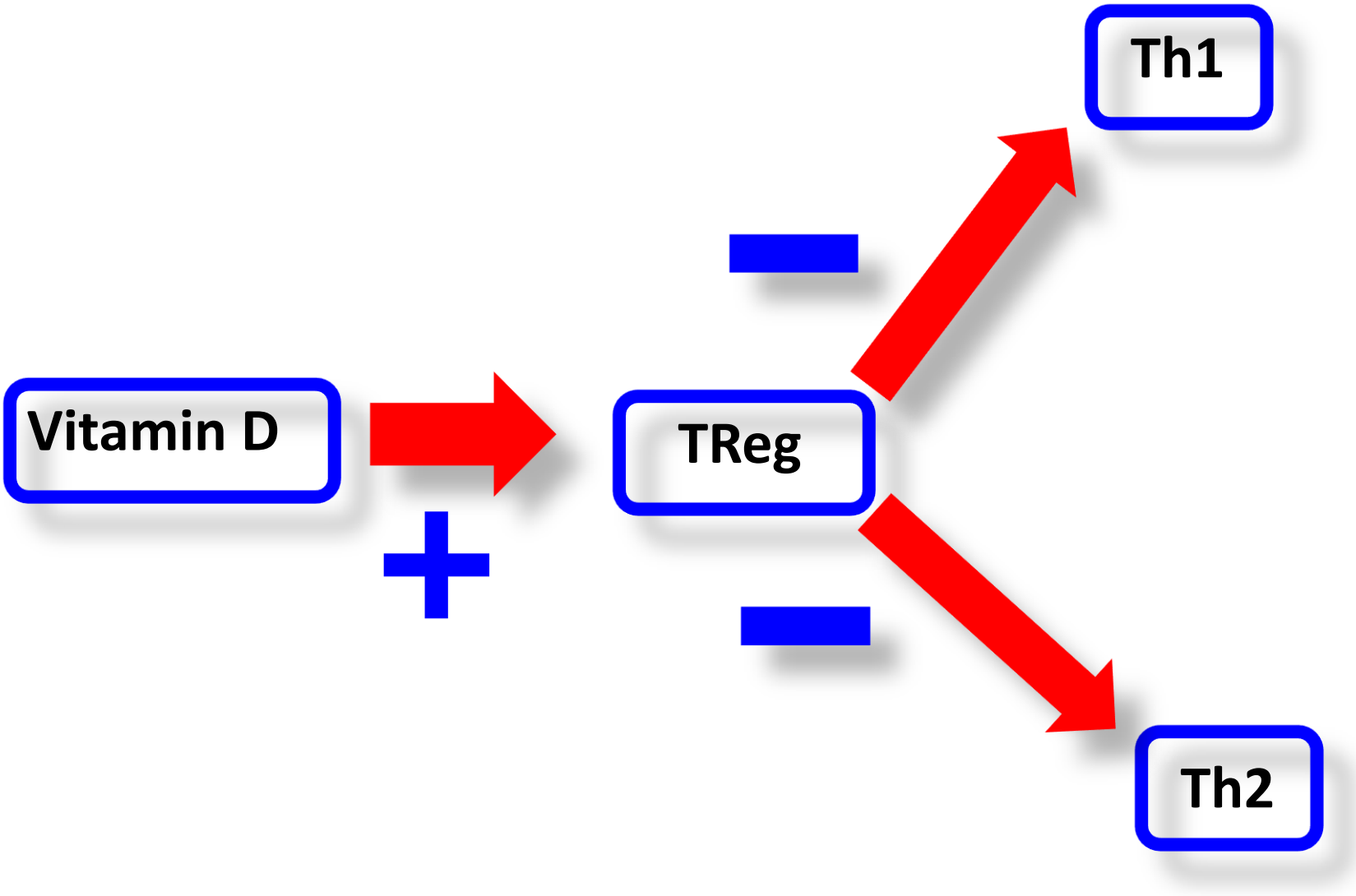
Solo 123 bambini !!

Back O et al. Acta Derm Venereol 2009; 89: 28–32

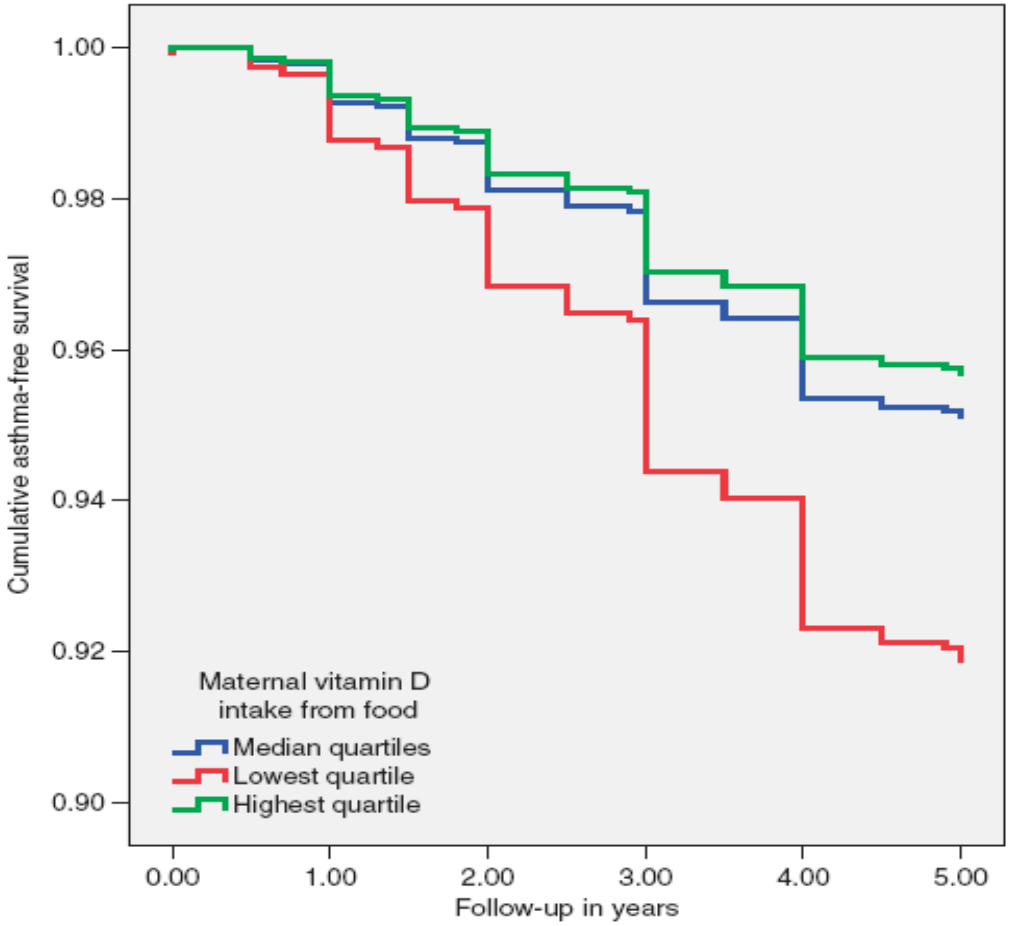
Vitamin D serum levels and allergic rhinitis



Wjst M et al. Allergy 2007;62:1085–1086


Th1
Vitamin D
TReg
Th2

Maternal vitamin D intake during pregnancy is inversely associated with asthma and allergic rhinitis in 5-year-old children



Curva di sopravvivenza senza asma a 5 anni

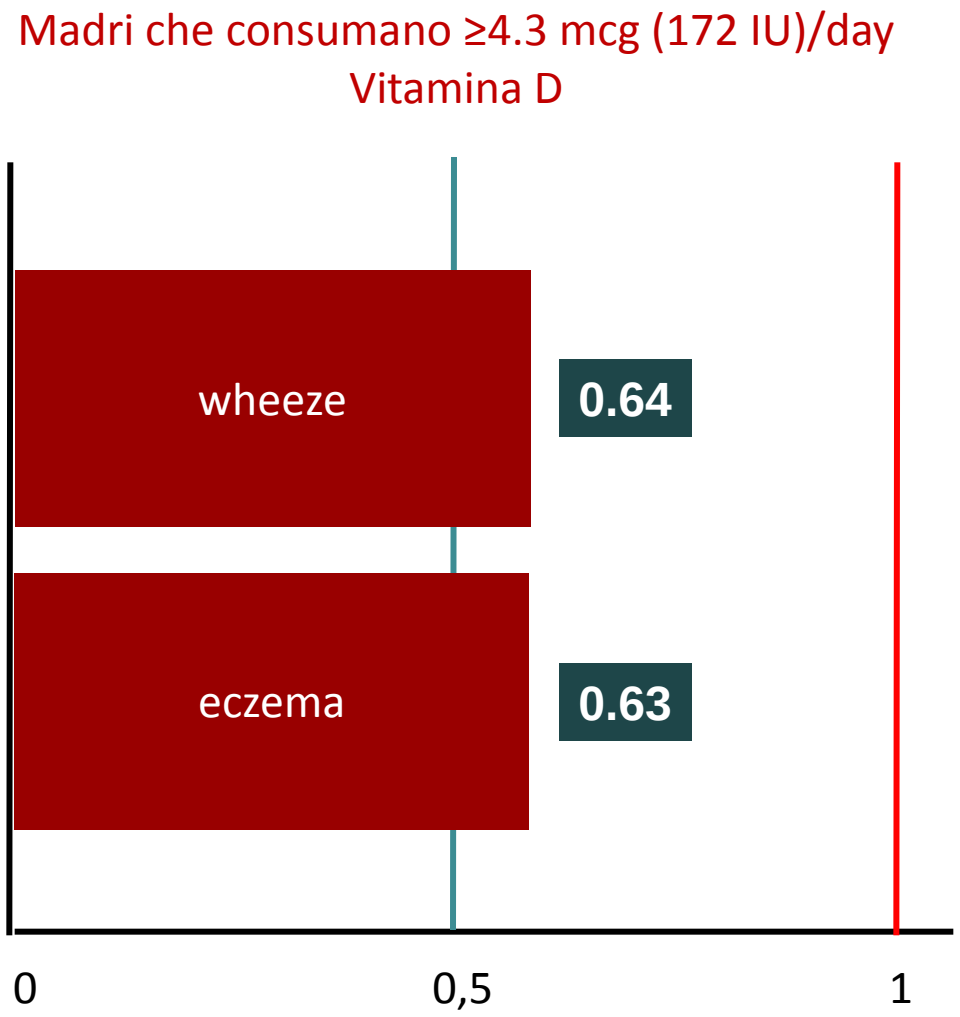
maggior introito di vitamina D durante la gravidanza

Meno figli con asma fino a 5 anni

Erkkola M et al. Clinical & Experimental Allergy 2009;39:875–882

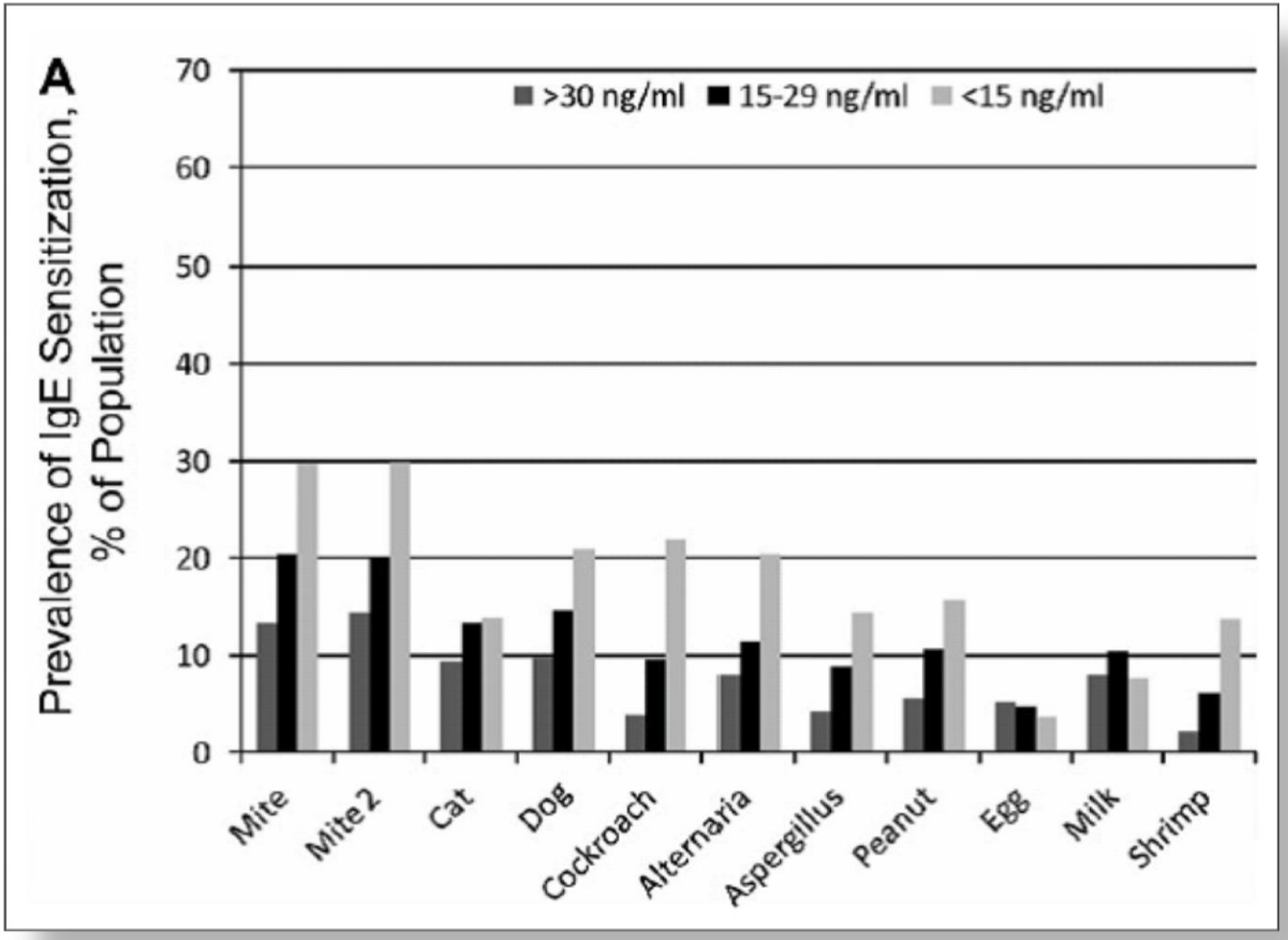
Dairy food, calcium, and vitamin D intake in pregnancy and wheeze and eczema in infants

- Consumo materno di prodotti caseari, calcio e vitamina D durante la gravidanza
- Rischio di wheeze e di eczema nei bambini a 16-24 mesi
- 763 coppie madre-figlio giapponesi



Miyake Y al. Eur Respir J 2010; 35: 1228–1234

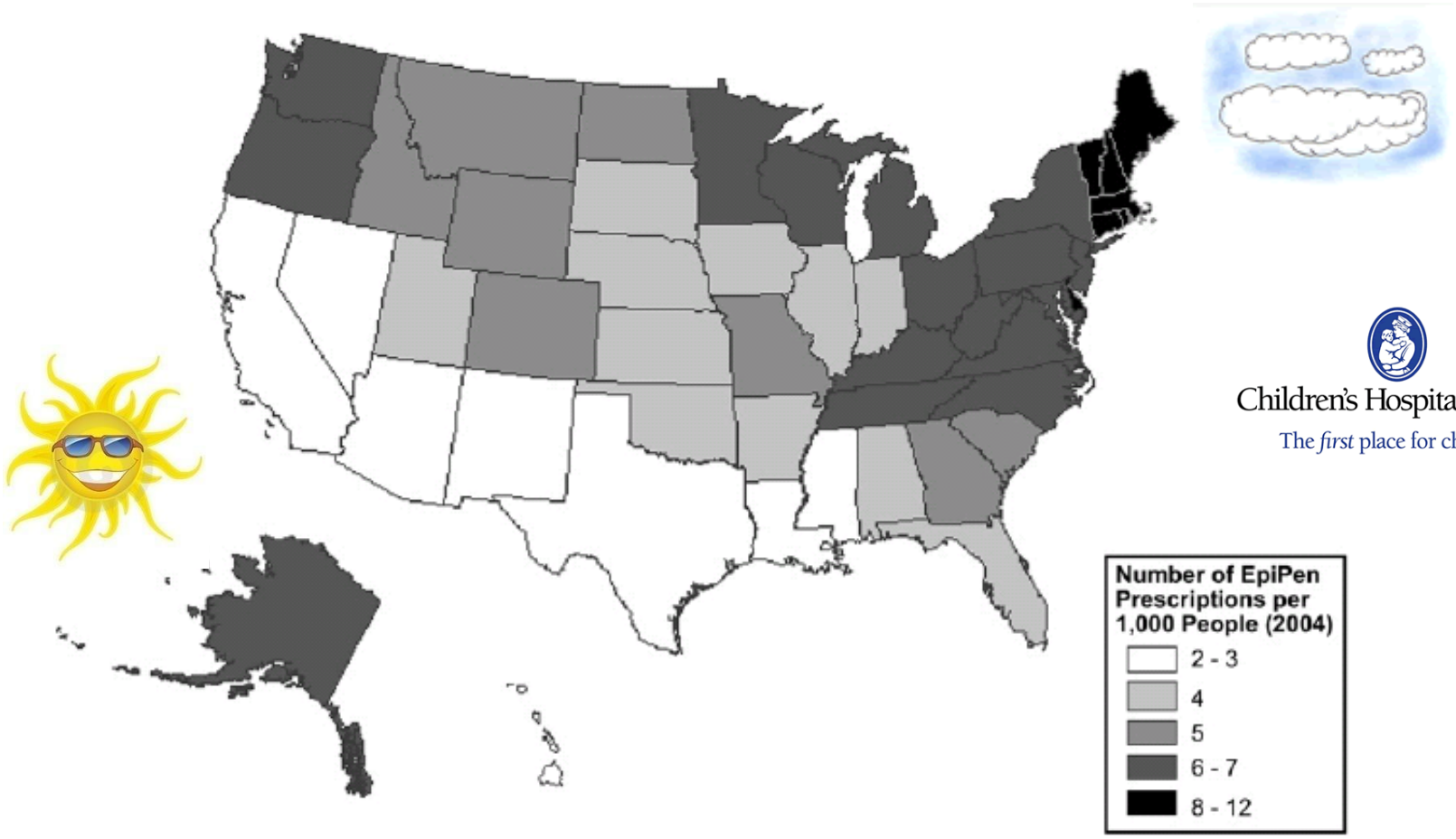
Vitamin D levels and food and environmental allergies in the United States: results from the National Health and Nutrition Examination Survey 2005-2006



3136 <18 anni
3454 >18 anni

Sharief S et al. J Allergy Clin Immunol. 2011 May;127(5):1195-202

Regional differences in EpiPen prescriptions in the United States: the potential role of vitamin D



Children's Hospital Boston
The *first* place for children

FIG 2. Regional differences in EpiPen prescriptions per 1000 persons.

Camargo CA jr et al. J Allergy Clin Immunol. 2007 Jul;120(1):131-6

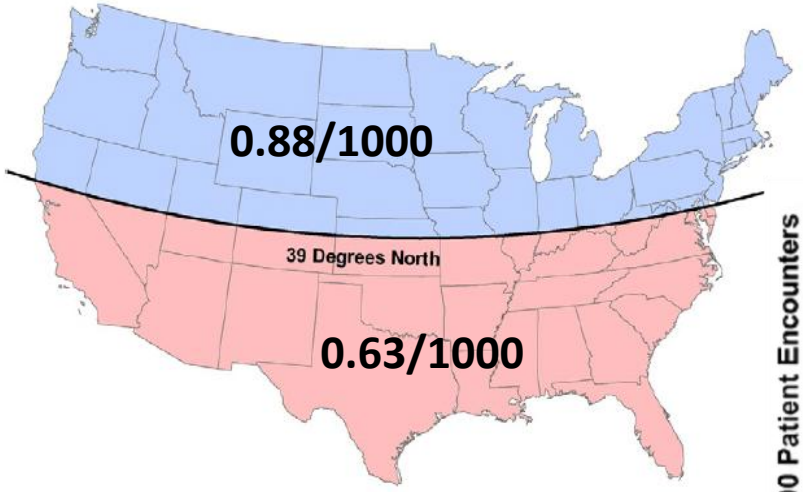
North-south differences in US emergency department visits for acute allergic reactions

Sex		
Female	1 [Reference]	
Male	0.65 (0.59-0.72)	<.001
Race		
White	1 [Reference]	
Black	0.96 (0.82-1.14)	.67
Other	1.28 (0.95-1.72)	.11
Ethnicity		
Non-Hispanic	1 [Reference]	
Hispanic	1.11 (0.93-1.31)	.25
Missing	0.95 (0.81-1.11)	.51
Metropolitan area		
Yes	1 [Reference]	
[illegible]	[illegible]	[illegible]
US region		
South	1 [Reference]	
Northeast	1.33 (1.14-1.56)	<.001
Midwest	0.84 (0.70-1.01)	.07
West	1.06 (0.89-1.25)	0.53

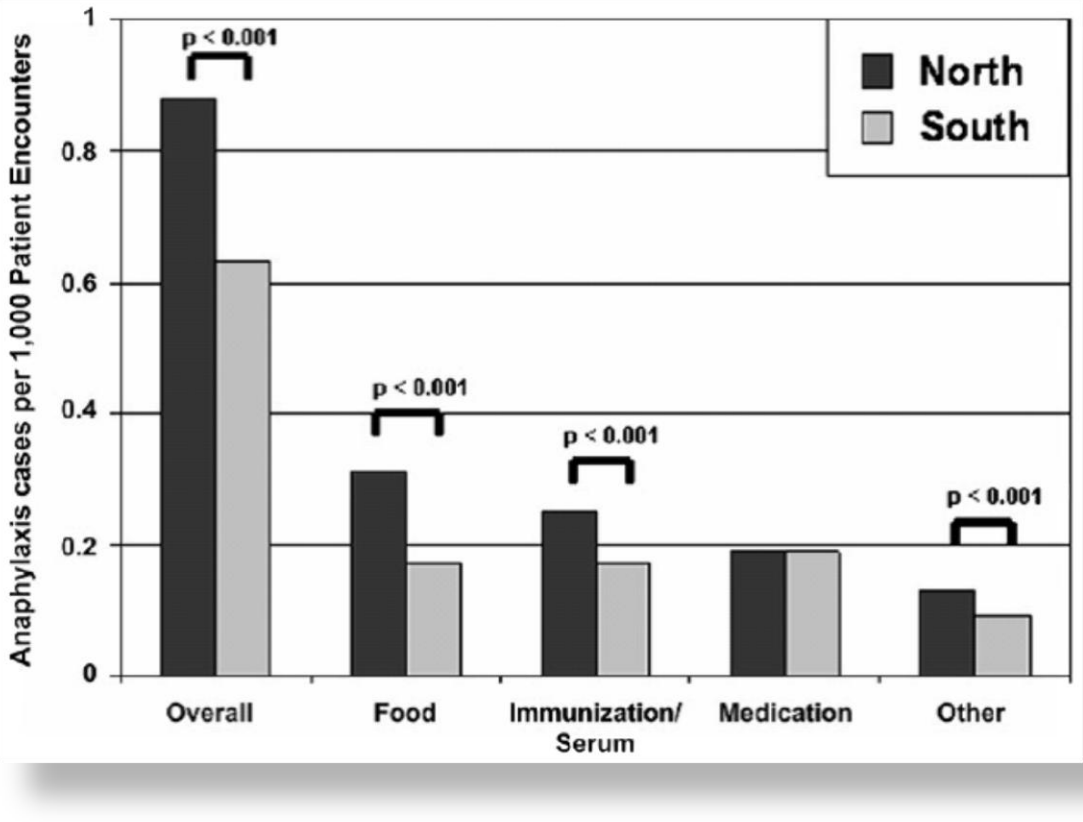
Children's Hospital Boston
The *first* place for children

Rudders SA et al. Ann Allergy Asthma Immunol. 2010 May;104(5):413-6

Higher incidence of pediatric anaphylaxis in northern areas of the United States

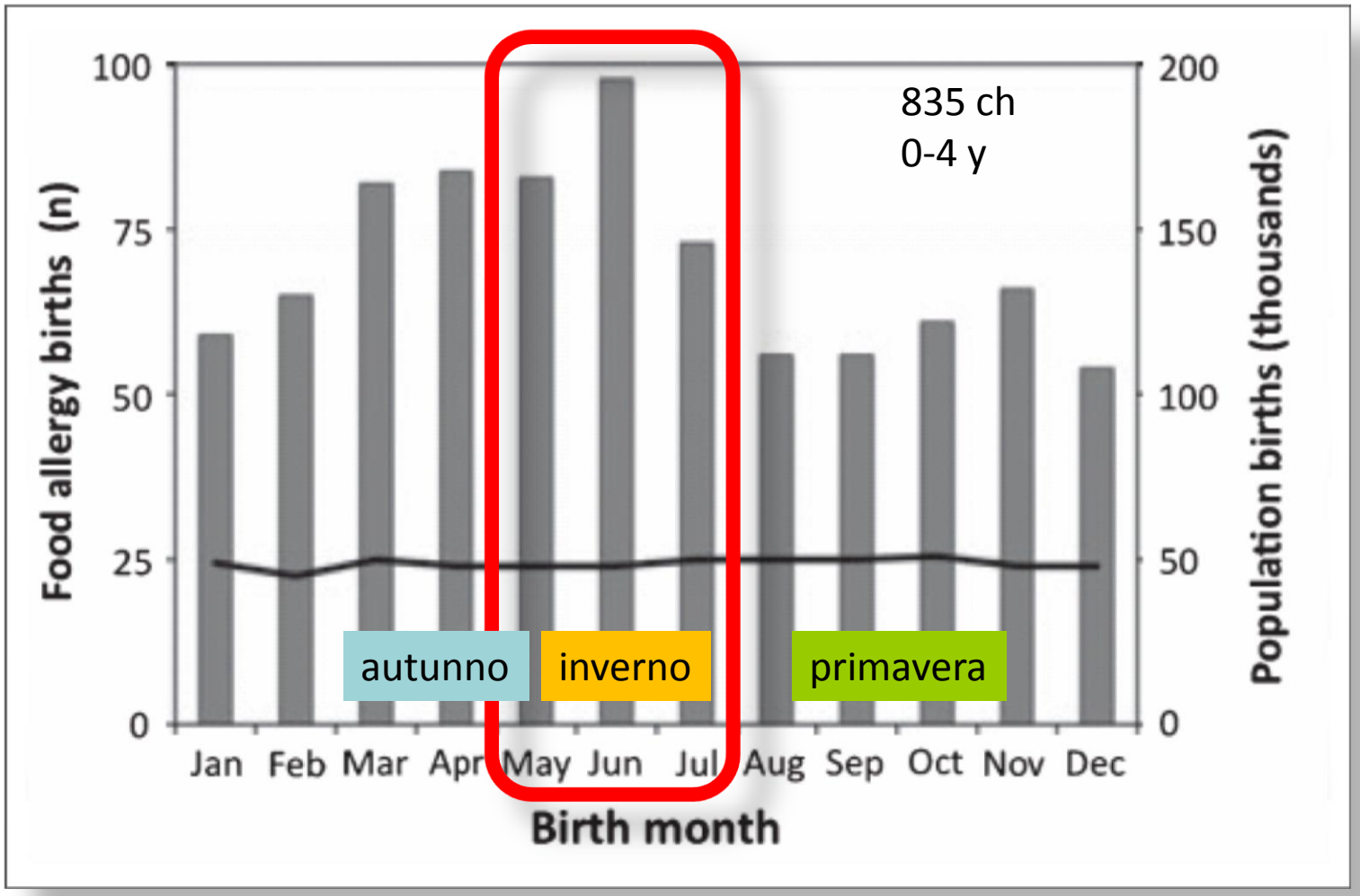


- ✓ 6,457 casi di anafilassi
- ✓ 8.589.583 pazienti
- ✓ periodo: 5 anni



Sheehan WJ et al. J Allergy Clin Immunol. 2009 October ; 124(4): 850–852.e2

Season of birth and childhood food allergy in Australia



Mullins RJ et al. Pediatr Allergy Immunol. 2011 Sep;22(6):583-9

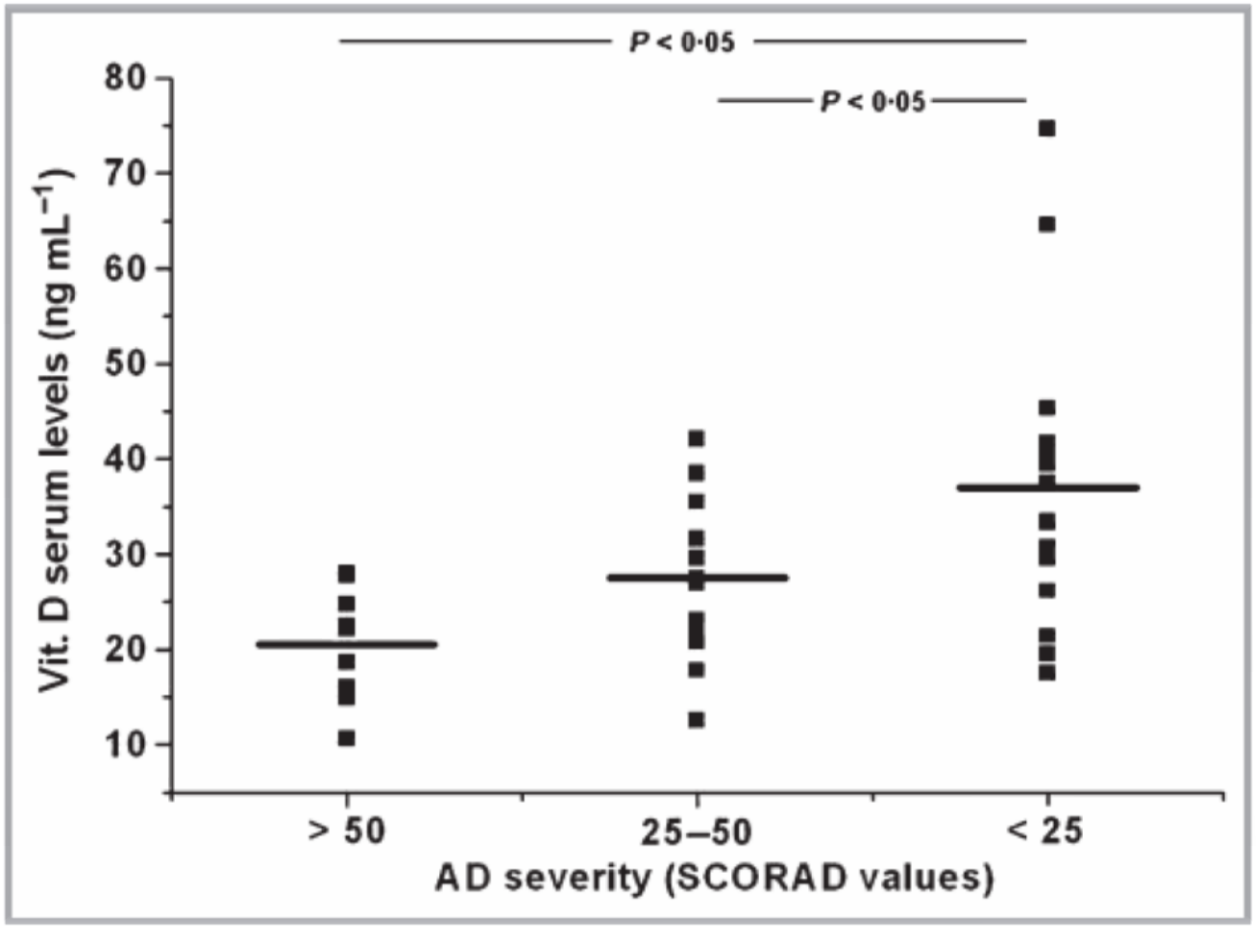
Dermatite atopica e vitamina D

Camargo (2007)		No correlation between maternal VD intake and AD
Sidbury (2008)		VD supplementation has mild beneficial effect on AD severity
Gale (2008)		Increased maternal VD levels predisposed AD
Oren (2008)		Increased prevalence of AD in obese children with low VD
Miyale (2010)		Increased maternal VD level reduces risk of AD
Peroni (2010)		Inverse correlation between severity of AD and VD levels
Javanbakht (2010)		Reduction of SCORAD after VD supplementation

Benson AA et al. Allergy 2012;67:296–301

Correlation between serum 25-hydroxyvitamin D levels and severity of atopic dermatitis in children

37 bb
8m-12a



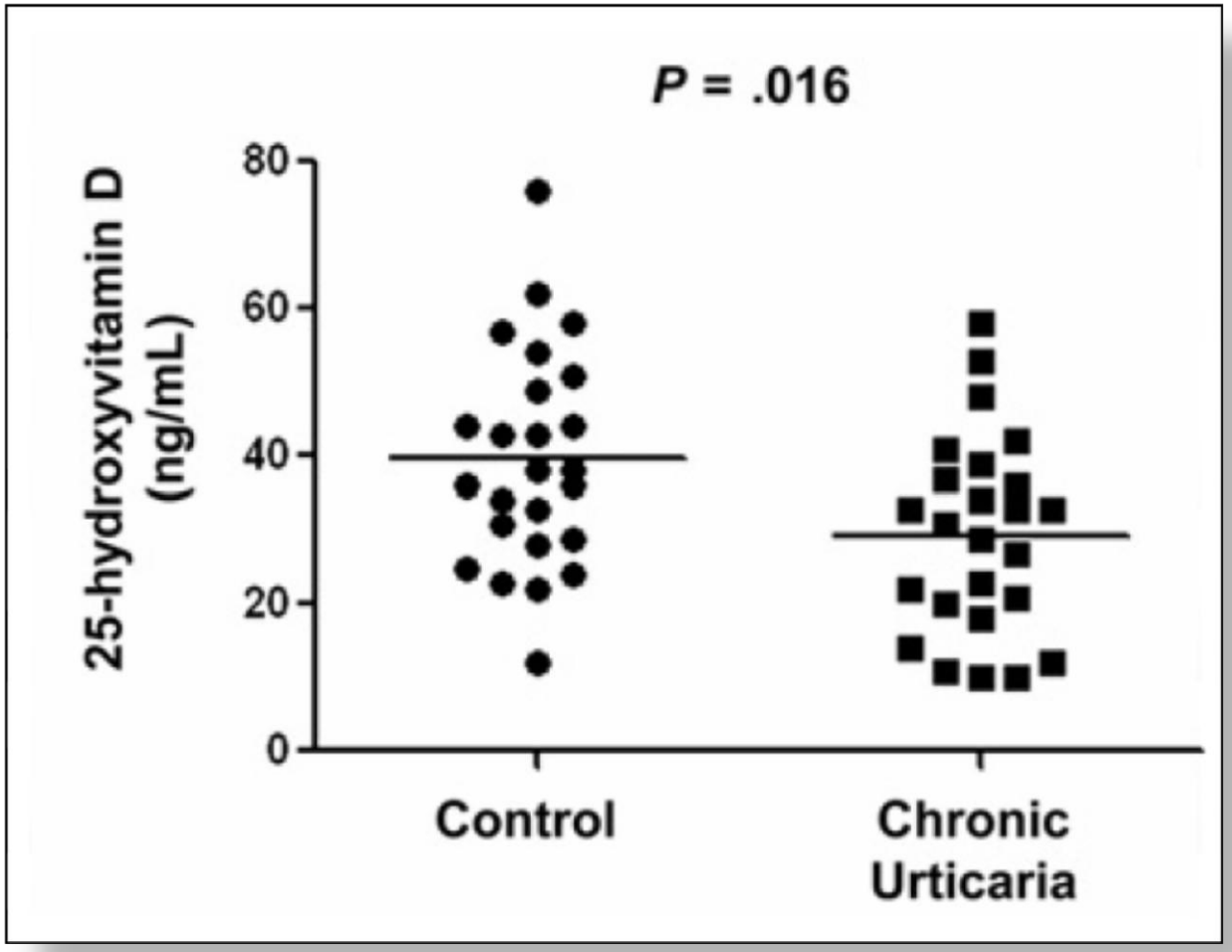
Peroni D et al. British J Dermatol 2011;164, pp1078–1082

Orticaria, DAC e vitamina D

ORTICARIA		
Thorp (2010)	↑	Pazienti con CU hanno livelli di vit.D più bassi dei controlli (AR)
Goetz (2011)	↑	70% di efficacia della terapia in pazienti con CU dopo supplementazione con vit.D
DERMATITE DA CONTATTO (DAC)		
Malley (2009)	↑	In modelli animali la DAC è più grave se i topi presentano deficit di vit.D

Benson AA et al. Allergy 2012;67:296–301

Reduced vitamin D levels in adult subjects with chronic urticaria



Thorp WA et al. J Allergy Clin Immunol. 2010 Aug;126(2):413

Vitamina D e…

sistema immunitario

infezioni respiratorie

asma

allergie

considerazioni terapeutiche

Prevention of rickets and vitamin D deficiency in infants, children and adolescents

- I bambini allattati al seno o parzialmente allattati dovrebbero ricevere un'aggiunta di **400 UI** di vit.D a partire dai primi giorni di vita
- I bambini non allattati al seno e quelli più grandi che assumono < di 1000ml/die di latte fortificato con vit.D dovrebbero ricevere **400 UI** di vit.D/die
- Gli adolescenti che non assumono sufficienti quantità di vit.D (latte e altri alimenti fortificati) dovrebbero ricevere un'aggiunta di **400 UI** /die di vit.D

Wagner, Pediatrics 2008;122:1142

Dietary guidelines for Calcium and Vitamin D: A New Era

TABLE 1 Selected Calcium and Vitamin D DRI Values for Children and Adolescents

Age	Calcium, mg/d		Vitamin D, IU/d	
	Recommended Intake[a]	Tolerable UL	Recommended Intake[a]	Tolerable UL
0–6 mo	200	1000	400	1000
6–12 mo	260	1500	400	1500
1–3 y	700	2500	600	2500
4–8 y	1000	2500	600	3000
9–18 y	1300	3000	600	4000

[a] Recommended intake values are the RDA values for children aged 1 year and older and AI values for infants younger than 1 year.

DRI = Dietary Recommended Intake

Efficacia di D_2 pari al 30% rispetto a D_3

Abrams SA, Pediatrics 2011;127;566

Safety

- ✓ L’intossicazione da vitamina D è estremamente rara
- ✓ Occorrono dosi > 50.000 UI al giorno per superare i 150 ng/mL (374 nmol/L) con rischio di ipercalcemia e iperfosfatemia
- ✓ Dosi di 10.000 UI di vit.D3 al giorno e fino a 5 mesi non causano tossicità
- ✓ E’ ben documentato che neonati e bambini possono tollerare dosi di vitamina D fino a 3000 UI/die senza effetti collaterali

Holick MF. NEJM 2007:357;266-81

A 21st century evaluation of the safety of oral vitamin D

- ✓ Dettagliata ricerca della letteratura
- ✓ Numerose evidenze dimostrano che 600-800 IU di vitamina D giornalmente e a lungo termine sono insufficienti a mantenere un livello sierico >75 nmol/L (30 ng/mL)
- ✓ È richiesto un supplemento di almeno 1500 IU/die.
- ✓ Un intake a lungo termine fino a 10000 IU non produce segni o sintomi di tossicità
- ✓ ***In conclusion, long-term daily intakes of up to and including 10000 IU of vitamin D maximize physiologic benefits and are safe.***

Glade MJ. Nutrition. 2012 Apr;28(4):344-56.

Aree di incertezza

- ✓ Dosaggi ottimali di vitamina D
- ✓ Effetti a lungo termine della supplementazione con dosi maggiori di 1000 UI/die
- ✓ Differenze esistenti in termini di efficacia e metabolismo tra le alte dosi intermittenti di vitamina D e le dosi giornaliere

Rosen, NEJM 2011;364:248



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