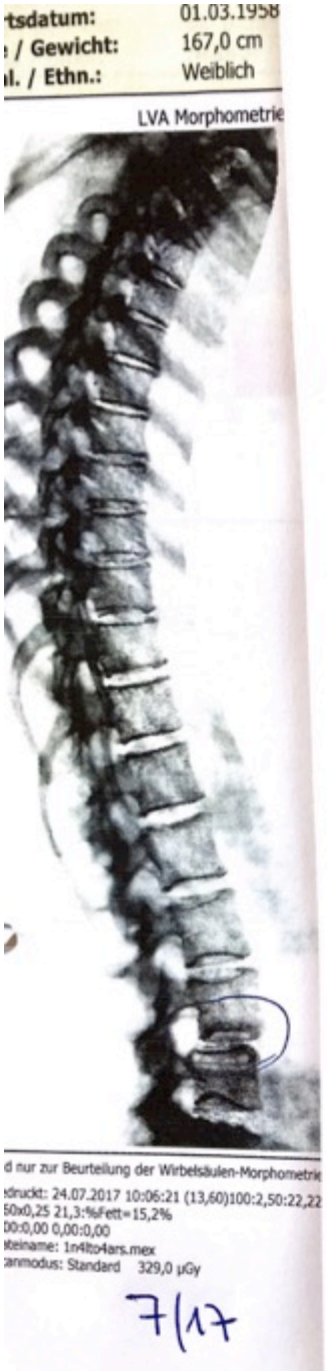
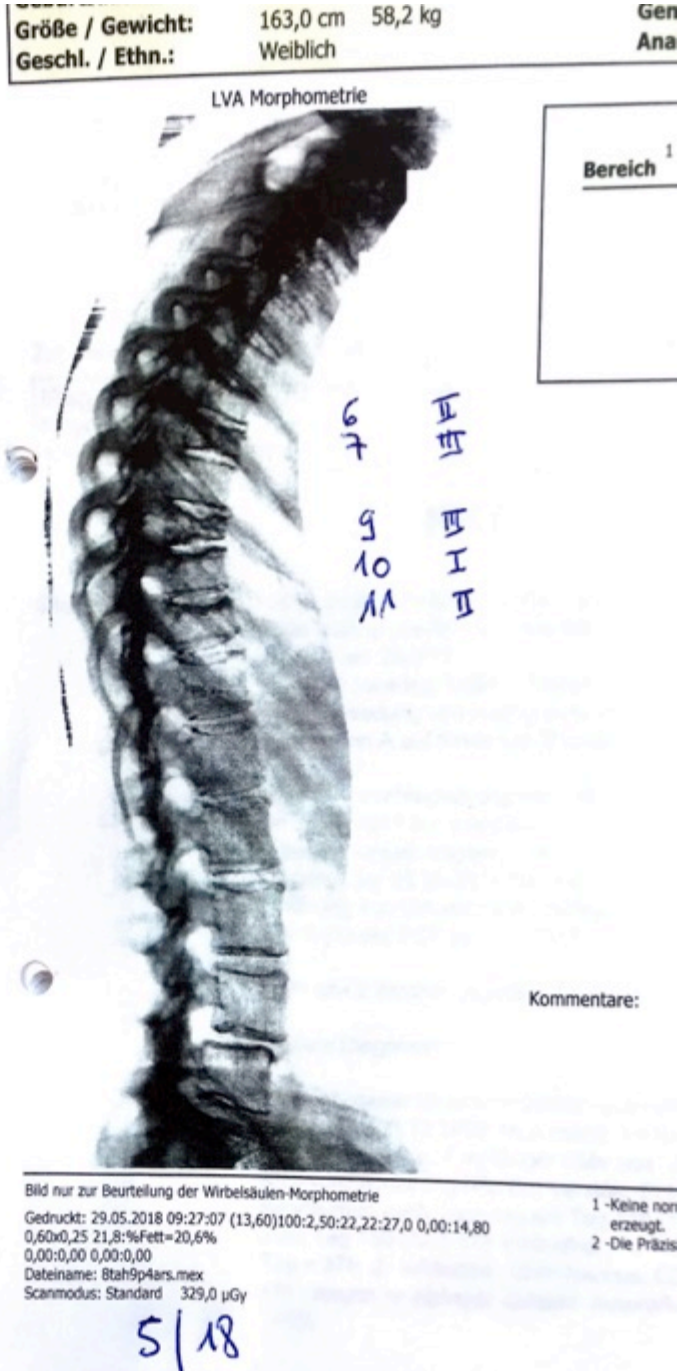
ERNÄHRUNG UND VITAMIN D IN DER OSTEOPOROSE

PD Dr. Karin Amrein, MSc
Hormoninstitut Dobnig
Abt. für Endokrinologie & Diabetologie
Medizinische Universität Graz

OSTEO-POROSE

DICHTE VS. FRAKTUR





20. OKTOBER = OSTEOPOROSETAG

- Laut WHO zählt die Osteoporose weltweit zu den 10 häufigsten Erkrankungen.
- Alle 30 Sekunden erleidet jemand in Europa einen Knochenbruch durch Osteoporose!
- ca. jede 3. Frau und jeder 5. Mann erleidet statistisch einen Knochenbruch durch Osteoporose.
- In Österreich gibt es ca. 500.000 Betroffene. davon sind ungefähr 390.000 Frauen betroffen und ca. 90.000 Männer.
- 51% der betroffenen Frauen und 52% der betroffenen Männer erhalten keine Therapie, da Ihre Erkrankung nicht erkannt wird.
- Osteoporose ist keine "Frauenkrankheit“, mehr Männer als bisher angenommen sind davon betroffen.

https://www.aktiongesundeknochen.at

ÜBERBLICK

- CALCIUM
- PHOSPHAT
- PROTEIN
- VITAMIN D
- VITAMIN K2
- (UNTER) ERNÄHRUNG, ANOREXIE
- ZÖLIAKIE, DIABETES 1, DIABETES 2

Review

Women's Health

Nutrition and bone health in women after the menopause

Osteoporosis affects one out of three postmenopausal women. Their remaining lifetime risk of fragility fractures exceeds that of breast cancer. The risk of osteoporosis and/or fragility fractures can be reduced through healthy lifestyle changes. These include adequate dietary intakes of calcium, vitamin D and protein, regular weight-bearing exercise, reduction in alcohol intake and smoking cessation. European guidance for the diagnosis and management of osteoporosis in postmenopausal women recommends a daily intake of at least 1000 mg/day for calcium, 800 IU/day for vitamin D and 1 g/kg body weight of protein for all women aged over 50 years. The development of programs that encourage lifestyle changes (in particular balanced nutrient intakes) are therefore essential for the reduction of osteoporosis risk.

René Rizzoli*[,1],
Heike Bischoff-Ferrari[2,3,4],
Bess Dawson-Hughes[5]
& Connie Weaver[6]

[1]Division of Bone Diseases, Department of Internal Medicine Specialties, Geneva University Hospitals & Faculty of Medicine, Geneva, Switzerland
[2]Geriatric Clinic, University Hospital Zurich, Zurich, Switzerland
[3]Centre on Aging & Mobility, University of Zurich, Switzerland

Rizzoli R Women's Health 2014

CALCIUM

- BEDARF
- SPIEGEL
- RACHITIS/OSTEOMALAZIE
- MYOKARDINFARKT???

IST DIESE PERSON AUSREICHEND MIT CALCIUM VERSORGT?

Ca Spiegel **2,6** mmol/l

Referenzwert: 2,0-2,7 mmol/l

Calcium-Slides: Danke, Maya Thun www.dieinternistin.at

IST DIESE PERSON AUSREICHEND MIT CALCIUM VERSORGT?

Ca-Spiegel

Gibt **KEINE Auskunft** über

Calcium Versorgung durch die Nahrung

Zur **Erhaltung der Calcium Spiegel (Homöostase)** spielt Parathormon und **Vitamin D +** Knochen eine Rolle

Ziel: Calcium Spiegel stabil halten !

Mannstadt M Nat Rev. 2017

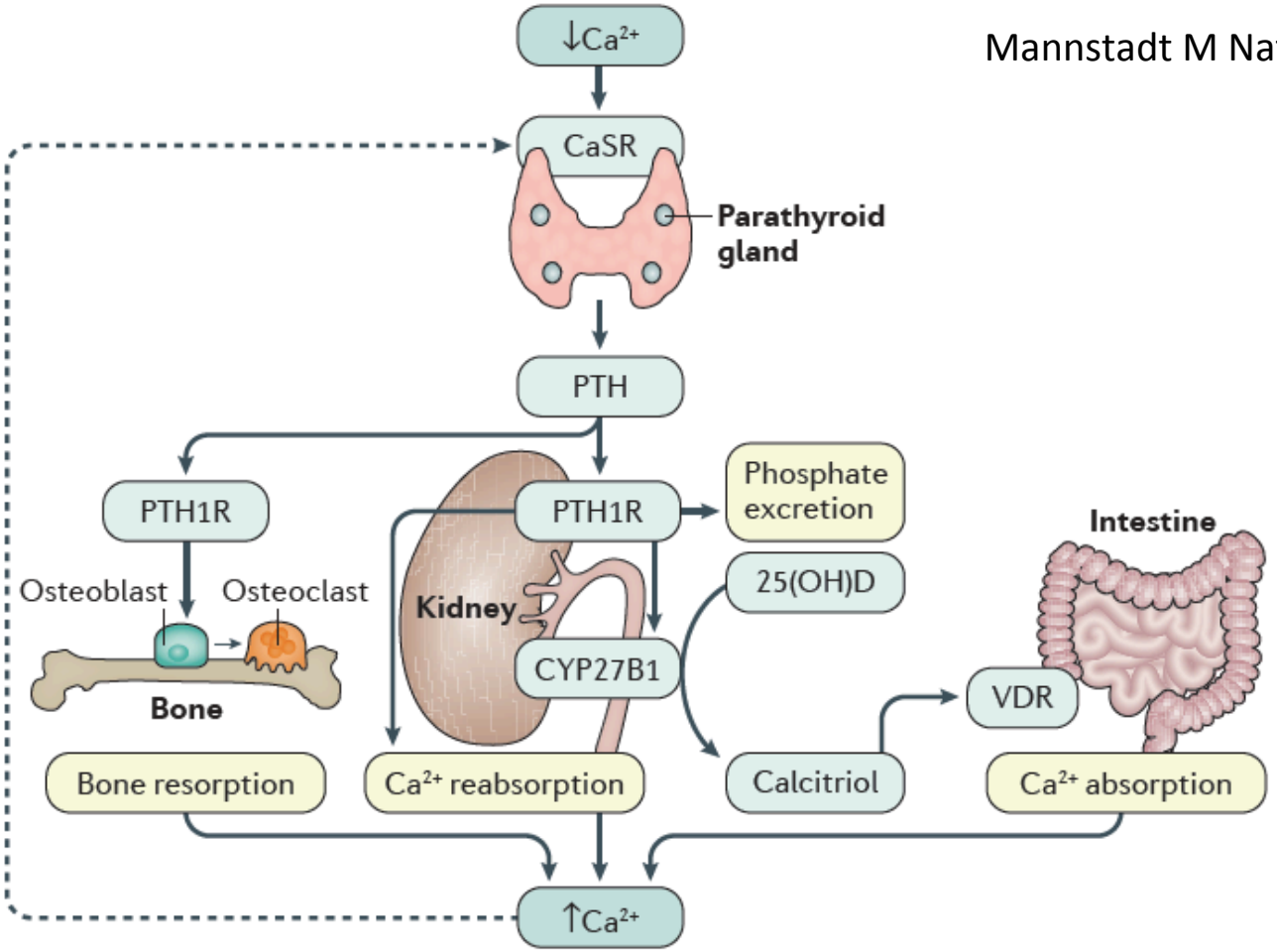


Figure 1 | **Regulation of extracellular calcium homeostasis.** Reduced activation of the extracellular calcium-sensing receptor (CaSR) owing to a reduction in extracellular calcium levels results in a rapid increase in parathyroid hormone (PTH) secretion.

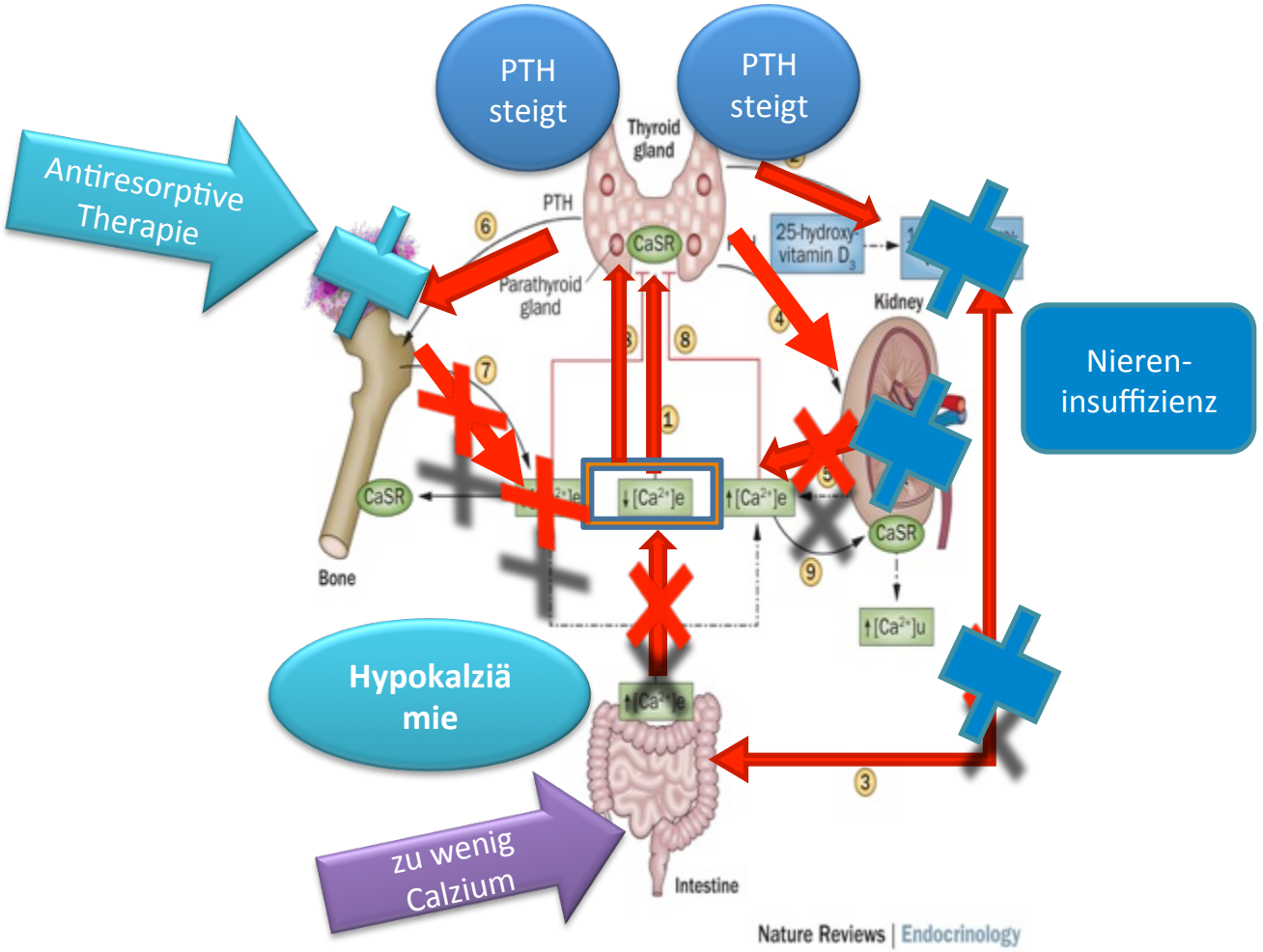
Ziel: Calcium Spiegel stabil halten !

HOMÖOSTASE BEZEICHNET DIE **AUFRECHTERHALTUNG** EINES **GLEICHGEWICHTSZUSTANDES** EINES OFFENEN DYNAMISCHEN SYSTEMS DURCH EINEN **INTERNEN REGULIERENDEN PROZESS**

WARUM IST DAS IN DER OSTEOLOGIE SO WICHTIG ?

In der Anwendung der **anti-resorptiven Therapie** ist die **Calcium Homöostase** auschlaggebend !

CALCIUM, VITAMIN D, PARATHORMON, ANTIRESORPTIVE THERAPIE



BEKOMMT DIESE PERSON AUSREICHEND CALCIUM ?

Ca Spiegel **2,1** mmol/l

Referenzwert: 2,0-2,7 mmol/l

BEKOMMT DIESE PERSON AUSREICHEND CALCIUM ?

Ca-Spiegel

Gibt KEINE Auskunft über

Calcium Versorgung durch die Nahrung

Bei Gesamt-Calcium Bestimmung spielt **Albumin** eine Rolle

Calcium (**Gesamt Ca/ionisiertes Ca**) Bestimmung

Gesamt-Calcium:

- Die Calcium-Konzentration im Serum wird durch das Gesamtprotein (insb. Albumin) stark beeinflusst.
- Ein **Abfall von Albumin** um **1g/dl** -**Erniedrigung des Gesamt-Ca** um **1mg/dl (0.25 mmol/l).**

- **Ionisiertes Calcium:**
  - besserer Indikator des Ca-Status = biologisch aktive Form

CALCIUM/ALBUMIN KORREKTUR RECHNER

Korrigiertes Ca (mmol/l)=

Calcium-Korrektur

= **Gemessenes Ca** (mmol/l) - 0.025 x Albumin (g/l) + 1.0

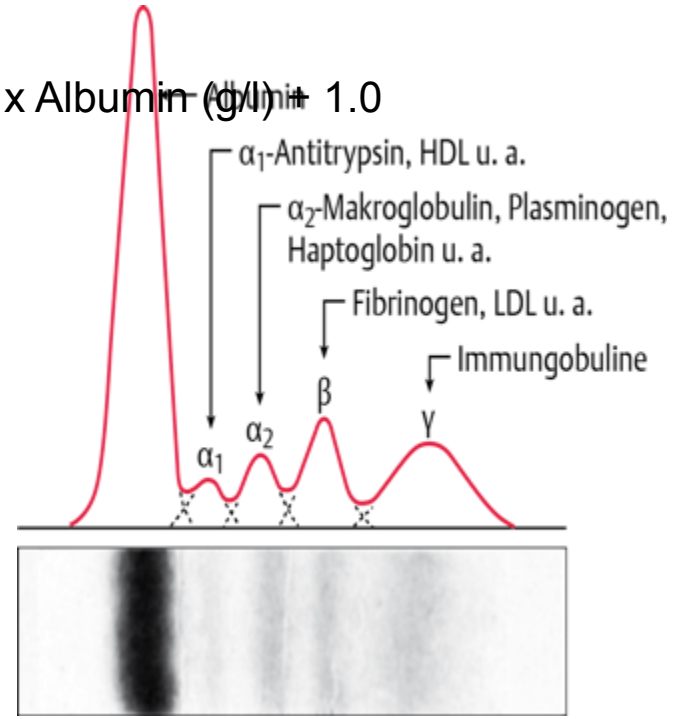
Korrektur des Serum-Calcium

Das Blut-Calcium liegt zu mehr als 50 % an Eiweiß, vor allem Albumin gebunden vor.

Calcium [Serum]:	2,1	[mmol/l]
Albumin [Serum]:	27	[g/l]

Berechnen Zurücksetzen

Korrigiertes Calcium:	2.42	[mmol/l]

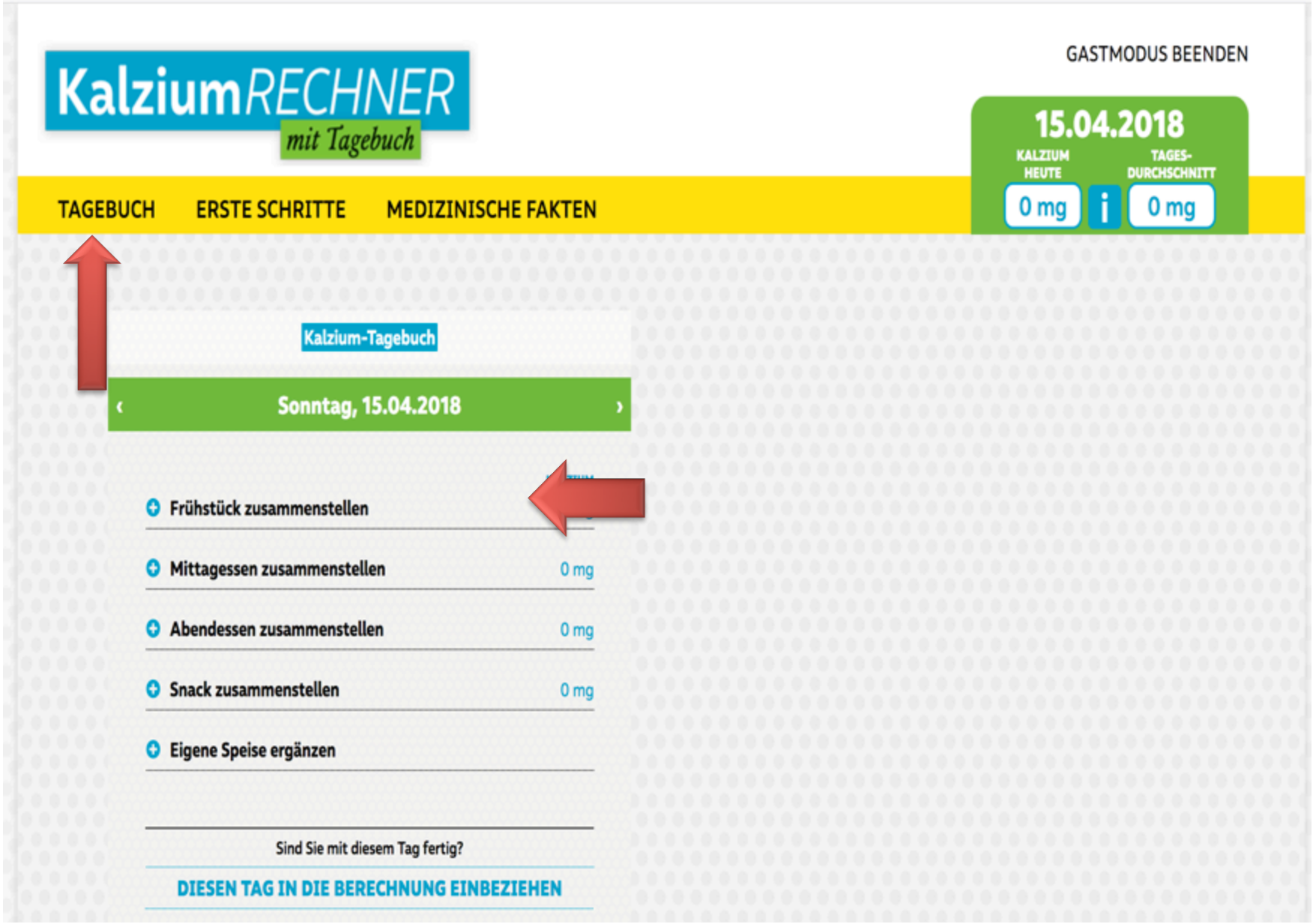


Payne RB, Little AJ, Williams RB, Milner JR.*nterpretation of serum calcium levels in patients with abnormal serum proteins*
Br Med J1973; 4: 643-646

ÄRZTIN: 40 LJ, 172CM, 47KG, ZÖLIAKIE, LAKTOSE-INTOLERANZ

- Frühstück:
  - ¼ l Joghurt laktosefrei, Obstsalat, Scheibe glutenfreies Brot
- Mittagessen:
  - Zander,-gebraten, Karotten, glutenfreies Weckerl, Portion Reis
- Abendessen:
  - Apfel
- Zwischendurch: 0
- Getränke:
  - 2x ¼ Liter Kaffee ohne Milch
  - 1,8 Liter Mineralwasser


Meistbesucht
Erste Schritte
http://cdn.yoox.biz/...
ICD-10 2010 Suche ...
sonderklasse
Co-Pro RemS2 - Ko...
Austria Codex Online
Erstattungskodex
Universitätsbibliothe...
Login-JSP
DFP-Kalend
KalziumRECHNER
mit Tagebuch
TAGEBUCH
ERSTE SCHRITTE
MEDIZINISCHE FAKTEN
Willkommen beim Kalzium-Tagebuch.
Auf dieser Website können Sie einfach und schnell
Ihre tägliche Kalzium-Zufuhr dokumentieren.
Die Ergebnisse können Sie anschließend
direkt mit Ihrem Arzt besprechen.
Um Ihre Eingaben speichern zu können,
müssen Sie sich bitte registrieren.
Mit
österreichischem
Speisezettel
E-MAIL ADRESSE
PASSWORT
PASSWORT VERGESSEN?
ANMELDEN
ODER
MIT FACEBOOK ANMELDEN
MIT GOOGLE ANMELDEN
REGISTRIEREN
GASTZUGANG


KalziumRECHNER
mit Tagebuch
GASTMODUS BEENDEN
15.04.2018
KALZIUM HEUTE
TAGES-DURCHSCHNITT
0 mg
i
0 mg
TAGEBUCH
ERSTE SCHRITTE
MEDIZINISCHE FAKTEN
Kalzium-Tagebuch
‹
Sonntag, 15.04.2018
›
Frühstück zusammenstellen
Mittagessen zusammenstellen
0 mg
Abendessen zusammenstellen
0 mg
Snack zusammenstellen
0 mg
Eigene Speise ergänzen
Sind Sie mit diesem Tag fertig?
DIESEN TAG IN DIE BERECHNUNG EINBEZIEHEN

GASTMODUS BEENDEN

15.04.2018

KALZIUM HEUTE 0 mg

TAGES-DURCHSCHNITT 0 mg

TAGEBUCH ERSTE SCHRITTE MEDIZINISCHE FAKTEN

Kalzium-Tagebuch

‹ Sonntag, 15.04.2018 ›

	KALZIUM
Frühstück zusammenstellen	0 mg
Mittagessen zusammenstellen	0 mg
Abendessen zusammenstellen	0 mg
Snack zusammenstellen	0 mg
Eigene Speise ergänzen	

Sind Sie mit diesem Tag fertig?

DIESEN TAG IN DIE BERECHNUNG EINBEZIEHEN

Mahlzeit zusammenstellen

Obstsalat

Frühstück | Mittagessen | Abendessen | Snack | Alle

Vorschläge

Obstsalat — 22,5 mg Kalzium/Portion

KalziumRECHNER mit Tagebuch

GASTMODUS BEENDEN

15.04.2018

KALZIUM HEUTE 23 mg | TAGES-DURCHSCHNITT 0 mg

TAGEBUCH ERSTE SCHRITTE MEDIZINISCHE FAKTEN

Mahlzeit zusammenstellen

obstsalat

Frühstück | Mittagessen | Abendessen | Snack | Alle

Vorschläge

Obstsalat 22,5 mg Kalzium/Portion

Mahlzeit zusammenstellen

Obstsalat

22,5 mg Kalzium/Portion

Portionsgröße 1 Portion (150g)

Anzahl Portionen 1

Kalzium 22,5 mg

zu meinen Favoriten

ZUM FRÜHSTÜCK HINZUFÜGEN

Hatten Sie Beilagen?

KalziumRECHNER mit Tagebuch

GASTMODUS BEENDEN

15.04.2018

KALZIUM HEUTE		TAGES-DURCHSCHNITT
233 mg	i	0 mg

TAGEBUCH | ERSTE SCHRITTE | MEDIZINISCHE FAKTEN

Mahlzeit zusammenstellen

joghurt

Frühstück | Mittagessen | Abendessen | Snack | Alle

Vorschläge

Cornflakes mit Milch oder Joghurt	243,9 mg Kalzium/Portion
Fruchtjoghurt 3,6 %	200 mg Kalzium/Portion
Fruchtjoghurt laktosefrei	210 mg Kalzium/Portion
Fruchtjoghurt light	200 mg Kalzium/Portion
Früchtemüsli mit Joghurt	254,8 mg Kalzium/Portion
Joghurt natur 1,5%	285 mg Kalzium/Portion
Joghurt natur 3,6 %	300 mg Kalzium/Portion
Joghurtdrink	120 mg Kalzium/Portion
Naturjoghurt laktosefrei	425 mg Kalzium/Portion
Polentaauflauf mit Joghurtdip	154 mg Kalzium/Portion

Mahlzeit zusammenstellen

Fruchtjoghurt laktosefrei

210 mg Kalzium/Portion

Portionsgröße	1 Becher (150g)
Anzahl Portionen	1
Kalzium	210.0 mg

zu meinen Favoriten

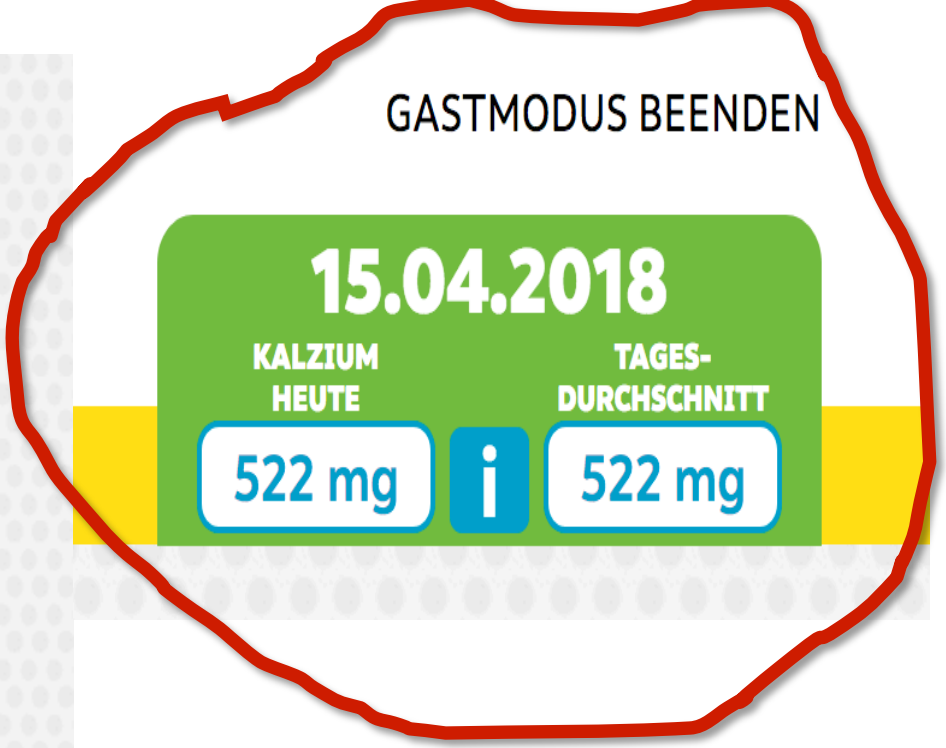
ZUM FRÜHSTÜCK HINZUFÜGEN

Hatten Sie Beilagen?

Nahrungsmittel suchen

Alt Wiener Suppentopf	29 mg Kalzium/Portion
Ananas	6,4 mg Kalzium/Portion
Antipasti Gemüse	43 mg Kalzium/Portion


‹ Sonntag, 15.04.2018 ›
KALZIUM
Frühstück zusammenstellen 245 mg
Obstsalat 1 Portion 23 mg
Fruchtjoghurt laktosefrei 1 Becher 210 mg
Mischbrot 1 Scheibe 8 mg
Schwarzer Kaffee 1 Häferl 4 mg
TIPPEN SIE AUF DIE SPEISE, UM DIE PORTIONEN ZU ÄNDERN
Mittagessen zusammenstellen 65 mg
gebratener Fisch 1 Portion 36 mg
Karottensalat 1 Portion 22 mg
Reis 1 Portion 3 mg
Schwarzer Kaffee 1 Häferl 4 mg
TIPPEN SIE AUF DIE SPEISE, UM DIE PORTIONEN ZU ÄNDERN
Abendessen zusammenstellen 8 mg
Apfel mittelgroß 1 Stück 8 mg
TIPPEN SIE AUF DIE SPEISE, UM DIE PORTIONEN ZU ÄNDERN
Snack zusammenstellen 205 mg
Mineralwasser Römerquelle 7 Glas 205 mg
TIPPEN SIE AUF DIE SPEISE, UM DIE PORTIONEN ZU ÄNDERN
Eigene Speise ergänzen
Dieser Tag ist abgeschlossen.

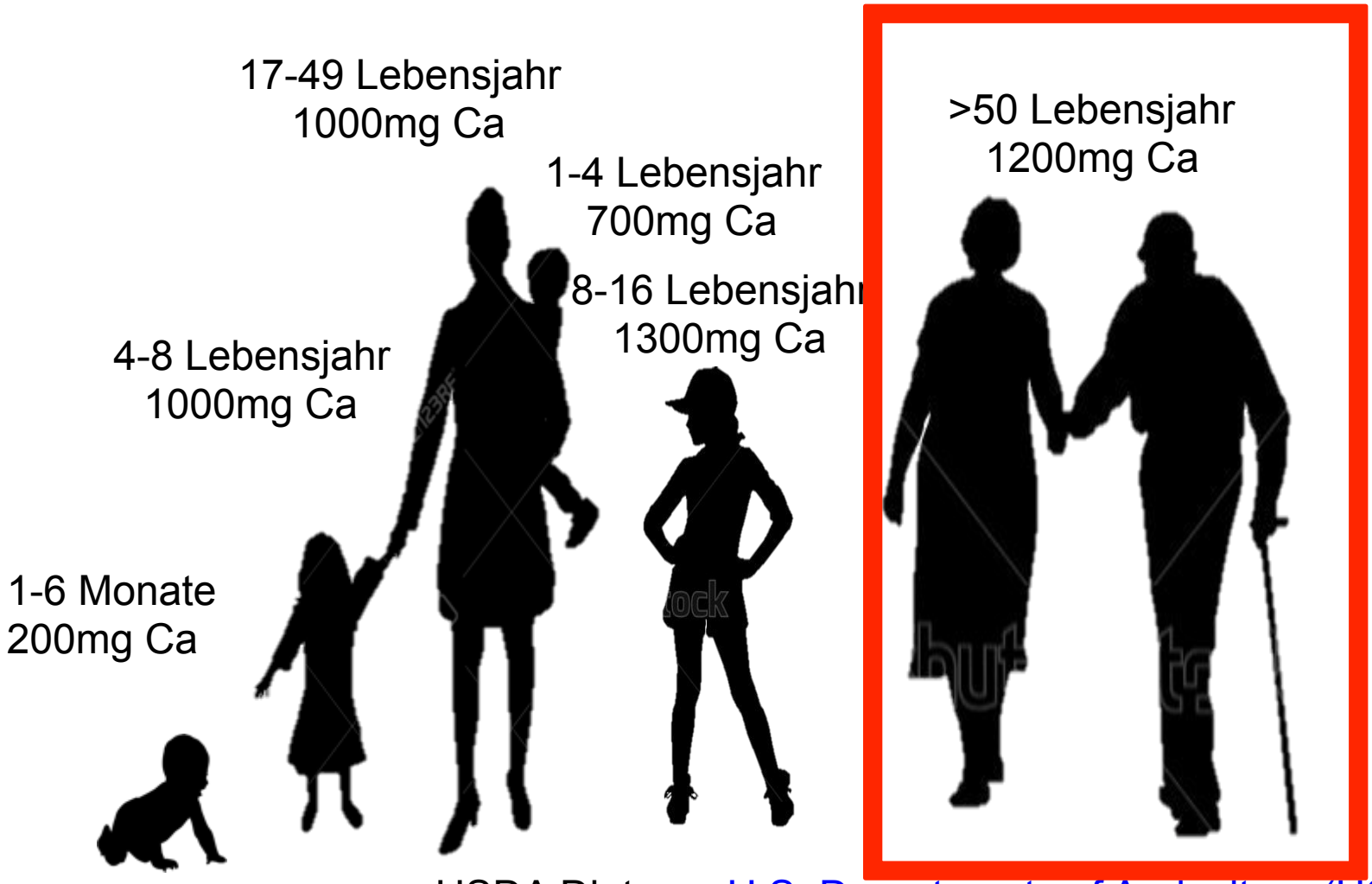

GASTMODUS BEENDEN
15.04.2018
KALZIUM HEUTE
522 mg
i
TAGES-DURCHSCHNITT
522 mg

WELCHE MENGE AN CALCIUM WIRD EMPFOHLEN?

DACH 2013

Säuglinge	Calcium mg/Tag
0 bis unter 4 Monate[a]	220
4 bis unter 12 Monate	330
Kinder	
1 bis unter 4 Jahre	600
4 bis unter 7 Jahre	750
7 bis unter 10 Jahre	900
10 bis unter 13 Jahre	1100
13 bis unter 15 Jahre	1200
Jugendliche und Erwachsene	
15 bis unter 19 Jahre	1200
19 bis unter 25 Jahre	1000
25 bis unter 51 Jahre	1000
51 bis unter 65 Jahre	1000
65 Jahre und älter	1000

TÄGLICHER CALCIUM-BEDARF



USDA Dietary= U.S. Departments of Agriculture (USDA)

WIEVIEL CALCIUM NEHMEN ÖSTERREICHERINNEN EIGENTLICH ZU SICH ?

Kann die Auswertung stimmen ?

TÄGLICHE CALCIUM-AUFNAHME IM DURCHSCHNITT

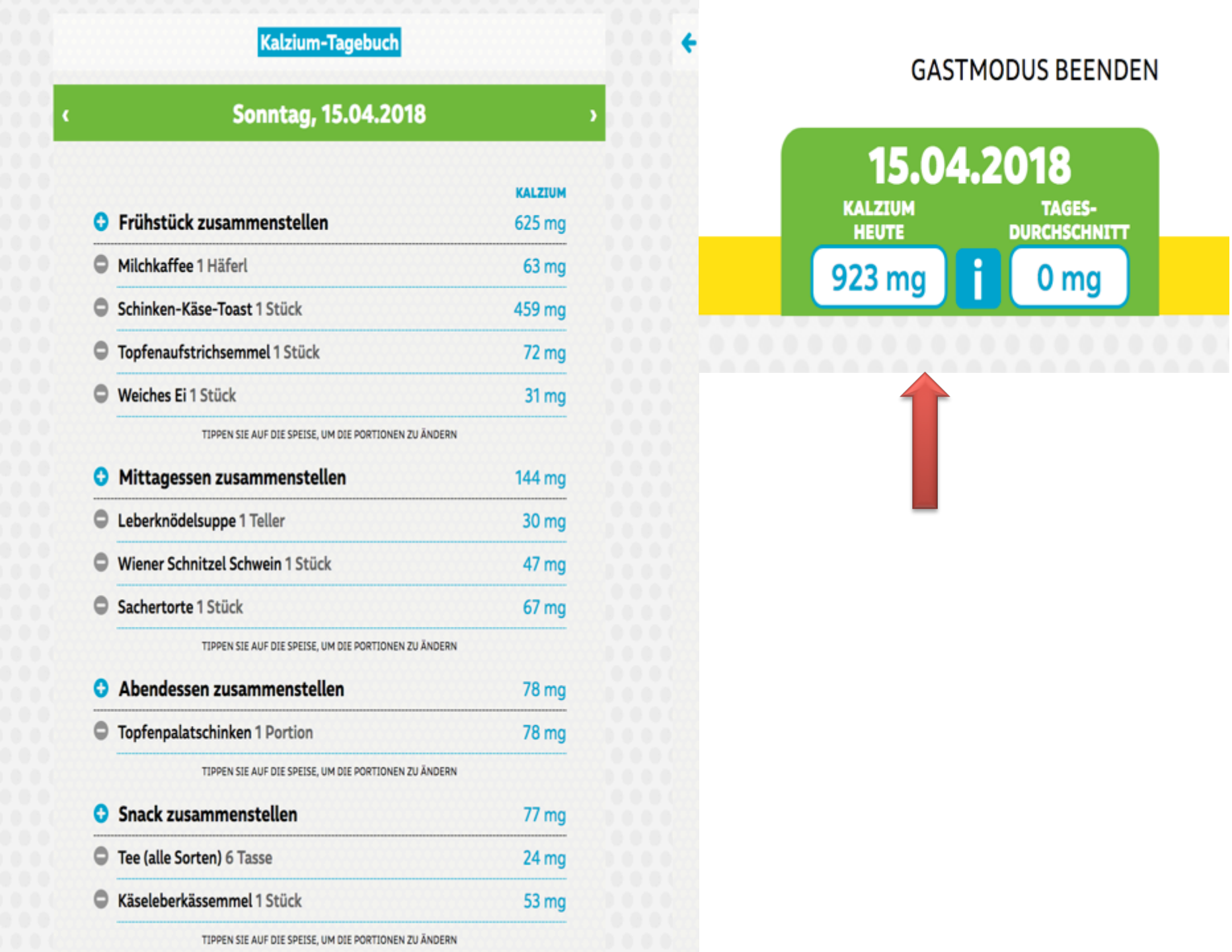
Zu wenig

	Frauen			
		–50 Jahre	51–64 Jahre (n=52)	D-A-CH 2012
Calcium (mg)		8 [779; 898]	786 [692; 881]	1000

	Männer			
	18–24 Jahre (n=17)	25–50 Jahre (n=87)	51–64 Jahre (n=44)	D-A-CH 2012
Calcium (mg)	991 [796; 1185]	881 [805; 958]	802 [690; 913]	1000

Eine „anständige“ Nahrungsaufnahme 100kg/180cm

- Frühstück:
  - Schinkenkäse Toast, Ei, Tasse Kaffee mit Milch, Topfenaufstrich Semmel
- Mittagessen:
  - Leberknödel Suppe, Wienerschnitzel, Sachertorte
- Abendessen:
  - Topfen Palatschinken
- Zwischendurch: Leberkäs Semmel
- Getränke:
  - 1,5 Liter Früchte Tee


Kalzium-Tagebuch
‹ Sonntag, 15.04.2018 ›
KALZIUM
Frühstück zusammenstellen 625 mg
Milchkaffee 1 Häferl 63 mg
Schinken-Käse-Toast 1 Stück 459 mg
Topfenaufstrichsemmel 1 Stück 72 mg
Weiches Ei 1 Stück 31 mg
TIPPEN SIE AUF DIE SPEISE, UM DIE PORTIONEN ZU ÄNDERN
Mittagessen zusammenstellen 144 mg
Leberknödelsuppe 1 Teller 30 mg
Wiener Schnitzel Schwein 1 Stück 47 mg
Sachertorte 1 Stück 67 mg
TIPPEN SIE AUF DIE SPEISE, UM DIE PORTIONEN ZU ÄNDERN
Abendessen zusammenstellen 78 mg
Topfenpalatschinken 1 Portion 78 mg
TIPPEN SIE AUF DIE SPEISE, UM DIE PORTIONEN ZU ÄNDERN
Snack zusammenstellen 77 mg
Tee (alle Sorten) 6 Tasse 24 mg
Käseleberkässemmel 1 Stück 53 mg
TIPPEN SIE AUF DIE SPEISE, UM DIE PORTIONEN ZU ÄNDERN
GASTMODUS BEENDEN
15.04.2018
KALZIUM HEUTE
923 mg
i
TAGES-DURCHSCHNITT
0 mg

CONCLUSIO CALCIUM

- Der **Calcium Spiegel** gibt **KEINE** ausreichende Information bzgl. Calcium Versorgung
- Österreicherinnen nehmen durchschnittlich **ZU WENIG CALCIUM** zu sich
- Eine **ausreichende Calzium-Versorgung** ist
  - **WESENTLICH** zur Osteoporose-Vorbeugung
  - **NOTWENDIG** bei antiresorptiver Therapie
- **Individuelle Auswertung** der Calziumaufnahme daher sinnvoll
- HILFREICH dafür ist der Kalziumrechner:

  Kalziumrechner.at

PHOSPHAT

VITAMIN D - MANGEL

- DEFINITION
- PRÄVALENZ
- MUSKEL, KNOCHEN
- IMMUNSYSTEM

LEITLINIEN

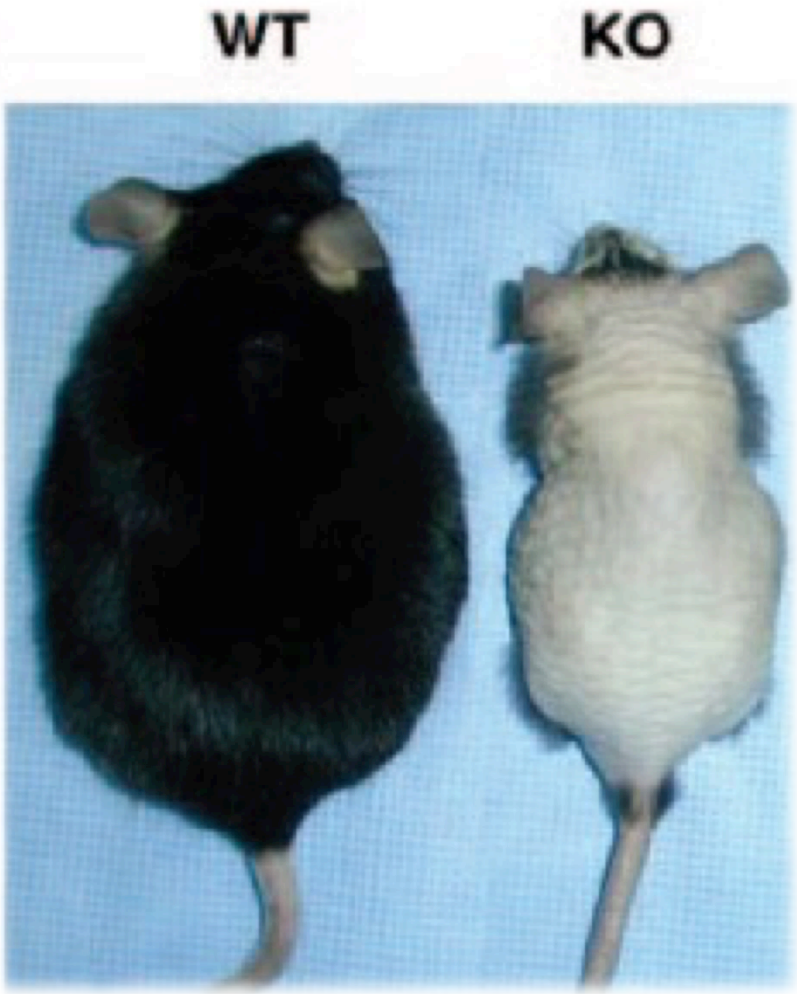
- **ZIEL 25(OH)D > 20ng/ml**
- **IOM (ALLGEMEINBEVÖLKERUNG)**
  - **600-800 IU/d, max. 4000 IU/d**
- **ENDOCRINE SOCIETY (RISIKOPAT.)**
  - **1500 – 2000 IU PRO TAG!!!**
  - **SICHERES LIMIT 10,000 IU/d**

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
- Obese children and adults (BMI > 30 kg/m^2)
- Granuloma-forming disorders
  - Sarcoidosis
  - Tuberculosis
  - Histoplasmosis
  - Coccidiomycosis
  - Berylliosis
- Some lymphomas

Ross 2011
Holick 2011

VDR KNOCKOUT (KO) MAUS



Bouillon R et al. Endocrine Reviews 2008; 29:726-776

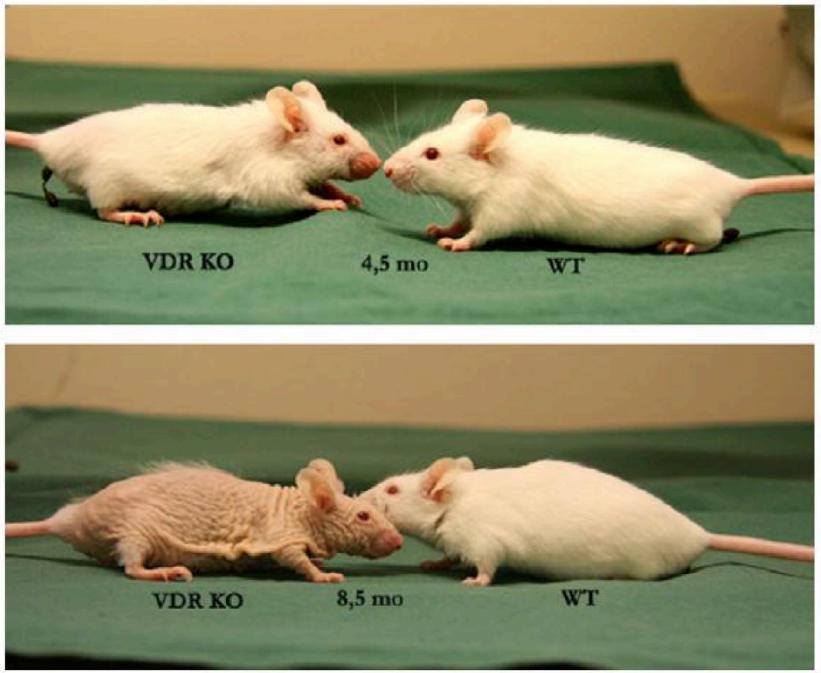


Fig. 2. Phenotype of VDR knockout mouse (KO) compared to wildtype littermate (WT; NMRI background strain) at the age of 4.5 (top) and 8.5 (bottom) months.

Keisala et al. Premature aging in vitamin D receptor mutant mice. J Steroid Biochem Mol Biol. 2009 Jul;115(3-5):91-7

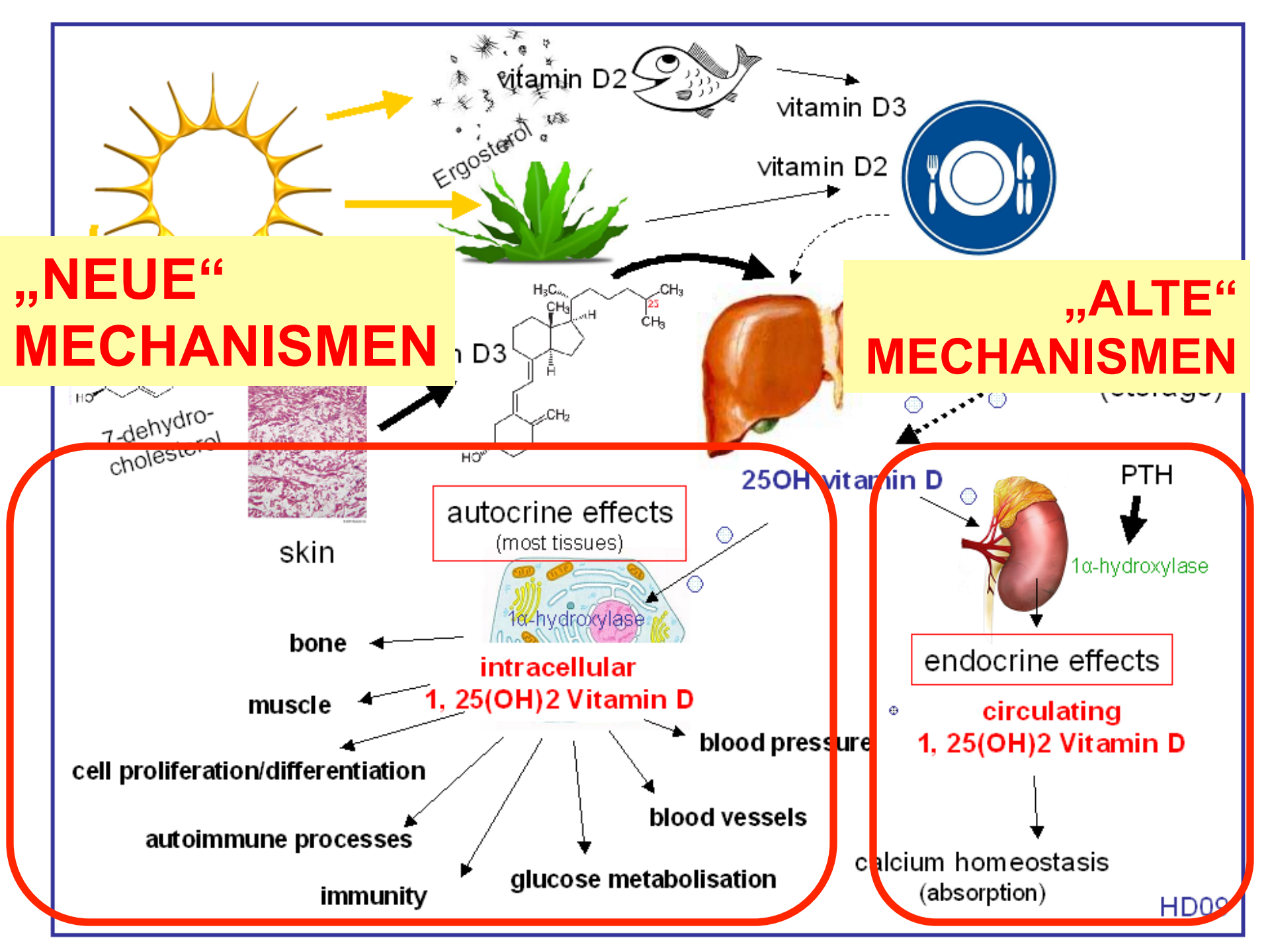
BASICS
VITAMIN D

- VITAMIN D IST EIN **STEROIDHORMON**

- VITAMIN D **REGULIERT ~ 200 GENE**

- CALCITRIOL (AKTIVES VITAMIN D) WIRD **NICHT NUR** IN DER NIERE PRODUZIERT

- VITAMIN D HAT NEBEN DER KALZIUMHOMÖOSTASE **VIELE ANDERE FUNKTIONEN**


„NEUE“ MECHANISMEN
„ALTE“ MECHANISMEN
vitamin D2
vitamin D3
vitamin D2
Ergosterol
7-dehydro-cholesterol
skin
autocrine effects
(most tissues)
1α-hydroxylase
bone
muscle
intracellular
1, 25(OH)2 Vitamin D
blood pressure
cell proliferation/differentiation
blood vessels
autoimmune processes
glucose metabolisation
immunity
25OH vitamin D
PTH
1α-hydroxylase
endocrine effects
circulating
1, 25(OH)2 Vitamin D
calcium homeostasis
(absorption)
HD09

BASICS
VITAMIN D BEI AKUT KRANKEN
(ERWACHSENE UND KINDER)

- EIN VITAMIN D MANGEL
  - IST HÄUFIG
  - MIT SCHLECHTEM OUTCOME ASSOZIIERT

  (MORTALITÄT, NIERENVERSAGEN, SEPSIS, …)

- **ZENTRALE FRAGE:**

  IST VITAMIN D NUR EIN MARKER ODER MEHR?

HADDAD
JCEM 1971

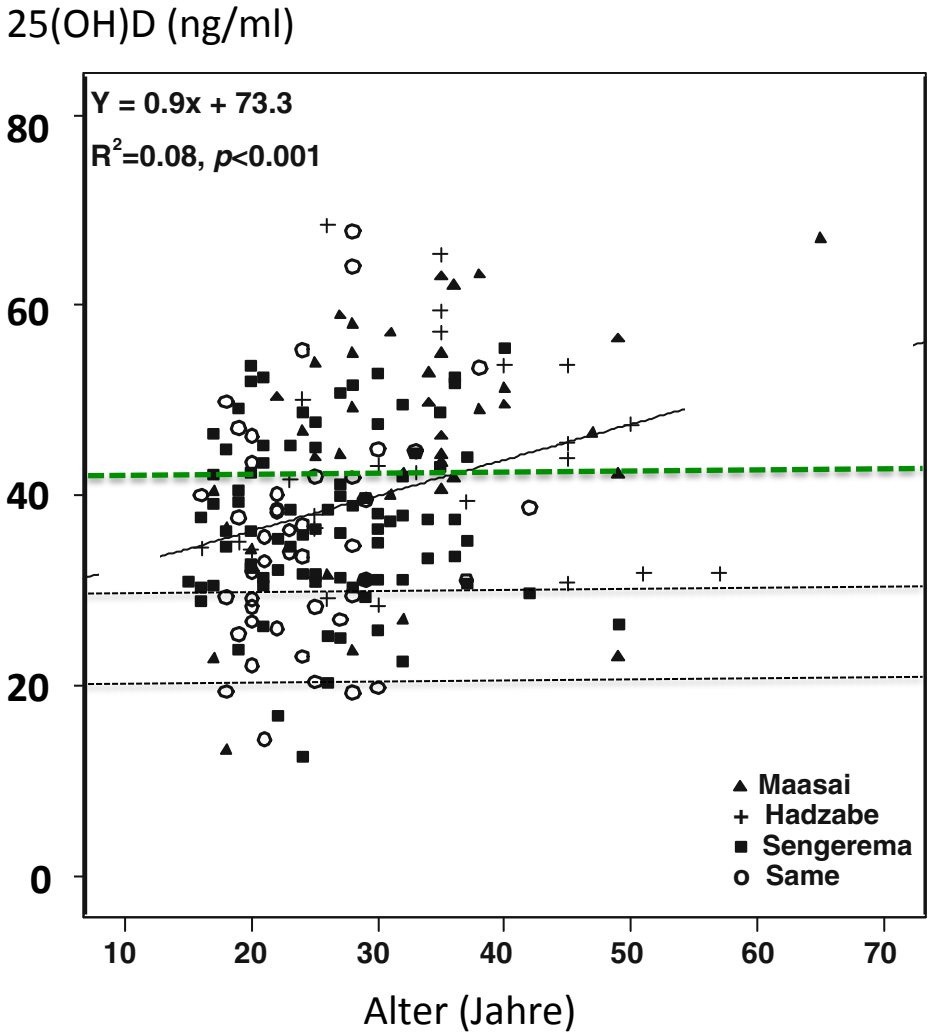
„markedly tanned lifeguards… ≥ 4 weeks at a local swimming pool“

TABLE II*

Group	No.	Age (years)	Consumption of D Weekly (Units)	Weekly Exposure to Sunlight (hours)	Plasma 25-HCC (ng/ml)
Normal Volunteers	40	30.2 ± 12.9	2230 ± 1041	8.8 ± 6.1	27.3 ± 11.8
Biliary Cirrhosis	4	1.5 - 55	2500 (est.)	——	6.4 ± 2.6*
Lifeguards	8	18.5 ± 2.0	2895 ± 677	53.0 ± 10.3	64.4 ± 8.7*

* $p < .001$ + values represent mean ± SD

VITAMIN D STATUS IN AFRIKA



MW: 42 ng/ml

30 ng/ml

20 ng/ml

N=367 Erwachsene, 82 Kleinkinder

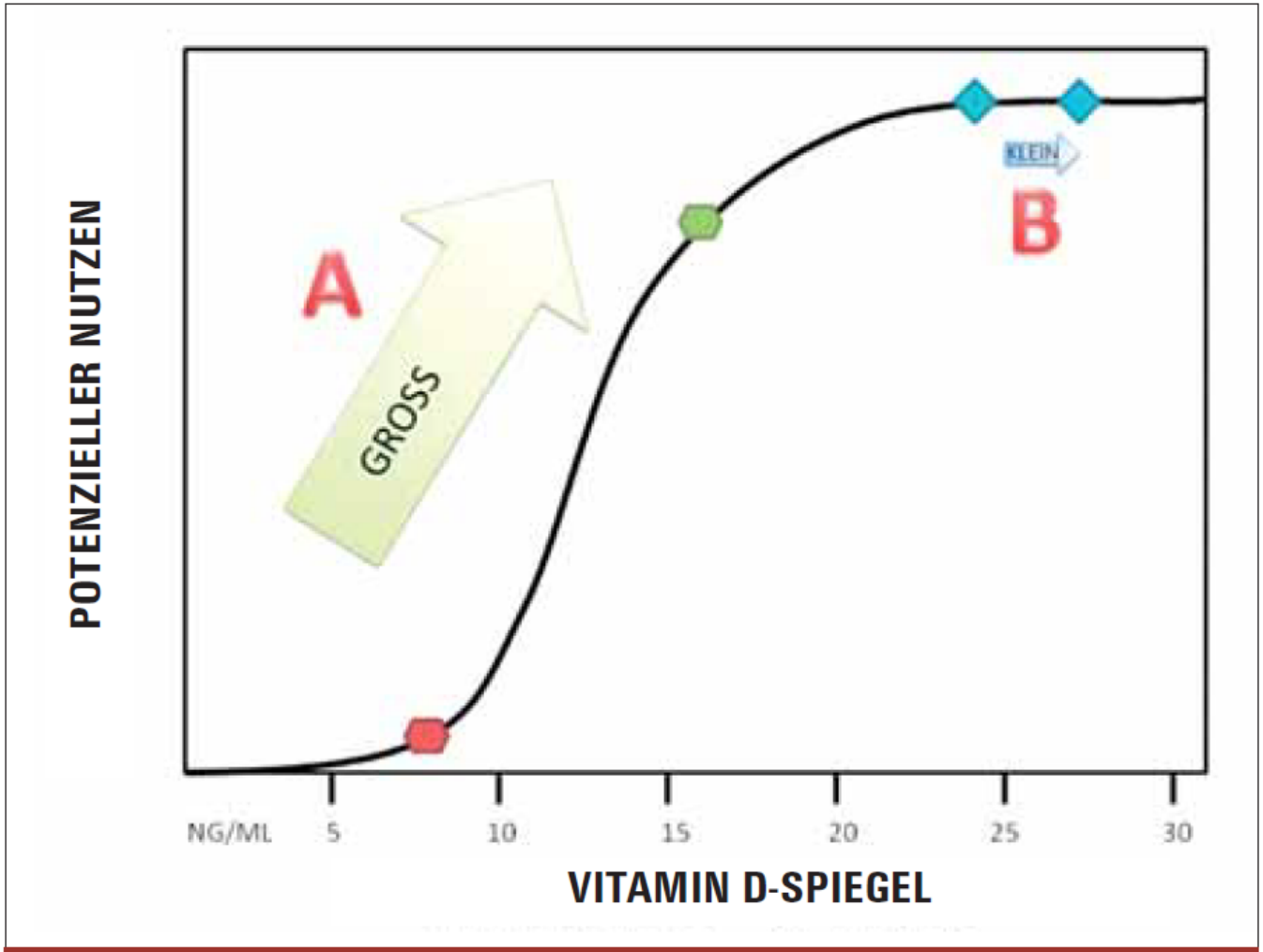
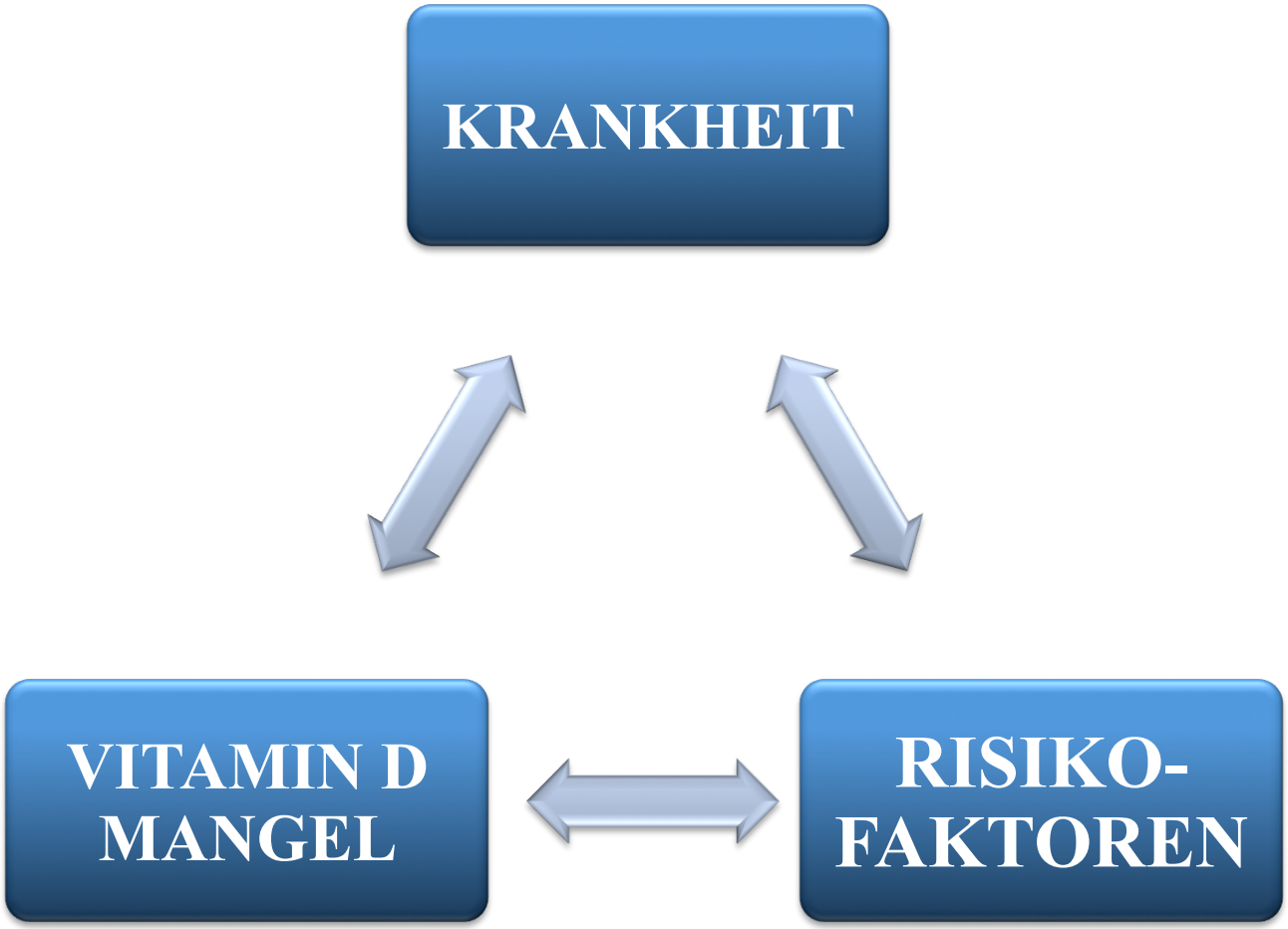


Abb.: Der potenzielle Nutzen einer Vitamin D-Gabe ist abhängig von Ausgangswert und erreichter Veränderung durch die Intervention. So wird wie in Szenario A das Anheben des 25(OH)D–Spiegels von 8 auf 16 ng einen weitaus größeren Effekt haben als wenn, wie in Szenario B, der Spiegel vorher bei 24 und nachher bei 27 ng/mL liegt.

REVERSE KAUSALITÄT!?!



MECHANISMEN VON VITAMIN D

	Allgemein-Bevölkerung	Akute Erkrankung
Infektionen	Atemwegsinfekte, Tuberkulose	Nosokomiale Infekte Sepsis, SIRS
Lunge/Muskel	COPD, Myopathie, Myalgia	Lungenversagen Prolong. Weaning, Critical Illness Myopathy
Herz	Herzinfarkt, Herzinsuffizienz, Sudden Cardiac Death	Kardiogener Schock, Arrhythmie

Adaptiert von: Lee P. et al., Intensive Care Med. 2009 Dec;35(12):2028-32

Effect of Vitamin D_3 Supplementation on Upper Respiratory Tract Infections in Healthy Adults

The VIDARIS Randomized Controlled Trial

David R. Murdoch, MD

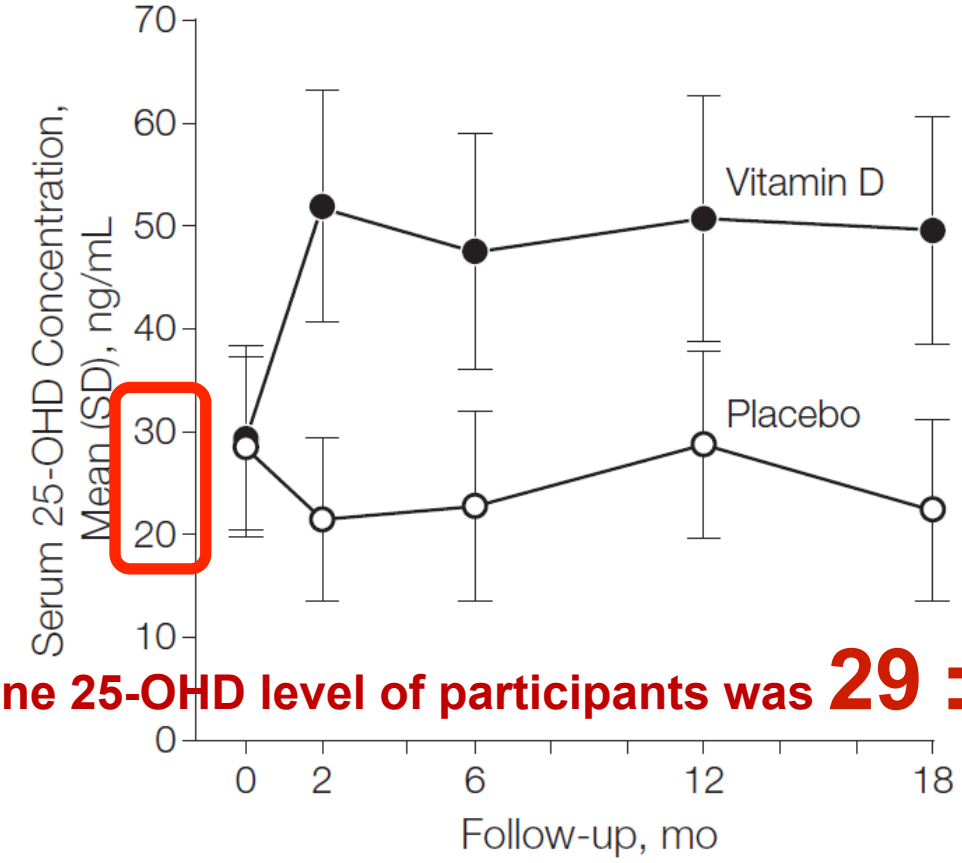
Context Observational studies have reported an inverse associat

- RCT, db, Christchurch, NZ, Start Februar (43°)
- 322 Gesunde, ca. 47 Jahre, 75% Frauen
- 200 000 IU Vitamin D3 po, 200 000 IU nach 1 Mon., dann 100 000 IU 1x/Mon. über 18 Monate
- PE: akute Atemwegsinfekte, KEIN EFFEKT

Murdoch JAMA 2012

MURDOCH 2012

Figure 2. Mean Serum 25-Hydroxyvitamin D (25-OHD) Levels Among the Intention-to-Treat Population



mean baseline 25-OHD level of participants was 29 ± 9 ng/mL

MURDOCH

- 25(OH)D Baseline: **29±9 ng/ml**
- 25(OH)D nach Intervention: > 48ng/ml
- PE: 593 URTI vs. 611
  - 5 participants < 10 ng/mL
  - No statistically significant differences were noted for any outcome when the data were reanalyzed by baseline 25-OHD levels less than 20 ng/mL (n=13, alle in Placebogruppe)

Randomized Trial of Vitamin D Supplementation and Risk of Acute Respiratory Infection in Mongolia

Carlos A. Camargo Jr, Davaasambuu Ganmaa, A. Lindsay Frazier, Franca F. Kirchberg, Jennifer J. Stuart, Ken Kleinman, Nyamjav Sumberzul and Janet W. Rich-Edwards

Pediatrics 2012;130;e561; originally published online August 20, 2012;

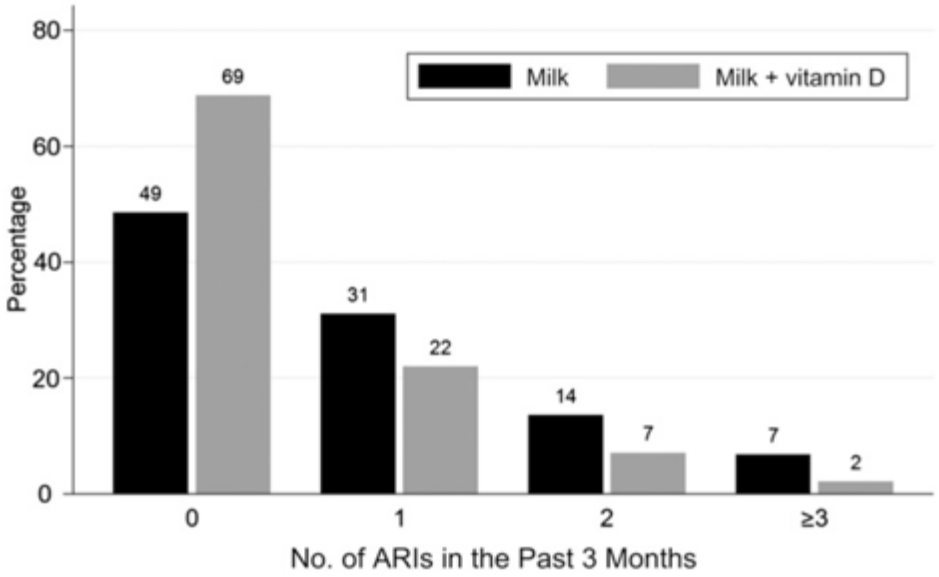
- RCT, db, Mongolei im Winter (48°)
- 247 Schulkinder, ca. 10 Jahre
- Milch ± 300 IU Vitamin D3/d über 2 Monate
- PE: akute Atemwegsinfekte (Eltern, > 24 Std.)

Randomized Trial of Vitamin D Supplementation and Risk of Acute Respiratory Infection in Mongolia

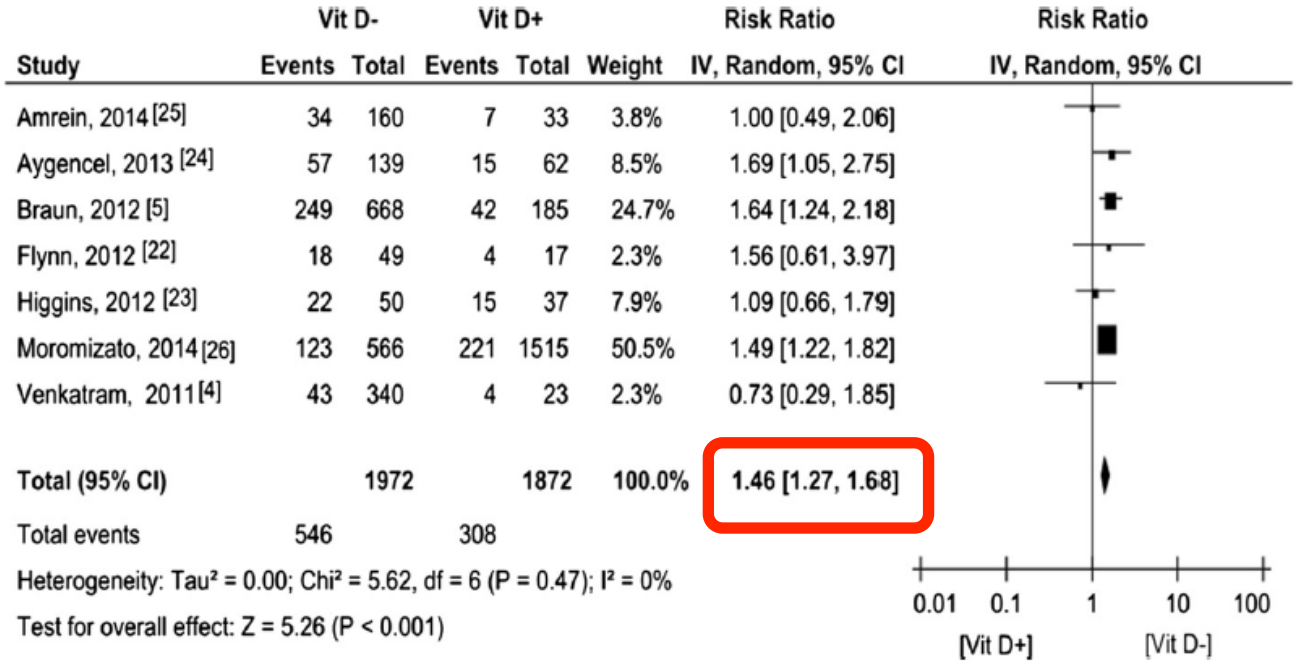
Carlos A. Camargo Jr, Davaasambuu Ganmaa, A. Lindsay Frazier, Franca F. Kirchberg, Jennifer J. Stuart, Ken Kleinman, Nyamjav Sumberzul and Janet W. Rich-Edwards

Pediatrics 2012;130;e561; originally published online August 20, 2012;

- 25(OH)D Baseline: **7ng/ml (IQ 5-10)**
- 25(OH)D nach Intervention: 7ng vs. 19ng/ml
- PE: 0.80 vs 0.45, P=0.047



VITAMIN D UND SEPSIS



Study	Vit D- Events	Total	Vit D+ Events	Total	Weight	Risk Ratio IV, Random, 95% CI
Amrein, 2014 [25]	34	160	7	33	3.8%	1.00 [0.49, 2.06]
Aygencel, 2013 [24]	57	139	15	62	8.5%	1.69 [1.05, 2.75]
Braun, 2012 [5]	249	668	42	185	24.7%	1.64 [1.24, 2.18]
Flynn, 2012 [22]	18	49	4	17	2.3%	1.56 [0.61, 3.97]
Higgins, 2012 [23]	22	50	15	37	7.9%	1.09 [0.66, 1.79]
Moromizato, 2014 [26]	123	566	221	1515	50.5%	1.49 [1.22, 1.82]
Venkatram, 2011 [4]	43	340	4	23	2.3%	0.73 [0.29, 1.85]
Total (95% CI)		**1972**		**1872**	**100.0%**	**1.46 [1.27, 1.68]**
Total events	546		308			

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 5.62$, df = 6 (P = 0.47); $I^2 = 0\%$

Test for overall effect: Z = 5.26 (P < 0.001)

Figure 2 Forest plot of studies comparing deficient vitamin D levels with sufficient vitamin D levels on sepsis. CI, confidence interval; IV, inverse variance; Vit D-, deficient vitamin D level; Vit D+, sufficient vitamin D level.

de Haan *et al. Critical Care* 2014, **18**:660
http://ccforum.com/content/18/6/660

VITAMIN D & MORTALITÄT

VITAMIN D UND SPITALSSTERBLICHKEIT

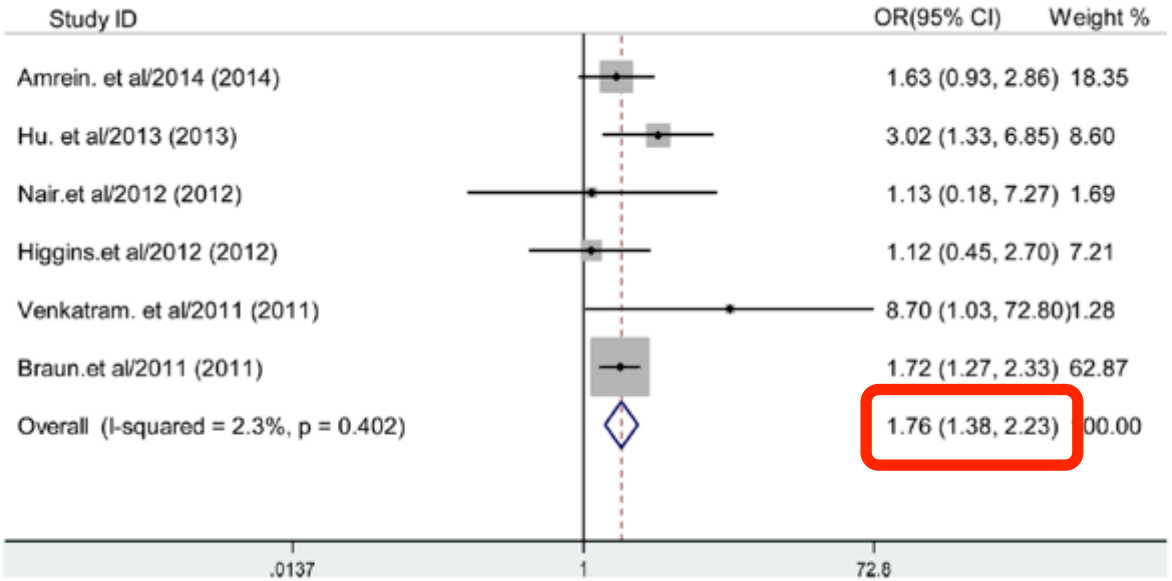
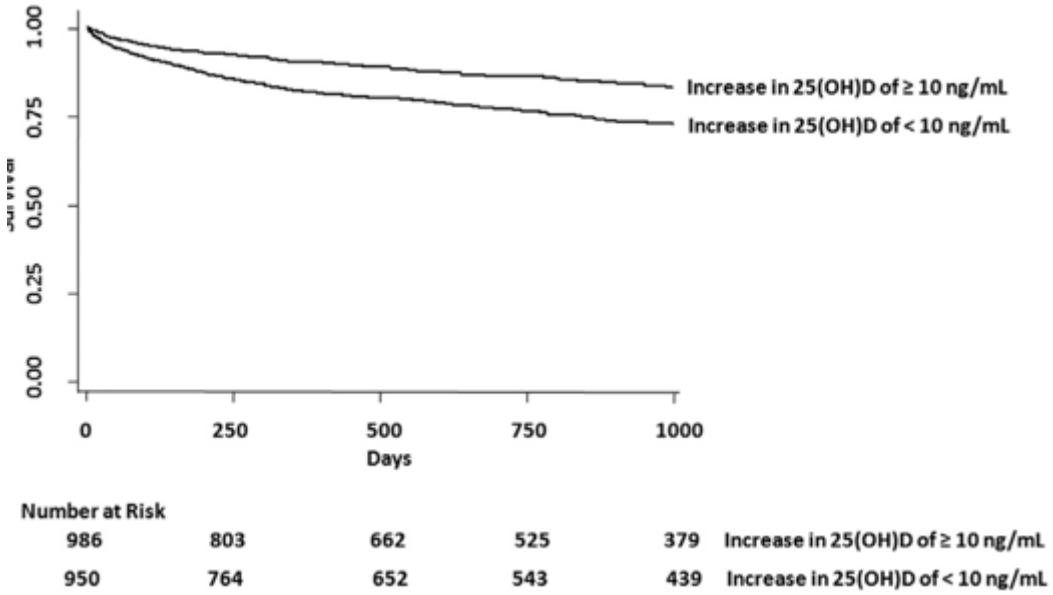


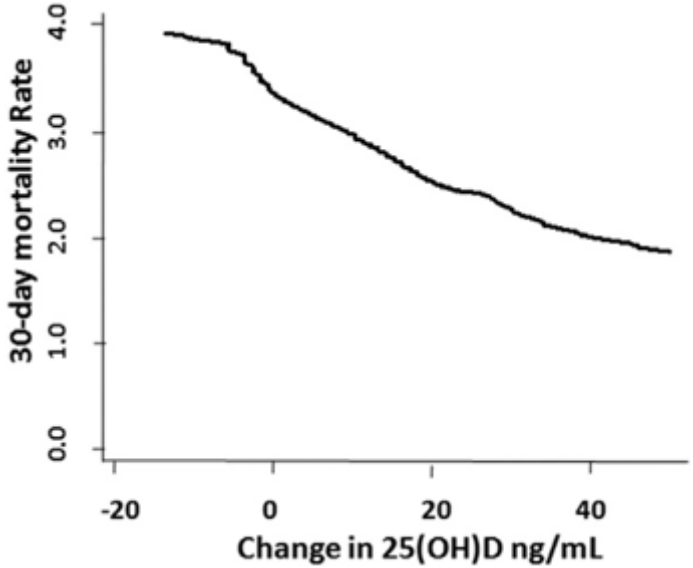
Figure 2 Forest plot showing the effect of vitamin D deficiency on hospital mortality. OR, odds ratio.

Zhang *et al. Critical Care* 2014, **18**:684
http://ccforum.com/content/18/6/684

VITAMIN D ANSTIEG BEI HOSPITALISIERTEN PAT.

- 4344 Erwachsene mit 2 Vitamin D Messungen 7-365 Tage vor einer Hospitalisierung
- Absoluter Anstieg > 10 ng/mL bei Pat. mit Vitamin D Mangel (n=1944):
  - Reduktion der 30-Tages-Mortalität um 48% (adjusted OR 0.52; 95%CI 0.30-0.93; P =0.026)





Amrein K et al. Clin Nutr. 2015

Vitamin D status and ill health: a systematic review

Philippe Autier, Mathieu Boniol, Cécile Pizot, Patrick Mullie

Lancet Diabetes Endocrinol 2013

Published Online
December 6, 2013
http://dx.doi.org/10.1016/
S2213-8587(13)70165-7

except colorectal cancer. Results from intervention studies did not show an effect of vitamin D supplementation on disease occurrence, including colorectal cancer. In 34 intervention studies including 2805 individuals with mean 25(OH)D concentration lower than 50 nmol/L at baseline supplementation with 50 µg per day or more did not show better results. Supplementation in elderly people (mainly women) with 20 µg vitamin D per day seemed to slightly reduce all-cause mortality. The discrepancy between observational and intervention studies suggests that low 25(OH)D is a marker of ill health. Inflammatory processes involved in disease occurrence and clinical course would reduce 25(OH)D, which would explain why low vitamin D status is reported in a wide range of disorders. In elderly people, restoration of vitamin D deficits due to ageing and lifestyle changes induced by ill health could explain why low-dose supplementation leads to slight gains in survival.

Wie viele mit schwerem Mangel?

	RCTs (n)	Appendix reference*	RCT duration (months)	Individuals included in trials (n)	Range of vitamin D dose (µg per day)	Baseline 25(OH)D in intervention groups (nmol/L)†	25(OH)D during the intervention (nmol/L)†	Intervention groups with mean 25(OH)D higher than 72 nmol/L in the trial (n)†	Number of outcomes assessed by trials (n)	Number of outcomes with significant improvement‡ (n [appendix reference])
(Continued from previous page)										
Infectious diseases										
Sputum conversion in tuberculosis patients	3	(30), (48), (49)	1–3	283	220–250	22·4–32·0	63·4–109·8	1	3	1 (48)
Restriction of mycobacteria growth	1	(50)	1·5	131	60	35·0	67·4	1	1	1 (50)
Tuberculosis score in tuberculosis patients	2	(51), (52)	1–12	485	17–20	17·5–77·4	50·0–97·8	1	2	0
Viral response in hepatitis C patients	1	(53)	6	72	50	22·4	92·4	1	1	1 (53)
Upper respiratory tract infections	5	(54), (55), (56), (57), (58)	3–62	6057	20–100	64·1–78·6	71·4–124·8	2	11	2 ([54], [57])
CD4 count and skin regulatory cells in patients with HIV	2	(59), (83)	2 and 12	76	20–89	25·0–60·2	80·9–179·7	2	7	0
Chronic obstructive pulmonary disease										
Chronic obstructive pulmonary disease	1	(60)	12	182	90	50·0	129·8	1	1	0
Mood and cognitive disorders										
Mood disorders	6	(61), (62), (63), (64), (65), (66††), (84)	0·2–60	7191	10–143	52·7–76·7	93·9–147·5	4	11	3 ([61], [65])
General dementia	1	(67¶)	84	4143	10	50·0	NR	NR	1	0
Physical functioning										
Physical functioning	3	(28), (38), (68)	3–5	354	10–100	20·1–51·92	39·9–83·4	1	13	2 ([28], [38])

IU: Faktor 40

Autier 2013

MORTALITY

Mortality									
All-cause mortality	2011 (2)	30	62 231	6493	1–84	5–50	Death	RR 0·96 (0·93–1·00)	0
All-cause mortality	2011 (3)	50	94 148	10 685	1–84 (median 24)	7·5–50	Death	RR 0·95 (0·91–0·99)	0
All-cause mortality	2012 (7); 2012 (7)	8**; 24	70 528; 88 097	3832; NR	36; 36	≥10; ≥10	Death; death	RR 0·93 (0·88–0·99); RR 0·94 (0·88–0·99)	0; 0
Cancer mortality	2011 (3)	3	39 200	863	1–84	8–20	Death	RR 0·89 (0·78–1·02)	0

RCT=randomised controlled trials. RR=relative risk. ES=effect size. NR=not reported. CO=the endpoint was a change in continuous variable measured in all individuals. Hb=haemoglobin. *References are listed in the appendix pp 13. †Our calculation. ‡From (8). §(4) and (2) have seven studies in common. ¶Meta-analysis done by authors, details in appendix p 4. ||(5) and (6) have six trials in common. **Pooled analysis of trials of 1000 individuals or more.

Table 4: Meta-analyses of randomised trials of vitamin D supplementation and non-skeletal endpoints

Results of meta-analyses and pooled analyses consistently showed that supplementation could significantly reduce the risk of all-cause mortality, with relative risks ranging from 0·93 to 0·96 (table 4). Most trials included elderly women and a sizeable proportion of individuals were living in institutions.

Autier 2013

Conclusions

Many prospective studies have shown associations between low 25(OH)D concentrations and a wide range of acute and chronic health disorders. However, an equally similar number of randomised trials have not confirmed that raising of 25(OH)D concentrations can modify the occurrence or clinical course of these disorders. Hence, associations between 25(OH)D and health disorders reported by investigators of observational studies are not causal. Low 25(OH)D could be the result of inflammatory processes involved in the occurrence and progression of disease. An exception would be slight gains in survival after the restoration of vitamin D deficits due to lifestyle changes induced by ageing and ill health. Five trials including

Autier 2013

The effect of vitamin D supplementation on skeletal, vascular, or cancer outcomes: a trial sequential meta-analysis

Mark J Bolland, Andrew Grey, Greg D Gamble, Ian R Reid

Methods We did a trial sequential meta-analysis of existing randomised controlled trials of vitamin D supplements, with or without calcium, to investigate the possible effect of future trials on current knowledge. We estimated the effects of vitamin D supplementation on myocardial infarction or ischaemic heart disease, stroke or cerebrovascular disease, cancer, total fracture, hip fracture, and mortality in trial sequential analyses using a risk reduction threshold of 5% for mortality and 15% for other endpoints.

Findings The effect estimate for vitamin D supplementation with or without calcium for myocardial infarction or ischaemic heart disease (nine trials, 48 647 patients), stroke or cerebrovascular disease (eight trials 46 431 patients), cancer (seven trials, 48 167 patients), and total fracture (22 trials, 76 497 patients) lay within the futility boundary, indicating that vitamin D supplementation does not alter the relative risk of any of these endpoints by 15% or more. Vitamin D supplementation alone did not reduce hip fracture by 15% or more (12 trials, 27 834 patients). Vitamin D co-administered with calcium reduced hip fracture in institutionalised individuals (two trials, 3853 patients) but did not alter the relative risk of hip fracture by 15% or more in community-dwelling individuals (seven trials, 46 237 patients). There is uncertainty as to whether vitamin D with or without calcium reduces the risk of death (38 trials, 81 173).

Interpretation Our findings suggest that vitamin D supplementation with or without calcium does not reduce skeletal or non-skeletal outcomes in unselected community-dwelling individuals by more than 15%. Future trials with similar designs are unlikely to alter these conclusions.

Bolland 2014

The effect of vitamin D supplementation on skeletal, vascular, or cancer outcomes: a trial sequential meta-analysis

Mark J Bolland, Andrew Grey, Greg D Gamble, Ian R Reid

	Participants (vitamin D / no vitamin D)	Age (years)	Sex (percentage female)	Duration	Treatment groups	Dose (vitamin D or vitamin D + calcium [for CaD])	Primary endpoint	Secondary endpoints	Baseline 25OHD concentrations in nmol/L; vitamin D/no vitamin D (N)*	Achieved 25OHD concentrations in nmol/L; vitamin D/no vitamin D (N)*
(Continued from previous page)										
Grant et al, 2005[46]	2649/2643	77	85%	45 months	2×2 factorial†: vitamin D, calcium, placebo	800 IU per day/1 g calcium per day	Fracture	MI, stroke, cancer, death	38 (60)	62/44 (60)
WHI trials, 2006–07[47–49]	18176/18106	62	100%	7 years	CaD and placebo	400 IU + 1 g per day	Fracture	MI, stroke, cancer, death	48 (357)	61/NS‡ (227/221)
Bolton-Smith et al, 2007[50]	62/61	69	100%	2 years	CaD and placebo	400 IU + 1 g per day	BMD	Fracture, death	57/62 (all)	75/49 (all)
Broe et al, 2007[51]	99/25	89	73%	5 months	Vitamin D and placebo	200, 400, 600, or 800 IU per day	Falls	Death	48/52 (All)	63/60 (all)
Burleigh et al, 2007[52]	100/103	83	59%	1 month	CaD and calcium	800 IU + 1·2 g per day/1·2 g per day	Falls	Fracture, death	25/22 (54)	27/22 (NS)
Lappe et al, 2007[53]	446/734	67	100%	4 years	CaD, calcium, placebo	1100 IU per day + 1·4–1·5 g per day/1·4–1·5 g per day	BMD	MI, stroke, cancer, death	72/72 (All)	96/71 (All)
Lyons et al, 2007[54]	1725/1715	84	76%	3 years	Vitamin D and placebo	100 000 IU every 4 months	Fracture	Death	NS	80/54 (102)
Smith et al, 2007[55]	4727/4713	79	54%	3 years	IM vitamin D and placebo	300 000 IU every year	Fracture	Death	56·5 (43)	+21%/NS (NS)
Björkman et al, 2008[56]	150/68	85	82%	6 months	Vitamin D and placebo	5600 or 16 800 IU per week	Biochemistry	Death	22/23 (all)	60/25 (all)

40 RCTs

Bolland 2014

COCHRANE META-ANALYSE 2014

Main results

We identified 159 trials, 56 randomised trials with 95,286 participants provided usable data on mortality. Most trials included women older than 70 years. The mean proportion of women was 77%. Forty-eight of the trials randomly assigned 94,491 healthy participants. Of these, four trials included healthy volunteers, nine trials included postmenopausal women and 35 trials included older people living on their own or in institutional care. The remaining **eight trials randomly assigned 795 participants with neurological, cardiovascular, respiratory or rheumatoid diseases. Vitamin D was administered for a weighted mean of 4.4 years.** Forty-five trials (80%) reported the baseline vitamin D status of participants based on serum 25-hydroxyvitamin D levels. Participants in 19 trials had vitamin D adequacy (at or above 20 ng/mL). Participants in the remaining 26 trials had vitamin D insufficiency (less than 20 ng/mL).

.... only vitamin D3 decreased mortality: **RR 0.94** (95% CI 0.91 to 0.98); P = 0.002; I2 = 0%; 75,927 participants; 38 trials). Trial sequential analysis supported our finding regarding vitamin D3, with the cumulative Z-score breaking the trial sequential monitoring boundary for benefit, corresponding to **150 people treated over five years to prevent one additional death.** Vitamin D3 statistically significantly decreased cancer mortality (RR 0.88 (95% CI 0.78 to 0.98); P = 0.02; I2 = 0%; 44,492 participants; 4 trials).

Bjelakovic 2014

Research

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Effect of High-Dose Vitamin D_3 on Hospital Length of Stay in Critically Ill Patients With Vitamin D Deficiency

The VITdAL-ICU Randomized Clinical Trial

Karin Amrein, MD, MSc; Christian Schnedl, MD; Alexander Holl, MD; Regina Riedl, MSc; Kenneth B. Christopher, MD; Christoph Pachler, MD; Tadeja Urbanic Purkart, MD; Andreas Waltensdorfer, MD; Andreas Münch, MD; Helga Warnitznig, MD; Tatjana Stojakovic, MD; Egbert Bisping, MD; Wolfgang Toller, MD; Karl-Heinz Smolle, MD; Andrea Berghold, PhD; Thomas R. Pieber, MD; Harald Dobnig, MD

Supplemental content at jama.com

IMPORTANCE Low vitamin D status is linked to increased mortality and morbidity in patients who are critically ill. It is unknown if this association is causal.

OBJECTIVE To investigate whether a vitamin D_3 treatment regimen intended to restore and maintain normal vitamin D status over 6 months is of health benefit for patients in ICUs.

DESIGN, SETTING, AND PARTICIPANTS A randomized double-blind, placebo-controlled, single-center trial, conducted from May 2010 through September 2012 at 5 ICUs that included a medical and surgical population of 492 critically ill adult white patients with vitamin D deficiency (≤20 ng/mL) assigned to receive either vitamin D_3 (n = 249) or a placebo (n = 243).

INTERVENTIONS Vitamin D_3 or placebo was given orally or via nasogastric tube once at a dose of 540 000 IU followed by monthly maintenance doses of 90 000 IU for 5 months.

MAIN OUTCOMES AND MEASURES The primary outcome was hospital length of stay. Secondary outcomes included, among others, length of ICU stay, the percentage of patients with 25-hydroxyvitamin D levels higher than 30 ng/mL at day 7, hospital mortality, and 6-month mortality. A predefined severe vitamin D deficiency (≤12 ng/mL) subgroup analysis was specified before data unblinding and analysis.

RESULTS A total of 475 patients were included in the final analysis (237 in the vitamin D_3 group and 238 in the placebo group). The median (IQR) length of hospital stay was not significantly different between groups (20.1 days [IQR, 11.1-33.3] for vitamin D_3 vs 19.3 days [IQR, 11.1-34.9] for placebo; $P = .98$). Hospital mortality and 6-month mortality were also not significantly different (hospital mortality: 28.3% [95% CI, 22.6%-34.5%] for vitamin D_3 vs 35.3% [95% CI, 29.2%-41.7%] for placebo; hazard ratio [HR], 0.81 [95% CI, 0.58-1.13]; $P = .18$. 6-month mortality: 35.0% [95% CI, 29.0%-41.5%] for vitamin D_3 vs 42.9% [95% CI, 36.5%-49.4%] for placebo; HR, 0.78 [95% CI, 0.58-1.04]; $P = .091$. For the severe vitamin D deficiency subgroup analysis (n = 200), length of hospital stay was not significantly different between the 2 study groups: 20.1 days (IQR, 12.9-39.1) for vitamin D_3 vs 19.0 days (IQR, 11.6-33.8) for placebo. Hospital mortality was significantly lower with 28 deaths among 98 patients (28.6% [95% CI, 19.9%-38.6%]) for vitamin D_3, compared with 47 deaths among 102 patients (46.1% [95% CI, 36.2%-56.2%]) for placebo (HR, 0.56 [95% CI, 0.35-0.90]; P for interaction = .04), but not 6-month mortality (34.7% [95% CI, 25.4%-45.0%] for vitamin D_3 vs 50.0% [95% CI, 39.9%-60.1%] for placebo; HR, 0.60 [95% CI, 0.39-0.93]; P for interaction = .12).

CONCLUSIONS AND RELEVANCE Among critically ill patients with vitamin D deficiency, administration of high-dose vitamin D_3, compared with placebo did not reduce hospital length of stay, hospital mortality, or 6-month mortality. Lower hospital mortality was observed in the severe vitamin D deficiency subgroup, but this finding should be considered hypothesis generating and requires further study.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT01130181

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Karin Amrein, MD, MSc, Division of Endocrinology and Metabolism, Department of Internal Medicine, Medical University of Graz, Auenbruggerplatz 15, A-8036 Graz, Austria (karin.amrein@medunigraz.at).

Section Editor: David C. Angus, MD, MPH, Associate Editor, JAMA (angusdc@upmc.edu).

JAMA. 2014;312(15):1520-1530. doi:10.1001/jama.2014.13204
Published online September 30, 2014

JAMA®

The Journal of the American Medical Association

K Amrein and coauthors

Effect of High-Dose Vitamin D_3 on Hospital Length of Stay in Critically Ill Patients With Vitamin D Deficiency: The VITdAL-ICU Randomized Clinical Trial

Published online September 30, 2014

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mobile.jamanetwork.com

The JAMA Network

VITDAL@ICU

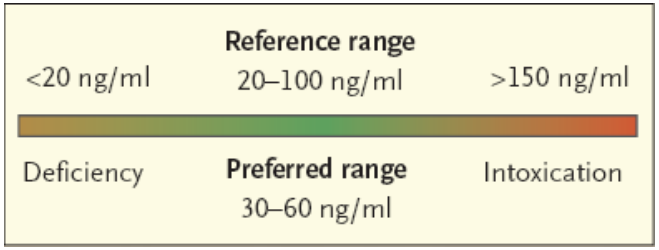
Correction of Vitamin D Deficiency in Critically Ill Patients
ClinicalTrials: NCT01130181

Setting	• randomisiert, doppelblind, placebokontrolliert • 5 ICUs (Neuro, Med, Chirurgie 3x) • 480 Pat. > 48 Std. auf ICU; 25(OH)D ≤ 20 ng/ml
Intervention	• 540,000 IU Vitamin D3 vs. Placebo 1x po/NGS • 90,000 IU/ Monat vs. Placebo 5x
Primärer Endpunkt	Aufenthaltsdauer im Spital
Sekundäre Endpunkte	Mortalität, Aufenthaltsdauer auf ICU, Labor, 6-Monats-Follow Up…

Amrein BMC Disorders 2012, JAMA 2014

DEFINITION

Holick M., NEJM 2007

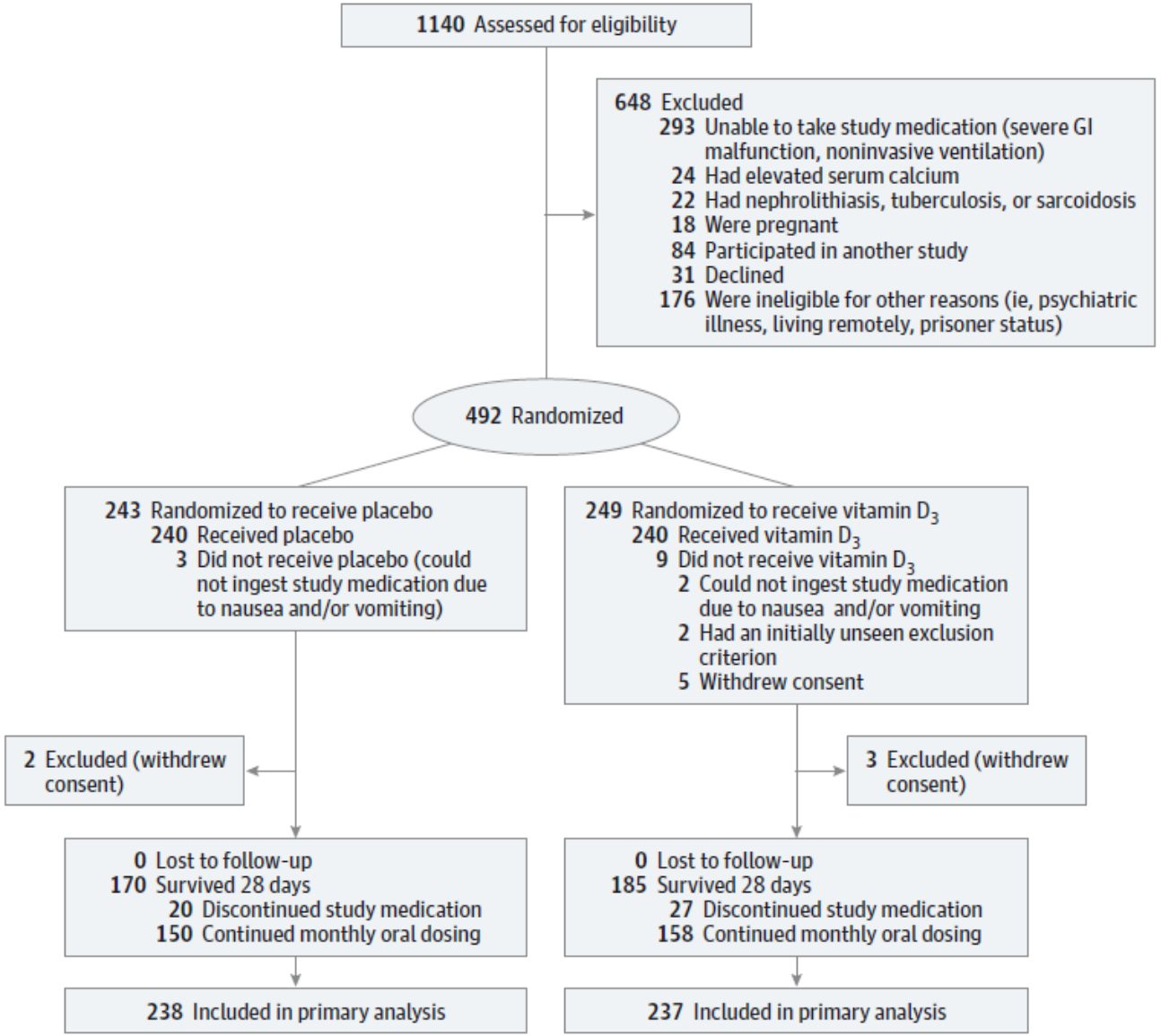


SCHWERER Mangel	< 12ng/ml	<30nmol/L
Mangel	< 20ng/ml	<50nmol/L
Insuffizienz	20-30ng/ml	50-75nmol/L
Normal	>30ng/ml	>75nmol/L

Baseline 25(OH)D Spiegel VITdAL-ICU:

	Placebo	Vitamin D3
25-hydroxy-vitamin D, ng/ml	**13.1 ± 4.3**	**13.0 ± 4.0**
≤12 ng/ml, No. (%)	102 (42.9)	98 (41.4)
13-20 ng/ml	136 (57.1)	139 (58.7)

Figure 1. Flow Diagram of the VITdAL-ICU Trial



N=475

Severe vitamin D deficiency n=200 (42%)

BASELINE CHARAKTERISTIKA

	Placebo (N=238)	Vitamin D3 (N=237)
Alter, Jahre	65.3±14.0	63.9±15.5
Frauen, n (%)	83 (34.9%)	83 (35.0%)
Body mass index, kg/m^2	27.1±5.5	27.2±5.0
SAPS II bei ICU Aufnahme	34.2±15.7	32.4±15.0
TISS-28 bei Studieneinschluss	38.0±8.2	37.7±7.6
Anteil mit mechanischer Beatmung	**154 (64.7%)**	**151 (63.7%)**
Anteil mit Noradrenalintherapie	126 (52.9%)	131 (55.3%)

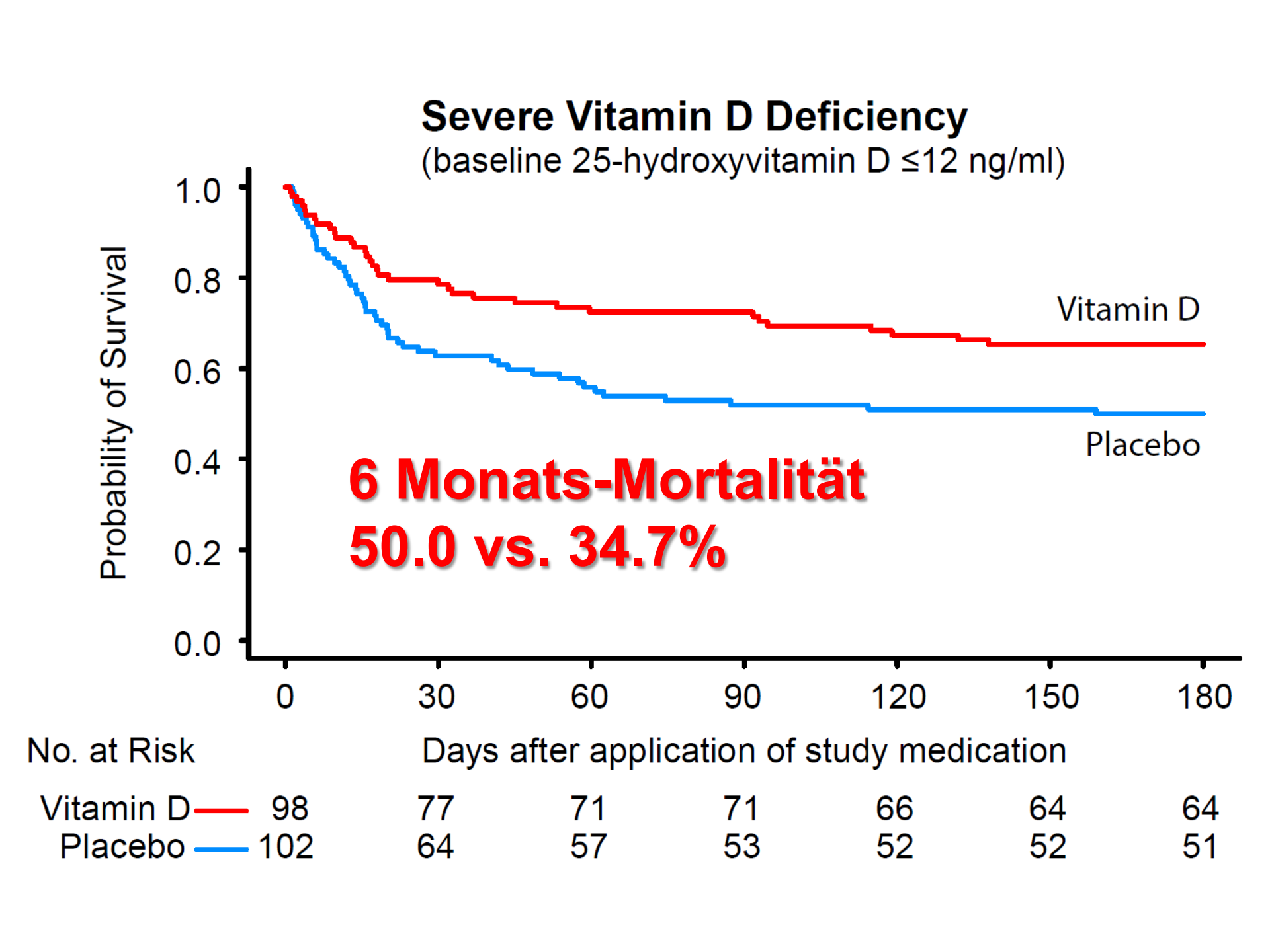
Alle n.s.

RESULTATE
PRIMÄRER ENDPUNKT

SPITALAUFENTHALT (Tage)

Vitamin D3: 20.1 [IQR 11.1-33.3]
Placebo: 19.3 [IQR 11.1-34.9]

P=0.981


Severe Vitamin D Deficiency
(baseline 25-hydroxyvitamin D ≤12 ng/ml)
Probability of Survival
1.0
0.8
0.6
0.4
0.2
0.0
Vitamin D
Placebo
6 Monats-Mortalität
50.0 vs. 34.7%
0
30
60
90
120
150
180
Days after application of study medication
No. at Risk
Vitamin D 98 77 71 71 66 64 64
Placebo 102 64 57 53 52 52 51

VITDAL-STUDIE...

PROTEIN

PROTEIN

- Protein **accounts for approximately 50% of bone volume and about a third of its mass.**
- Cross-linking of collagen molecules in bone involves the modification of amino acids, and many of the collagen fragments released during the bone remodeling process **cannot be reused** to build new bone.
- Adequate supplies of dietary protein are therefore required for healthy bone maintenance.
- Variations in protein intake within the 'normal' range (around 0.8–1.5 g/kg body weight/day) **account for 3–4% of the variance in peak bone mass** attainment in well-nourished children and adolescents

Rizzoli 2014

VITAMIN K

WARFARIN AND VITAMIN K INTAKE IN THE ERA OF PHARMACOGENETICS

- The effect of gross changes in vitamin K intake on anticoagulation is a **classic**.
- Case reports have described decreased anticoagulant response due to **sudden excessive vitamin K intake**. The causes were **usually vitamin K rich, vegetable-based, weight reducing diets and food supplements or multivitamins**. The culprit amounts of vitamin K consumed ranged from 25 to 6000 mg/day
- Excessive anticoagulation has also been described after **unrecorded dietary modification or discontinuation of multivitamin use**

Lurie Y, Brit J Clin Pharmacol 2010

VITAMIN K – EIN UPDATE

Deutsche Herzstiftung

Vitamin K in Lebensmitteln

(Durchschnittswert in µg pro 100 g essbarem Anteil)

Ananas (frisch)	0,10
Ananas (in Dosen)	0,30
Apfel	3,7
Apfelmus	0,60
Apfelsaft	0,10
Apfelsine	3,8
Aprikose	3,3
Aubergine	0,50
Auster	0,10
Avocado	19
Birne	4,9
Bleichsellerie	29
Blumenkohl	57
Broccoli (gekocht, abgetropft)	270
Broccoli (roh)	155
Brunnenkresse	250

Haferflocken	63
Hafermehl	4,1
Haselnuss	9,0
Himbeere	10
Honig	25
Hühnerei (gesamt)	8,9
Hühnerleber	80
Hüttenkäse	0,40
Joghurt (mind. 3,5 % Fett)	0,34
Johannisbeere (rot)	11
Johannisbeere (schwarz)	30
Kakaobutter	15
Kalbsleber	88
Kartoffel	2,1
Kichererbse (Samen, trocken)	264
Kirsche (süß)	1,5

Butter	7,0
Butterschmalz	8,0
Cashewnuss	26
Champignon	14
Chesterkäse	2,3
Chinakohl	80
Diestelöl	11
Emmentalerkäse (45 % Fett)	2,6
Erbse (grün)	29
Erbse (trocken)	81
Erdbeere	5,0
Erdnussöl	0,70
Fenchel (Blatt)	240
Grünkohl	817
Gurke	13
Hafer (ganzes Korn)	50

Kiwi	33
Kohlrabi	7,0
Kokosfett	10
Kopfsalat	109
Kuhmilch (3,5 % Fett)	0,50
Kuhmilch (fettarm)	0,20
Kuhmilch (Magermilch)	0,10
Kuhmilch (Rohmilch)	0,36
Kürbiskernöl	112
Lauch	47
Leinsamen	5,0
Limabohne	6,0
Linse (trocken)	122
Mais (ganzes Korn)	40
Maiskeimöl	31
Makrele	7,1

Schekl A, Ernährungsumschau 2017

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Effect of **vitamin K** in **bone** metabolism and vascular calcification: A review of mechanisms of action and evidences.
Villa JKD et al. Crit Rev Food Sci Nutr. (2017)

Vitamin K and osteoporosis: Myth or reality?
Palermo A et al. Metabolism. (2017)

Regulation of **bone** remodeling by vitamin K2.
Myneni VD et al. Oral Dis. (2017)

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1. **Vitamin K** in Chronic Kidney Disease.
Cozzolino M, Mangano M, Galassi A, Ciceri P, Messa P, Nigwekar S.
Nutrients. 2019 Jan 14;11(1). pii: E168. doi: 10.3390/nu11010168. Review.
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BMJ Case Rep. 2019 Jan 14;12(1). pii: bcr-2018-227520. doi: 10.1136/bcr-2018-227520.
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3. Evaluation of **vitamin K** status and rationale for **vitamin K** supplementation in dialysis patients.
Caluwé R, Verbeke F, De Vriese AS.
Nephrol Dial Transplant. 2018 Dec 26. doi: 10.1093/ndt/gfy373. [Epub ahead of print]
PMID: 30590803
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4. Retraction: Paper "Differential Effect of **Vitamin K** and Vitamin D Supplementation on **Bone** Mass in Young Rats Fed Normal or Low Calcium Diet" by Iwamoto J, et al. [Yonsei Med J 2004;45(2):314-324].

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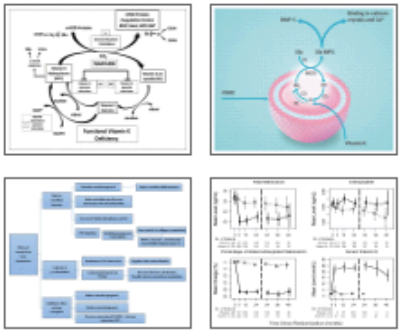

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Bone mineral density and **vitamin K** status in children with celiac di [Turk J Gastroenterol. 201

Combined treatment of **vitamin K** and teriparatide on **bone** metab [Exp Ther Med. 201

Vitamin K and **bone**.
[Clin Cases Miner Bone Metab. 2

K1 vs. K2

- K1: v.a. GRÜNGEMÜSE
- K2: wird von DARMBAKTERIEN synthetisiert

K2-HYPE

Metabolism 2017

Review

Vitamin K and osteoporosis: Myth or reality?

Andrea Palermo[a,1], Dario Tuccinardi[a,*,1], Luca D'Onofrio[b,2], Mikiko Watanabe[c,2], Daria Maggi[a], Anna Rita Maurizi[a], Valentina Greto[a], Raffaella Buzzetti[b], Nicola Napoli[a], Paolo Pozzilli[a], Silvia Manfrini[a]

[a] Department of Endocrinology and Diabetes, University Campus Bio-Medico of Rome, 00128 Rome, Italy
[b] Department of Experimental Medicine, Polo Pontino, Sapienza University of Rome, 00185 Rome, Italy
[c] Department of Experimental Medicine, Section of Medical Physiopathology and Endocrinology, Sapienza University of Rome, 00161 Rome, Italy

ARTICLE INFO

Article history:
Received 13 June 2016
Accepted 28 January 2017

Keywords:
Osteoporosis
Vitamin K1
Vitamin K2
BMD
Fracture

ABSTRACT

Vitamin K is a liposoluble vitamin. The predominant dietary form, phylloquinone or vitamin K1, is found in plants and green vegetables; whereas menaquinone, or vitamin K2, is endogenously synthesized by intestinal bacteria and includes several subtypes that differ in side chain length. Aside from its established role in blood clotting, several studies now support a critical function of vitamin K in improving bone health. Vitamin K is in fact required for osteocalcin carboxylation that in turn regulates bone mineral accretion; it seems to promote the transition of osteoblasts to osteocytes and also limits the process of osteoclastogenesis. Several observational and interventional studies have examined the relationship between vitamin K and bone metabolism, but findings are conflicting and unclear. This systematic review aims to investigate the impact of vitamin K (plasma levels, dietary intake, and oral supplementation) on bone health with a particular interest in bone remodeling, mineral density and fragility fractures.

VITAMIN K

Metabolism 2017

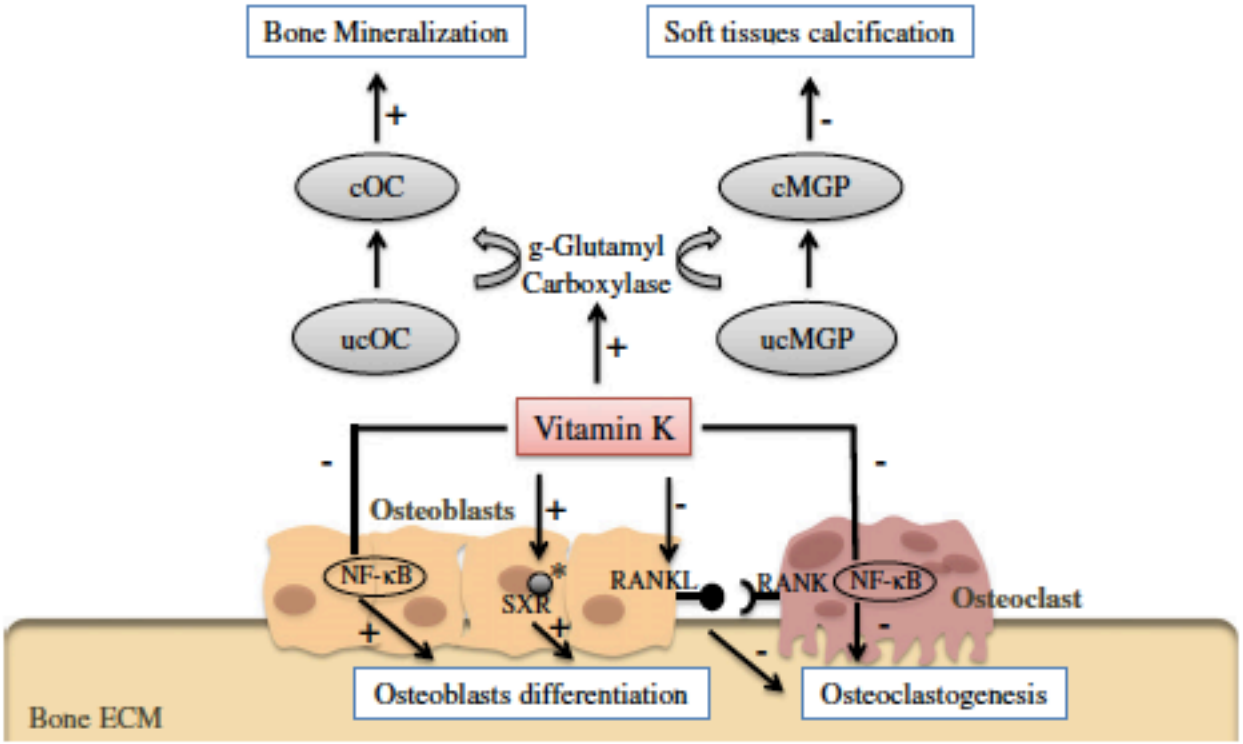

Fig. 1 – Mechanisms of action in bone. *: Evidence in animal models; ucOC: undercarboxylated Osteocalcin; cOC: carboxylated Osteocalcin; ucMGP: undercarboxylated Matrix Gla Protein; cMGP: carboxylated Matrix Gla Protein; NF-κB: nuclear factor κB; SXR: Steroid and Xenobiotic Receptor; RANKL: Receptor Activator of Nuclear factor Kappa B Ligand; RANK: Receptor Activator of Nuclear factor Kappa B; ECM: Extracellular matrix.

VITAMIN K

Metabolism 2017

Randomized controlled trials							
Author, year	Country	n	Subjects	Trial duration	Intervention	Co-interventions*	Results
Kruger MC et al. 2006 [54]	New Zealand	82	Premenopausal women aged 20-35	16 weeks	K1 (80 mcg/day) vs. placebo	Fortified skim milk (Ca 1000 mg/day)	Decreased ucOC, CTX, P1NP
Bügel S et al. 2007 [55]	Denmark	48	Postmenopausal women	6 weeks	K1 (200, 500 mcg/day) vs. placebo	Vitamin D3 10 mcg/day	Decreased ucOC, increased cOC, increased total OC with maximum dose supplementation. No differences in other BTM.
Bolton-Smith C et al. 2007 [56]	UK	209	Healthy postmenopausal women	2 years	K1 (200 mcg/day) and/or vitamin D (400 IU) plus calcium (1000 mg/day) vs. placebo		Decreased %ucOC and PTH
Kanellakis S et al. 2012 [19]	Greece	219	Postmenopausal women	1 year	K1 or K2 (100 mcg/day) vs. placebo	Fortified dairy products (vitamin D 10 mcg and calcium 800 mg)	Decreased %ucOC and urine deoxypyridinoline levels vs. placebo and vs. group without vitamin K addiction
Cheung AM et al. 2008 [63]	Canada	440	Postmenopausal women with osteopenia and normal levels of vitamin D	4 years	K1 (500 mcg/day) vs. placebo		Decreased ucOC and total OC levels, no differences in CTX
Koitaya N et al. 2013 [57]	Japan	50	Healthy postmenopausal women	1 year	MK-4 (1.5 mg/day) vs. placebo		Decreased ucOC
Binkley N et al. 2009 [58]	US	381	Postmenopausal women	1 year	MK-4 (45 mg/day), K1 (1 mg/day) vs. placebo	Calcium and Vitamin D	Decreased ucOC, no differences in BALP and NTX
Emaus N et al. 2010 [59]	Norway	334	Healthy early post-menopausal women	1 year	MK-7, in the form of natto capsules.		Decreased ucOC, increased cOC
Knapen MHJ et al. 2013 [60]	Netherlands	244	Healthy postmenopausal women	3 years	MK-7 (180 mcg/day) vs. placebo		Decreased ucOC, increased cOC
Martini LA et al. 2006 [64]	US	21	Postmenopausal women	84 days	K1 depletion and repletion up to 450 mcg/day		No effects of acute K1 depletion in terms of bone biomarkers, repletion reduced serum NTX
Yasui T et al. 2006 [61]	Japan	34	Postmenopausal women with osteopenia or osteoporosis	1 year	K2 (45 mg/day) or K2 and vitamin D3 (0.75 mcg/day)		Decreased ucOC in both groups, decreased OC and BALP in K2 plus vitamin D group
Miki T et al. 2003 [62]	japan	20	Elderly osteoporotic women with vertebral fractures	2 weeks	MK-4 (45 mg/day)	Calcium (600 mg/day)	Decreased ucOC, no change in OC

ANDERES

- ZINK?
- CAROTINOIDE?
- MAGNESIUM?
- ???

ERKRANKUNGEN

- (UNTER) ERNÄHRUNG
- ANOREXIE
- ZÖLIAKIE
- DIABETES 1
- DIABETES 2

DIABETES

DEUTLICH ERHÖHTES FRAKTURRISIKO!!!

LEITLINIE VON MUSCHITZ ET AL. (ÖGKM) KOMMT

2019

TAKE HOME

- **UNTERERNÄHRUNG IST EIN PROBLEM**
  - **ANOREXIE, ZÖLIAKIE (v.a. MALCOMPLIANCE)**
  - **ÄLTERE, PROTEINMANGEL, SARKOPENIE, CALCIUMZUFUHR**
- **VITAMIN D MANGEL HÄUFIG**
  - **ERFORDERLICHE DOSIS oft > 2000 IU/d**
- **VITAMIN K/2**
  - **WENIGE DATEN**

TAKE HOME

Executive summary

- Factors that maintain bone health include nutrition, weight-bearing exercises and avoidance of deleterious influences.
- Calcium and vitamin D reduce fall and fracture risk.
- Adequate dietary protein intakes are required for healthy bone maintenance.
- Dairy products provide more calcium, protein, phosphorus, potassium, zinc and magnesium per calorie than any other food.
- There is a need to educate subjects about the importance and potential sources of calcium, vitamin D and protein.

Rizzoli R Women‘s Health 2014


Vitamin D-Mangel -
Aktuelle Diagnostik und Prophylaxe in Fallbeispielen
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