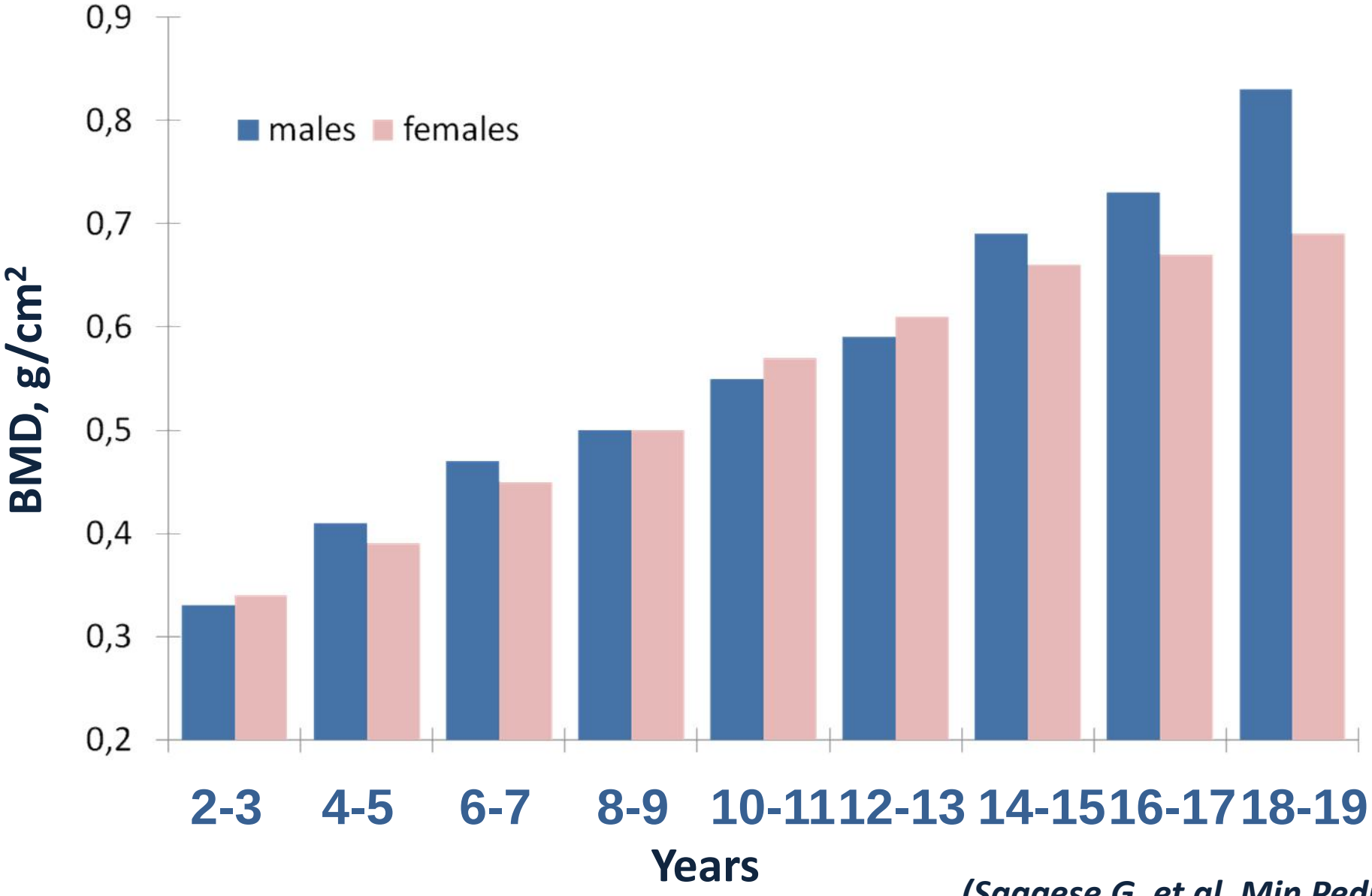
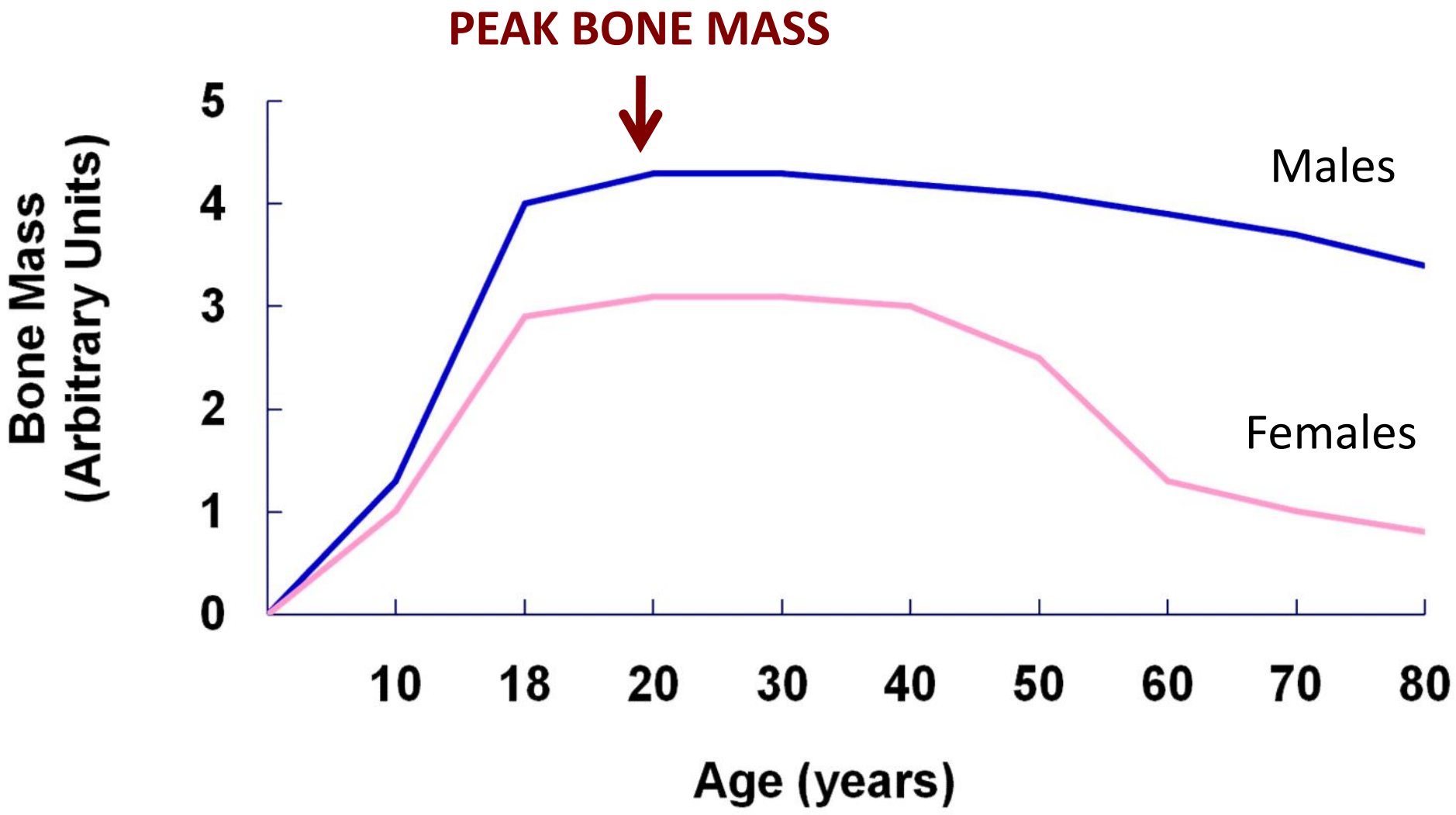
Acquisizione massa ossea

Radial bone mineral density during childhood and adolescence measured by single-photon absorptiometry (SPA)



(Saggese G. et al, Min Pediatr 1986)

Changes in bone mass with age



(Cooper C. 1990)

Picco di massa ossea

"Livello più elevato di massa ossea raggiungibile durante la vita come risultato di una crescita normale"

Significato clinico

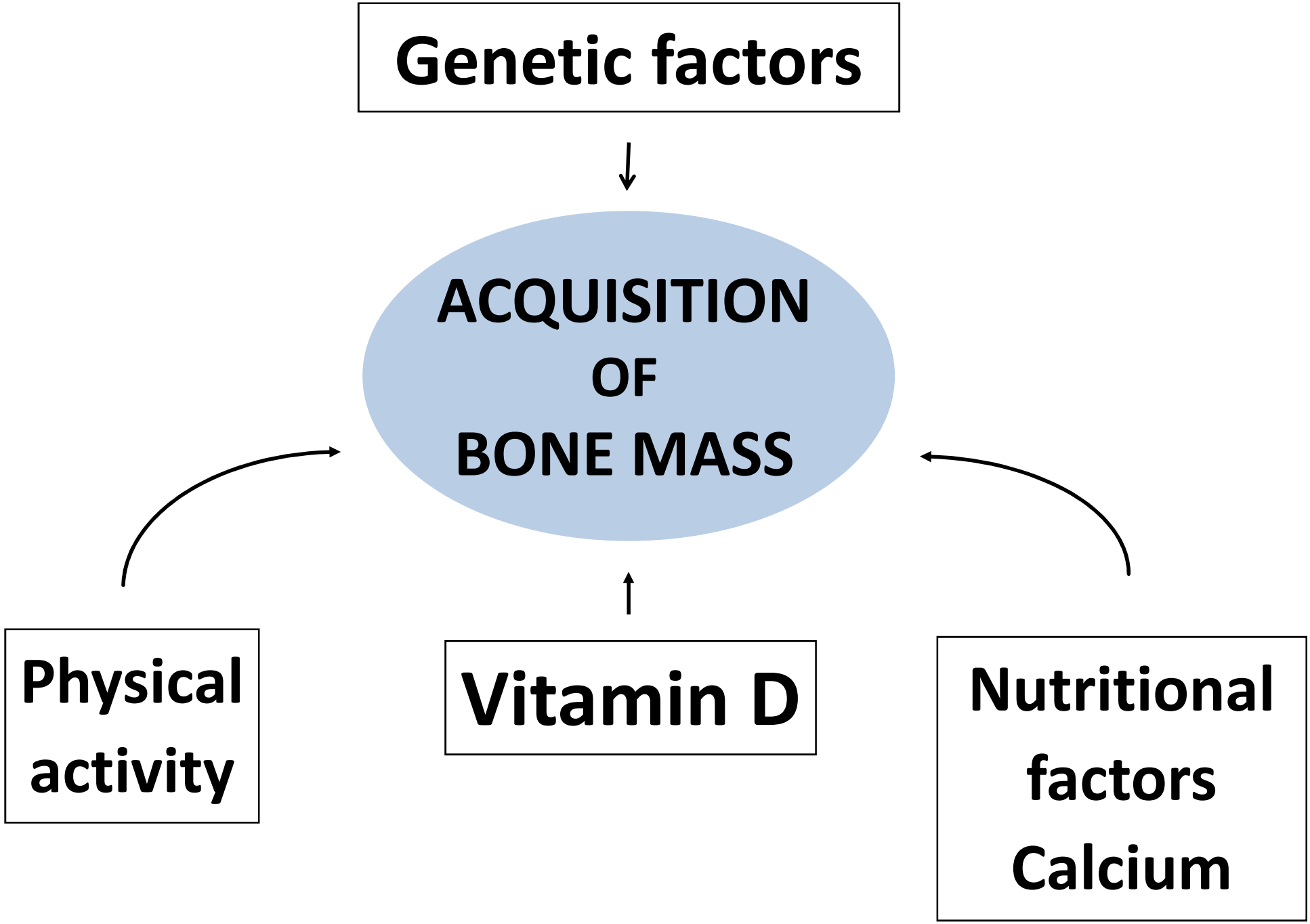
L'acquisizione di un ottimale picco di massa ossea rappresenta uno dei fattori più importanti per la prevenzione dell'osteoporosi.

To prevent the osteoporosis playing in advance

Suboptimal bone development leads to a reduction in peak bone mass, and a higher risk of osteoporotic fracture later in life.

Preventative strategies against osteoporosis can be aimed at either optimizing the peak bone mass obtained, or reducing the rate of bone loss. Optimization of peak bone mass may be more amenable to public health strategies.

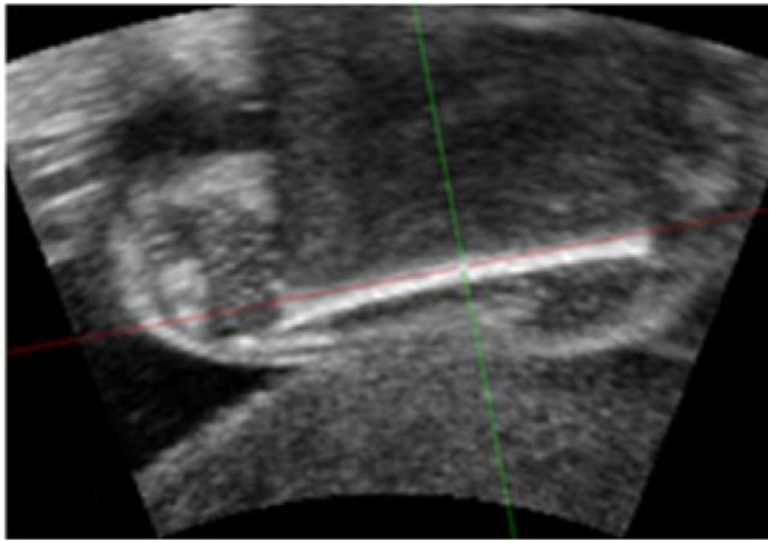
Clinical Cases in Mineral and Bone Metabolism 2013; 10(2): 83-85

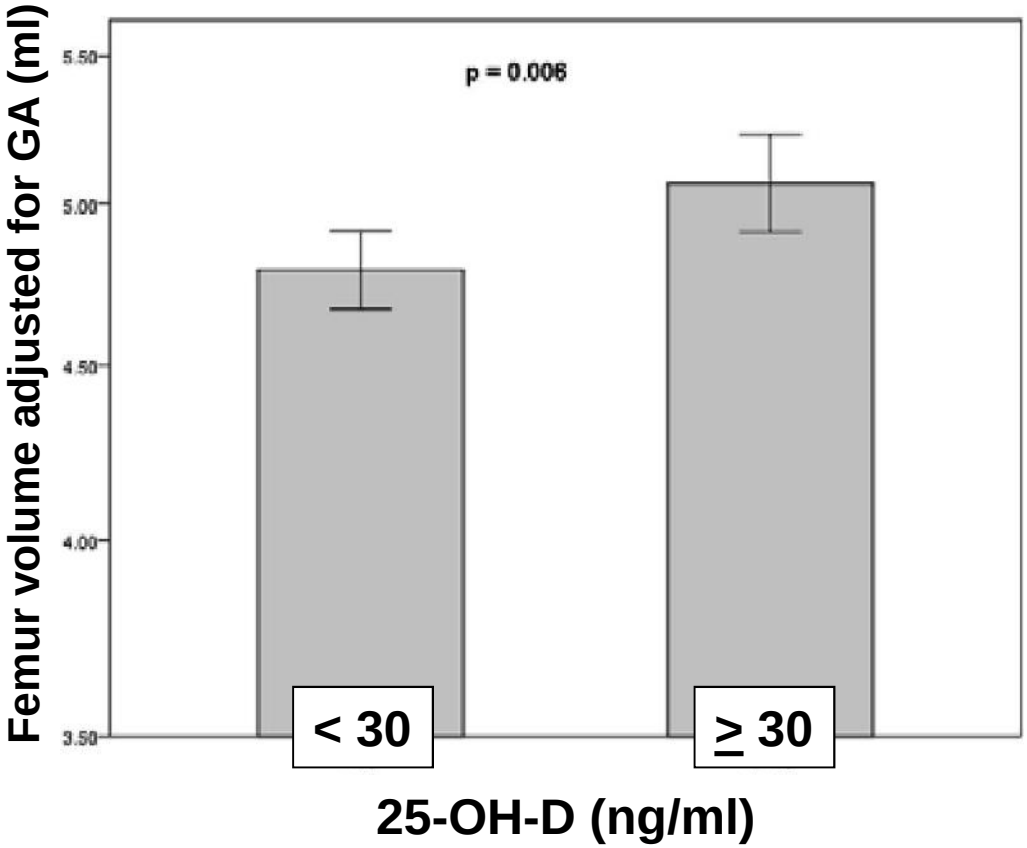

Genetic factors
ACQUISITION
OF
BONE MASS
Physical
activity
Vitamin D
Nutritional
factors
Calcium

Studio	N	Paese	Età	Vit. D	Gruppi	Durata supplem.	25(OH)D basale, ng/ml (media ± DS)	25(OH-D) al follow-up, ng/ml (media ± DS)	Parametri valutati	Effetto della supplementazione sulla massa ossea e/o muscolare
Andersen 2008***	26	Danimarca	10,1-14,7 anni (F Pakistane)	D3	• 400 UI/die • 800 UI/die • placebo	12 mesi	6,8 (4,8-8,4)^ 3,5 (2,1-6,8)^ 2,9 (2,1-9,4)^	18,8 (11,5-24,6)^ 11,7 (11,4-25,6)^ 2,3 (2,0-6,4)^	DXA corpo intero e lombare, markers tutti over ossei	Nessun effetto della supplementazione con vitamina D sui markers di tutti over ossei né sulla massa ossea.
Hettiarachchi 2010	60	Sri Lanka	3-5 anni	*	• 100 UI/die + 450 mg/die calcio • controlli (non supplem.)	9 mesi	28,8 ± 12,9 41,4 ± 10,6	38,5 ± 11,0 38,5 ± 14,8	DXA lombare e femorale	La supplementazione con calcio e vitamina D aumentava i livelli di BMD lombare.
Molgaard 2010	221	Danimarca	11-12 anni (F)	D3	• 200 UI/die • 400 UI/die • placebo	12 mesi	16,8 ± 7,0 17,8 ± 6,6 17,4 ± 6,8	21,2 ± 6,5 23,2 ± 5,7 15,9 ± 7,1	DXA corpo intero e lombare, markers di tutti over ossei	La supplementazione aumentava i livelli di BMC e BMD del corpo intero nei soggetti con genotipo FF del VDR.
Viljakainen 2006***	228	Finlandia	11-12 anni (F)	D3	• 200 UI/die • 400 UI/die • placebo	12 mesi	18,5 ± 7,0 18,7 ± 6,5 19,1 ± 7,3	Incremento di 2,2 ± 6,1 Incremento di 4,8 ± 5,4 Decremento di 2,0 ± 4,8	DXA lombare e femorale, markers di tutti over ossei	Nei gruppi supplementati aumentavano i valori di BMC femorali e si riducevano i markers di riassorbimento osseo. La supplementazione con 400 UI/die aumentava i livelli di BMC lombare.
Al-Shaar' 2013	338	Libano	10-17 anni	D3	• 1.400 UI/sett. (M) • 14.000 UI/sett. (M) • placebo (M) • 1.400 UI/sett. (F) • 14.000 UI/sett. (F) • placebo (F)	12 mesi	15,2 (12,1-18,8)° (M) 15,5 (11,7-18,7)° (M) 16,0 (12,9-19,5)° (M) 11,3 (8,7-15,6)° (F) 12,6 (10,0-18,7)° (F) 11,7 (8,7-11,7)° (F)	Incremento di 3,7 ± 5,0 (M) Incremento di 18,6 ± 9,4 (M) Incremento di 0,9 ± 5,1 (M) Incremento di 3,2 ± 9,2 (F) Incremento di 23,8 ± 30,3 (F) Incremento di 1,5 ± 5,4 (F)	DXA anca e composizione corporea; software per analisi strutturale dell'anca	Nelle F la suppl. con vit. D (alte e basse dosi) aumentava i livelli di BMD e riduceva il rapporto di instabilità a livello del collo femorale, aumentava i livelli di BMD e la cross sectional area a livello della regione intertrocanterica ed il diametro esterno della diafisi (geometria ossea).
Ebbott 2011	60	India	2-4 anni	D3	• 30.000 UI/mese + 405 mg calcio (5/7 giorni) • 30.000 UI/mese + 156 mg calcio (5/7 giorni)	12 mesi	10,0 ± 10,8 7,6 ± 10,8	25,7 ± 9,6 23,2 ± 4,8	DXA corpo intero, composizione corporea	La supplementazione con calcio e vit. D aumentava i livelli di BMC e BA del corpo intero ed i livelli di massa magra e massa grassa in entrambi i gruppi. I livelli di BMC del corpo intero aumentavano di più nel gruppo che riceveva più calcio.
El-Hajj Fuleihan 2006***	179	Libano	10-17 anni (F)	D3	• 1.400 UI/sett. • 14.000 UI/sett. • placebo	12 mesi	14 ± 9 14 ± 8 14 ± 7	17 ± 6 38 ± 31 16 ± 8	DXA lombare, anca, avambraccio, corpo intero, composizione corporea	La massa magra aumentava in entrambi i gruppi supplementati. I valori di BA e di BMC dell'anca aumentavano nel gruppo supplementato con alte dosi. Nelle F pre-menarca la massa magra ed i livelli di BMC del trocantere aumentavano in entrambi i gruppi supplementati, i livelli di BMD lombare aumentavano nel gruppo supplementato con basse dosi.
Khadilkar 2010	50	India	14-15 anni (F)	D2	• 300.000 UI/3 mesi + 250 mg/die calcio • placebo + 250 mg/die calcio	12 mesi	9,8 (5,1-13,3)^ 8,3 (5,1-12,2)^	30,1 (25,7-34,2)^ 11,2 (6,7-13,6)^	DXA corpo intero e lombare	Nelle F entro due anni dal menarca la supplementazione con vitamina D aumentava i livelli di BA e BMC del corpo intero e di BMC lombare.
Ward 2010	73	Regno Unito	12-14 anni (F)	D2	• 150.000 UI/3 mesi • placebo	12 mesi	7,2 ± 3,2 7,2 ± 3,0	22,4 ± 3,6 6,3 ± 2,6	DXA lombare, pQCT radiale e tibiale	La supplementazione con vitamina D non aveva effetto sulla massa ossea né sulla geometria ossea.

Effect of maternal vitamin D concentrations on fetal bone

- **n. 357 pregnant women**
- **fetal 3D ultrasound and maternal 25-OH-D levels were assessed at <u>34 wk</u>**



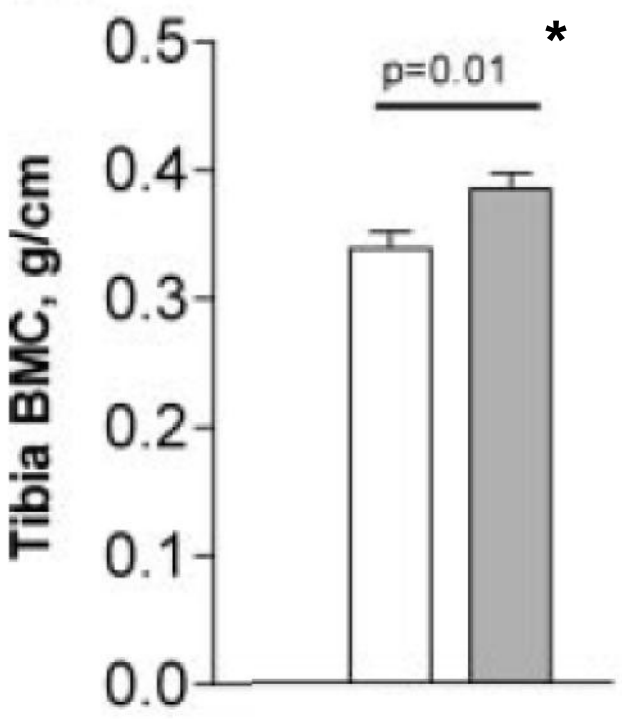


- **Fetus from vitamin D sufficient mothers have higher femur volume.**
- **Maternal vitamin D concentrations are significant predictors of femoral volume.**

(Ioannou C et al. JCEM Nov 2012)

Maternal vitamin D status determines bone variables in term newborns

- N = 125 pregnant women.
- Maternal 25-OH-D assessed during the first trimester (8-10 w) and 2 days postpartum
- Median value of maternal 25-OH-D: 17 ng/ml.
- Bone variables were measured by pQCT at the newborn tibia on 10 ± 11 days postpartum



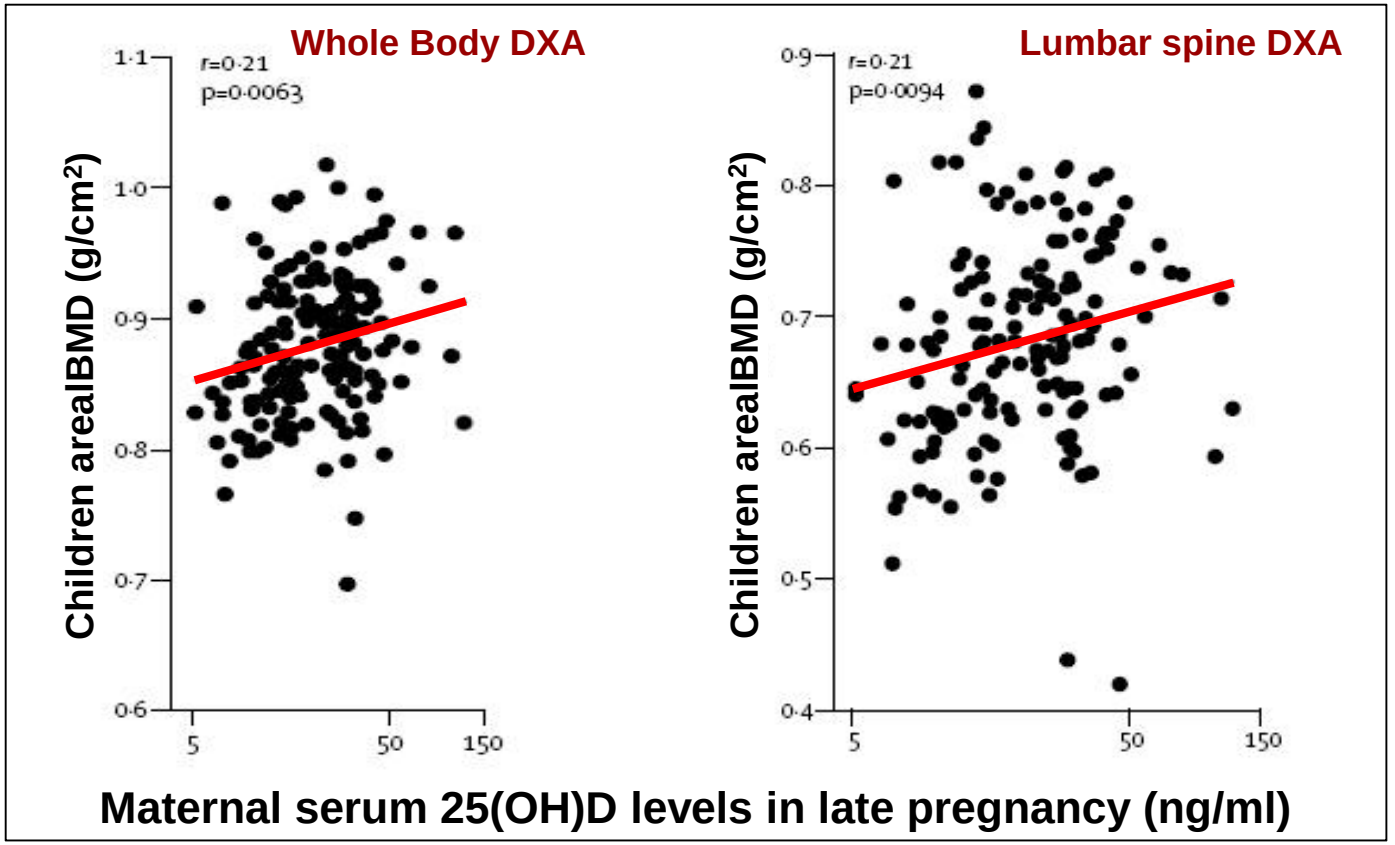
* Adjusted for birth weight, maternal height and age at pQCT measurement

- 71% of pregnant women were vitamin D deficient (25-OH-D < 20 ng/ml).
- Newborns of deficient mothers had lower tibial bone mineral content.
- Maternal vitamin D status affects bone mineral accrual during the intrauterine period.

(Viljakainen HT et al. JCEM 2010)

Maternal vitamin D status during pregnancy and childhood bone mass at age 9 years

- **N = 198 children (M = 104)**
- **Serum 25(OH)D levels measured at 34 weeks**
- **Singleton pregnancy, at term**
- **BMD assessment (DXA) at 9 yrs**



At 9 yr children BMD was positively related with 34 w maternal 25(OH)D. Maternal vitamin D status seems to influence the programming of the acquisition of bone mass of the child.

(Javaid MK et al. Lancet 2006)

Association of maternal vitamin D status during pregnancy with BMC in offspring: a prospective cohort study

- **3.960 mothers and offspring pairs, mainly of white European origin**
- **Mean offspring age was 9,9 years.**
- **77% mothers had sufficient, 28% insufficient, and 6% deficient 25(OH)D concentrations in pregnancy.**
- **TBLH and spinal BMC did not differ between offspring of mothers in the lower two groups versus sufficient 25(OH)D concentration.**
- **No associations with offspring BMC were found for any trimester, including the third trimester, which is thought to be most relevant.**

Maternal vitamin D status in pregnancy was not associated with offspring BMC in late childhood.

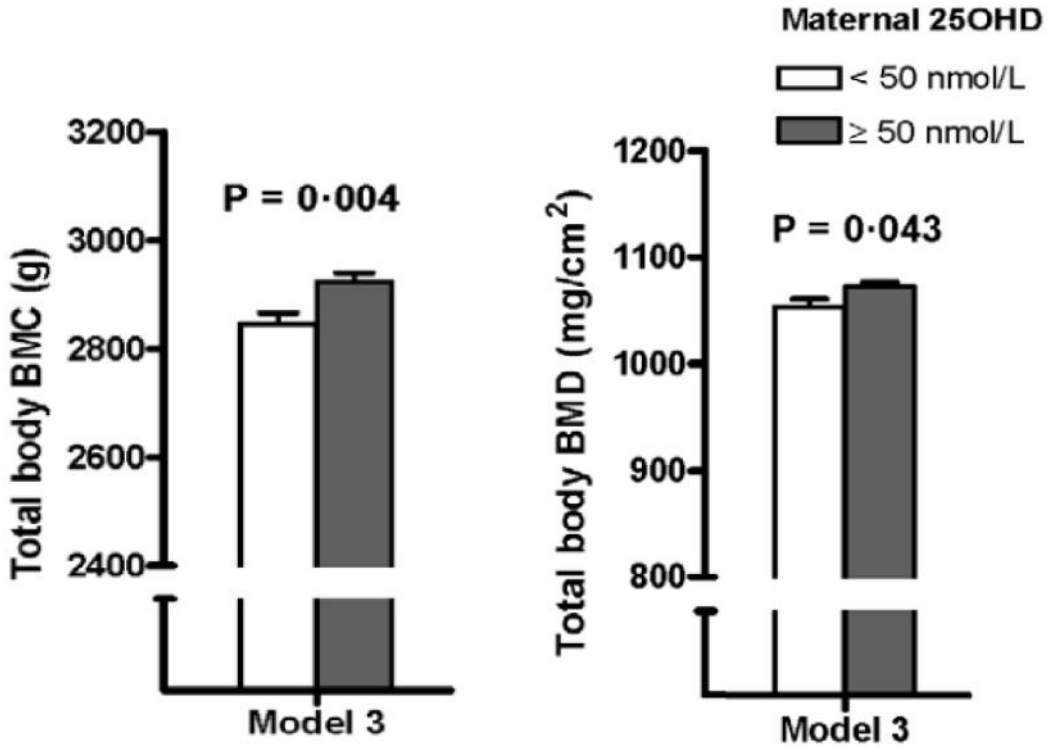
(Lawlor DA et al. Lancet 2013)

Maternal vitamin D status during pregnancy and bone mass in offspring at 20 years of age

N = 341 mother and offspring pairs

- Maternal serum samples at 18 wks gestation
- BMC and BMD measured by DXA in offspring at 20 yrs

In the 132 offspring whose mothers had 25-OH-D levels <50 nmol/L (20 ng/ml) at 18 weeks gestation, total body BMC and BMD were significantly lower than in the offspring of women whose had 25OHD ≥ 50 nmol/L



Model 3 = adjustment for season of sampling, maternal factors and offspring factors (sex, birth weight, and age, height, lean mass and fat mass at 20 y)

Vitamin D deficiency in pregnant women is associated with lower peak bone mass in their offspring at 20 yrs of age. This may increase fracture risk in the offspring in later life

(Zhu K et al. JBMR 2013)

Vitamin D supplementation in pregnancy: A systematic review

Nicholas C Harvey[1,2,*], Christopher Holroyd[1,*], Georgia Ntani[1], Kassim Javaid[3], Philip Cooper[1], Rebecca Moon[1], Zoe Cole[1], Tannaze Tinati[1], Keith Godfrey[1,2], Elaine Dennison[1], Nicholas J Bishop[4], Janis Baird[1], and Cyrus Cooper[1,2,3]

- Five of the eight observational studies relating maternal 25(OH)-vitamin D status to offspring bone outcomes demonstrated positive associations. The one small intervention study identified did not, but the methodology is unclear and a statistically significant result is unlikely based on the sample size.
- Thus observational studies suggest that maternal 25(OH)-vitamin D status may influence offspring bone development, but do not allow public health recommendations to be made. Further high-quality intervention studies are required here, such as the ongoing MAVIDOS Maternal Vitamin D Osteoporosis Study

Health Technol Assess. 2014 July ; 18(45): 1–190.

J Clin Densitom. 2015 Jan-Mar;18(1):60-7. doi: 10.1016/j.jocd.2014.04.121. Epub 2014 May 28.

Vitamin D status is associated with bone mineral density and bone mineral content in preschool-aged children.

Hazell TJ[1], Pham TT[2], Jean-Philippe S[2], Finch SL[2], El Hayek J[3], Vanstone CA[2], Agellon S[2], Rodd CJ[4], Weiler HA[5].

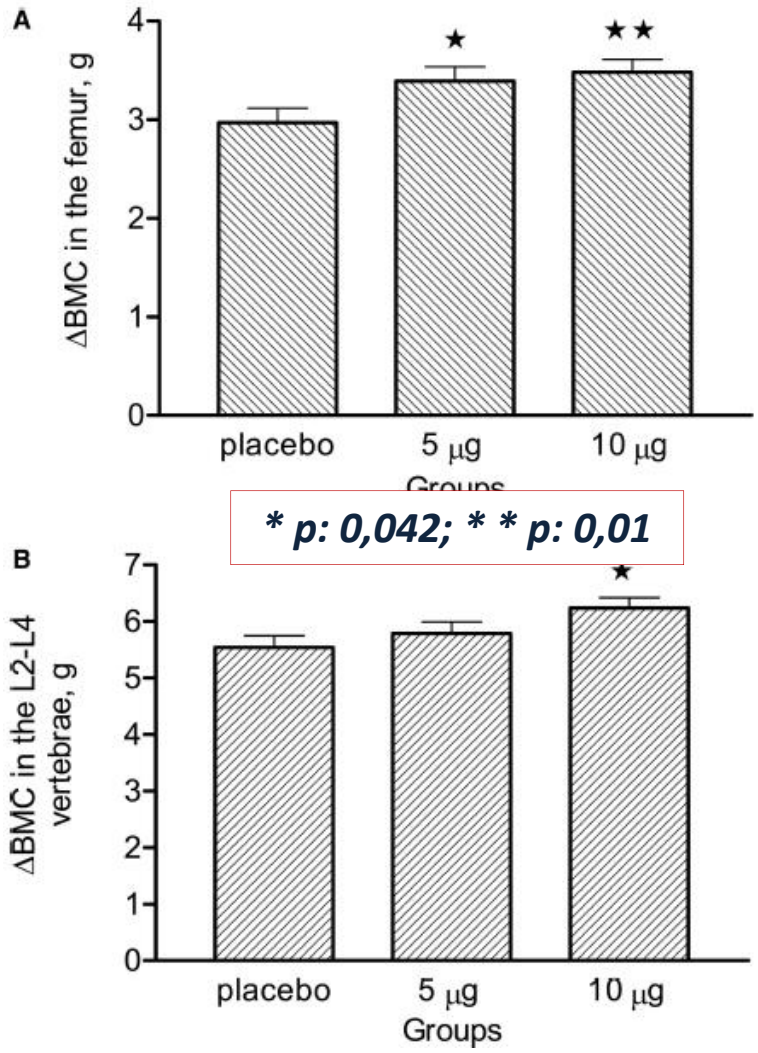
Objective: **associations between vitamin D status, bone mineral content (BMC), areal bone mineral density (aBMD), and markers of calcium homeostasis in preschool-aged children.**

Children: n=488; age range: 1,8-6,0 y

Higher vitamin D status (>75 nmol/L) is linked to higher BMC and aBMD of forearm and whole body in preschool-aged children ($p<0,036$).

J Clin Densitom, Mar 2015

A positive dose-response effect of vitamin D supplementation on site-specific bone mineral augmentation in adolescent girls



**** p: 0,042; * * p: 0,01***

**** p: 0,013***

228 girls; mean age: 11,4±0,4 years
25(OH)D: 47 nM

Bone mineral augmentation in the femur was significantly higher (14,3% and 17,2%) in the groups receiving 5 and 10 ug of Vitamin D/day for 1 yr , respectively, compared with the placebo group, but only 10 ug increased lumbar spine BMC augmentation significantly.

(Viljakainen et al. Journal of bone and mineral research 2006)

The relation between 25-hydroxyvitamin-D with peak bone mineral density and body composition in healthy young adults

(n = 464, age 17-31 yrs)

Correlation coefficients between 25-OH-D and DXA variables

	Total body BMD	Lumbar spine vBMD	Femoral neck vBMD	Lean body mass	% fat
Males	**0,23°**	-0,13	0,12	**0,26°**	0,14
Females	0,07	-0,02	**0,16***	0,05	**-0,21^**

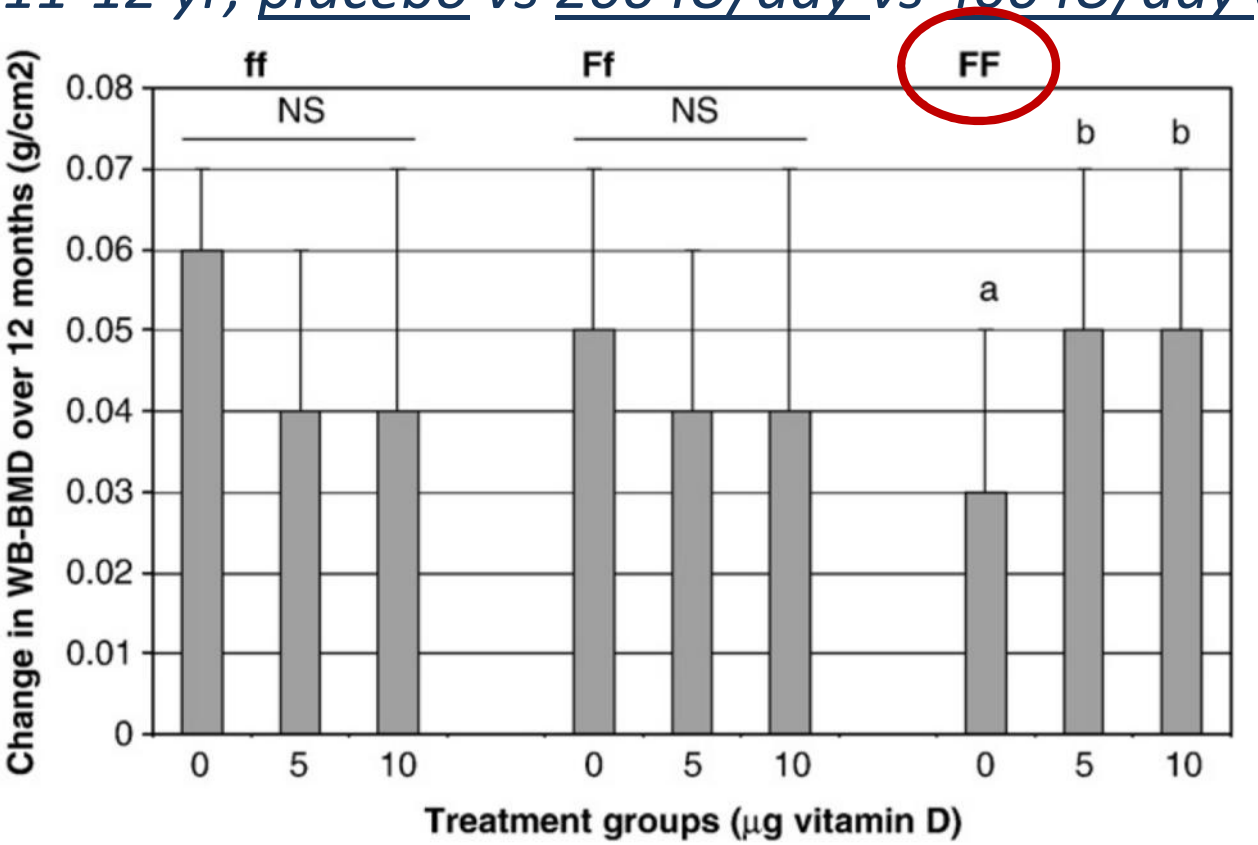
° p<0.05; *p<0.01; ^p<0.001

- ***25-OH-D levels were related to the achievement of peak bone mass.***
- ***Vitamin D status was negatively associated with body fat in females and positively with lean body mass in males.***

(Boot AM et al. J Pediatr Endocr Met 2011)

Does vitamin D supplementation of healthy Danish Caucasian girls affect bone turnover and bone mineralization?

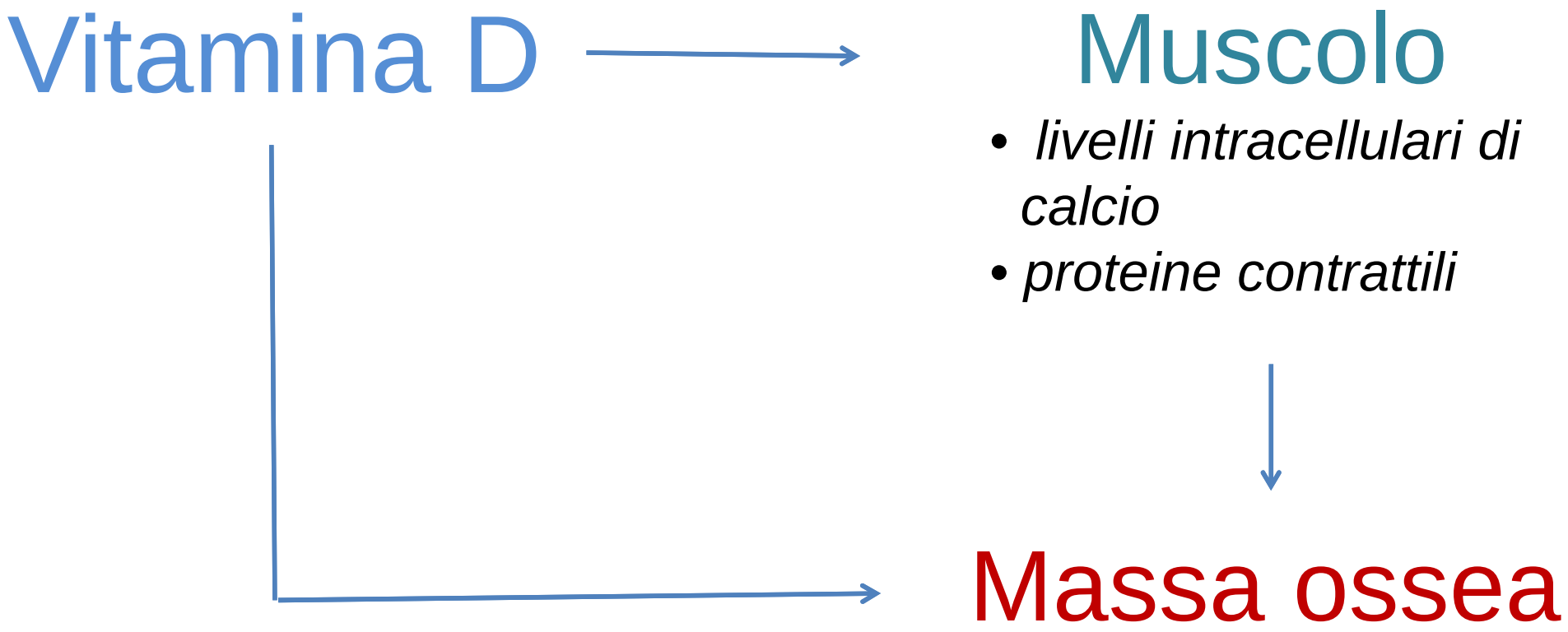
(n = 221, 25OHD: 11-12 yr; placebo vs 200 IU/day vs 400 IU/day of Vit.D3 for 1 yr)



(Molgaard C et al . Bone 2010)

- **Supplementation with vitamin D (200 or 400 IU/day) over 1 year increased 25OHD concentration, but there was no effect on indices of bone health in the entire group of girls.**
- **However, there was an effect on BMD for a subgroup with the FF VDR genotype indicating an influence of genotype**

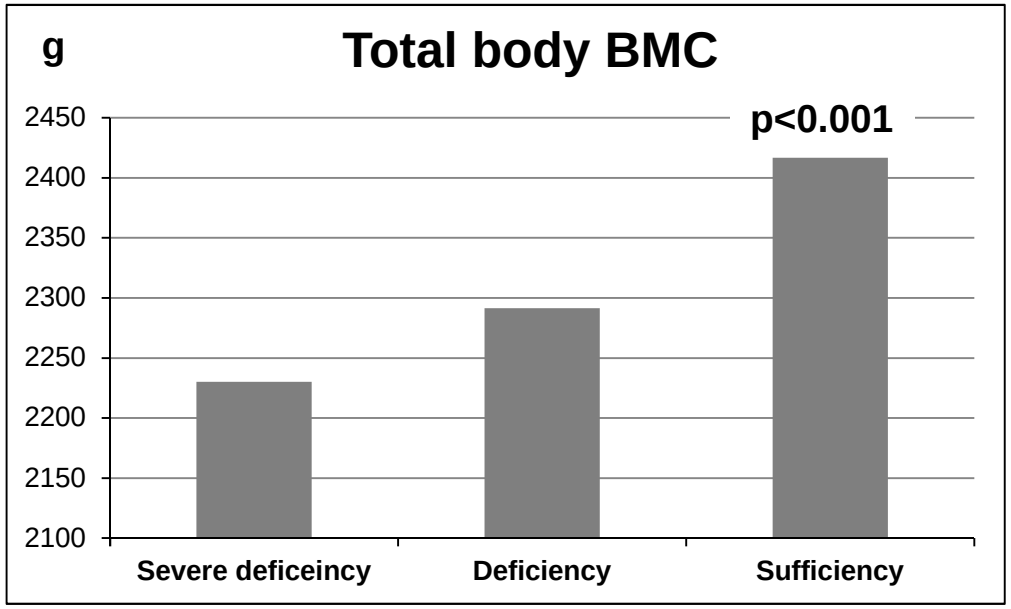
“Mechanostat theory” (Frost, 1994)

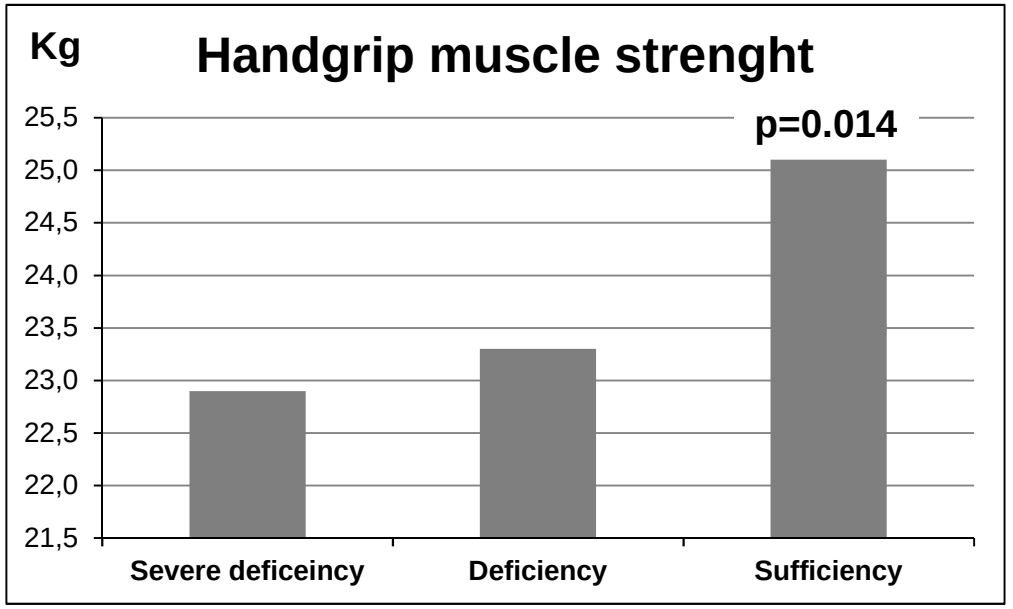


Sufficient vitamin D status has a positive influence on bone mass and muscle strength in adolescent girls

(n = 301, 15.0 ± 0.4 yr)

- **Sufficiency (25-OH-D > 20 ng/ml): 11.0%**
- **Deficiency (25-OH-D: 10-20 ng/ml): 57.8%**
- **Severe deficiency (25-OH-D < 10 ng/ml): 31.2%**

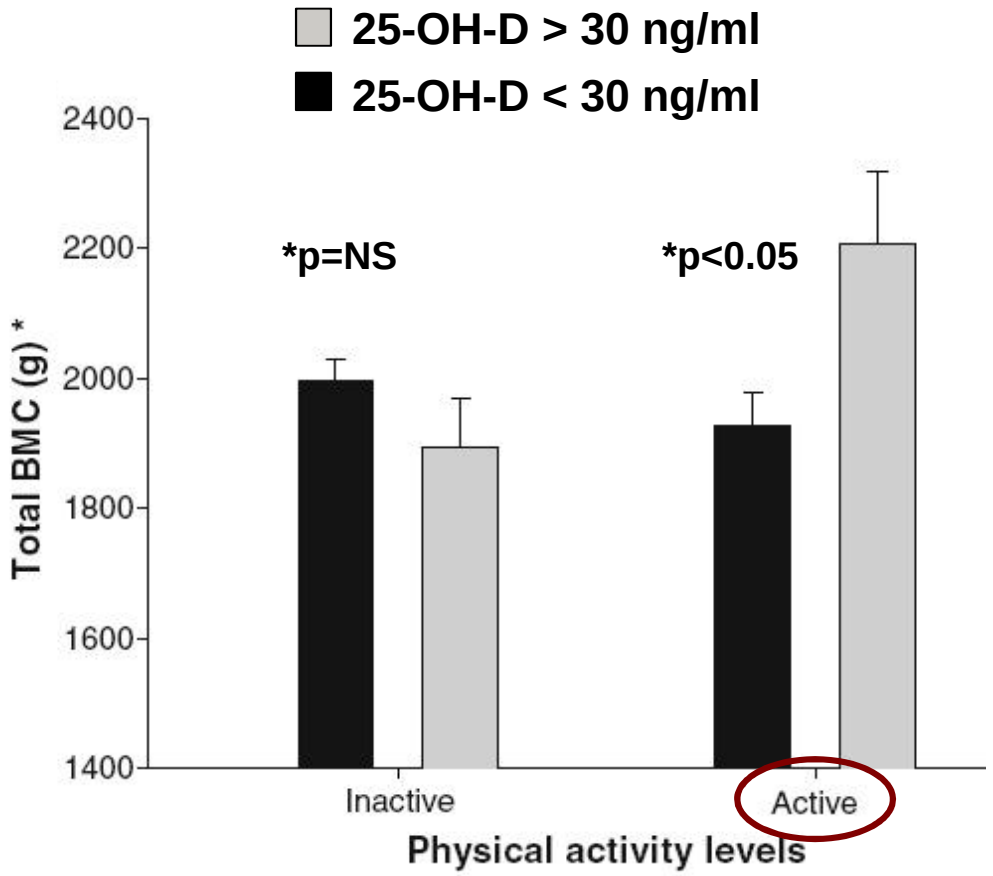




Adequate vitamin D status is important in enhancing muscle strength and in attaining higher peak bone mass.

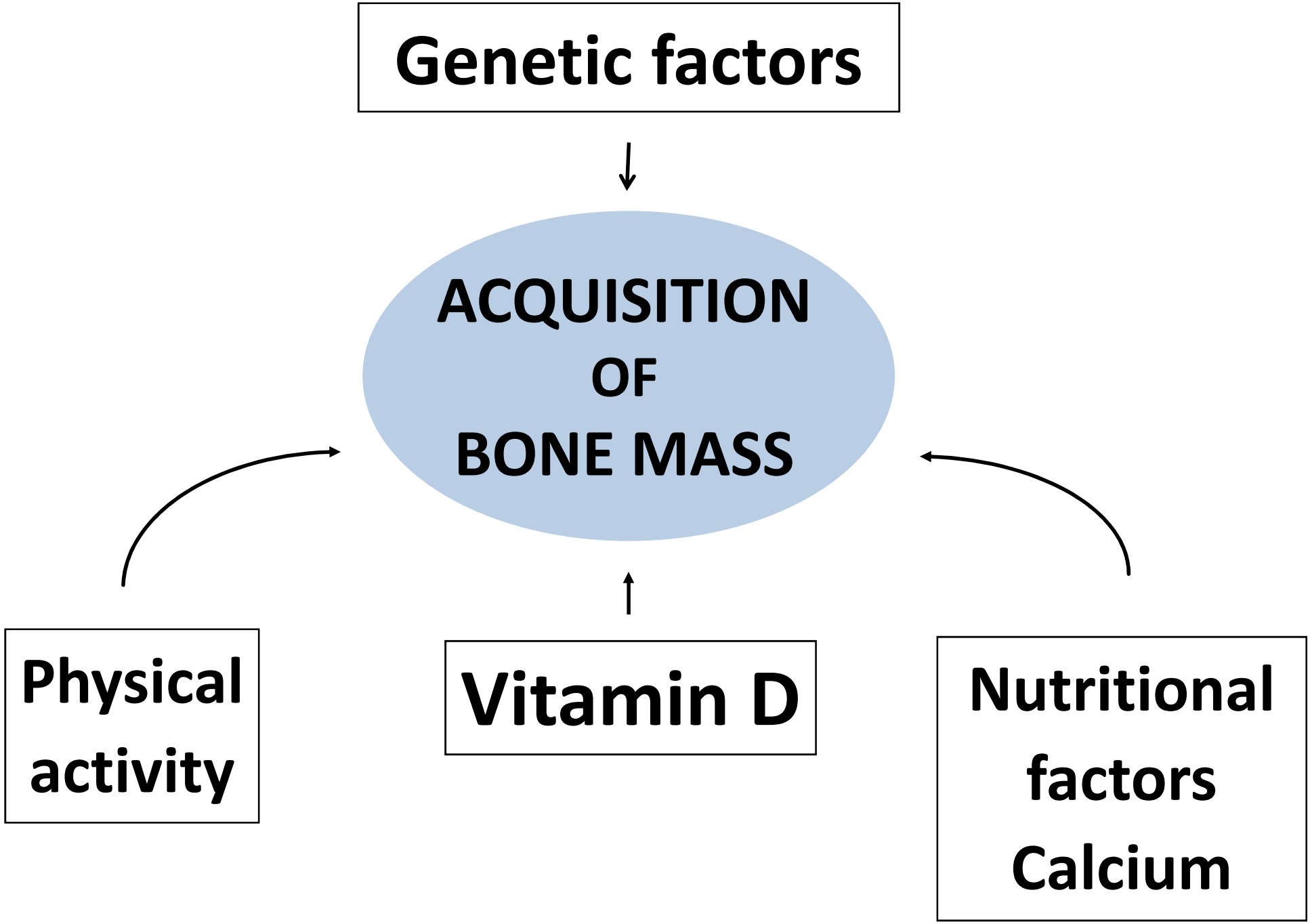
(Foo LH et al. J Nutr 2009)

Vitamin D status and physical activity (PA) have a sinergic action in improving bone mass in adolescents (n = 100, age 12.5-17.5 yr)



Vitamin D and PA might interact to determine BMC in two possible directions: 25(OH)D sufficiency levels improve bone mass only in active adolescents, or PA has a positive influence on BMC in individuals with replete vitamin D levels.

(Valtuena J et al. Osteoporos Int 2012)


Genetic factors
ACQUISITION
OF
BONE MASS
Physical
activity
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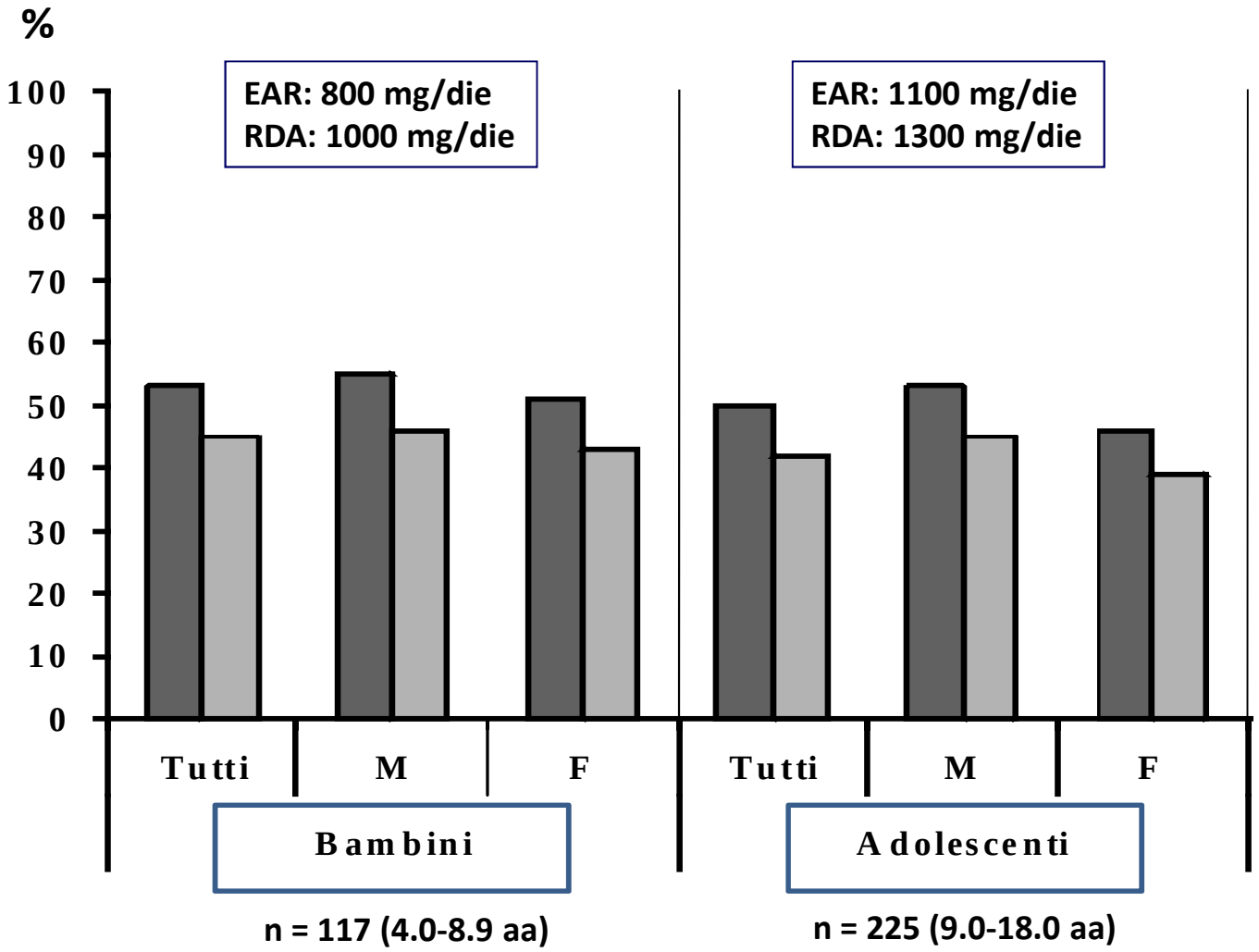
Nutritional
factors
Calcium

Intake di calcio espresso come percentuale dei fabbisogni raccomandati (IOM 2010)

Clinica Pediatrica Università di Pisa (n = 272; M = 124)



- EAR % (Estimated Average Requirement)
- RDA % (Recommended Dietary Allowance)

WinFood

Vitamina D e massa ossea

- L'evidenza attuale basata sugli studi di associazione e di supplementazione disponibili sembra confermare un effetto positivo della supplementazione con vitamina D sui processi di acquisizione della massa ossea in bambini ed adolescenti con ipovitaminosi.

- Per quanto riguarda la gravidanza, gli studi disponibili, essenzialmente di associazione, sembrano indicare che lo stato vitaminico D materno possa influenzare i processi di acquisizione della massa ossea del feto e del nascituro, anche nelle epoche successive della vita fino al raggiungimento del picco di massa ossea.

- **Il mantenimento di un adeguato stato vitaminico durante l'età evolutiva è verosimilmente necessario per l'acquisizione di un ottimale picco di massa ossea.**

Molecular and Cellular Endocrinology 410 (2015) 11–18

Conflicting reports on vitamin D supplementation: Evidence from randomized controlled trials

Richard D. Lewis *,[1], Emma M. Laing [1]

Key variables to consider in studies involving Vitamin D interventions on bone mineral accrual in children

Variable
Baseline 25(OH)D
Vitamin D dose
Form of vitamin D supplement
Calcium intake
Sunlight exposure/season of testing
Vitamin D assay
Race
Sex
Muscle
Physical activity
Age/pubertal maturation
Statistical analysis methods
Bone outcome measures

Vitamina D e massa ossea

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Vitamina D: azioni scheletriche

- **Rachitismo**
- **Acquisizione massa ossea**

Vitamin D and child health: extraskeletal aspects

Although there are currently many studies that have demonstrated associations with vitamin D status and potential extraskeletal benefits of vitamin D, there is limited evidence at present of causation when examined in intervention studies (RCTs).

Until there is evidence that vitamin D is beneficial beyond its effects on the skeleton, we do not feel there should be widespread vitamin D supplementation of the population.

(Shaw NJ, Mughal MZ. Arch Dis Child Mar 2013)

Minerva Pediatr. 2013 Jun;65(3):253-60.

Is vitamin D supplementation necessary in healthy full-term breastfed infants? A follow-up study of bone mineralization in healthy full-term infants with and without supplemental vitamin D.

Bagnoli F[1], Casucci M, Toti S, Cecchi S, Iurato C, Coriolani G, Tiezzi M, Vispi L.

METHODS:

Bone mineralization was studied by performing ultrasound scans of 73 healthy full-term subjects at the age of 3 months.

The infants were divided into three group:

group A: breastfed without supplemental vitamin D (BF);

group B: breastfed with supplement of 400 IU/day of vitamin D(BFD);

group C: fed with formula (with and without supplemental vitamin D 400 IU/day) (FF).

RESULTS:

n 75% of subjects of group A mcSOS and mcBTT values were ≤ the 10th percentile, while in group B they were between the 10th and 50th percentile. In FF infants given supplemental vitamin D mcSOS and mcBTT values were between the 25th and 75th percentile

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