



Vitamin D in Diabetes and Vascular Health

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Declarations of interest

- Personal pecuniary

 Internis Consultancy
- Non-personal non-pecuniary
 - Director of Manchester SAS Vitamin D laboratory



Overview

- Vitamin D:
 - Physiology
 - Deficiency
- Role of vitamin D in:
 - Diabetes incidence and outcomes
 - CVD incidence and outcomes
 - Mortality
- Conclusions



Vitamin D metabolism





Rickets/Osteomalacia









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Osteomalacia and Vitamin D



Peacock, 1984



What is sufficient vitamin D?



Initial 250HD (nmol/l)

Peacock 1985





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Dietary Reference Intakes fo	r Vitamin D and Ca	alcium	Released: November 30, 2010 Dietary Reference Intakes for Calcium and Vitamin D		
Topics: Food and Nutrition, Public Health					

Threshold of 50 nmol/l (20ng/ml)



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What level do we need?



Deficient <30 nmol/l (12ng/ml) Insufficient Sufficient >50 nmol/l (20ng/ml)

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Vitamin D and Season



Peacock,1984



Problem with sunshine







Hypponen, 2007





Other Effects of Vitamin D

- Bone and Fracture
 - Bone loss
 - Falls
- Vascular Disease
- Diabetes
- Cancer
- Infection
- Inflammation





Other Effects of Vitamin D

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PubMed citations of Diabetes and Vitamin D



Central Manchester University Hospitals

Total = 2838 April 2014



PubMed citations of Cardiovascular Disease and Vitamin D



Total = 3601 April 2014

Diabetes and vitamin D Meta analyses

- 290 cohort studies
- Cohort studies show relationship between 250HD and health outcome

Diabetes – 2 studies:

Diabetes incidence					
Diabetes incidence	2013 (8)§	14	76220	4996	0-62 (0-54-0-70)
Diabetes incidence	2013 (9)§	16	72 204	4877	0-67 (0-60-0-75)

10 studies in common

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CVD and vitamin D Meta analyses

- 290 cohort studies
- Cohort studies show relationship between 250HD and health outcome
- CVD more studies:

Cardiovascular disease incidence and mortality					
Cardiovascular disease	2010 (4)†	5	19376	2417	0-42 (0-28-0-65)
Cardiovascular disease	2011 (5)†	7	27620	2530	0-60 (0-44-0-81)
Cardiovascular disease	2012 (6)†	17	65994	6123	0-66 (0-56-0-77)
Coronary heart disease	2012 (6)	8	33249	1973	0-72 (0-64-0-83)

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Diabetes and vitamin D Intervention meta analysis

- 172 RCTs
- Interventional studies no effect of vit D on same health outcomes
- Diabetes Single study:

Glucose metabolism								
HbA _{ic}	2013¶ (appendix pp 6–7)	16	1491	CO	1-12	20–317	% of total Hb	ES -0·01 (-0·25 to 0·23)

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Diabetes and vitamin D Meta analysis HbA1c

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CVD and vitamin D Intervention meta analyses

- 172 RCTs
- CVD More studies:

Cardiovascular diseases								
Cardiovascular diseases	2010 (1)	4	41346	1976	12-60	10-25	Incidence	RR 0·99† (0·89–1·09)
Myocardial infarction	2011 (2)	6	39 879	1353	1-84	8–25	Incidence	RR 1.02 (0.93-1.13)
Stroke	2011 (2)	6	39 879	1006	1–84	10-25	Incidence	RR 1.05 (0.88–1.25)
Systolic blood pressure	2011 (2)	14	NR	СО	1–84	NR	Change (mm Hg)	ES -0.06 (-1.98 to 1.87
Diastolic blood pressure	2011 (2)	14	NR	СО	1–84	NR	Change (mm Hg)	ES -0·34 (-1·03 to 0·35)
Cardiovascular mortality	2011 (3)	7	41879	1229	1-84	8–35	Deaths	RR 1.02 (0.91–1.13)

Still no effect

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Mortality and vitamin D Meta analysis

Chowdhury, 2014

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Mortality and vitamin D Meta analysis

		No of participants/deaths			
	No of studies	Intervention group	Control group	Relative risk (95% CI)	Relative risk (95% CI)
Trials reporting on vit	amin D ₃ a	alone			
Community dwelling	5	3940/549	3926/601		0.91 (0.81 to 1.01)
Hospital based	9	2886/538	2885/576		0.84 (0.65 to 1.09)
All studies	14	6826/1087	6811/1177		0.89 (0.80 to 0.99)
Trials reporting on vit	amin D ₂ a	alone			
Community dwelling	4	8313/1420	8408/1393		1.05 (0.94 to 1.17)
Hospital based	4	180/20	178/17		1.15 (0.63 to 2.11)
All studies	8	8493/1440	8586/1410	+	1.04 (0.97 to 1.11)
			0	0.5 0.75 1 1.75	2
			V s t	/itamin D Contro supplement bette better	l r

Chowdhury, 2014

BUT

- Prospective study meta analysis included 3 studies using active vitamin D and one looking at exercise and vitamin D
- If they are excluded RR → 0.92 (0.84 - 1.02)
- Must read the small print!

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Trial Sequential Analysis

Bolland 2014

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Summary

- Low vitamin D is common in people:
 - With diabetes
 - With CVD
 - Who are likely to die
- Giving vitamin D doesn't seem to help

Possible Explanation

- Disease
- ↓nutrition
- reduced sunlight exposure

• ↓ 250HD

Other Effects of Vitamin D

- Falls
- Vascular Disease
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- Cancer
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Dietary Reference Intakes for Type: Consensus Study	Vitamin D and Ca	alcium Released: November 30, 2010 Dietary Reference Intakes for Calcium and Vitamin D			

"Only robust evidence is in regards bone disease"

Conclusion

- Low vitamin D levels in diabetes and CVD are probably the result of underlying disease states than their cause
- There is no evidence to indicate any benefit of vitamin D replacement on the incidence or consequences of diabetes or CVD

Vitamin D and Bone Health: A Practical Clinical Guideline for Patient Management

http://www.nos.org.uk/document.doc?id=1352