Vitamin D Supplementation During Pregnancy and the 1st Year of Life and Why

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Centre for Children's Bone & Musculoskeletal Health

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  - Speaker fees
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Outline

- Case of nutritional rickets
- Vitamin D and calcium in pregnancy
- Nutritional rickets
- Prevention and Treatment of Nutritional Rickets
- Controversies in Vitamin D

SPECIAL FEATURE

Consensus Statement

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, and Wolfgang Högler*

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Munns et al *JCEM* 2016; 101(2)

Case

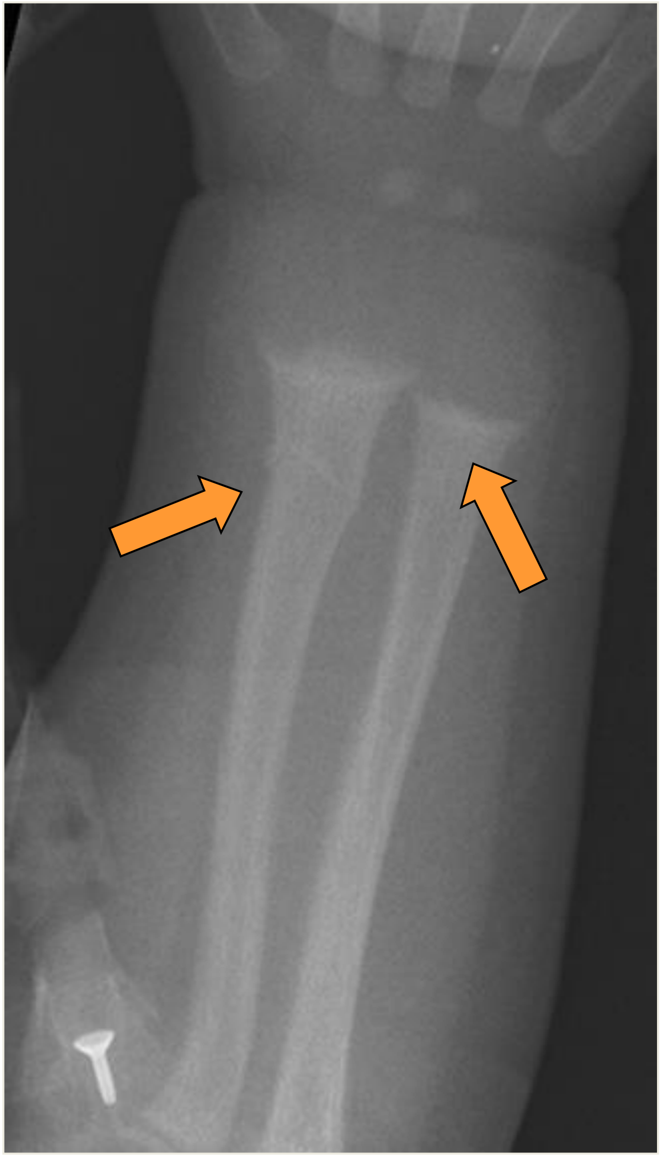
- 3 month old female
- Irritable
- Painful leg and bruise

- Term, LSCS, Birth Weight 2490 g
- Mother not supplemented with vitamin D during pregnancy
- Breast fed
- Pakistani parents
- Mother wears traditional modest clothing

Examination

- Painful left leg
- Irritable
- Rachitic rosary, flaring wrists
- Poor weight gain
- Systemic examination otherwise normal


L



Further Investigation

• Calcium	1.59 mmol/L	(2.10-2.65)
• Phosphorus	0.80 mmol/L	(1.20-2.10)
• Magnesium	0.72 mmol/L	(0.71-0.96)
• Alk-phos	1453 U/L	(160-400)
• 25-(OH)vit D	<12 nmol/L	(>50)
• PTH	62.9 pmol/L	(1.0-7.0)

Mother

- 25 (OH) vit D 12 nmol/L
- Calcium 2.40 mmol/L

Treatment

- Calcitriol 60 nanograms/kg/day
- Oral calcium 100 mg/kg/day
- Cholecalciferol 2000 IU daily for 3 months
- Calcium 150 mg bd
- Maintenance vitamin D 400 IU daily
- Treat mother
  - Cholecalciferol 5000 IU daily 3 months
  - Calcium 600 mg bd

Further Investigations

	Baseline	24 hours	48 hours	72 hours
Calcium (2.1-2.6 mmol/L)	1.59	1.63	2.00	2.14
Phosphorus (1.2-2.1 mmol/L)	0.80	0.98	0.87	0.82
Alk Phos (140-360 IU/L)	1453			
PTH (1-7 pmol/L)	62.9			
25-OHD (>50 nmol/L)	<12			

Oral calcium 100 mg/kg/day
Calcitriol 60 ng/kg/day

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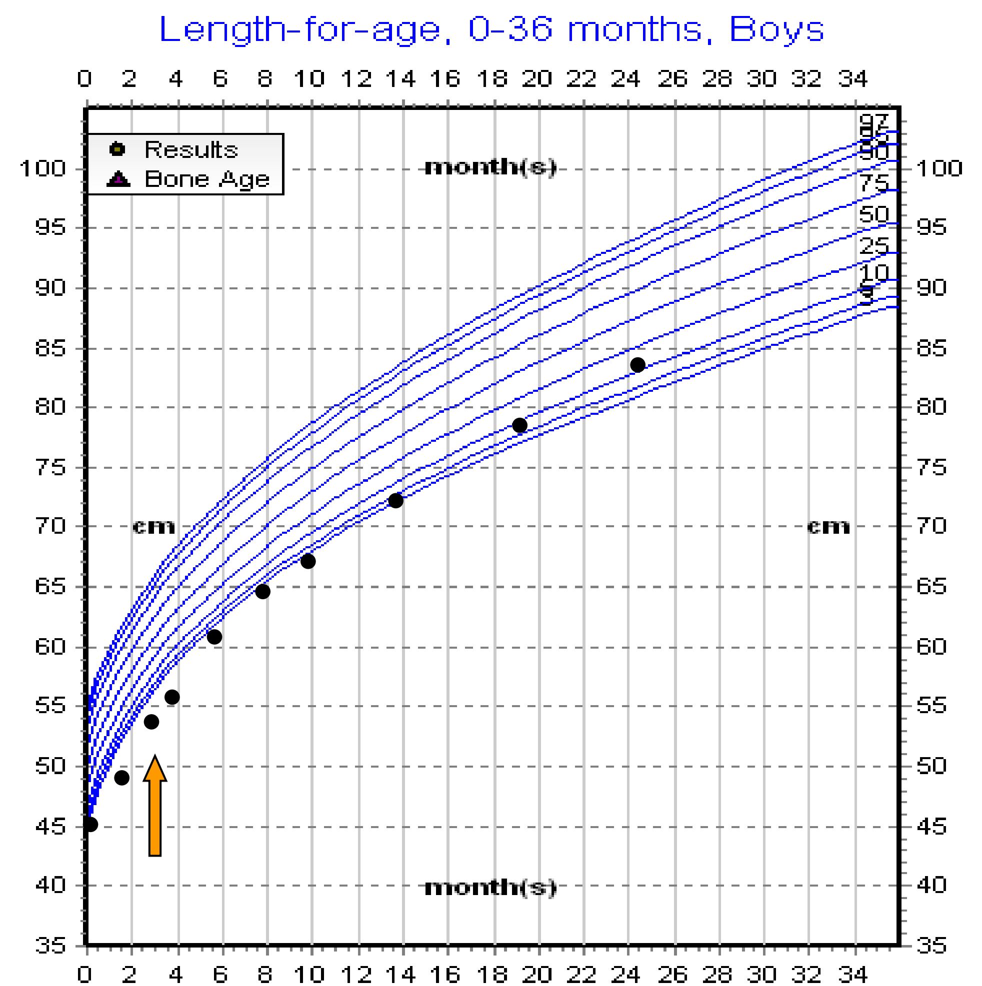
Follow-up


3 months


6 months


Length-for-age, 0-36 months, Boys
Results
Bone Age
month(s)
cm
0 2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34
35 40 45 50 55 60 65 70 75 80 85 90 95 100
97 90 75 50 25 10 3

Calcium and Vitamin D in Pregnancy and Lactation

- Increased demands on calcium homeostasis with pregnancy and lactation
  - Foetal skeletal mineralisation
  - Calcium for breast milk

Pregnancy

- Term foetal skeletal has about 30 g of calcium
- 80% of this is accrued in the last trimester
- Calcium comes from a doubling of maternal intestinal calcium absorption
  - Mediated by 1,25-(OH)D (calcitriol)
  - ?Prolactin or placental lactogen
- Mild increase in maternal bone turnover from 12 weeks gestation
- Pregnancy does not lead to any significant reduction in maternal BMD or risk of developing osteoporosis in later life

Sowers. *J Bone Miner Res 1996;11*

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Lactation

- 210 mg of calcium lost in breast milk daily
- Comes from demineralisation of maternal skeleton
  - PTHrP (breast) and fall in oestradiol levels
- Fall in BMC of 3 – 10% after 2 – 6 months of lactation at trabecular sites (spine, hip and distal radius)
- Fall in BMC correlated with amount of calcium in breast milk
- Supplementation with high-dose calcium does not prevent BMC loss

Laskey et al. *Am J Clin Nutr* 1998;67

Kalkwarf et al. *N Engl J Med* 1997;337

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Lactation

- After weaning there is regaining of BMC
- Lactation does not appear to be a risk factor for subsequent osteoporotic fractures

Sowers. *J Bone Miner Res 1996;11*

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Vitamin D Metabolism

7-dehydrocholesterol

Solar UVB

Skin

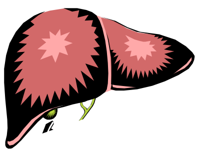
Previtamin D_3

Heat

Vitamin D_3

Dietary
Vitamin D_2
(Ergocalciferol)
or
Vitamin D_3
(Cholecalciferol)

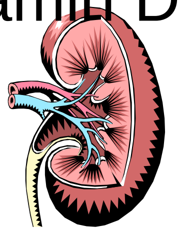
Vitamin D-25 hydroxylase



Liver

25-hydroxyvitamin D_3

25(OH)-1α-hydroxylase
CYP27B1



Kidney

1,25-dihydroxyvitamin D_3

Vitamin D Receptor (VDR)

Vitamin D in Pregnancy and Lactation

- Maternal vitamin D levels do not change throughout pregnancy or lactation

	Recommended Daily Allowance (RDA)	Upper Level Intake
14 – 18 year old	600 IU daily	4000 IU daily
>18 year old	600 IU daily	4000 IU daily

- RDA is the dose that will keep 97.5% of the population >50 nmol/L

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OIM. Dietary reference intakes for calcium and vitamin D. The National Academies Press; 2011
Munns et al *JCEM* 2016; 101(2)

Vitamin D Deficiency (<50nmol/L) and Pregnancy

25OHD level	Westmead	Campbelltown	Adelaide	ACT	Shepparton	Brisbane
>50 nmol/L	59%	55%	26%	65%	74%	91%
25 – 49 nmol/L	32%	34%	42%	31%	21%	6%
<25 nmol/L	9%	12%	32%	4%	5%	3%

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Lau et al. *MJA 2011*;194(7)
Perampalam et al. *ANZJOG* 2011;51
Thomas et al. *BMJ* 2011;2
Teale et al. *ANZOG* 2010;50
McLeod et al. *MJA* 2011;195(7)

Classical Features of Vitamin D Deficiency During Pregnancy

- Worsening of hypocalcaemia
- Osteomalacia
- Limb / bone pain
- Myopathy / myalgia
- Obstetric problems during labor

Kovacs. *Endocrinol Metab Clin N Am* 2011;40

What are the Typical Features and Biochemistry of Vitamin D Deficiency in Pregnancy?

- Asymptomatic
- 25 OHD <50 nmol/L

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Treatment of Vitamin D Deficiency in Pregnancy

25OHD level	Treatment Dose	Maintenance Dose
Mild 25 - 50nmol/L	1,000 IU daily for 3 months	600 – 1000 IU daily
Moderate 12.5 – 25 nmol/L	2,000 IU daily for 3 months	600 – 1000 IU daily
Severe <12.5 nmol/L	2,000 IU daily for 3 months	600 – 1000 IU daily

Paxton et al. *MJA* 2013;198(3)

2,000 IU daily for 3 months will raise 25OHD by ~ 25 nmol/L

4,000 IU daily for 3 months will raise 25OHD by ~ 40 nmol/L

Higher doses may be needed (4,000 IU daily)
Safety of high-dose Stoss therapy uncertain
Need to recheck vitamin D levels in third trimester

Hollis et al. *J Bone Miner Res* 2011; 26(10)

Neonatal Calcium and Vitamin D

- In utero foetal calcium = maternal calcium
- Unless mother hypocalcaemic, foetal development normal

- Neonatal vitamin D is 75% of maternal vitamin D
- Little vitamin D in breast milk – 25 IU/L
- Half life of vitamin D about 8 weeks
- Un-supplemented neonate can quickly become vitamin D deficient

Rickets and Osteomalacia

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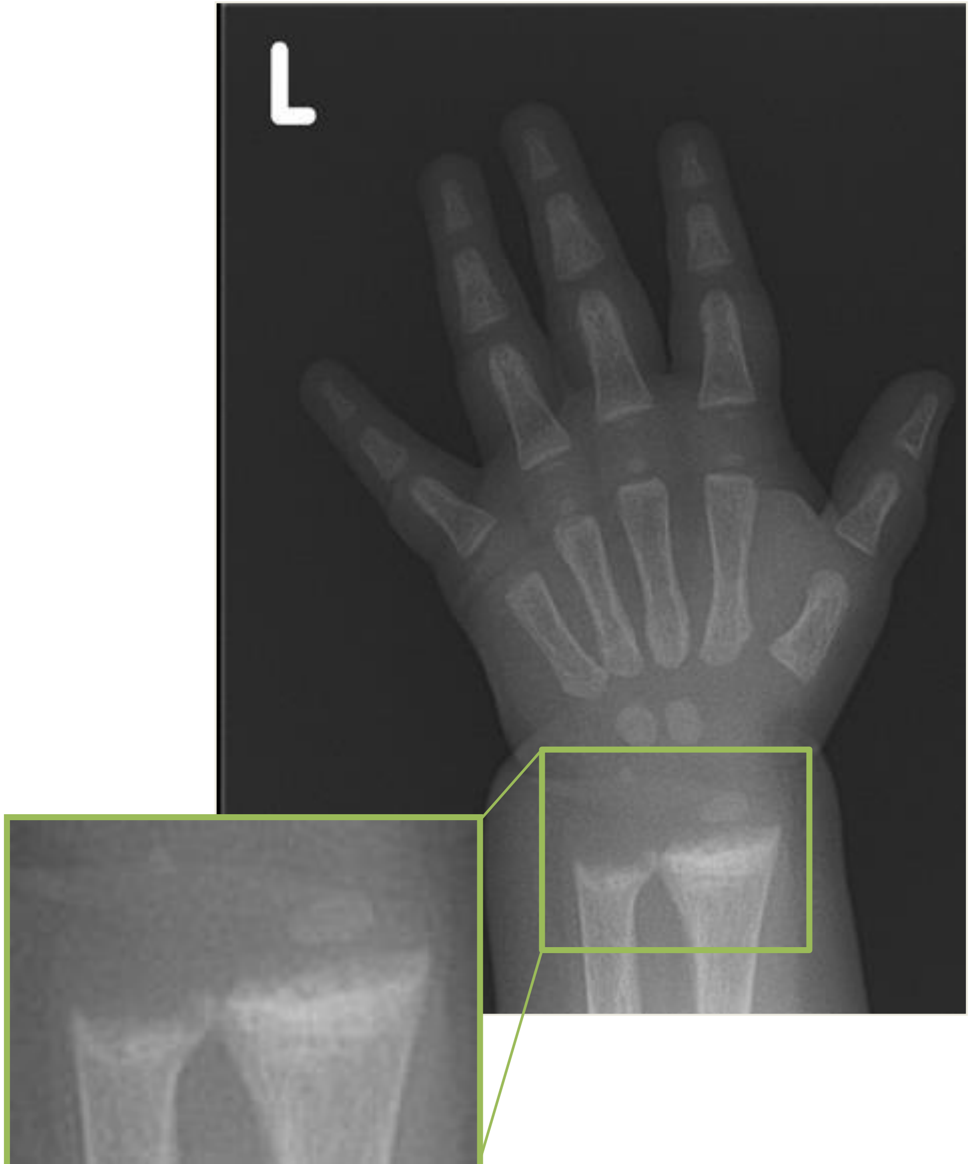
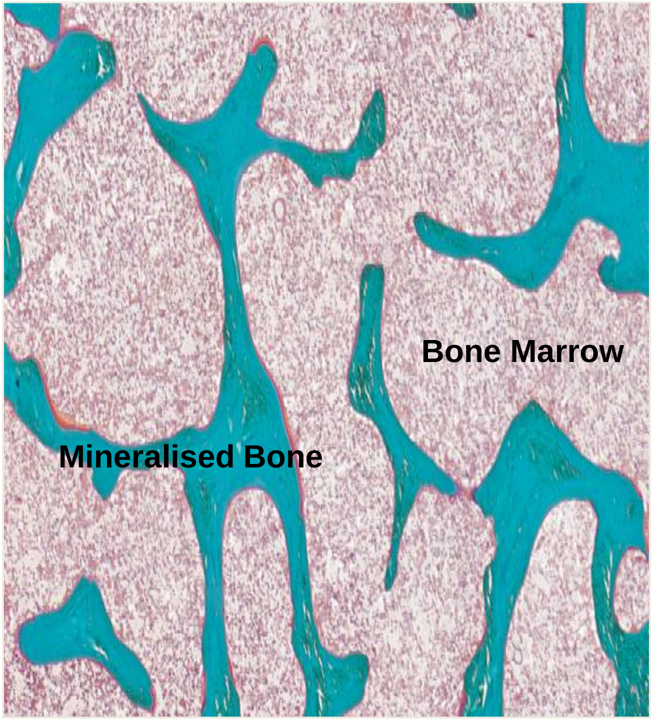
X-Ray of 7 month old Girl with Nutritional Rickets

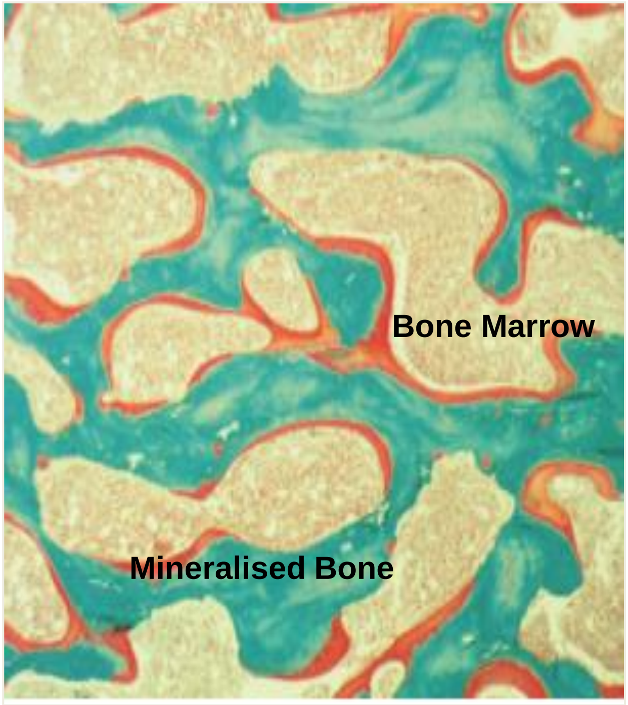


Osteomalacia

Normal



Osteomalacia



Pediatric Bone; 2003

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Clinical Features of Nutritional Rickets

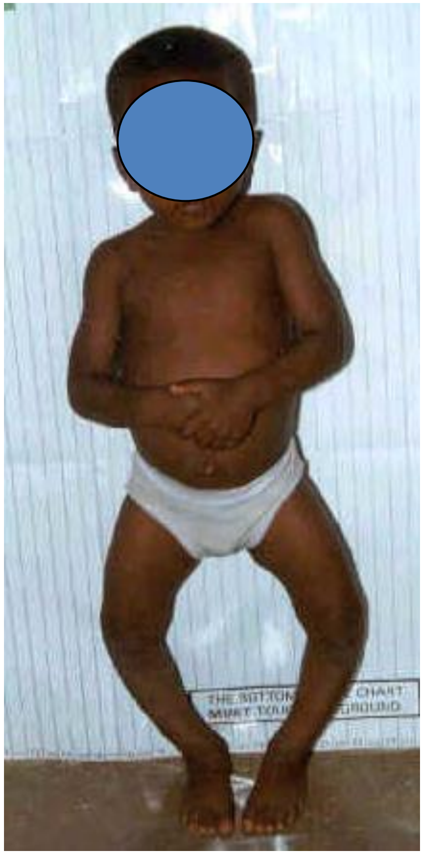
- Metabolic Disturbance
  - Hypocalcemic seizures
  - Neonatal tetany
  - Laryngospasm

- Skeletal abnormalities
  - Bowed legs
  - Pathological fractures
  - Craniotabes

- Growth and Developmental abnormalities
  - Failure to thrive
  - Developmental Delay
  - Cardiomyopathy and death
  - Association with iron deficiency anaemia

Limb Deformity

Genu Valgum



Genu Varum

Wind Swept

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Countries with Reports on Nutritional Rickets

North America	South America	Europe	Asia	Africa/Middle East
Canada	Argentina	Algeria	India	Ethiopia
U.S.	Chile	Denmark	Bangladesh	Kenya
	Columbia	Finland	China	Nigeria
		France	Indonesia	Sudan
		Netherlands	Israel	S. Africa
		Norway	Japan	Saudi Arabia
		Spain	Kuwait	Yemen
		Sweden	Lebanon	
		U.K.	Mongolia	
		Germany	New Zealand	
			Vietnam	
			Australia	

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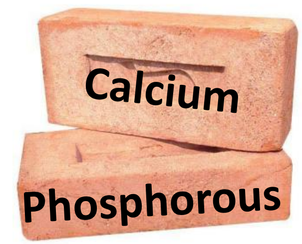
Incidence

- Nutritional Rickets:
  - 2.9, 4.9, 7.5, and 24 per 100,000 children in Canada, Australia, UK, and the USA, respectively
- Hypocalcaemic seizures due to Vitamin D deficiency in the UK:
  - 3.49 per 1 Million children (age 0-15)
- Vitamin D and/or calcium deficiency:
  - Worldwide, widespread

Munns et al JCEM 2016; 101(2)

The 3 primary causes rickets and osteomalacia

- Lack of Mineral Supply (Calcium, Phosphporus)
  - – Calcium deficiency rickets
  - – Hypophosphataemic rickets



- Lack of the Mineral Supplier (Vitamin D)
  - – Vitamin D deficiency
  - – Vitamin D resistance

- Lack of Mineral Deposition (TNSALP)
  - – Hypophosphatasia

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What Happens when Vitamin D and Dietary Calcium are not Maintained?

Hypocalcaemia

↓

Hyperparathyroidism

↓ ↓

↑Alkaline phosphatase   Hypophosphataemia

↓

Osteomalacia and Rickets

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Vitamin D, Calcium and Nutritional Rickets

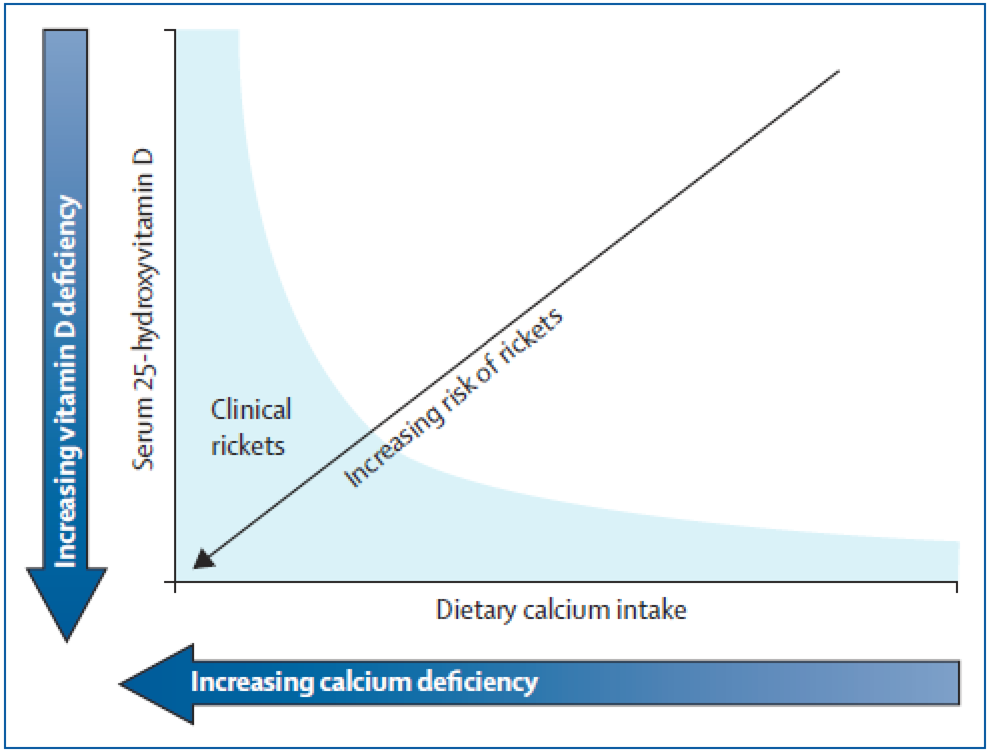

Figure: Vitamin D and dietary calcium deficiency—detrimental to bone in combination

Högler W, Munns CF Lancet Glob Health. 2016 Apr;4(4):e229-30.

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What is the definition of vitamin D deficiency?

Classified by serum 25OHD level

	Serum 25OHD
Sufficiency	> 50 nmol/L
Insufficiency	30-50 nmol/L
Deficiency	<30 nmol/L

1+++

Strong recommendation
High quality evidence

Functional outcomes of this definition

- Depend on balance between dietary calcium intake and 25OHD level
- Majority of children asymptomatic and detected through screening
- Osteomalacia and rickets most significant outcome
- Biochemical results and bone density are associated outcomes

No indication for routine screening for vitamin D deficiency

Munns et al JCEM 2016; 101(2)

Risk Factors for Vitamin D Deficiency

- Reduced intake or synthesis of vitamin D
  - Maternal vitamin D deficiency
  - Prolonged exclusive breast feeding (>6 months)
  - Darker skin colour
  - Limited sun exposure
    - Disability
    - Clothing
    - Sunscreen
- Abnormal gut function / malabsorption
  - Small bowel: Coeliac disease
  - Pancreatic insufficiency: Cystic fibrosis
  - Biliary obstruction
- Reduced synthesis / increased degradation / sequestration
  - Chronic liver disease
  - Medication: antiepileptic, glucocorticoids
  - Obesity

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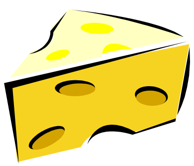
Munns et al *MJA* 2006; 185(5)
Adams et al. *JCEM* 2009;95(2)

Definition of dietary calcium deficiency

- For infants 0-6 and 6-12 months of age, the adequate calcium intake is 200 and 260mg/day, respectively. **(**1+++**)**
- For children > 12 months of age
  - Dietary calcium intake of <300mg/day increases the risk of rickets independent of serum 25OHD levels. **(**1++O**)**
  - **Classified by dietary calcium intake**: **(**1++O**)**

	Daily calcium intake
Sufficiency	>500mg
Insufficiency	300 – 500mg
Deficiency	<300mg



Assessment: Dietary questionnaire specific to the diet of country/ region

Munns et al JCEM 2016; 101(2)

Treatment of Nutritional Rickets

Vitamin D2 or D3

Age	Daily oral dose for 3 months	Single dose (D3>D2)	Maintenance daily dose
< 3 months	2000 IU	N/A	400 IU
3 to 12 months	2000 IU	50,000 IU	400 IU
12 months to 12 years	3000 - 6000 IU	150,000 IU	600 IU
> 12 years	6000 IU	300,000 IU	600 IU

Reassess response to treatment after 3 months as further treatment may be required.

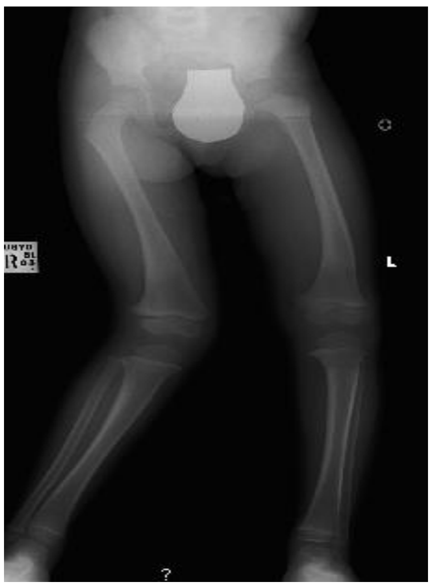
IU to µg: divide by 40

Calcium

Ensure a daily calcium intake of at least 500mg

Munns et al JCEM 2016; 101(2)

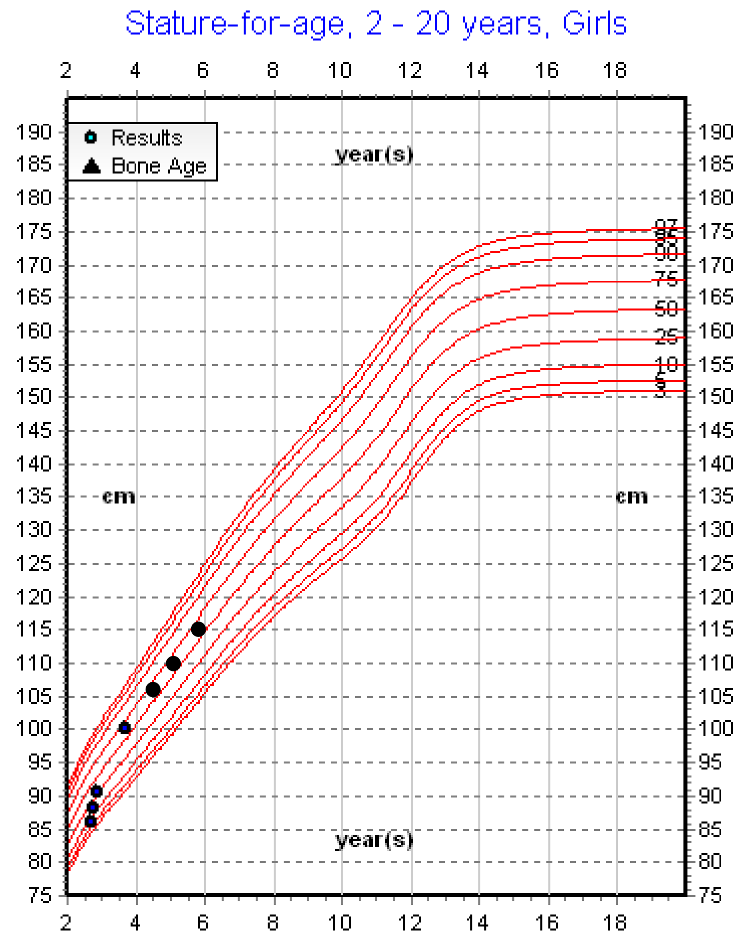
Follow-up Images



6 months

18 months

30 months



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Prevention of Rickets

- **First 12 months of life**
  - 400 IU/day (10µg) prevents rickets in infants and is recommended for **all** infants in the 1st year of life
- **Beyond 12 months of age**
  - Everybody needs to meet their nutritional requirement for vitamin D (diet or supplementation), which is at least 600 IU/day (15µg), as recommended by the IOM.
  - **Supplement**
    - All children with a history of symptomatic vitamin D deficiency requiring treatment.
    - Children and adults at high risk of vitamin D deficiency, with factors that reduce synthesis or intake of vitamin D.
    - All pregnant women 600 – 1000 IU daily

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Munns et al JCEM 2016; 101(2)

Public health strategies for Rickets Prevention

- **Provide Vitamin D Supplementation for**
  - ALL infants from birth to at least 12 months of age
  - ALL pregnant women
  - ALL risk groups, for life

Incorporate Vitamin D Supplementation into
Childhood primary health care programs
AND
Antinatal care programs

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Munns et al JCEM 2016; 101(2)

Public health strategies for Rickets Prevention

Food Fortification

- Fortify staple foods with vitamin D and calcium, as appropriate.
- Food fortification can prevent rickets and improve vitamin D status if
  - appropriate foods are used
  - sufficient fortification is provided
  - fortification is supported by relevant legislation
  - the process is adequately monitored
  - Indigenous food sources of calcium should be promoted or subsidized in children

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Munns et al JCEM 2016; 101(2)

Are there other reasons to supplement mothers and babies with vitamin D?

Cochrane Library

Cochrane Database of Systematic Reviews

2016

Vitamin D supplementation for women during pregnancy (Review)

De-Regil LM, Palacios C, Lombardo LK, Peña-Rosas JP

De-Regil LM, Palacios C, Lombardo LK, Peña-Rosas JP.
Vitamin D supplementation for women during pregnancy.
Cochrane Database of Systematic Reviews 2016, Issue 1. Art. No.: CD008873.
DOI: 10.1002/14651858.CD008873.pub3.

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Maternal Vitamin D and Birth Length

Analysis 1.17. Comparison 1 Vitamin D alone versus no treatment/placebo (no vitamins or minerals), Outcome 17 Birth length (cm) (ALL).

Review: Vitamin D supplementation for women during pregnancy

Comparison: 1 Vitamin D alone versus no treatment/placebo (no vitamins or minerals)

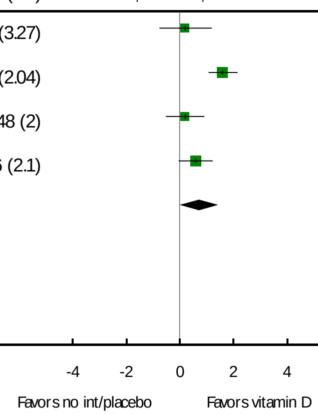
Outcome: 17 Birth length (cm) (ALL)

Study or subgroup	Vitamin D N	Mean(SD)	No intervention/placebo N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Brooke 1980	59	49.7 (2.3)	67	49.5 (3.27)		20.7 %	0.20 [-0.78, 1.18]
Marya 1988	100	50.06 (1.79)	100	48.45 (2.04)		28.1 %	1.61 [1.08, 2.14]
Roth 2010	74	48.2 (2.5)	73	48 (2)		24.8 %	0.20 [-0.53, 0.93]
Sablok 2015	108	46.61 (1.8)	57	46 (2.1)		26.3 %	0.61 [-0.03, 1.25]
Total (95% CI)	**341**		**297**			**100.0 %**	**0.70 [-0.02, 1.43]**

Heterogeneity: $Tau^2 = 0.42$; $Chi^2 = 13.09$, df = 3 (P = 0.004); $I^2 = 77\%$

Test for overall effect: Z = 1.89 (P = 0.058)

Test for subgroup differences: Not applicable



Trend to increase in birth length with vitamin D supplementation

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De-Regil et al. *Cochrane Database Syst Rev* 2016 14(1)

Maternal Vitamin D and Birthweight

Analysis 1.19. Comparison 1 Vitamin D alone versus no treatment/placebo (no vitamins or minerals), Outcome 19 Birthweight (g) (ALL).

Review: Vitamin D supplementation for women during pregnancy

Comparison: 1 Vitamin D alone versus no treatment/placebo (no vitamins or minerals)

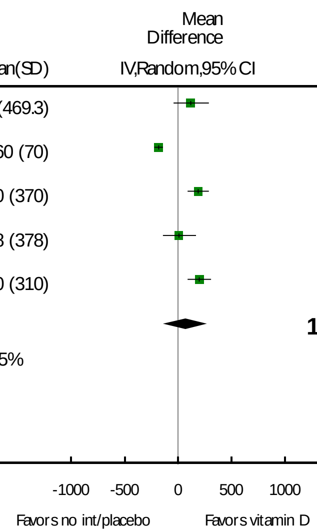
Outcome: 19 Birthweight (g) (ALL)

Study or subgroup	Vitamin D N	Mean(SD)	No intervention/placebo N	Mean(SD)	Weight	Mean Difference IV,Random,95% CI
Brooke 1980	59	3157 (468.5)	67	3034 (469.3)	18.9 %	123.00 [-41.07, 287.07]
Mallet 1986	48	3280 (86)	29	3460 (70)	21.3 %	-180.00 [-215.23, -144.77]
Marya 1988	100	2990 (360)	100	2800 (370)	20.4 %	190.00 [88.82, 291.18]
Roth 2010	73	2802 (543)	74	2788 (378)	19.2 %	14.00 [-137.44, 165.44]
Sablok 2015	108	2600 (410)	57	2400 (310)	20.2 %	200.00 [88.39, 311.61]
Total (95% CI)	**388**		**327**		**100.0 %**	**66.60 [-137.22, 270.41]**

Heterogeneity: Tau^2 = 50334.96; Chi^2 = 88.39, df = 4 (P<0.00001); I^2 =95%

Test for overall effect: Z = 0.64 (P = 0.52)

Test for subgroup differences: Not applicable



When Mallet study excluded form the analysis the result became significant Summary effect 146.5 g (95% CI 67.8 to 225.2) in favour of maternal vitamin D supplementation

De-Regil et al. *Cochrane Database Syst Rev* 2016 14(1)

Maternal Vitamin D and Head Circumference

Analysis 1.18. Comparison 1 Vitamin D alone versus no treatment/placebo (no vitamins or minerals), Outcome 18 Head circumference at birth (cm) (ALL).

Review: Vitamin D supplementation for women during pregnancy

Comparison: 1 Vitamin D alone versus no treatment/placebo (no vitamins or minerals)

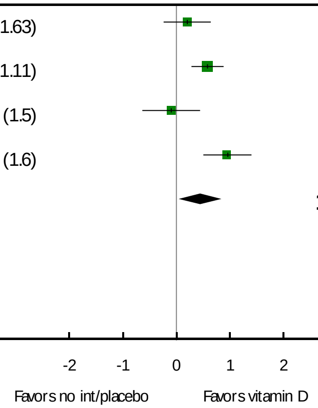
Outcome: 18 Head circumference at birth (cm) (ALL)

Study or subgroup	Vitamin D N	Mean(SD)	No intervention/placebo N	Mean(SD)	Mean Difference IV,Random,95% CI	Weight	Mean Difference IV,Random,95% CI
Brooke 1980	59	34.5 (0.76)	67	34.3 (1.63)		24.8 %	0.20 [-0.24, 0.64]
Marya 1988	100	33.99 (1.02)	100	33.41 (1.11)		29.6 %	0.58 [0.28, 0.88]
Roth 2010	73	32.9 (1.8)	74	33 (1.5)		21.5 %	-0.10 [-0.64, 0.44]
Sablok 2015	108	33.85 (0.96)	57	32.9 (1.6)		24.2 %	0.95 [0.50, 1.40]
Total (95% CI)	**340**		**298**			**100.0 %**	**0.43 [0.03, 0.83]**

Heterogeneity: $Tau^2 = 0.12$; $Chi^2 = 10.66$, df = 3 (P = 0.01); $I^2 = 72\%$

Test for overall effect: Z = 2.13 (P = 0.033)

Test for subgroup differences: Not applicable



Maternal vitamin D supplementation associate with an increase in head circumference at birth

De-Regil et al. *Cochrane Database Syst Rev* 2016 14(1)

Maternal Vitamin D and Low Birth Weight (<2500g)

Analysis 1.11. Comparison 1 Vitamin D alone versus no treatment/placebo (no vitamins or minerals), Outcome 11 Low birthweight (less than 2500 g) (ALL).

Review: Vitamin D supplementation for women during pregnancy

Comparison: 1 Vitamin D alone versus no treatment/placebo (no vitamins or minerals)

Outcome: 11 Low birthweight (less than 2500 g) (ALL)

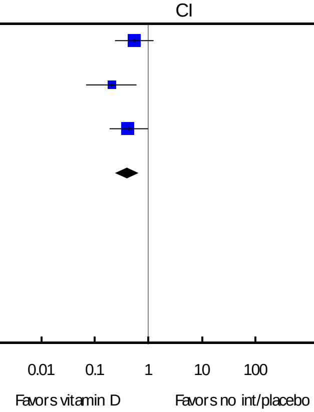
Study or subgroup	Vitamin D n/N	No intervention/placebo n/N	Risk Ratio M-H,Random,95% CI	Weight	Risk Ratio M-H,Random,95% CI
Brooke 1980	7/59	15/69		37.7 %	0.55 [0.24, 1.25]
Marya 1988	4/100	19/100		24.1 %	0.21 [0.07, 0.60]
Sablok 2015	9/108	11/57		38.2 %	0.43 [0.19, 0.98]
Total (95% CI)	**267**	**226**		**100.0 %**	**0.40 [0.24, 0.67]**

Total events: 20 (Vitamin D), 45 (No intervention/placebo)

Heterogeneity: $Tau^2 = 0.01$; $Chi^2 = 2.08$, df = 2 (P = 0.35); $I^2 = 4\%$

Test for overall effect: Z = 3.49 (P = 0.00048)

Test for subgroup differences: Not applicable



Maternal vitamin D supplementation appeared protective against LBW

De-Regil et al. *Cochrane Database Syst Rev* 2016 14(1)

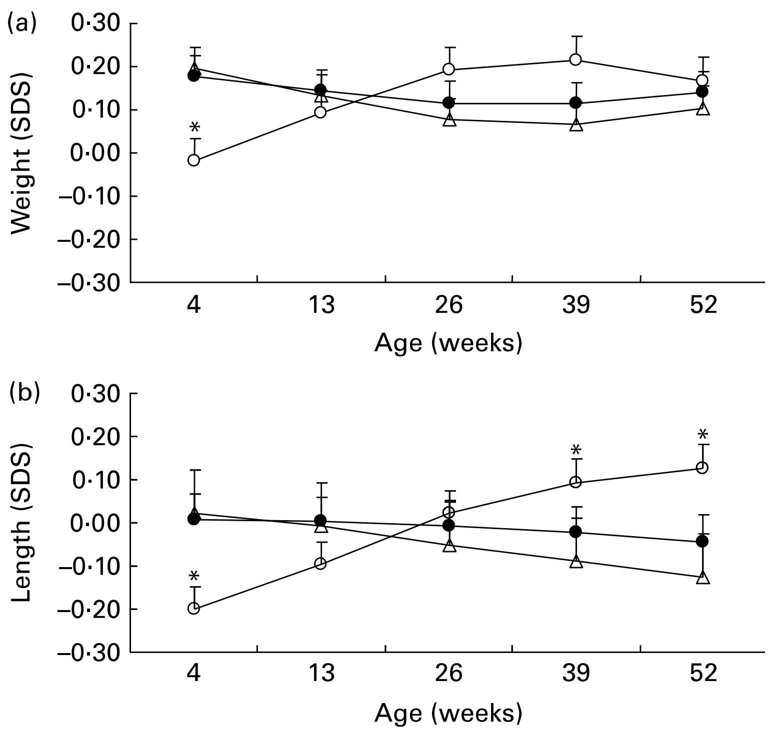
Maternal Vitamin D and Low Birth Weight (<2500g)

Nested case control study from Canada

- Maternal vitamin D <50nmol/L was protective of LBW compared to >75nmol/L
- OR 0.47 95% CI 0.23-0.97

Morgan et al. *Arch Gynecol Obstet* 2016; 293(4)

Linear Growth in First Year of Life



–○–, Deficient; –●–, insufficient; –△–, adequate.

25OHD <30nmol/L associated with reduced birth weight and length with increased growth velocity over first 12 months of age (end up longer)

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Leffelaar et al. *Brit J Nutrit* 2010;104

Fetal Effects of Vitamin D

- Childhood Bone Mass and Maternal Vit D Supplementation
  - Conflicting data with weak evidence on DXA
  - Reduced bone size and BMC
  - Normal vBMD
- Maternal Vit D status does not appear associated with childhood fracture in offspring (outside infantile nutritional rickets)

De-Regil et al. *Cochrane Database Syst Rev* 2016 14(1)
Viljakainen et al. *JCEM* 2010; 95(4)
Javaid et al. *Lancet* 2006; 367
Lawlor et al. *Lancet* 2013; 38
Petersen et al. PLOS One 2014; Dec
Theodoratou et al. *BMJ* 2014; 348

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Meta-analysis of Maternal Vitamin D and Childhood BMD (DXA)

Region	Number of Studies	Reported Summary Effect (95% CI)	P value
Total body	5	0.1 (−0.06 to 0.26)	0.22
Forearm	2	0.04 (−0.36 to 0.45)	0.86
Hip	4	0.06 (−0.18 to 0.29)	0.63
Lumbar spine	5	0.15 (−0.01 to 0.31)	0.07

Theodoratou et al. *BMJ* 2014; 348

Maternal vitamin D status does not influence childhood BMD

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Childhood Vitamin D Supplementation / Levels

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Vitamin D and Dental Caries

- 38 studies in meta-analysis
  - Summary effect 0.53 (95% CI 0.43 – 0.65)
  - Vitamin D supplementation associated with less dental caries
- NHANES 2005-2006
  - No significant association between vitamin D status and dental caries

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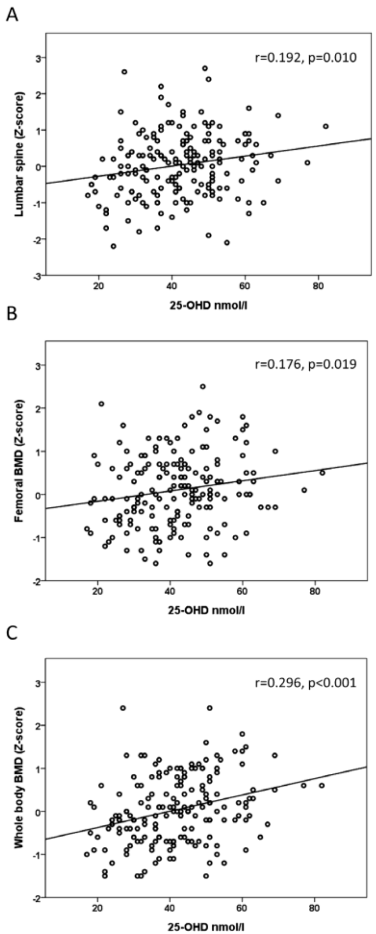
Theodoratou et al. *BMJ* 2014; 348
Hujoel et al. *Nurt Rev* 2013; 71
Herzog et al. *J Am Dent Assoc* 2016; 147(6)

Vitamin D and Bone Mass Accrual in Childhood

Bone Mineral Density



After controlling for calcium intake

Lehtonen-Veromaa et al showed BMD change over a 3 year period was 4% smaller in those with 25-OHD <20nmol/L than in those with 25-OHD >37.5nmol/L.

BMD appears to continue to increase as 25-OHD increases.

Pekkinen et al . *PLoS ONE* 2012;7(7)
Lehtonen-Veromaa et al. *Am J Clin Nutr*; 76
Theodoratou et al. *BMJ* 2014; 348

Fracture and Vitamin D and Rickets

Femoral Fracture

Rickets

Table 3: Clinical presentation of cases of vitamin D-deficiency rickets reported between July 1, 2002, and June 30, 2004

Characteristic	Age group, yr; no. (%) of cases* < 1 *n = 34*	1-2 *n = 56*	> 2-7 *n = 14*	Total *n = 104*
Age, yr, mean (SD)	0.6 (0.3)	1.4 (0.3)	3.2 (1.3)	1.4 (1)

Canadian Paediatric Surveillance Unit
Nutritional rickets 2002-2004
11% cases had fracture.

~20% of rickets present with fracture

Munns et al. *JCEM* 2016; 101(2)
Ward et al. *CMAJ* 2007;177(2)
Moon et al. *Osteoporos Int* 2014; 25(12)

Fracture and Vitamin D

- Simple vitamin D deficiency does not appear associated with increased fracture risk in children with normal or pathological bone
- There are data to suggest increased lifetime risk of fracture in children who had rickets in infancy (n=129) compared to healthy controls (n=411) – 22.5% v 13.5% (p=0.01)

Munns et al. *JCEM* 2016; 101(2)
Gorter et al. *J Clin Res Pediatr Endo* 2016;8(4)
Minkowitz et al. *J Pediatr Orhop* 2017; 37(1)
Contreras et al. *Pediatr Emerg Care* 2014; 30(11)
Moon et al. *Osteoporos Int* 2014; 25(12)

Take Home Messages

- Vitamin D deficiency = 25OHD <30 nmol/L
- Deficient Calcium Intake <300 mg/day
- Rickets (why we supplement with vitamin D)
  - Radiological diagnosis, occurring when low calcium intake is combined with low 25OHD (LCMS)
  - Affects cardiac & skeletal muscle, and bones
  - Features reversible & fully preventable, but long-term sequelae & deaths if untreated
- Supplement
  - ALL infants 1st year of life (400IU, 10μg)
  - ALL pregnant mothers (600 – 1000 IU, 15 - 25μg)
  - ALL risk groups, for life
- Food fortification programs should be considered for high-risk populations

Munns et al JCEM 2016; 101(2)

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Thank you

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kids Westmead

Centre for Children's Bone & Musculoskeletal Health