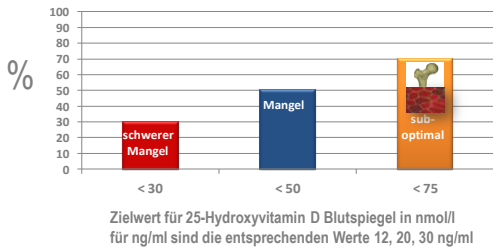


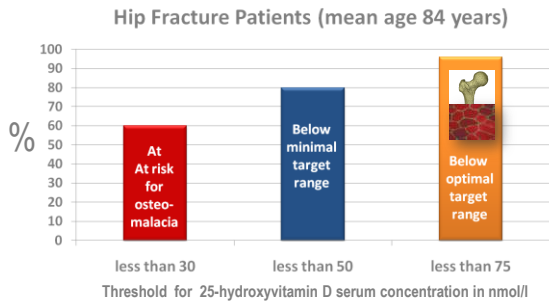
Ausgangslage:
 Erwachsene in Europa
 2010 EU-Parlament



http://www.ccm.be/news_eurnews.php?id=1119
 van der Wielen RP, et al. Serum vitamin D concentrations among elderly people in Europe. Lancet 1995;346:207-10 (SENECA).
 Burnand B, Burchardt P et al. Serum 25-hydroxyvitamin D: Swiss population. Am J Clin Nutr 1992;56:537-42.



Hüftbruchpatienten



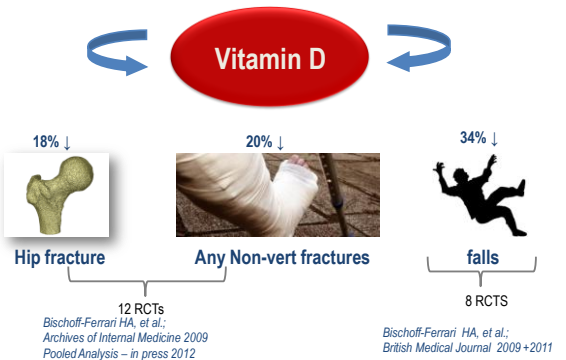
Bischoff-Ferrari HA, Staehelin HB, Theiler R et al.; Severe Vitamin D Deficiency in Swiss Hip Fracture Patients; Bone 2008

KINDER in Deutschland - KIGGS


Verteilung für 25-Hydroxy-Vitamin-D (Calcidol) im Serum [nmol/l] mit Median (Med) und 90. Perzentilbereich (p5, p95)

Altersgruppe Jahre	Jungen		Mädchen		Gesamt	
	Med	p5-p95	Med	p5-p95	Med	p5-p95
1-2	63,6	20,5-119,0	59,8	19,4-114,0	61,9	19,4-115,0
3-6	44,0	13,9-97,4	44,1	16,1-93,6	44,1	15,0-95,8
7-10	42,9	15,2-90,8	40,3	14,1-86,9	41,7	14,8-89,1
11-13	39,6	14,9-87,9	35,7	9,0-74,5	38,0	12,7-80,9
14-17	36,8	11,9-88,8	41,1	13,5-104,0	39,3	12,3-96,3
Gesamt	42,4	14,1-96,2	41,4	13,8-96,4	41,9	13,9-96,3
Migrant	35,5	10,1-89,7	34,2	8,0-94,1	34,8	8,9-92,5
Nicht-Migrant	43,9	15,1-97,2	42,9	15,4-97,0	43,5	15,2-97,2

Evidenz von randomisierten Doppelblind Studien



Warum?

- 

Main Source of Vitamin D

 - We expose less than 5% of our skin to the sun + we wear sunscreen
 - Very little vitamin D production from November to May in all of Europe
 - Vitamin D production in the skin decreases 4 times with age
 - Seniors avoid the sun: lowest levels in the Mediterranean (SENECA study)

2. Nutritional sources of vitamin D are limited

- not enough  in the sea

Chen TC, Holick MF, et al. Factors that influence the cutaneous synthesis and dietary sources of vitamin D. Arch Biochem Biophys 2007;8:8.



Neue Richtlinien 2011 Unterschiede



IOM

- Zielwert Serum Spiegel = 50 nmol/l

IOF / Endo Society

- Zielwert Serum Spiegel = 75 nmol/l



Neue Richtlinien 2011 Gemeinsamkeiten



IOM / IOF / Endo Society

- Empfehlen generell ab 70 Jahren 800 IU Vitamin D am Tag

- IOF bereits ab 60 Jahren 800 IU Vitamin D am Tag

Monitoring

TABLE 2. Indications for 25(OH)D measurement (candidates for screening)

Rickets
Osteomalacia
Osteoporosis
Chronic kidney disease
Hepatic failure
Malabsorption syndromes
Cystic fibrosis
Inflammatory bowel disease
Crohn's disease
Bariatric surgery
Radiation enteritis
Hyperparathyroidism
Medications
Antiseizure medications
Glucocorticoids
AIDS medications
Antifungals, e.g. ketoconazole
Cholestyramine
African-American and Hispanic children and adults
Pregnant and lactating women
Older adults with history of falls
Older adults with history of nontraumatic fractures
Diseases in children and adults (BMI > 30 kg/m ²)
Granuloma-forming disorders
Sarcoidosis
Tuberculosis
Histoplasmosis
Coccidiomycosis
Berylliosis
Some lymphomas

Evaluation, Treatment, and Prevention of Vitamin D Deficiency: an Endocrine Society Clinical Practice Guideline

Michael F. Holick, Neil C. Binkley, Heike A. Bischoff-Ferrari, Catherine M. Gordon, David A. Hanley, Robert P. Heaney, M. Hassan Murad, and Conrad M. Weaver
Boston University School of Medicine (M.F.H.), Boston, Massachusetts 02118; University of Wisconsin (N.C.B.), Madison, Wisconsin 53706; University Hospital Zurich (H.A.B.), CH-8091 Zurich, Switzerland; Children's Hospital Boston (C.M.G.), Boston, Massachusetts 02115; University of Calgary Faculty of Medicine (D.A.H.), Calgary, Alberta, Canada T2N 1N6; Creighton University (R.P.H.), Omaha, Nebraska 68178; Mayo Clinic (M.M.), Rochester, Minnesota 55905; and Purdue University (C.M.W.), West Lafayette, Indiana 47907

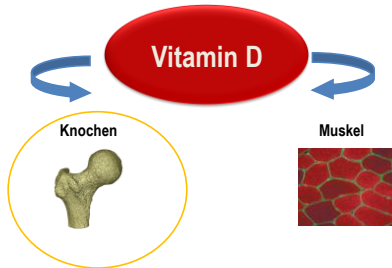
J Clin Endocrinol Metab, July 2011, 96(7)

Wann soll man 25(OH)D Spiegel messen?

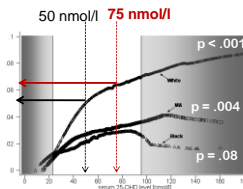
- kein Screening tool
- Endocrine Society definiert Indikationen



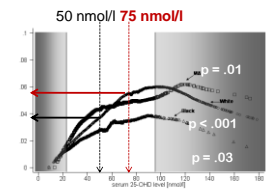
EPIDEMIOLOGY: positive association between 25(OH)D status and hip BMD in 13,432 individuals in NHANES III



Younger adults (ages 20 to 49)



Older adults (age ≥50)

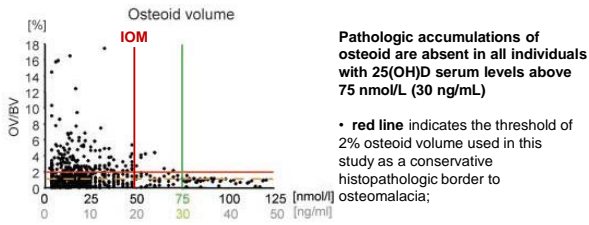


Serum 25-hydroxyvitamin D in nmol/l

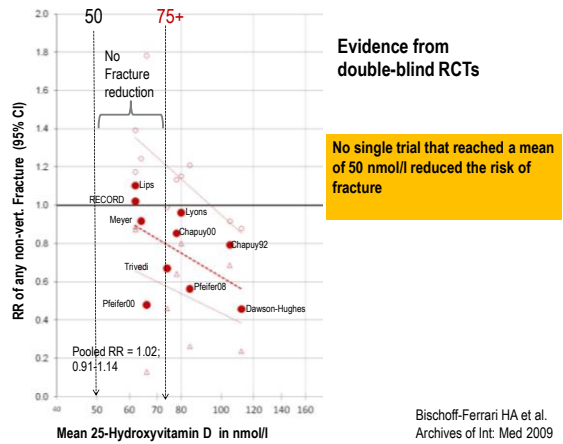
Adjustments: sex, age, BMI, smoking, daily calcium intake, and estrogen use

Bischoff-Ferrari HA, et al. Am J Med 2004

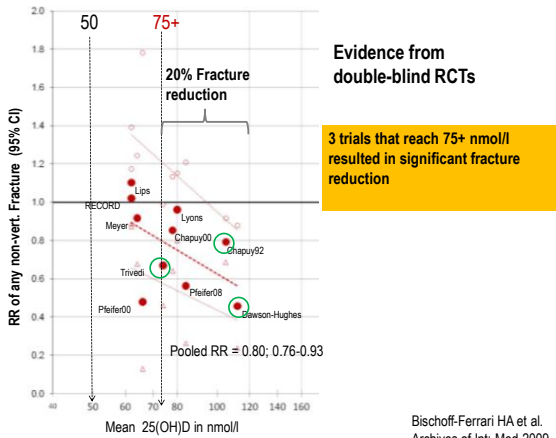
25(OH)D level for optimal mineralization
675 iliac crest bone biopsies



Priemel et al.; JBMR 2010



Bischoff-Ferrari HA et al. Archives of Int. Med 2009



Bischoff-Ferrari HA et al. Archives of Int. Med 2009

D – Risiko?



Benefit/Risk assessment based on clinical studies 2010
10,000 IU / day

2010 IOM recommendations
Safe upper intake = 4000 IU / day

Bischoff-Ferrari HA, Shao A, Dawson-Hughes B, Giovannucci E, Willett WC; Benefit-Risk Assessment of Vitamin D; OP International 2010



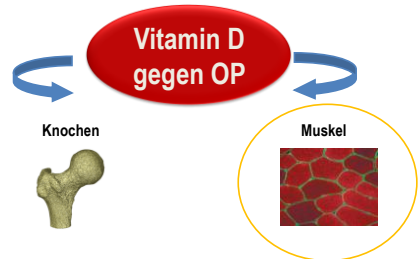
A large dose of vitamin D once a year is not recommended

- 500'000 IU D3 orally once a year (Australia)
- Double-blind, placebo-controlled trial of 2256 community-dwelling women, aged 70 years or older, considered to be at high risk of fracture
- RR for fracture in the vitamin D group was 1.26 (95% CI, 1.00-1.59)
- A temporal pattern in a post hoc analysis of falls.
 - RR of falling in the vitamin D group vs the placebo group was 1.31 in the first 3 months after dosing and 1.13 during the following 9 months (test for homogeneity; $P = .02$)

Why?

- down-regulation of 1,25(OH)2D
- less down time by better function and less infections

Sanders K et al. JAMA 2010





Vitamin D – Muscle Link

- (1) Severe deficiency -- Myopathie
- (2) VDR present in muscle
(Bischoff-Ferrari, JBMR 2004)
- (1) Type II muscle fibre atrophy in biopsies of patients with severe deficiency
 - Fast twitch
 - First to recruit for fall prevention
- (4) Two small studies demonstrate increase in relative number and size of type II fibers

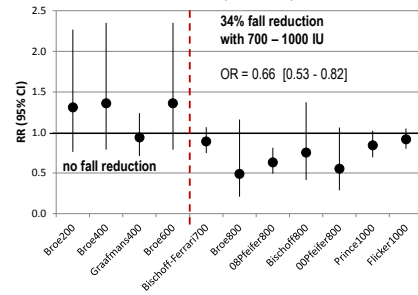


after treatment with 1-alpha vitamin D (3 mo)
(Soerensen OH et al. Clin Sci 1979)
after treatment with 1000 IU D2 (2 yrs)
(Sato et al. 2005; Cerebrovasc Dis)



Meta-Analysis of double-blind RCTs of vitamin D and fall reduction

8 RCTs (n = 2426)



Trial and treatment dose of vitamin D in IU per day

Bischoff-Ferrari et al. BMJ 2009 and 2011

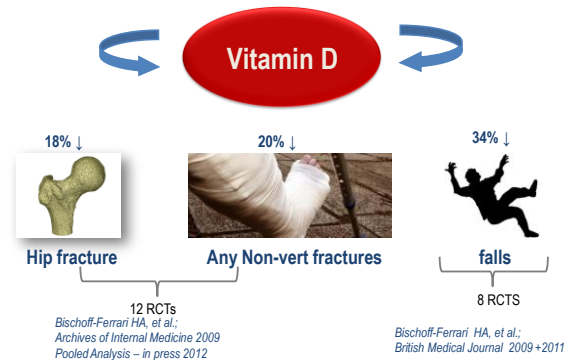
Clinical Guidelines



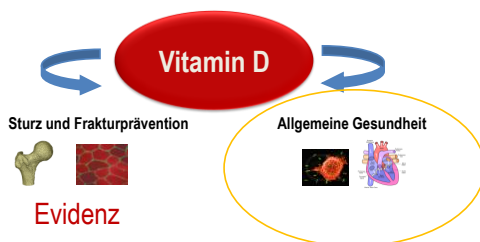
All institutions but the IOM identified vitamin D as an effective strategy in fall prevention – based on the same evidence

- 2011 assessment of the Agency for Healthcare Research and Quality (AHRQ) for the U.S. Preventive Services Task Force
- 2011 US Endocrine Society task force on vitamin D
- 2010 American Geriatric Society/British Geriatric Society Clinical Practice Guideline
- 2010 Position Statement on Vitamin D by IOF

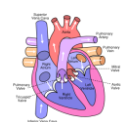
Evidenz von randomisierten Doppelblind Studien



Small clinical trials, mechanistic and large cohort studies suggest benefit of vitamin D on cardio-vascular health



Large clinical trials needed to confirm such benefits



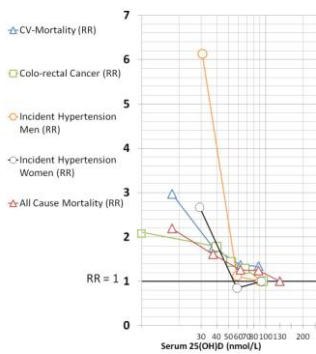
Mouse without the VDR: has hypertension and dies from heart failure

Small clinical trials in humans: UVB-irradiation or 800 IU vitamin D reduces blood pressure by about 6 mmHG

Large cohort studies: vitamin D levels of at least 75 nmol/l compared to levels below 36 nmol/l
6-fold lower risk of hypertension among men
3-fold lower risk among women
2.5-fold lower risk of myocardial infarction

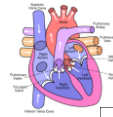
*Giannuzzi E et al. Archives of Int. Med. 2008; Pfleger M et al. J Clin Endocrinol Metab. 2007; Krause et al. The Lancet 1998
Bouillon R, Bischoff-Ferrari H, Willett W. JBMR 2008; Erdo I et al. Endocrinology 2003*

Serum 25-hydroxyvitamin D concentrations of 75 - 110 nmol/l confer the lowest risk for

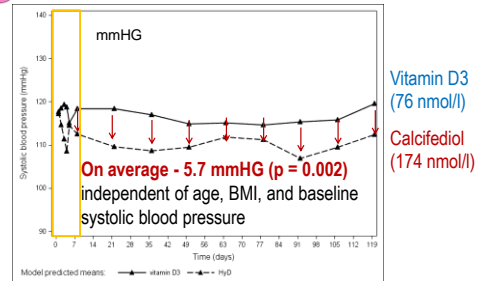


.... cardiovascular disease, mortality, and colo-rectal cancer with a 2-6 fold decreased risk compared to levels < 30 nmol/l

Bischoff-Ferrari HA et al.
Benefit Risk Assessment of Vitamin D
(Osteoporosis International 2010).



Calcifediol versus D3 effects on blood pressure



Bischoff-Ferrari HA, Dawson-Hughes B et al.; JBM 2011

Zusammenfassung

- **Vitamin D Supplementation zur Osteoprose / Sturz Prävention:**
 - Evidenz-basiert
 - 800 IU Vitamin D / Tag – 20% Risikoreduktion
 - Wichtiger Doppeleffekt: Knochen + Muskel
 - Einnahme täglich, wöchentlich oder monatlich
 - Optimaler Blutwert: 75 nmol/l (30 ng/ml) Vitamin
- **Weitere Wirkungen sind bisher in grossen Interventionsstudien NICHT bewiesen:**
 - Grosse Kohortenstudien weisen darauf hin, dass ein Vitamin D Mangel möglicherweise das Risiko für CV – Erkrankungen / Infekte / Immunerkrankungen erhöht



VIELEN DANK !!