# VITAMIN D
# HYPE ODER HOPE

## JUNI 2025

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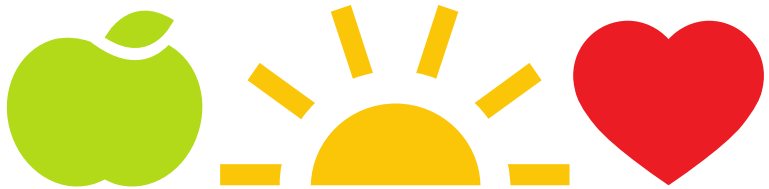

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# ÜBERSICHT

- NEWS 2024 & 2025: KREBS, INFEKTE, PREFRAILTY, AGEING CLOCKS, MS
- GRUNDLAGEN
- PRÄVALENZ MANGEL IN GERIATRIE, MORTALITÄT, FRAKTUREN

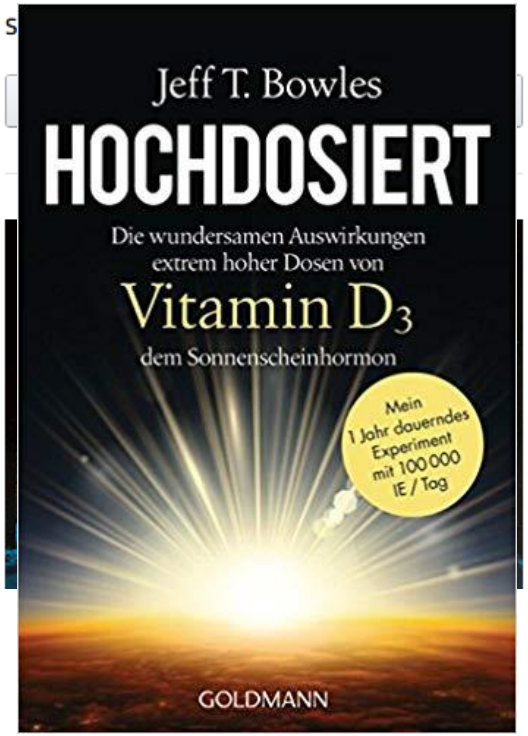
# HYPE!

## 420 Kundenrezensionen

4,4 von 5 Sternen

| | |
|---|---|
| 5 Sterne | 74% |
| 4 Sterne | 8% |
| 3 Sterne | 7% |
| 2 Sterne | 4% |
| 1 Stern | 7% |

### Dieses Produkt bewerten




### Lesen Sie Rezensionen, die folgende Stichworte enthalten

jeff bowles | gesund in 7 tagen | hohen dosen | vitamin d mangel | augen geöffnet | verständlich geschrieben | tolles buch | buch gelesen | hochdosiertes vitamin | raimund von helden | multiple sklerose

Spitzenrezensionen

Timo Rieger

**Sehr empfehlenswert!**

6. Oktober 2018

Format: Kindle Ausgabe | Verifizierter Kauf

Vitamin D3 hat mich gerettet!
Hatte vor mehreren Jahren eine nächtliche Panikattacke und nachfolgend Angstzustände. Ich war immer schlapp und müde, konnte aber nicht schlafen. Das war das Allerschlimmste. Durch den Schlafentzug wurde ich immer antriebsloser und lag eigentlich nur noch auf dem Sofa... Mit ständigen Heulattacken... Mein Hausarzt sagte mir.... Organisch ist alles in Ordnung.... Meine Beschwerden wären wohl psychischer Natur...Niemand konnte mir sagen, was mir fehlte.
Meine Schwester (gelernte Kinderkrankenschwester) machte mich auf Vitamin D3 aufmerksam. Ich las zunächst das Buch "Gesund in sieben Tagen" von Dr. Raimund von Helden. Habe mir dann im Internet einen Arzt gesucht, der Vitamin D - Berater war... Dort wurde ein Bluttest gemacht und ich hatte einen 25-OH-Calciferol-Spiegel von 9ng/ml!!!!!! Also quasi nichts vorhanden! Habe dann hochdosiert Vitamin 3 bekommen und konsequent genommen.... Nach nur ein paar Tagen!!!..... Konnte ich wieder schlafen!!!!! Das war das Größte!!!! Meine Stimmung besserte sich und war wieder deutlich fitter.... Habe dann nach der Auffülltherapie die Erhaltungstherapie weitergemacht mit 40.000IE/Woche Dekristol aber ohne Vitamin K2.... Darüber wusste ich damals noch nichts.... Habe dann schleichend immer weniger Vitamin D3 genommen.... Also öfter mal vergessen usw. Bis ich dann über

# HOPE!

**NEUE RCT Daten – konsistente kleine Benefits (10-20% RR)**

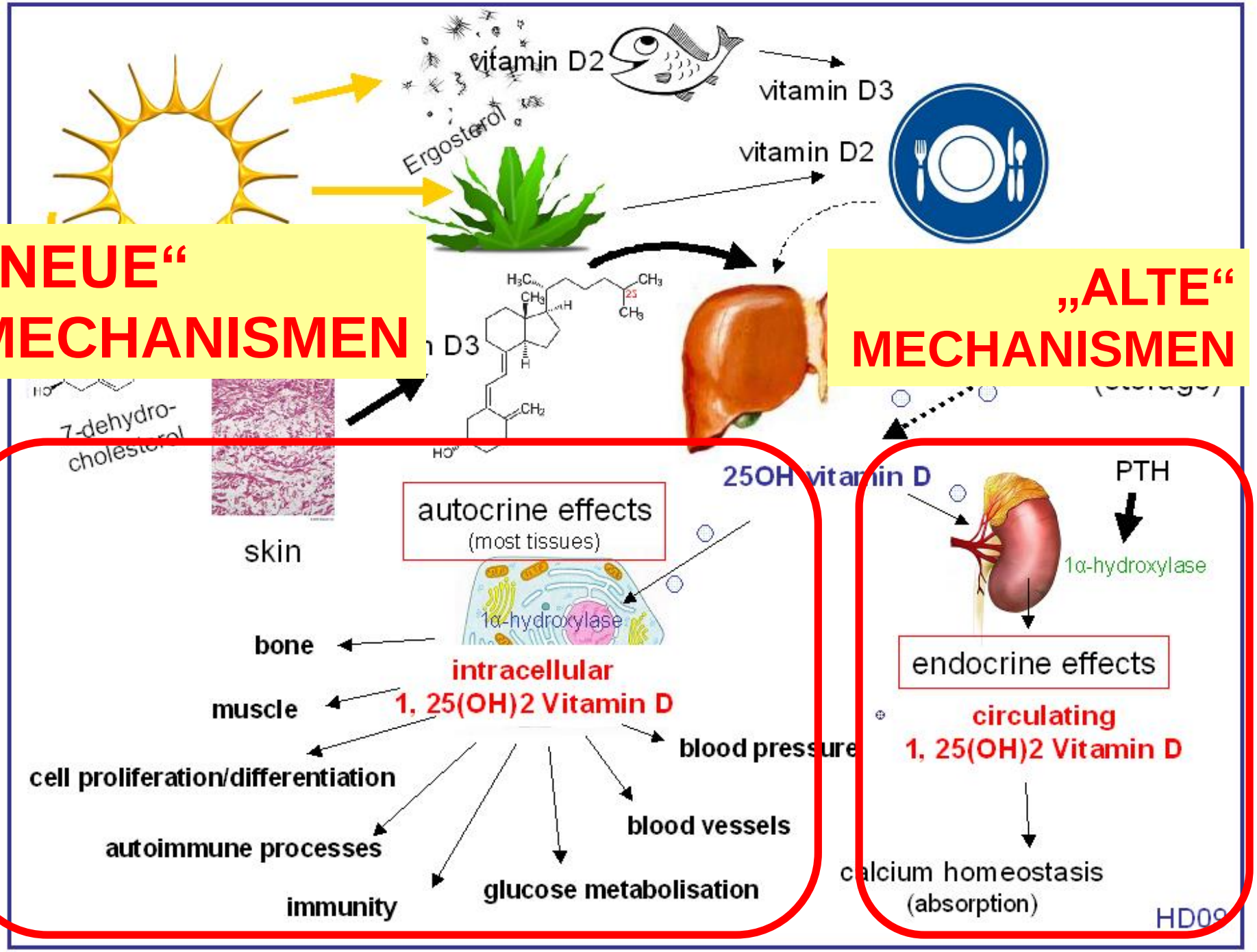
- weniger MS Aktivität (D-lay, Thouvenot, Frankreich, JAMA 2025)

- weniger Frailty / langsameres Altern (Do HEALTH, Bischoff-Ferrari, CH, Nature 2025)

- weniger metastasierte / tödliche Krebserkrankungen (VITAL und DO HEALTH)

- weniger autoimmune Erkrankungen (VITAL, Hahn, US, BMJ 2022, Costenbader)

- Weniger Diabetes (Tobias / VITAL, Nature 2025, Pittas IPDMA 3 RCTs, Annals IM 2023)


„NEUE“ MECHANISMEN
„ALTE“ MECHANISMEN
vitamin D2
Ergosterol
vitamin D3
vitamin D2
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)

# VITAMIN D QUELLEN

**Table 1. Dietary, Supplemental, and Pharmaceutical Sources of Vitamins $D_2$ and $D_3$.***

| Source | Vitamin D Content |
|---|---|
| **Natural sources** | |
| Salmon | |
| Fresh, wild (3.5 oz) | About 600–1000 IU of vitamin $D_3$ |
| Fresh, farmed (3.5 oz) | About 100–250 IU of vitamin $D_3$ or $D_2$ |
| Canned (3.5 oz) | About 300–600 IU of vitamin $D_3$ |
| Sardines, canned (3.5 oz) | About 300 IU of vitamin $D_3$ |
| Mackerel, canned (3.5 oz) | About 250 IU of vitamin $D_3$ |
| Tuna, canned (3.6 oz) | About 230 IU of vitamin $D_3$ |
| Cod liver oil (1 tsp) | About 400–1000 IU of vitamin $D_3$ |
| Shiitake mushrooms | |
| Fresh (3.5 oz) | About 100 IU of vitamin $D_2$ |
| Sun-dried (3.5 oz) | About 1600 IU of vitamin $D_2$ |
| Egg yolk | About 20 IU of vitamin $D_3$ or $D_2$ |
| Exposure to sunlight, ultraviolet B radiation (0.5 minimal erythemal dose)† | About 3000 IU of vitamin $D_3$ |

Holick M NEJM 2007

# BASICS VITAMIN D

- VITAMIN D IST EIN **STEROIDHORMON**
- VITAMIN D **REGULIERT HUNDERTE GENE**
- CALCITRIOL (AKTIVES VITAMIN D) WIRD **NICHT NUR** IN DER NIERE PRODUZIERT

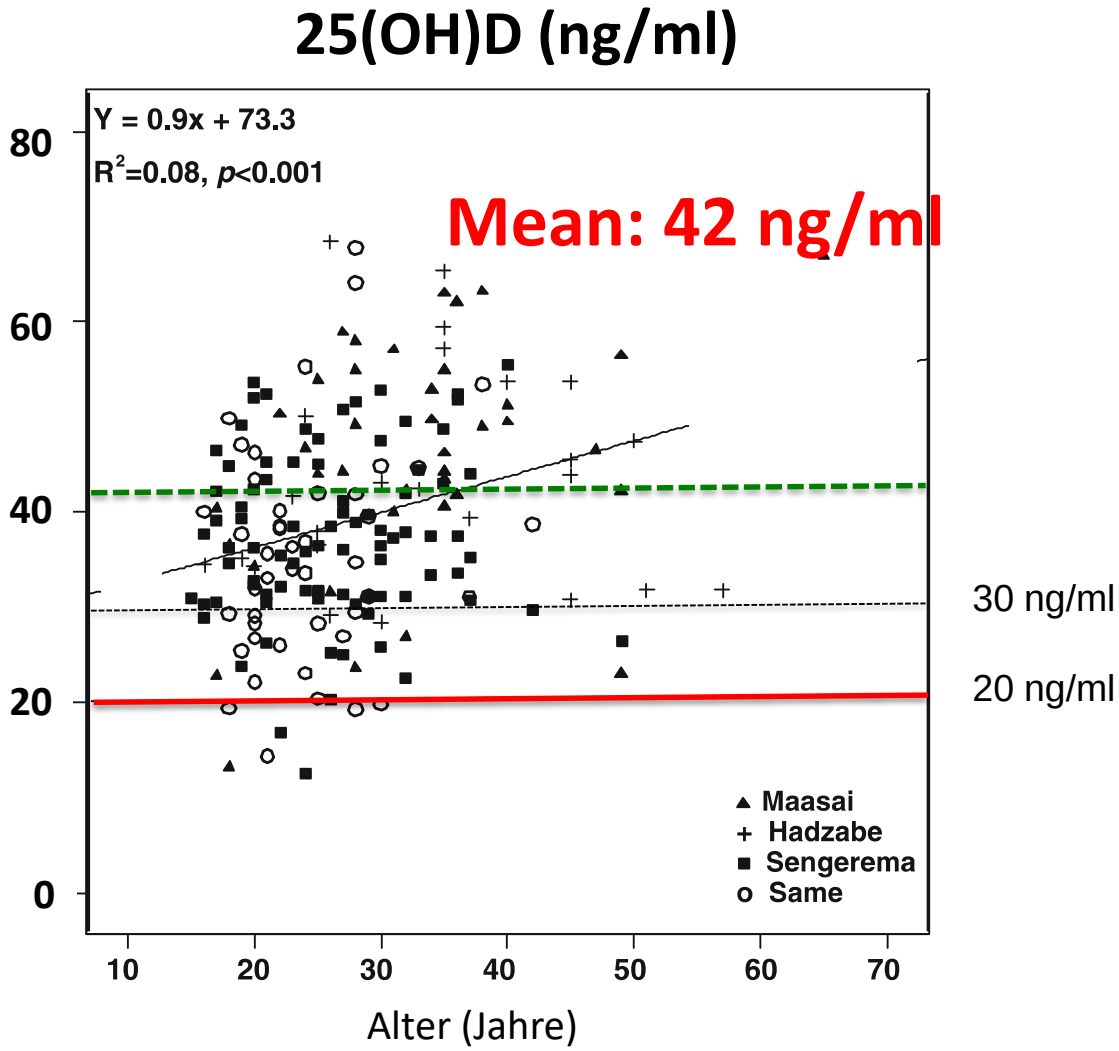
# BASICS VITAMIN D

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

- NG/ML ≠ NMOL/L

- **METABOLITE:** AKTIVES; NATIVES, ...

# VITAMIN D STATUS OHNE BÜRO


N=367 Erwachsene, 82 Kleinkinder

Luxwolda M et al. 2013 Eur J Nutr 52:1115-25

# VITAMIN D STATUS OHNE BÜRO

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



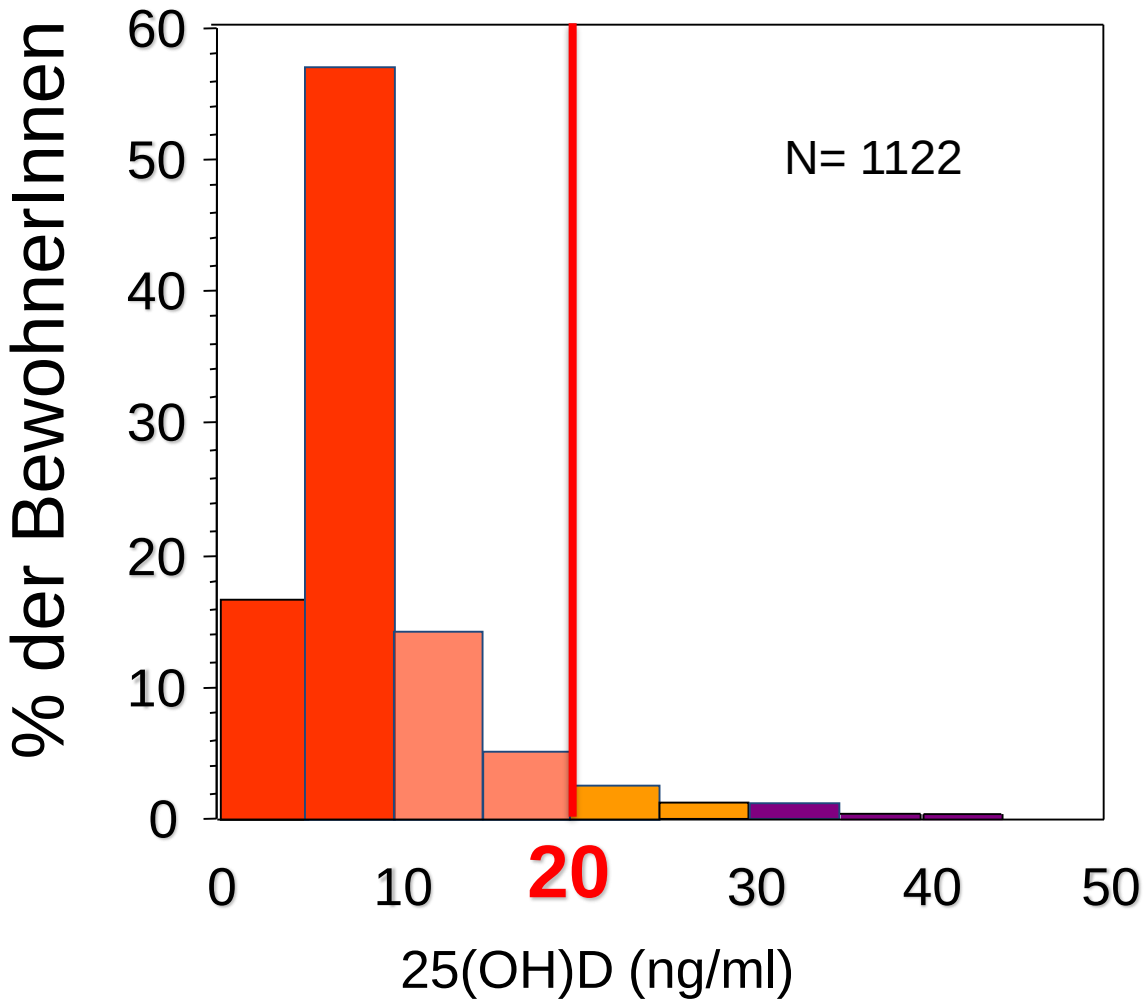
TABLE II*

| 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

Haddad, JCEM 1971

# VITAMIN D STATUS IM PFLEGEHEIM




Dobnig et al. J Clin Endocrinol Metab. 2006; 91(9):3355-63

# MORTALITÄT - 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%**... **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....**

.... 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

# NEWS !

**ENDO 2024 Leitlinie**

**NEUE RCT Daten – konsistente kleine Benefits (10-20% RR)**

- weniger MS Aktivität (D-lay, Thouvenot, Frankreich, JAMA 2025)

- weniger Frailty / langsameres Altern (Do HEALTH, Bischoff-Ferrari, CH, Nature 2025)

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- weniger autoimmune Erkrankungen (VITAL, Jill Hahn, US, BMJ 2022)

- Weniger Diabetes (Tobias / VITAL , Nature 2025, IPDMA 3 RCTs, Annals IM 2023)

*The Journal of Clinical Endocrinology & Metabolism*, 2024, **00**, 1–41
https://doi.org/10.1210/clinem/dgae290
Advance access publication 3 June 2024
**Clinical Practice Guideline**

# Vitamin D for the Prevention of Disease: An Endocrine Society Clinical Practice Guideline

**Marie B. Demay,[1] Anastassios G. Pittas,[2] Daniel D. Bikle,[3] Dima L. Diab,[4] Mairead E. Kiely,[5] Marise Lazaretti-Castro,[6] Paul Lips,[7] Deborah M. Mitchell,[8] M. Hassan Murad,[9] Shelley Powers,[10] Sudhaker D. Rao,[11,12] Robert Scragg,[13] John A. Tayek,[14,15] Amy M. Valent,[16] Judith M. E. Walsh,[17] and Christopher R. McCartney[18,19]**

[1]Department of Medicine, Endocrine Unit, Massachusetts General Hospital and Harvard Medical School, Boston, MA 02114, USA
[2]Division of Endocrinology, Diabetes and Metabolism, Department of Medicine, Tufts Medical Center, Boston, MA 02111, USA
[3]Departments of Medicine and Dermatology, University of California San Francisco, San Francisco VA Medical Center, San Francisco, CA 94158, USA

### Recommendation 4

In the general population aged 50 to 74 years, we suggest against routine vitamin D supplementation. (2 | ⊕⊕⊕◯)

### Technical remark

- This recommendation relates to empiric vitamin D supplementation that exceeds the DRIs established by the IOM. Adults in this age group should follow the Recommended Daily Allowance established by the IOM (600 IU [15 μg] daily for those aged 50 to 70 years; 800 IU [20 μg] daily for those older than 70 years).

### Recommendation 6

In the general population aged 75 years and older, we suggest empiric vitamin D supplementation because of the potential to lower the risk of mortality. (2 | ⊕⊕⊕◯)

### Technical remarks

- Empiric vitamin D may include daily intake of fortified foods, vitamin formulations that contain vitamin D and/or daily intake of a vitamin D supplement.
- For empiric supplementation, daily, lower-dose vitamin D is preferred over nondaily, higher doses.
- In the clinical trials included in the systematic review that reported on the mortality outcome, vitamin D dosage ranged from 400 to 3333 IU (10 to 83 μg) daily equivalent. The estimated weighted average was approximately 900 IU (23 μg) daily. Participants in many trials were allowed to remain on their routine supplements, including up to 800 IU (20 μg) of vitamin D daily.

# FÜR WEN EMPIRISCHE HOCHDOSIERTE VITAMIN D SUPPLEMENTATION? ENDO SOCIETY 2024

| Ages 1-18 | Ages 19-49 | Ages 50-74 | Ages ≥75 | Pregnancy | Prediabetes |
|---|---|---|---|---|---|
| **Empiric vitamin D supplementation*** To prevent nutritional rickets and because of the potential to lower the risk of respiratory tract infections. | **No empiric vitamin D supplementation*** Follow the Institute of Medicine Recommended Daily Allowance. | | **Empiric vitamin D supplementation*** Because of the potential to lower the risk of mortality. | **Empiric vitamin D supplementation*** Because of the potential to lower the risk of preeclampsia, intrauterine mortality, preterm birth, small for gestational age birth and neonatal mortality. | **Empiric vitamin D supplementation*** Because of the potential to lower the risk of progression to diabetes. |

The panel assumed that all should follow the Recommended Dietary Reference Intakes (DRI) established by the US Institute of Medicine (currently the National Academy of Medicine). The Recommended Daily Allowance (RDA) in the DRI is 600 IU (15 μg) for persons aged 1-70 years and 800 IU (20 μg) for persons older than 70 years. The RDA established by the the Institute of Medicine and the American College of Obstetricians and Gynecologists (ACOG) is 600 IU (15 μg) during pregnancy.

* **Empiric vitamin D supplementation** refers to vitamin D (cholecalciferol [$D_3$] or ergocalciferol [$D_2$]) intake (usually in pill or drop form) that (a) exceeds the DRIs and (b) is implemented without testing for 25-hydroxyvitamin D. Vitamin D doses in the included clinical trials varied considerably (see technical remarks under recommendations); hence, optimal doses remain unclear.

For people older than 50 years for whom vitamin D treatment is indicated, the panel suggests supplementation via daily administration of vitamin D, rather than intermittent high doses.

The panel suggests against routine 25-hydroxyvitamin D testing for generally healthy individuals who do not otherwise have established indications for 25-hydroxyvitamin D testing (e.g., hypocalcemia). The panel did not specifically address whether and how those who present with low levels of 25-hydroxyvitamin D should be evaluated and/or treated.

* Importantly, this guideline does not address individuals with underlying conditions that substantially alter vitamin D physiology, including various conditions associated with decreased absorption (e.g., short gut, gastric bypass, inflammatory bowel disease), increased catabolism/decreased activation (e.g., some medications), and increased renal losses (e.g., nephrotic syndrome). In addition, this guideline does not address persons known to be at high risk for fractures.

Demay JCEM 2024:https://doi.org/10.1210/clinem/dgae290

# PRÄDIABETES

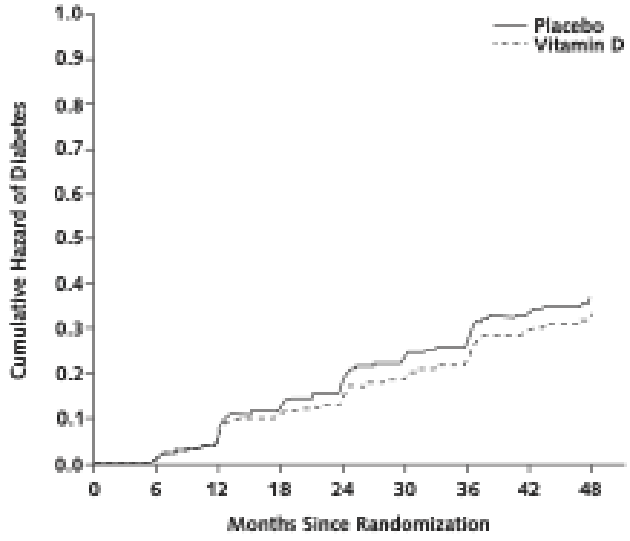
Annals of Internal Medicine REVIEW

## Vitamin D and Risk for Type 2 Diabetes in People With Prediabetes

### A Systematic Review and Meta-analysis of Individual Participant Data From 3 Randomized Clinical Trials

Anastassios G. Pittas, MD, MS; Tetsuya Kawahara, MD, PhD; Rolf Jorde, MD, PhD; Bess Dawson-Hughes, MD; Ellen M. Vickery, MS; Edith Angellotti, MD; Jason Nelson, MPH; Thomas A. Trikalinos, MD; and Ethan M. Balk, MD, MPH

*Figure 2.* Incidence curves for new-onset diabetes among adults with prediabetes: intention-to-treat analysis.

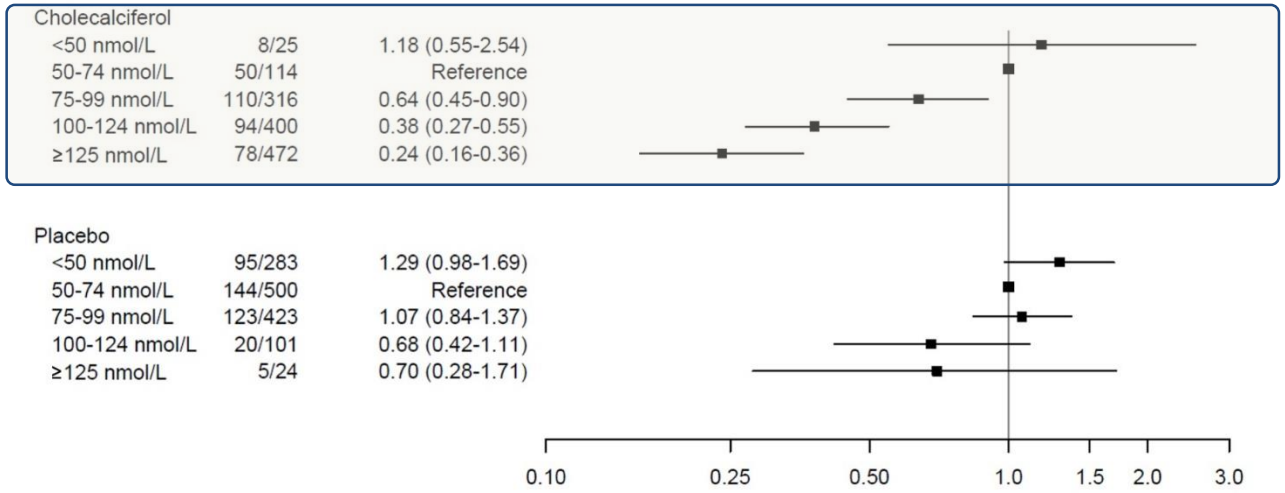



At risk, *n*

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Vitamin D | 2097 | 2040 | 1908 | 1745 | 1527 | 1298 | 1105 | 429 | 281 |
| Placebo | 2093 | 2032 | 1900 | 1714 | 1488 | 1239 | 1050 | 397 | 255 |

Vitamin D reduced risk for diabetes by 15% (hazard ratio, 0.85 [95% CI, 0.75 to 0.96]) in adjusted analyses, with
a 3-year absolute risk reduction of 3.3% (CI, 0.6% to 6.0%).

**-15%**



Annals of Internal Medicine

REVIEW

# Vitamin D and Risk for Type 2 Diabetes in People With Prediabetes

## A Systematic Review and Meta-analysis of Individual Participant Data From 3 Randomized Clinical Trials

**Anastassios G. Pittas, MD, MS; Tetsuya Kawahara, MD, PhD; Rolf Jorde, MD, PhD; Bess Dawson-Hughes, MD; Ellen M. Vickery, MS; Edith Angellotti, MD; Jason Nelson, MPH; Thomas A. Trikalinos, MD; and Ethan M. Balk, MD, MPH**

**Background:** The role of vitamin D in people who are at risk for type 2 diabetes remains unclear.

**Purpose:** To evaluate whether administration of vitamin D decreases risk for diabetes among people with prediabetes.

**Data Sources:** PubMed, Embase, and ClinicalTrials.gov from database inception through 9 December 2022.

**Study Selection:** Eligible trials that were specifically designed and conducted to test the effects of oral vitamin D versus placebo on new-onset diabetes in adults with prediabetes.

**Data Extraction:** The primary outcome was time to event for new-onset diabetes. Secondary outcomes were regression to normal glucose regulation and adverse events. Prespecified analyses (both unadjusted and adjusted for key baseline variables) were conducted according to the intention-to-treat principle.

**Data Synthesis:** Three randomized trials were included, which tested cholecalciferol, 20 000 IU (500 mcg) weekly; cholecalciferol, 4000 IU (100 mcg) daily; or eldecalcitol, 0.75 mcg daily, versus matching placebos. Trials were at low risk of bias. Vitamin D reduced risk for diabetes by 15% (hazard ratio, 0.85 [95% CI, 0.75 to 0.96]) in adjusted analyses, with a 3-year absolute risk reduction of 3.3% (CI, 0.6% to 6.0%). The effect of vitamin D did not differ in prespecified subgroups. Among participants assigned to the vitamin D group who maintained an intratrial mean serum 25-hydroxyvitamin D level of at least 125 nmol/L (≥50 ng/mL) compared with 50 to 74 nmol/L (20 to 29 ng/mL) during follow-up, cholecalciferol reduced risk for diabetes by 76% (hazard ratio, 0.24 [CI, 0.16 to 0.36]), with a 3-year absolute risk reduction of 18.1% (CI, 11.7% to 24.6%). Vitamin D increased the likelihood of regression to normal glucose regulation by 30% (rate ratio, 1.30 [CI, 1.16 to 1.46]). There was no evidence of difference in the rate ratios for adverse events (kidney stones: 1.17 [CI, 0.69 to 1.99]; hypercalcemia: 2.34 [CI, 0.83 to 6.66]; hypercalciuria: 1.65 [CI, 0.83 to 3.28]; death: 0.85 [CI, 0.31 to 2.36]).

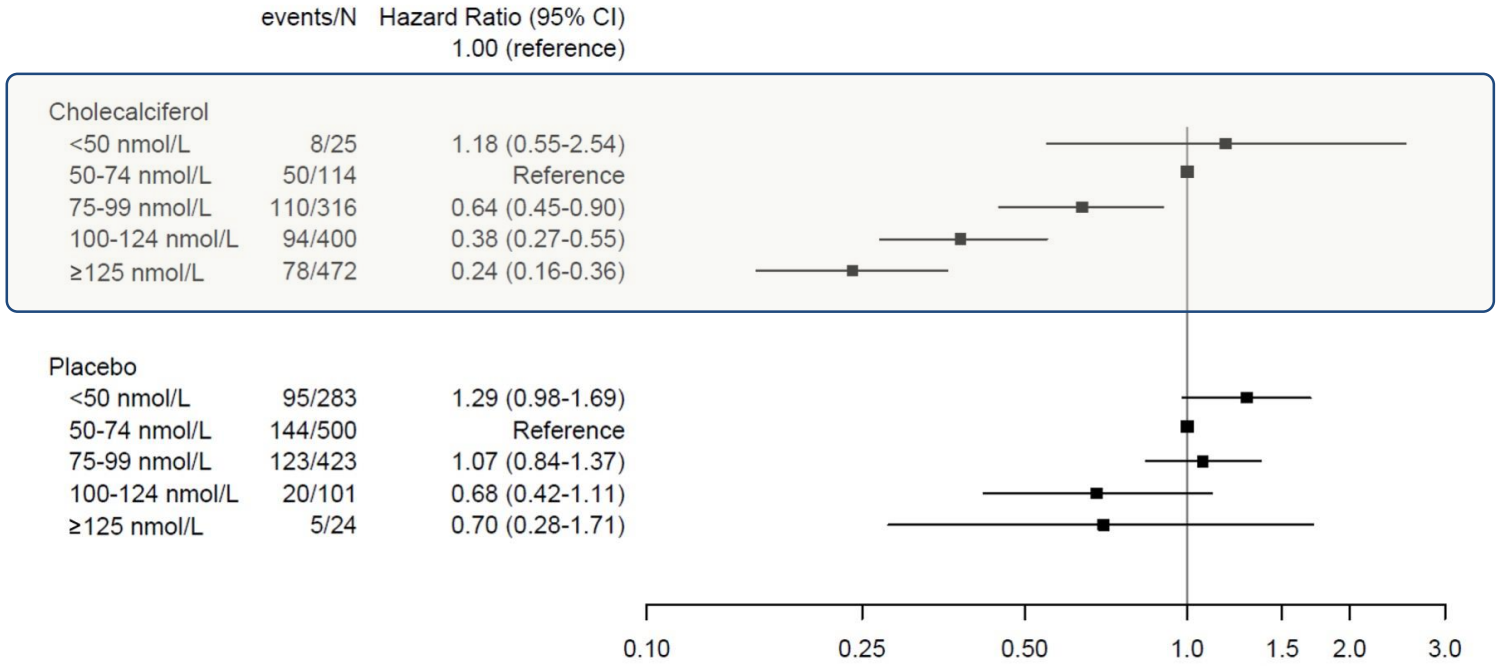
**Limitations:** Studies of people with prediabetes do not apply to the general population. Trials may not have been powered for safety outcomes.

**Conclusion:** In adults with prediabetes, vitamin D was effective in decreasing risk for diabetes.

**Primary Funding Source:** None. (PROSPERO: CRD42020163522)

*Ann Intern Med.* doi:10.7326/M22-3018 Annals.org
For author, article, and disclosure information, see end of text.
This article was published at Annals.org on 7 February 2023.

USA
NORWEGEN
JAPAN




Adjusted for baseline age, gender, body mass index, race, and hemoglobin A1c

# Intra-trial vitamin $D_3$ exposure and risk of new-onset diabetes

Pittas, Kawahara, Jorde et al Ann Int Med 2023

# NNT

INTENSIVE LIFESTYLE, NNT = 7

METFORMIN, NNT = 14 (BMI > 30)

VITAMIN D, NNT = 30 (BMI < 30)

# MULTIPLE SKLEROSE, JAMA 2025

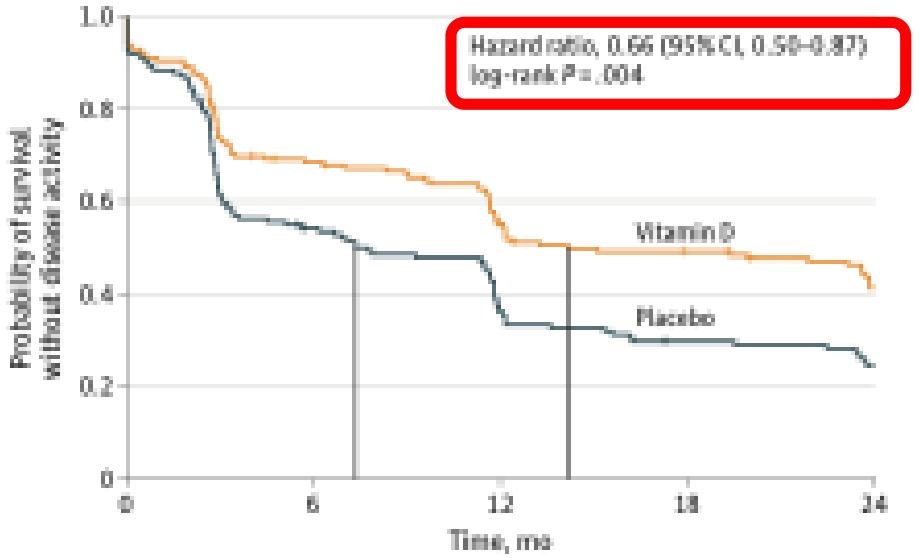
**- 34%**

**OBJECTIVE** To evaluate the efficacy of high-dose cholecalciferol as monotherapy in reducing disease activity in patients with clinically isolated syndrome (CIS) typical for MS.

**DESIGN, SETTING, AND PARTICIPANTS** The D-Lay MS trial was a parallel, double-blind, randomized placebo-controlled clinical trial in 36 MS centers in France. Patients were enrolled from July 2013 to December 2020 (final follow-up on January 18, 2023). Untreated patients with CIS aged 18 to 55 years with CIS duration less than 90 days, serum vitamin D concentration less than 100 nmol/L, and diagnostic magnetic resonance imaging (MRI) meeting 2010 criteria for dissemination in space or 2 or more lesions and presence of oligoclonal bands were recruited.

**INTERVENTION** Patients were randomized 1:1 to receive oral cholecalciferol 100 000 IU (n = 163) or placebo (n = 153) every 2 weeks for 24 months.

Figure 2. Disease Activity in the Treatment Groups During the 2 Years of Follow-Up



# VITAL vs. DO HEALTH

## UNTERSCHIEDE

N= >25,000 vs. > 2100

50 + vs. 70+

+ Turnen in DO HEALTH

US vs Europa

## ÄHNLICH

Beide 2000 IU & 1000mg Omega 3

800 IU Vitamin D in Placeboarm erlaubt

Nicht selektioniert für Mangel

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

# Vitamin D Supplements and Prevention of Cancer and Cardiovascular Disease

JoAnn E. Manson, M.D., Dr.P.H., Nancy R. Cook, Sc.D., I-Min Lee, M.B., B.S., Sc.D., William Christen, Sc.D., Shari S. Bassuk, Sc.D., Samia Mora, M.D., M.H.S., Heike Gibson, Ph.D., David Gordon, M.A.T., Trisha Copeland, M.S., R.D., Denise D'Agostino, B.S., Georgina Friedenberg, M.P.H., Claire Ridge, M.P.H., Vadim Bubes, Ph.D., Edward L. Giovannucci, M.D., Sc.D., Walter C. Willett, M.D., Dr.P.H., and Julie E. Buring, Sc.D., for the VITAL Research Group*

## ABSTRACT

**BACKGROUND**

It is unclear whether supplementation with vitamin D reduces the risk of cancer or cardiovascular disease, and data from randomized trials are limited.

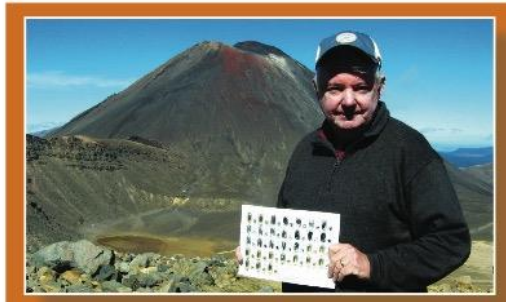
Fr
Bri
Ha

# 2018 VITAL...

„KEIN“ EFFEKT AUF CV & ONKO-NEUERKRANKUNGEN, ABER...

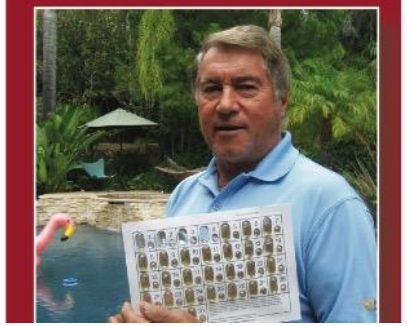
## VITAL on the Go

**Joyce S.**, of Maryland, writes, “In a ‘crabby’ mood in Annapolis, Maryland! Home of the Great Blue! Great dipped in butter! Enjoyed a tasty feast with family. Haven’t missed a pill in five years.”



**Daniel D.**, of Mississippi, at the Tongariro Alpine Crossing in New Zealand, writes that “[t]he volcano in the background [Mount Ngauruhoe] served as ‘Mount Doom’ in the Lord of the Rings movies.”

**Chris J.**, of California, at the Uyuni Salt Flats in Bolivia, is on a quest to visit 100 countries before her 80th birthday. She reports, “I have about 21 countries to go to reach my goal.”



**Leeann S.**, of Massachusetts, with chinstrap penguins in Antarctica, writes, “I teach nutrition and health, and I spend a lot of time answering questions about supplements. Now I get to be a part of the research on two popular supplements. Nothing impresses students more than real life experience...”

JAMA Network Open

Original Investigation | Oncology

# Effect of Vitamin $D_3$ Supplements on Development of Advanced Cancer
## A Secondary Analysis of the VITAL Randomized Clinical Trial

Paulette D. Chandler, MD, MPH; Wendy Y. Chen, MD, MPH; Oluremi N. Ajala, MD, MPH; Aditi Hazra, PhD, MPH; Nancy Cook, ScD; Vadim Bubes, PhD; I-Min Lee, MBBS, ScD; Edward L. Giovannucci, MD, ScD; Walter Willett, MD, DrPH; Julie E. Buring, ScD; JoAnn E. Manson, MD, DrPH; for the VITAL Research Group

## Abstract

**IMPORTANCE** Epidemiologic and trial data suggest that vitamin D supplementation may reduce metastatic cancer and cancer mortality, reflecting shared biological pathways.

**OBJECTIVE** To follow up on the possible reduction in cancer death in the Vitamin D and Omega-3 Trial (VITAL) with an evaluation of whether vitamin D reduces the incidence of advanced (metastatic

## Key Points

**Question** Does vitamin $D_3$ supplementation reduce the risk of developing advanced (metastatic or fatal) cancer among adults without a diagnosis of cancer at baseline?

JAMA Network Open

Original Investigation | Oncology

# Effect of Vitamin $D_3$ Supplements on Development of Advanced Cancer
## A Secondary Analysis of the VITAL Randomized Clinical Trial

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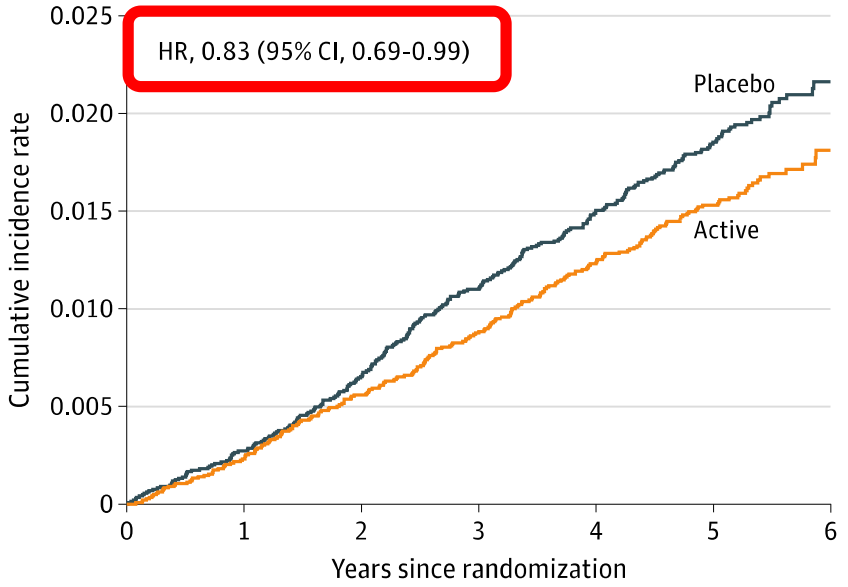
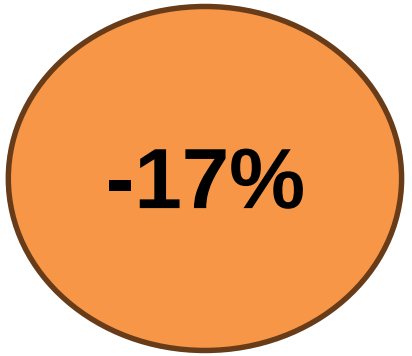
**Figure 2. Vitamin D (Active) and Placebo: Cumulative Incidence Rates of Metastatic and Fatal Cancer of Any Type**




No. at risk

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Active | 12 927 | 12 738 | 12 543 | 12 341 | 11 992 | 9557 | 744 |
| Placebo | 12 944 | 12 765 | 12 567 | 12 345 | 11 985 | 9543 | 746 |



# INVASIVE CANCER

**DO HEALTH**
Vitamin D, Omega & Turnen



| Treatment | Treatment Event /Total | Control Event /Total | Hazard Ratio (95%CI) |
|---|---|---|---|
| Vitamin D | 36 /1076 | 45 /1051 | 0.76 ( 0.49 - 1.18 ), p= 0.225 |
| Omega-3 | 32 /1073 | 49 /1054 | 0.7 ( 0.44 - 1.09 ), p= 0.115 |
| SHEP | 35 /1081 | 46 /1076 | 0.74 ( 0.48 - 1.15 ), p= 0.183 |
| Omega-3 + Vitamin D | 15 /529 | 28 /537 | 0.53 ( 0.28 - 1 ), p= 0.051 |
| Vitamin D + SHEP | 11 /539 | 21 /539 | 0.56 ( 0.3 - 1.04 ), p= 0.068 |
| Omega-3 + SHEP | 12 /539 | 26 /542 | 0.52 ( 0.28 - 0.97 ), p= 0.039 |
| Vitamin D + Omega-3 + SHEP | 4 /264 | 12 /270 | 0.39 ( 0.18 - 0.85 ), p= 0.017 |

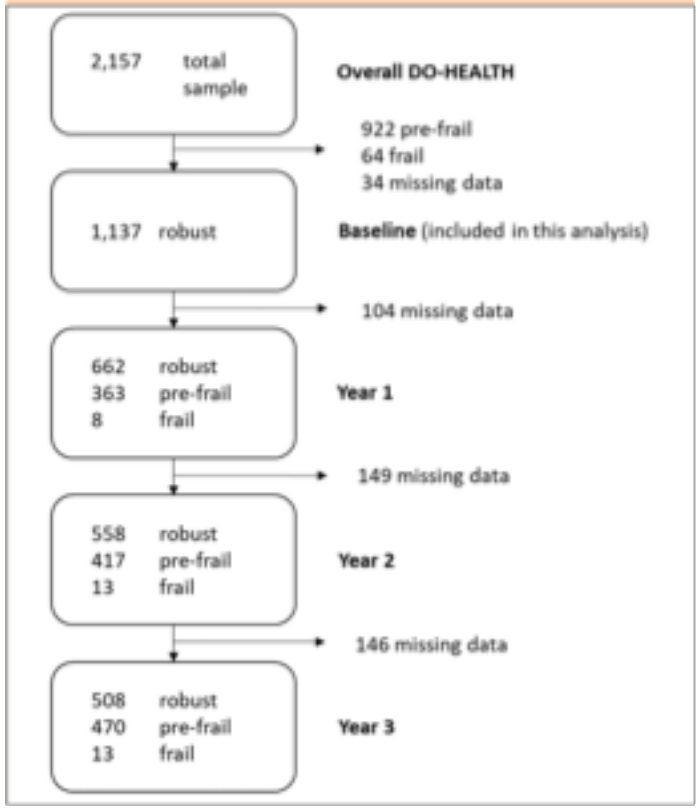

**FIGURE 2 |** Primary endpoint—effect of treatments on the prevention of any invasive cancer. Cox-proportional hazard model adjusted for history of cancer, sex, BMI, prior fall, age, and study center. The comparison group is always the group that does not have the respective treatment(s) of interest. For all three treatments, it is the group who received only the placebo. All verified new invasive cancer cases (*n* = 81) among all 2,157 participants. Abbreviation: SHEP, Simple home exercise program.

**VIT D -24%**
**Alle -61%**

# PREFRAILTY



**Figure 1.** Flow chart of included participants




For this analysis we included only participants considered robust at baseline from the total DO-HEALTH study population according to the applied frailty phenotype

**DO HEALTH**

Vitamin D, Omega & Turnen

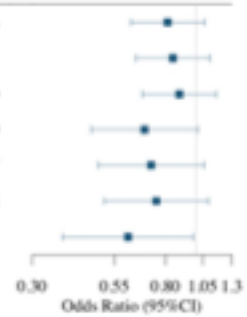
Gagesch M. et. al. 2023

Vit D -19
alle -39%



**Figure 2.** Treatment effects on the odds of becoming pre-frail during the follow-up

| Treatments | Incidence in Treatment Group | Incidence in Control Group | Odds Ratio (95% CI) | P-values |
|---|---|---|---|---|
| Vit D vs No Vit D | 333/528 (63.1%) | 363/535 (67.9%) | 0.81 (0.62-1.07) | p=0.134 |
| Omega-3 vs No Omega-3 | 334/520 (64.2%) | 362/543 (66.7%) | 0.84 (0.64-1.11) | p=0.221 |
| SHEP vs No SHEP | 343/540 (63.5%) | 353/523 (67.5%) | 0.89 (0.67-1.16) | p=0.379 |
| Vit D+ Omega-3 vs No VitD + Omega-3 | 160/251 (63.8%) | 189/266 (71.1) | 0.69 (0.46-1.01) | p=0.059 |
| Vit D + SHEP vs No VitD + SHEP | 166/264 (62.9%) | 186/259 (71.8%) | 0.72 (0.49-1.06) | p=0.097 |
| Omega-3 + SHEP vs No Omega-3 + SHEP | 164/266 (61.7%) | 183/269 (68.0%) | 0.75 (0.51-1.10) | p=0.135 |
| Vit D + Omega-3 + SHEP vs Placebo | 80/126 (63.5%) | 96/130 (73.9%) | 0.61 (0.38-0.98) | p=0.041 |




Vit D = Vitamin D supplementation, Omega-3 = Omega-3 fatty acids supplementation, SHEP = simple home exercise program

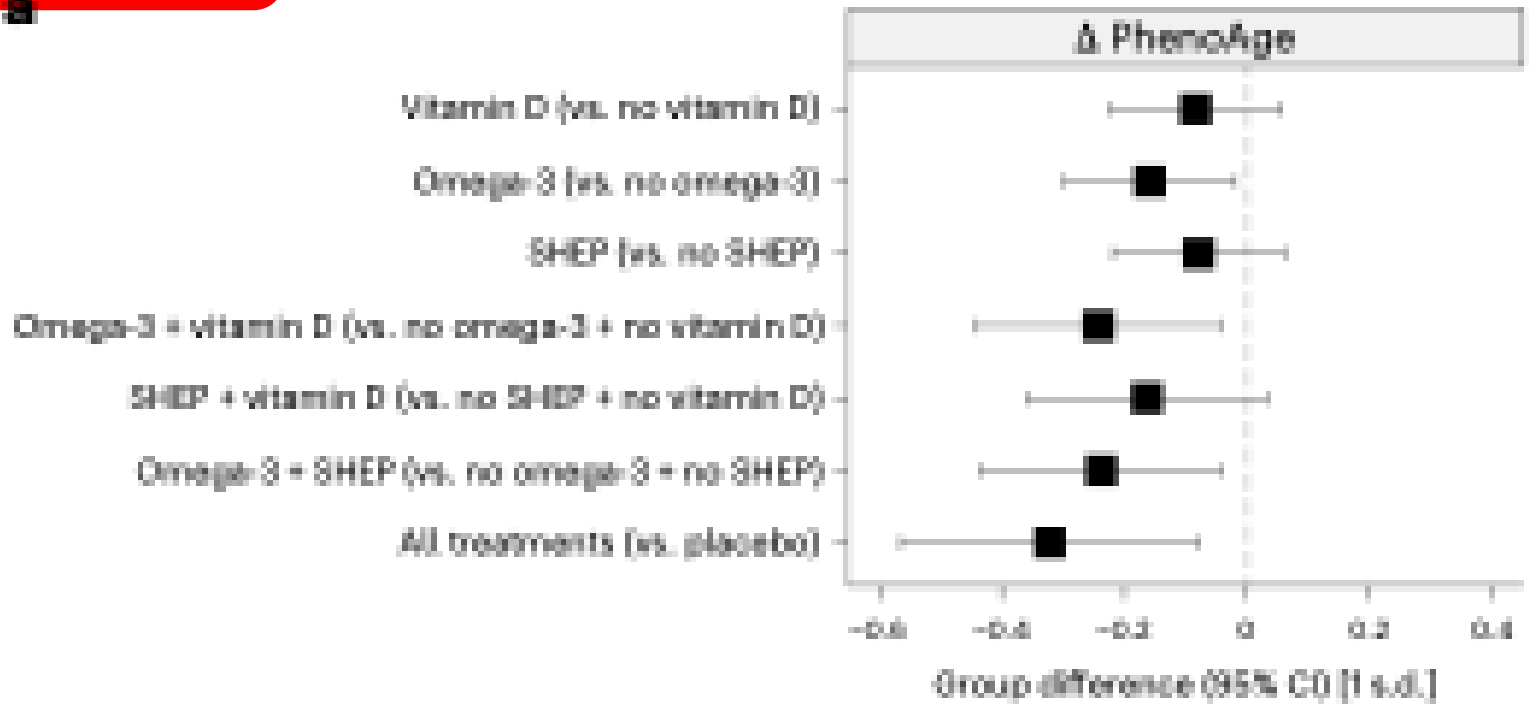
# AGEING

GrimAge2 and DunedinPACE) over 3 years. Omega-3 alone slowed the DNAm clocks PhenoAge, GrimAge2 and DunedinPACE, and all three treatments had additive benefits on PhenoAge. Overall, from baseline to year 3, standardized effects ranged from 0.16 to 0.32 units (2.9–3.8 months). In summary, our trial indicates a small protective effect of omega-3 treatment on slowing biological aging over 3 years across several clocks, with an additive protective effect of omega-3, vitamin D and exercise based on PhenoAge.

**DO HEALTH**

Vitamin D, Omega & Turnen

Bischoff Ferrari et. al. Nature Med 2025



# VITAL

Arthritis & Rheumatology
Vol. 76, No. 6, June 2024, pp 973–983
DOI 10.1002/art.42811
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American College of Rheumatology
Empowering Rheumatology Professionals

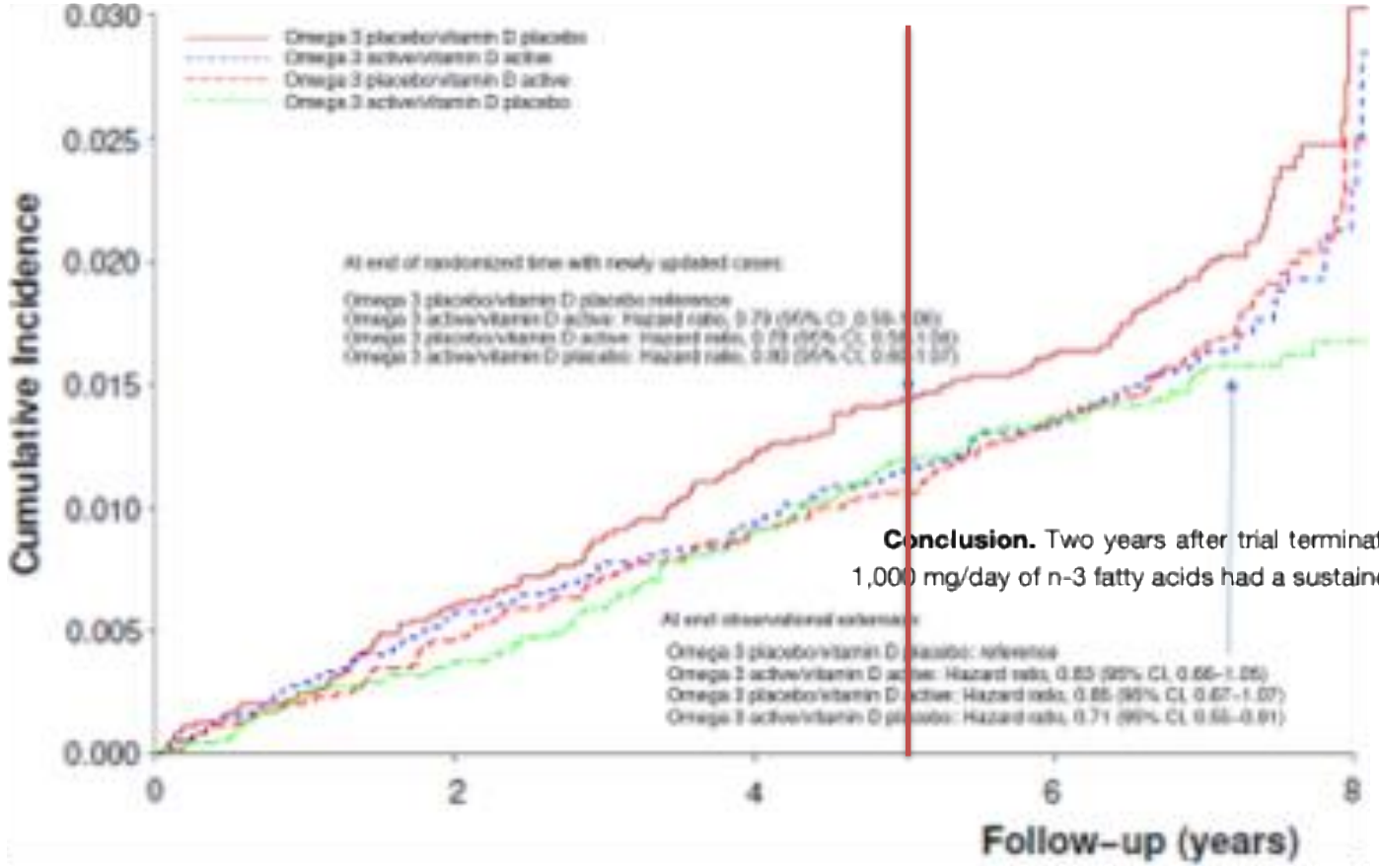


## Vitamin D and Marine n-3 Fatty Acids for Autoimmune Disease Prevention: Outcomes Two Years After Completion of a Double-Blind, Placebo-Controlled Trial



Karen H. Costenbader,[1] Nancy R. Cook,[1] I-Min Lee,[1] Jill Hahn,[2] Joseph Walter,[3] Vadim Bubes,[3] Gregory Kotler,[3] Nicole Yang,[1] Sonia Friedman,[1] Erik K. Alexander,[1] and JoAnn E. Manson[1]

- 22%




**Conclusion.** Two years after trial termination, the protective effects of 2000 IU/day of vitamin D dissipated, but 1,000 mg/day of n-3 fatty acids had a sustained effect in reducing AD incidence.

**Figure 3.** Cumulative incidence curves for autoimmune disease incidence in the four arms of VITAL (N = 25,871) over a median of 5.3 years of randomized follow-up and 2 years of observational follow-up after trial termination. CI, confidence interval; VITAL, Vitamin D and Omega-3 Trial.

# VITAL

nature communications

Article

https://doi.org/10.1038/s41467-025-58721-6

# Vitamin D supplementation vs. placebo and incident type 2 diabetes in an ancillary study of the randomized Vitamin D and Omega-3 Trial

- 9%
ns

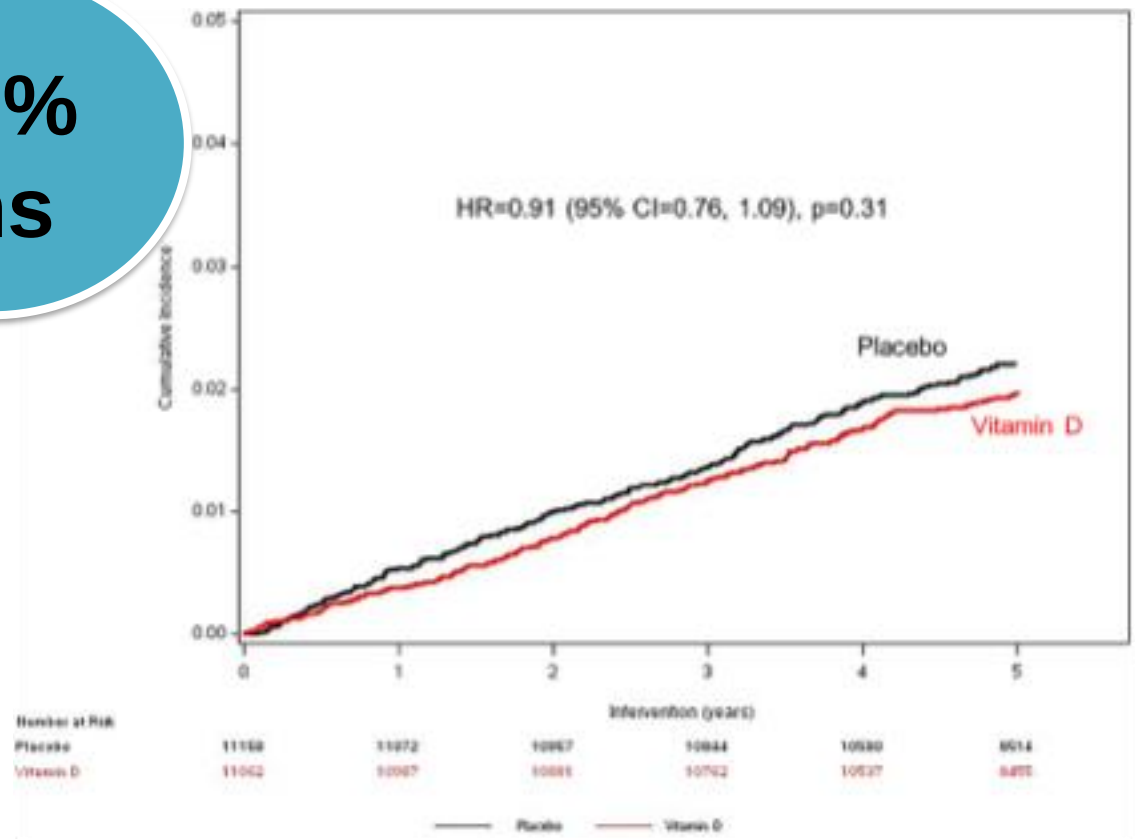



**Fig. 1 | Cumulative incidence of T2D by randomized vitamin D vs. placebo in VITAL-T2D.** The cumulative incidence plot and intention-to-treat hazard ratio and 95% confidence interval of T2D by randomized vitamin D vs. placebo were calculated using a Cox proportional hazards regression model adjusted for age at baseline, sex, and randomized omega-3 treatment group (active vs. placebo) using two-sided hypothesis tests. Source data are provided as a Source Data file. HR hazard ratio CI 95% confidence interval.

US adults. The study design is an ancillary analysis (VITAL-T2D) of The Vitamin D and Omega-3 Trial (VITAL), a completed randomized, double-blind, placebo-controlled 2 × 2 trial of daily vitamin $D_3$ (cholecalciferol; 2000 IU/day) and omega-3 fatty acids (1 g/day) for the primary prevention of cancer and cardiovascular disease. We also conducted a systematic review and meta-analysis of

**2000 IU vs. Placebo**
**(800 IU erlaubt!)**

**nicht selektioniert**
**für T2D Risiko**

**Table 2 | Effect of randomization to vitamin D vs. placebo on T2D incidence in VITAL-T2D**

| Treatment group | T2D cases, No. (%) | T2D incident rate | HR (95% CI) | P-value |
|---|---|---|---|---|
| Placebo | 254 (2.27%) | 4.37 cases/1000 PY | Reference | |
| Vitamin D | 230 (2.08%) | 3.98 cases/1000 PY | 0.91 (0.76, 1.09) | 0.31 |

Intention-to-treat Cox proportional hazards regression model is adjusted for age at baseline randomization, self-reported sex, and omega-3 treatment group a… 2 diabetes; *PY* person years, *CI* confidence interval.

| | | |
|---|---|---|
| Vitamin D supplement use ≤800 IU/d[c] | 4880 (43.7) | 4845 (43.8) |
| Serum 25-hydoxyvitamin D, median (IQR), ng/ml | 31 (25—37) | 31 (25—37) |
| <20 ng/ml | 838 (12.2) | 765 (11.3) |

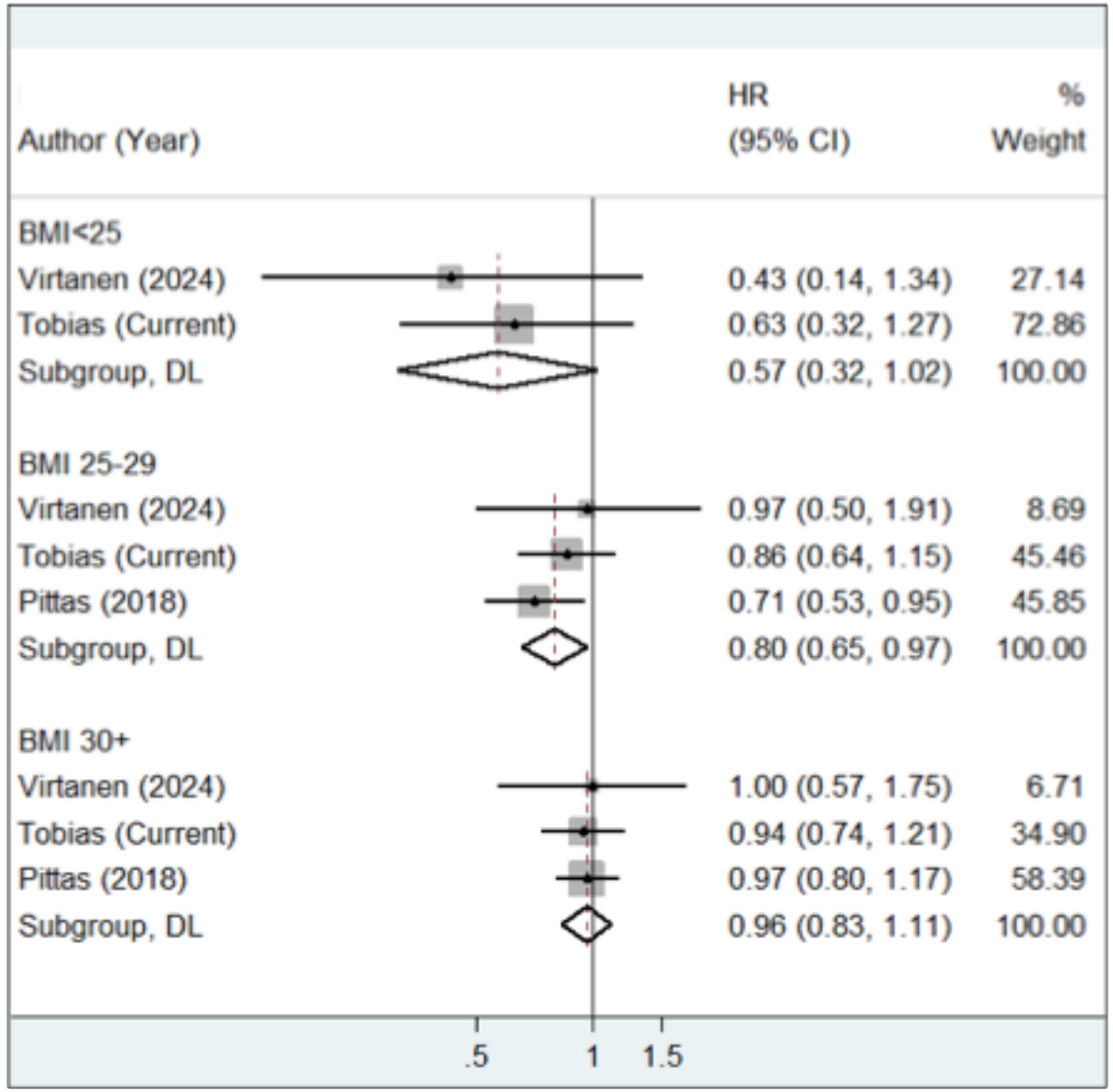
vitamin D had no effect on glycemic traits at 2 years. Meta-analysis of 4 trials ($n = 5205$; 936 T2D cases) obtained HR = 0.89 (CI = 0.80, 0.99). In conclusion, Vitamin D supplementation did not reduce T2D in older US adults, but a modest reduction was observed when meta-analyzed with prior trials. **Trial Regis-**

**-11%**

for the primary prevention of CVD[14]. The meta-analyzed estimate of VITAL with the other 3 RCTs indicated randomized vitamin D led to a 11% lower risk of T2D vs. placebo (pooled HR = 0.89 [0.80-0.99]; $p = 0.035$; $I^2 = 0\%$) (Supplementary Fig. 2). D2d and FIND also reported results stratified by BMI, and when combined with the VITAL-T2D in our meta-analysis there was a suggested dose-response of lower T2D for vitamin D vs. placebo across BMI strata, with BMI < 25.0 kg/m$^2$ HR = 0.57 (0.32, 1.02), BMI 25.0-29.0 kg/m$^2$ HR = 0.80 (0.65, 0.97), and BMI ≥ 30.0 kg/m$^2$ HR = 0.96 (0.83, 1.11); however, the statistical interaction by BMI category was not significant ($p = 0.10$).

**BMI Interaktion**

(B) Stratified by baseline body mass index (kg/m$^2$).



# INTERAKTION MIT BMI

**Kleinerer oder kein Effekt bei BMI > 25 or 30:**

- Multiple Sklerose
- Fortgeschrittene Krebserkrankung
- Autoimmunerkrankung
- Diabetes

# BOLUS
# praktisch, aber wirkungslos

# Perspective: Vitamin D supplementation prevents rickets and acute respiratory infections when given as daily maintenance but not as intermittent bolus: implications for COVID-19

**Authors:** George Griffin,[A] Martin Hewison,[B] Julian Hopkin,[C] Rose Anne Kenny,[D] Richard Quinton,[E] Jonathan Rhodes,[F] Sreedhar Subramanian[G] and David Thickett[H]

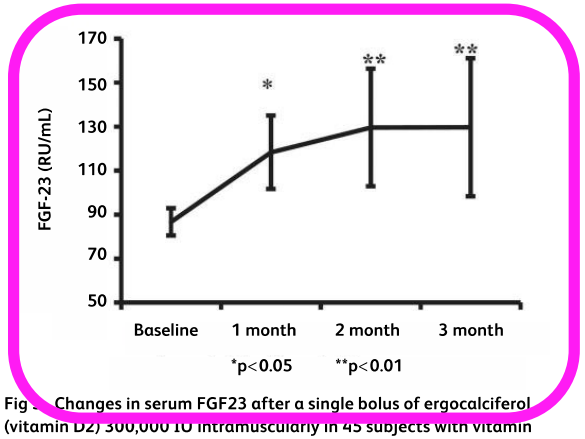



**Fig 2. Changes in serum FGF23 after a single bolus of ergocalciferol (vitamin D2) 300,000 IU intramuscularly in 45 subjects with vitamin D deficiency/insufficiency.** FGF23, which inhibits 1α -hydroxylase activity, is increased by 50% ($P<0.01$) 3 months after the bolus. Reproduced with permission from Turner *et al.*[29]

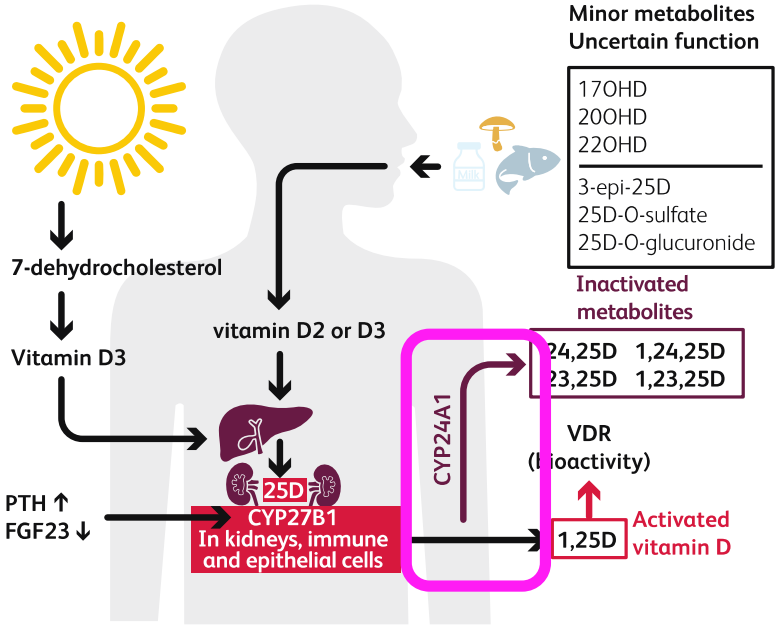



**Fig 1. The complexity of vitamin D metabolism.** D2 is from plant sources via ultraviolet action on ergosterol and D3 from animal sources via ultraviolet action on 7-dehydrocholesterol. Activation is via 25-hydroxylation in the liver followed by 1α-hydroxylation (CYP27B1) in kidneys, immune cells and many epithelia, to 1,25(OH)2D. Increased FGF23 suppresses 1α-hydroxylation. Free 25(OH)D appears to be preferentially taken up by monocytes,19 so the reduction in DBP in illness may have a protective effect via increased availability of free 25(OH)D. Either 25(OH)D or 1,25(OH)2D can be degraded via 24-hydroxylation (CYP24A1) to 24,25(OH)D or 1,24,25(OH)3D respectively.

# VITAMIN D & ICU

# BASICS

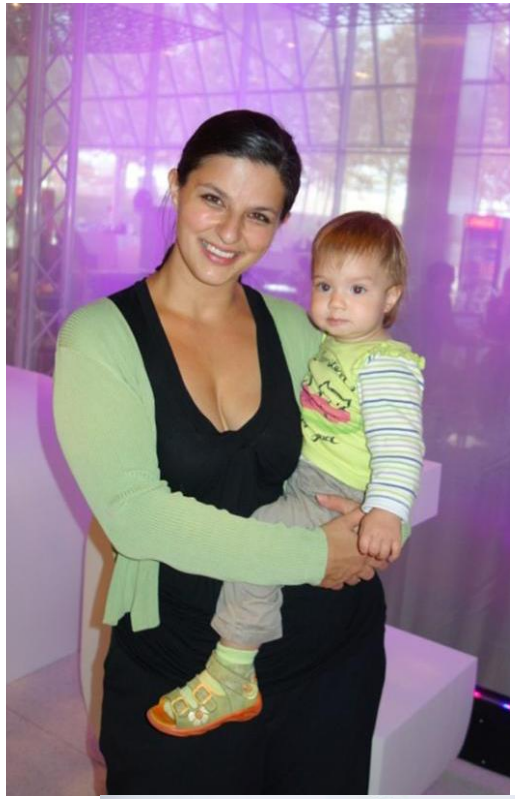
## VITAMIN D BEI AKUT KRANKEN

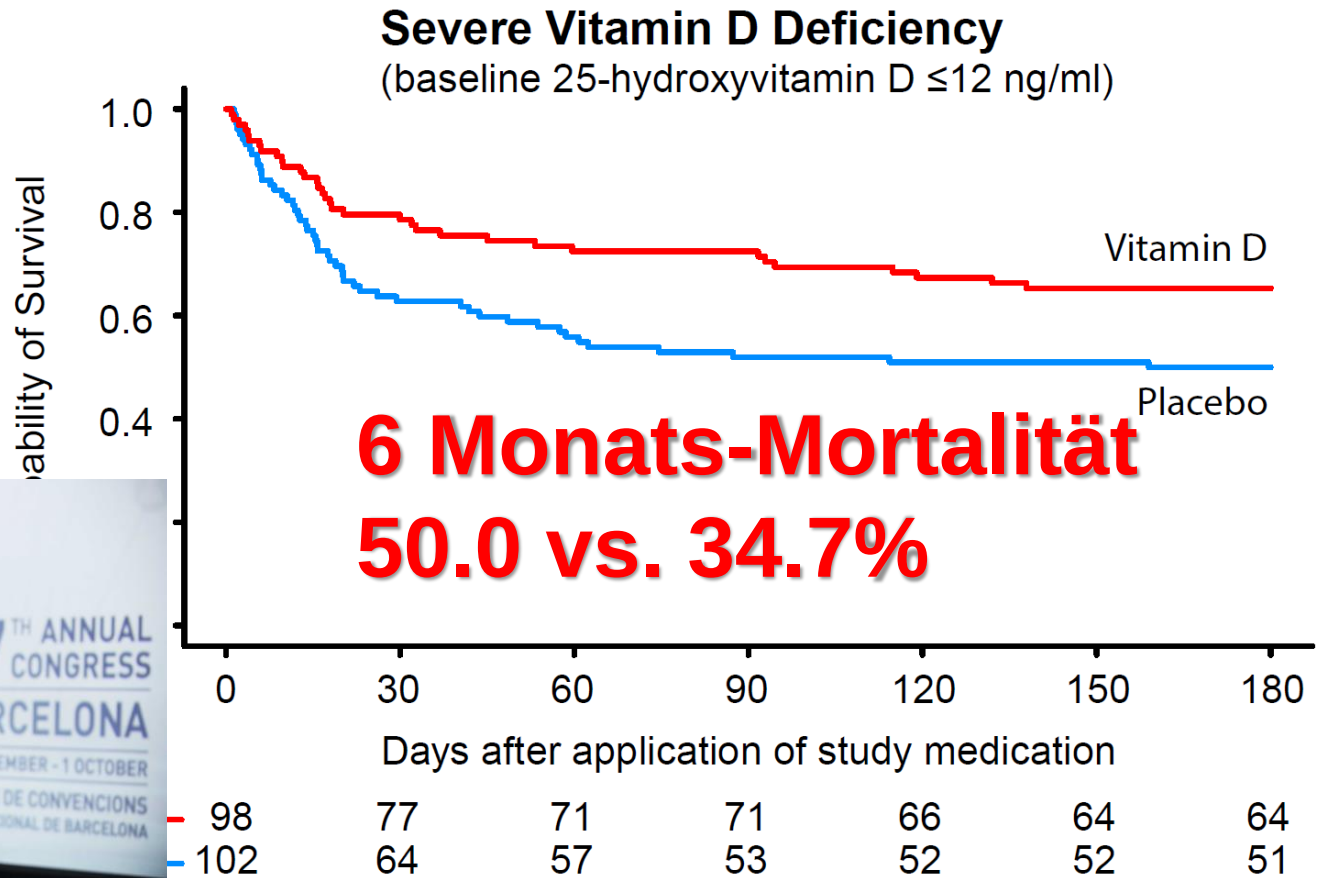
### (ERWACHSENE UND KINDER)

- EIN VITAMIN D MANGEL
  - IST HÄUFIG
  - MIT SCHLECHTEM OUTCOME ASSOZIIERT
    - MORTALITÄT, NIERENVERSAGEN, SEPSIS

**IST VITAMIN D NUR EIN MARKER ODER MEHR?**

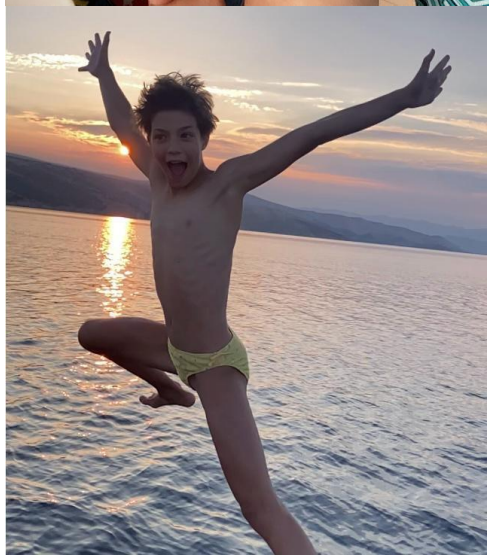
# VITDAL-ICU




**6 Monats-Mortalität**

**50.0 vs. 34.7%**



JAMA 2014

# VITDALIZE – Start 2017, A, D, B, UK

EFFECT OF HIGH-DOSE VITAMIN D3 ON 28-DAY MORTALITY IN ADULT CRITICALLY ILL PATIENTS WITH SEVERE VITAMIN D DEFICIENCY; NCT03188796

| | |
|---|---|
| Setting | • randomized, double blind, placebo controlled<br>• mixed ICUs (medical, surgical, neurologic)<br>• **2400** ICU patients; **25(OH)D ≤ 12 ng/ml** |
| Intervention | • 540,000 IU Vitamin D3 vs. Placebo 1x po/tube<br>• 4,000 IU daily for 90 days |
| Primary Endpoint | **28-DAY MORTALITY** |
| Secondary Endpoints | morbidity, LOS, lab, duration of mech.vent./circulatory support, readmissions etc. |

**n > 1985, 2025: 288!**

# TOXIZITÄT

nutrients

MDPI

*Review*

## Development of Vitamin D Toxicity from Overcorrection of Vitamin D Deficiency: A Review of Case Reports

**Kornelia Galior, Stefan Grebe and Ravinder Singh ***

Department of Laboratory Medicine and Pathology, Mayo Clinic, Rochester, MN 55905, USA; Galior.Kornelia@mayo.edu (K.G.); Grebe.Stefan@mayo.edu (S.G.)

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Received: 5 June 2018; Accepted: 16 July 2018; Published: 24 July 2018

# GALIOR et al.

| Age (years) | Vitamin D dose | Form of Intake | Reason | Vitamin D, Serum (ng/m) | Total Ca, Serum (mg/dL) | Symptoms |
|---|---|---|---|---|---|---|
| 0.4–4.2 ($n = 7$) | 260,000–800,000 IU/day | Fish oil supplements | Labeling errors | 340–962 | 13.4–18.8 | Weakness, loss of appetite, vomiting |
| 1–2 ($n = 2$)<br>1 | 200 IU/day (2–4weeks)<br>200 IU/day (1 month) | Oral preparation<br>Oral preparation | Labeling errors<br>Labeling errors | >160<br>760 | 13.7–19.3<br>19.4 | Abdominal pain, vomiting<br>Poor appetite, vomiting |
| 58<br>40 | 1,864,000 IU (2 months)<br>970,000 IU (1 month) | Oral supplements<br>Oral supplements | Labeling errors<br>Labeling errors | 1220<br>645 | 15<br>13.2 | Fatigue, thirst, polyuria<br>Nausea, vomiting, thirst, polyuria, muscle aches |
| 42 | 156,000–2,604,000 IU/day (2 years) | Oral supplements | Labeling errors | 487.3 | 15 | Dehydration, fatigue, loss of apetite |
| 0.3 | 50,000 IU/day (2 months) | Oral supplements | Inappropriate administration | 294 | 18.7 | Vomiting, diarrhea, dehydration |
| 0.3–0.2 ($n = 2$) | 20,000 IU/day (1.5 weeks) | Oral supplements | Inappropriate administration | 644<br>680 | 15 L<br>21 L | Poor appetite, lethargy, crying |
| 19 | 15,000,000 IU (1 year) | Injection | Inappropriate administration | 150 | 14.8 | Anorexia, nausea, vomiting |
| 42–86 ($n = 16$) | 2,220,000–6,360,000 IU (1–3 months) | Injection or oral sachets | Iatrogenic (body aches and fatigue) | 175–1161 | 11.1–15.7 | Nausea, vomiting, constipation |
| 48–75 ($n = 0$) | 3,000,000–60,000,000 IU (1–4 months) | Injection or oral sachets | Iatrogenic (various indications) | 164–306 | 12–13.98 | Vomiting, polyuria, anorexia |
| 45 | 6,000,000 IU (2 weeks) | Injection | Iatrogenic (knee surgery) | 150 | 23.1 | Anorexia, vomiting, abdominal pain |
| 42–85 ($n = 15$) | 600,000 IU (1 month–3 years) | Oral supplements + injections | Iatrogenic (improve health) | 103–164 | 10.9–15.2 | Altered sensorium, dehydration, vomiting, anorexia |
| 45–89 ($n = 19$) | 4,200,000–9,000,000 IU (1–5 months) | Oral tablets or injections | Iatrogenic (bone pain, aches, fatigue) | 190–988 | 11.9–15.2 | Vomiting, altered sensorium, AKI, constipation, |
| 75 | 50,000 IU/day (1 year) | Oral supplements | Iatrogenic (hypoparathyroidism) | 243 | 15.3 | Altered mental status |

# CONCLUSIO


- **VITAMIN D – MANGEL häufig...**
- RISIKOGRUPPEN SIND ZAHLREICH
- EMPFEHLUNG 800-4000 IU/d
- VEREINZELT MEHR NÖTIG (MEDIKATION etc.)
- SPIEGEL SINNVOLL BEI SPEZIELLEN FRAGESTELLUNGEN

  (z.B.: noch höhere Dosis nötig?)

# CONCLUSIO

- SPANNENDE BENEFITS BEI NEUEN ENDPUNKTEN
- INTERAKTION BMI
- EINZELNE BOLUS DOSEN FUNKTIONIEREN NICHT (SIND ABER NÖTIG AUF ICU)
- VITDALIZE FINALE 2026


# Gesund altern
# Vitamin D

## Karin Amrein & Christian Muschitz


**www.oegkm.at**

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