

Vitamin D Deficiency

Update October 2016

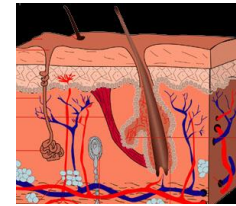
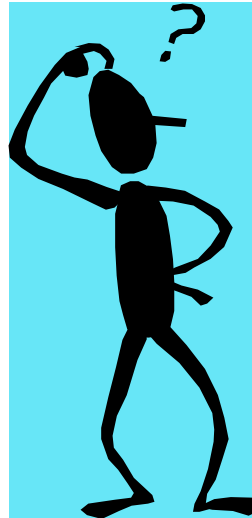
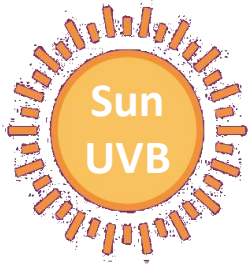


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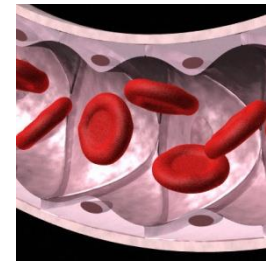
Vitamin D Physiology



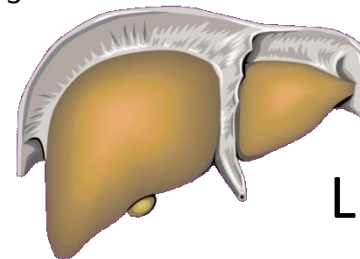
SKIN

7-dehydrocholesterol

Vitamin D₃



BLOOD



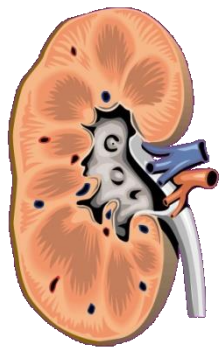
LIVER

25-hydroxyvitamin D₃
(25OHD₃)



PTH

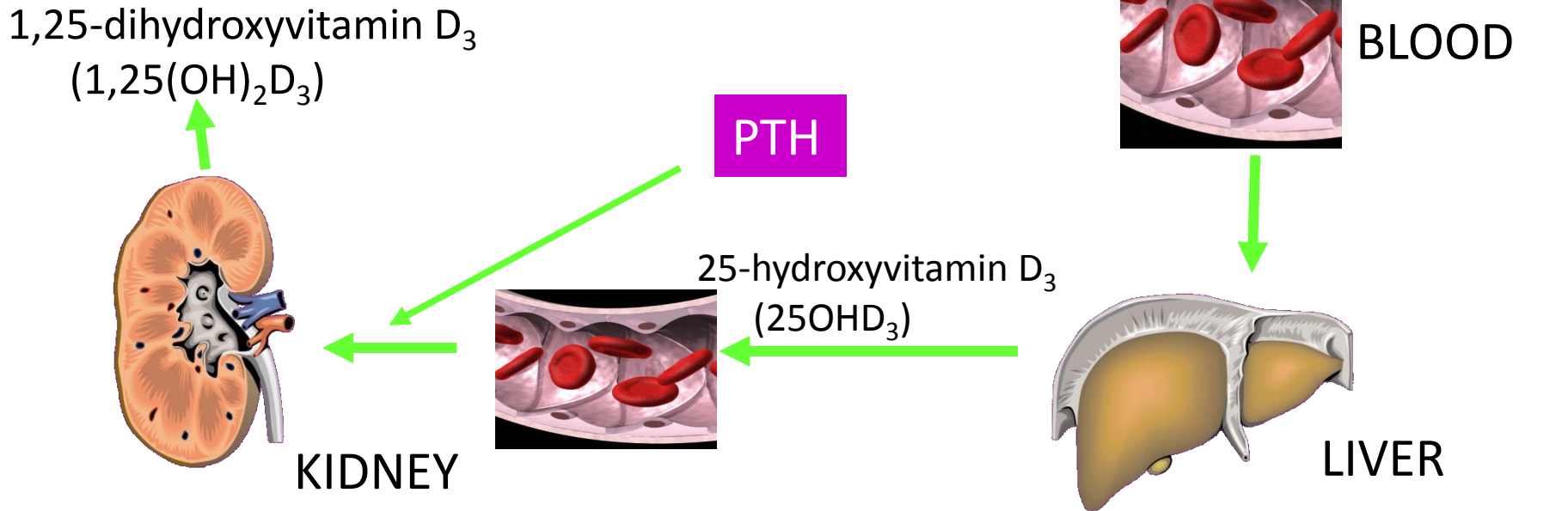
KIDNEY



1,25-dihydroxyvitamin D₃
(1,25(OH)₂D₃)

Diet:

Milk, eggs, fish

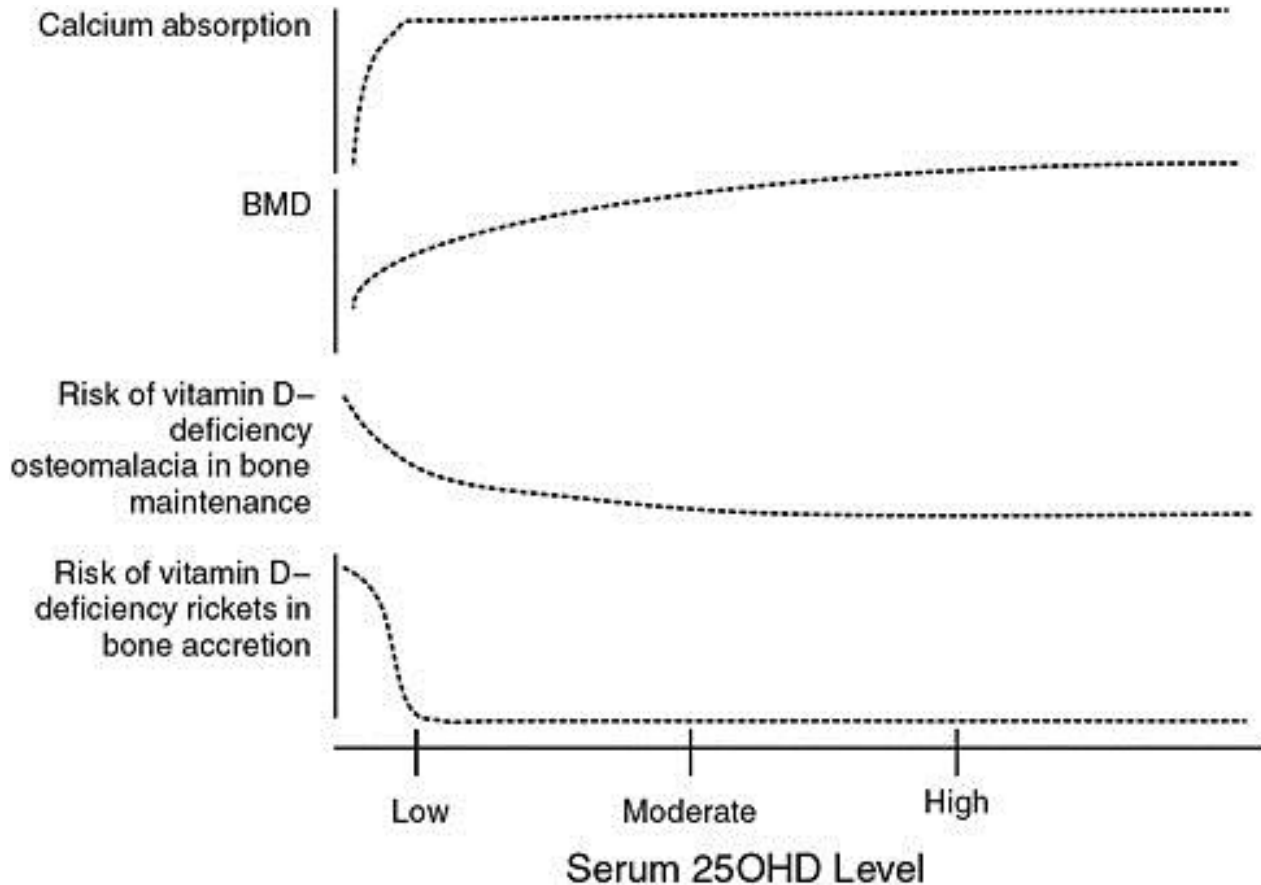


Non Calcaemic Effects of Vitamin D?

- VDR widely expressed
- Numerous observational studies showing association with vitamin D deficiency
 - Malignancies (at least a dozen!)
 - Autoimmune disease (T1DM, RA, MS, etc.)
 - Cardiovascular disease (HT, IHD, etc.)
 - Mortality
- Intrigue, lack of data around causality
- Further research needed

Institute of Medicine

Integrated Bone Health Outcomes and Vitamin D Exposure



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

National Osteoporosis Society Practical Guides

Endorsed by:

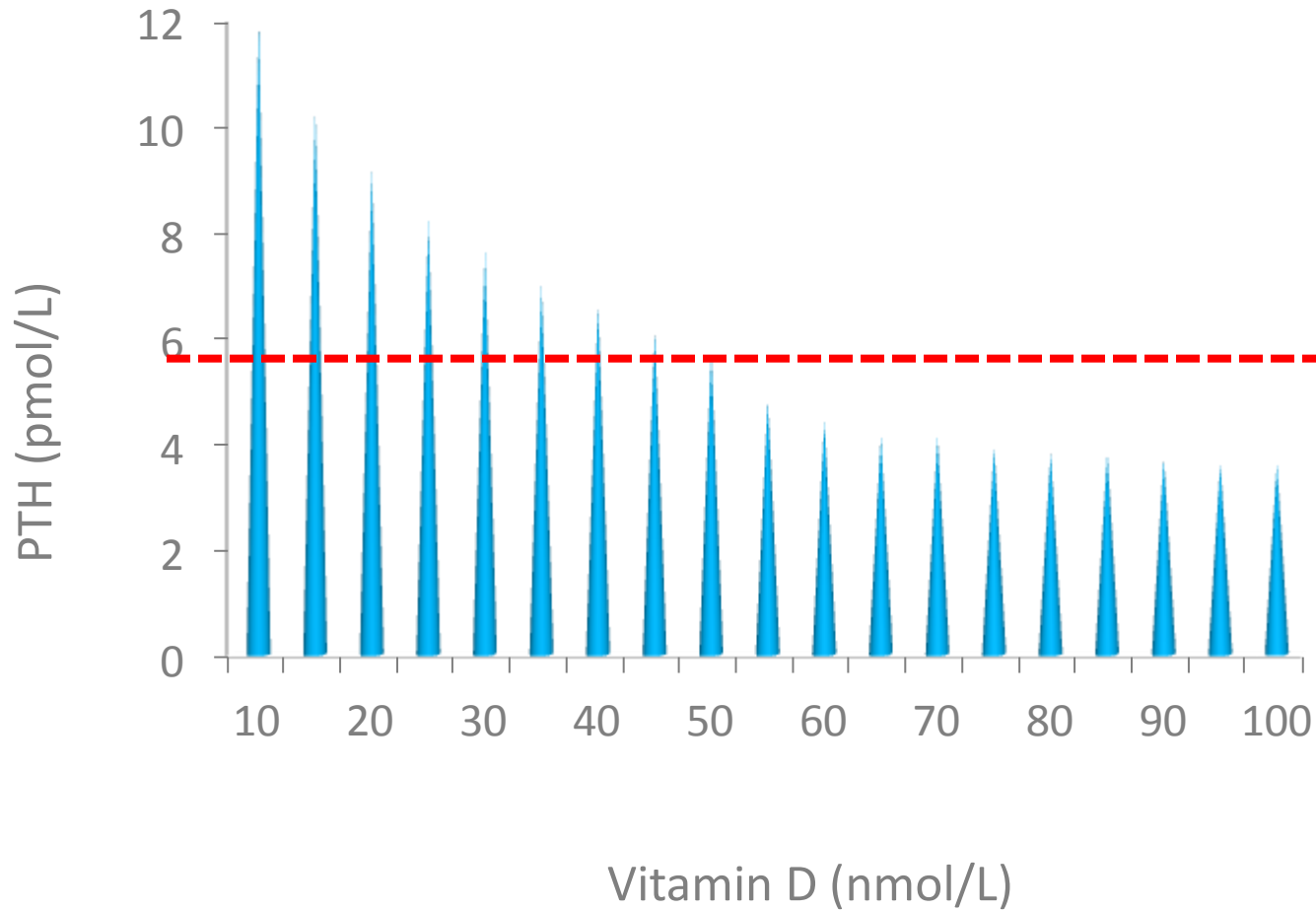


for a breakfree future

How do we define vitamin D deficiency?

- Major controversy
- IOM determined
 - Rickets/osteomalacia not seen if 25OHD >30 nmol/L
 - 25OHD between 30-50 nmol/L
 - Sufficient for bone health in 50% healthy people
 - 25OHD >50 nmol/L
 - Sufficient for bone health in 'majority'
- NOS Guidelines align to IOM
 - 25OHD <30 nmol/L = deficient
 - 25OHD 30-50 nmol/L = may be inadequate in some
 - 25OHD >50 nmol/L = sufficient for majority

Vitamin D and PTH



Rickets/Osteomalacia

- Deficiency of vitamin D
- Rickets when affects *growing* skeleton
- Osteomalacia when affects *adult* skeleton
- Bone unduly *soft* in both situations
- Lack of *mineralisation* of collagen component
- Failure to absorb sufficient calcium from GI tract
- Lack of sunlight/dietary, rarely inherited

Osteomalacia



Bone pain

Myopathy

Increased fracture risk

Increased falls risk

- Low/undetectable 25OH-vitamin D
- High PTH
- High ALP
- Low serum calcium

Vitamin D levels in man past and present



Serum 25OHD measurement is recommended for

- Patients with bone diseases that may be improved with vitamin D treatment
- Patients with bone diseases, prior to specific treatment where correcting vitamin D deficiency is appropriate
- Patients with musculoskeletal symptoms that could be attributed to vitamin D deficiency.

Vitamin D

Public Health v Patient Management

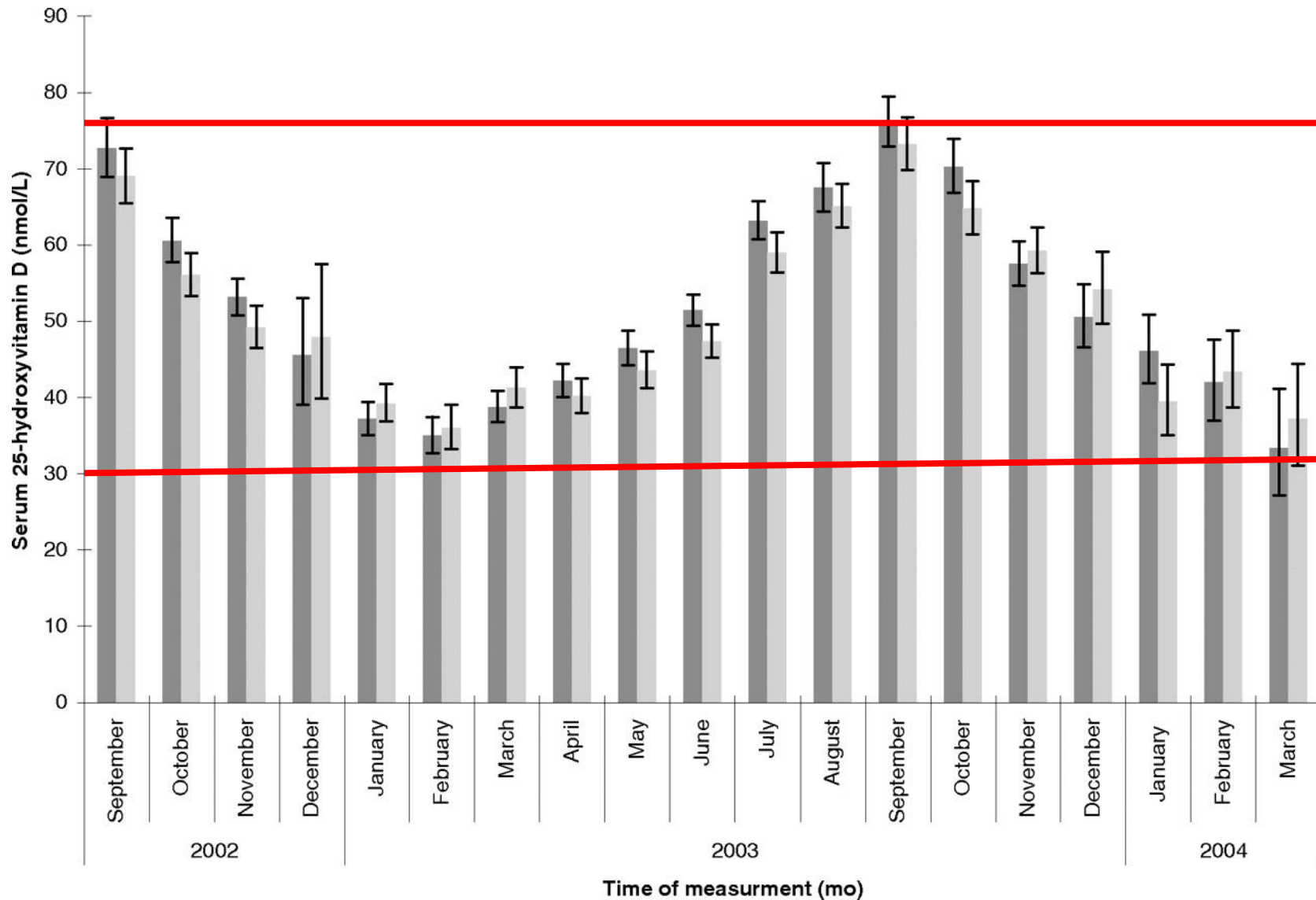
- 15-30% of the adult UK population are vitamin D deficient
- Increases with ethnicity, age and obesity

People at risk of vitamin D deficiency	Daily vitamin D supplement
<ul style="list-style-type: none"> ■ All pregnant and breastfeeding women 	10µg/day=400iU
<ul style="list-style-type: none"> ■ All infants and children from 6 months to 5 years, unless they are drinking 500ml (a pint) or more of infant formula a day at any time during this age range (Infants aged 0–6 months may not need supplements as they should get adequate amounts from breastmilk or infant formula milk. If there is any doubt about the mother's use of vitamin supplements during pregnancy and/or breastfeeding, breastfed infants will benefit from vitamin D supplements from 1 month) 	6 months to 5 years – 7µg/day
<ul style="list-style-type: none"> ■ People who are not exposed to much sun, e.g. people confined indoors for long periods and those who cover their skin for cultural reasons 	10µg/day=400iU
<ul style="list-style-type: none"> ■ People aged 65 years and over 	10µg/day=400iU

Measuring 25OHD

- D2 = plant derived
- D3 = animal & sunlight derived
- Vitamin D rapidly converted to 25OHD
- Total 25OHD best indicator of vitamin D stores
- Measurements in nmol/L (UK) or ng/ml (US)
- HPLC or Tandem MS assays

Geometric mean (95% CI) monthly variation in serum 25-hydroxyvitamin D [25(OH)D] concentrations in men (n = 3725) and women (n = 3712) in the 1958 British birth cohort at age 45 y.



Who do we treat?

- 25OHD <30 nmol/L
- 25OHD 30-50 nmol/L in presence of
 - Fragility #, OP, high # risk
 - Treatment with antiresorptive drug for bone disease
 - Symptoms suggestive of vitamin D deficiency
 - Increased risk of vitamin D deficiency in future due to
 - E.g. reduced UV
 - Raised PTH
 - Anti-epileptic drugs or glucocorticoids
 - Malabsorption

How do we treat?

- Use adequate dose to correct deficiency
- *Timely* reversal of clinical consequences of vitamin D deficiency
- Avoid toxicity (rare, >10,000 IU/d)
- D3 preferential to D2 but D2 acceptable
 - D2 quicker clearance
 - D2 lower bioavailability
- Oral preferred to IM (not recommended)
 - Bioavailability (inter-individual variability)
 - Slower repletion

Practical dosing

- Where rapid correction of vitamin D is required
 - Symptomatic
 - Prior to potent antiresorptive treatment
 - Up to 300,000 IU in divided doses
 - 50,000 IU capsules once weekly 6/52 (300,000 IU)
 - 20,000 IU capsules two weekly 7/52 (280,000 IU)
 - 800 IU capsules 5/d for 10/52 (280,000 IU)
- » *Not Combined Ca/D preparations*
- Maintenance
 - Consider 1/12 after loading
 - 800 – 2,000 (<4,000) IU/d
 - May be all that is required if no ‘urgency’ to correction

Do not use calitriol/alfacalcidol

Vitamin D dose requirements for fracture prevention



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ORIGINAL ARTICLE

A Pooled Analysis of Vitamin D Dose Requirements for Fracture Prevention

Heike A. Bischoff-Ferrari, M.D., Dr.P.H., Walter C. Willett, M.D., Dr.P.H., Endel J. Orav, Ph.D., Paul Lips, M.D., Pierre J. Meunier, M.D., Ronan A. Lyons, M.D., M.P.H., Leon Flicker, M.D., John Wark, M.D., Ph.D., Rebecca D. Jackson, M.D., Jane A. Cauley, Dr.P.H., Haakon E. Meyer, M.D., Ph.D., Michael Pfeifer, M.D., Kerrie M. Sanders, Ph.D., Hannes B. Stähelin, M.D., Robert Theiler, M.D., and Bess Dawson-Hughes, M.D.

N Engl J Med 2012; 367:40-49 | [July 5, 2012](#)

30% reduction in hip fractures

14% reduction in non-vertebral fractures

...our data suggest that high-dose vitamin D supplementation (≥ 800 IU per day) may reduce the risk of hip fracture in persons 65 years of age or older, independently of type of dwelling, age, and sex...

Monitoring and follow up

- Routine monitoring of 25OHD is not recommended
 - Consider repeat if symptoms/malabsorption
 - Not before 3/12
- Check serum calcium 1/12 after loading
 - To check for (unmasked) primary hyperparathyroidism
- 800-1,000 IU vitamin D/d should increase 25OHD by ~25 nmol/L over 3 months

Licensed vs unlicensed vitamin D

- MHRA – ‘do not use unlicensed product where licensed product exists’
- Quality issues
 - 17-170% stated dose
- Licensed in the UK
 - Fultium-D3[®] (Internis)
 - Desunin[®] (Meda)
 - InVita D3[®] (Consilient)

Update

Latest advice for medicines users

Off-label or unlicensed use of medicines:
prescribers' responsibilities

Article date: April 2009

A licensed medicine meets acceptable standards of efficacy, safety, and quality

Summary

- Much confusion around vitamin D
 - Target levels, non-classical effects, public health v disease, etc.
- Strongest evidence around bone health
- Problems with vitamin D preparations
- Multiple disparate guidelines in use
- National guidelines
 - Clarify good practice
 - Pragmatism in absence of good evidence