

# Vitaminpillen - mehr Schaden als Nutzen?

Prof. Dr. med Ingrid Mühlhauser



**Es gilt das gesprochene Wort!**

# Meine Interessenkonflikte

# 3 Szenarien

A decorative graphic consisting of a solid blue horizontal bar that spans the width of the slide. Below this bar, on the right side, there are three parallel white horizontal lines of varying lengths, creating a stepped effect.

# Prävention von Knochenbrüchen

Frauen mit ...	Medikamente 1000 Frauen über 7 Jahre	Placebo 1000 Frauen über 7 Jahre
Hüftbruch	10	11
Wirbelbruch mit Beschwerden	10	11
Unterarm- oder Handgelenkbruch	31	31
Irgendeinem Knochenbruch	115	119
Nierensteinen	25	21

Ich würde die Medikamentenbehandlung empfehlen:

**A** eher ja

**B** eher nein

# Prävention von Knochenbrüchen

Frauen mit ...	<b>Calcium+Vit. D</b> 1000 Frauen über 7 Jahre	<b>Placebo</b> 1000 Frauen über 7 Jahre
Hüftbruch	10	11
Wirbelbruch mit Beschwerden	10	11
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Nierensteinen	25	21

Ich würde die **Calcium+Vitamin D** Behandlung empfehlen:

**A** eher ja

**B** eher nein

*The* NEW ENGLAND  
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

FEBRUARY 16, 2006

VOL. 354 NO. 7

Calcium plus Vitamin D Supplementation  
and the Risk of Fractures

Rebecca D. Jackson, M.D., Andrea Z. LaCroix, Ph.D., Margery Gass, M.D., Robert B. Wallace, M.D., John Robbins, M.D., Cora E. Lewis, M.D., Tamsen Bassford, M.D., Shirley A.A. Beresford, Ph.D., Henry R. Black, M.D., Patricia Blanchette, M.D., Denise E. Bonds, M.D., Robert L. Brunner, Ph.D., Robert G. Brzyski, M.D., Bette Caan, Dr.P.H., Jane A. Cauley, Dr.P.H., Rowan T. Chlebowski, M.D., Steven R. Cummings, M.D., Iris Granek, M.D., Jennifer Hays, Ph.D., Gerardo Heiss, M.D., Susan L. Hendrix, D.O., Barbara V. Howard, Ph.D., Judith Hsia, M.D., F. Allan Hubbell, M.D., Karen C. Johnson, M.D., Howard Judd, M.D., Jane Morley Kotchen, M.D., Lewis H. Kuller, M.D., Robert D. Langer, M.D., Norman L. Lasser, M.D., Marian C. Limacher, M.D., Shari Ludlam, M.P.H.,

## Frauengesundheitsstudie (WHI Studie), USA

- 36.282 Frauen, 50 bis 79 Jahre
- 1000 mg Calcium + 400 IU Vitamin D<sub>3</sub> im Vergleich zu Placebo
- Studiendauer 7 Jahre

Johanna M. Manson, M.D., M.P.H., Bette Caan, D.P.H., Jane A. Cauley, D.P.H., Rowan T. Chlebowski, M.D., Steven K. Cummings, M.D., Iris Granek, M.D., Jennifer Hays, Ph.D., Gerardo Heiss, M.D., Susan L. Hendrix, D.O., Barbara V. Howard, Ph.D., Judith Hsia, M.D., F. Allan Hubbell, M.D., Karen C. Johnson, M.D., Howard Judd, M.D., Jane Morley Kotchen, M.D., Lewis H. Kuller, M.D., Robert D. Langer, M.D., Norman L. Lasser, M.D., Marian C. Limacher, M.D., Shari Ludlam, M.P.H.,



# Prävention von Prostatakrebs

- In einer randomisiert-kontrollierten Studie mit insgesamt 35.533 Männern zur Prävention von Prostatakrebs mit Vitamin E über etwa 5,5 Jahre betrug die relative Risikodifferenz 17%;  
 $p=0.008$ .

Ich würde die Vitaminbehandlung empfehlen:

**A** eher ja

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# Prävention von Prostatakrebs

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# Zunahme statt Abnahme von Prostatakrebs

## Vitamin E and the Risk of Prostate Cancer The Selenium and Vitamin E Cancer Prevention Trial (SELECT)

Eric A. Klein, MD

Ian M. Thompson Jr, MD

Catherine M. Tangen, DrPH

John J. Crowley, PhD

M. Scott Lucia, MD

Phyllis J. Goodman, MS

Lori M. Minasian, MD

Leslie G. Ford, MD

Howard L. Parnes, MD

J. Michael Gaziano, MD, MPH

**Context** The initial report of the Selenium and Vitamin E Cancer Prevention Trial (SELECT) found no reduction in risk of prostate cancer with either selenium or vitamin E supplements but a statistically nonsignificant increase in prostate cancer risk with vitamin E. Longer follow-up and more prostate cancer events provide further insight into the relationship of vitamin E and prostate cancer.

**Objective** To determine the long-term effect of vitamin E and selenium on risk of prostate cancer in relatively healthy men.

**Design, Setting, and Participants** A total of 35 533 men from 427 study sites in the United States, Canada, and Puerto Rico were randomized between August 22, 2001, and June 24, 2004. Eligibility criteria included a prostate-specific antigen (PSA) of 4.0 ng/mL or less, a digital rectal examination not suspicious for prostate cancer, and age 50 years or older for black men and 55 years or older for all others. The primary analysis included 34 887 men who were randomly assigned to 1 of 4 treatment

2011

ORIGINAL CONTRIBUTION

# Vitamin E and the Risk of Prostate Cancer

## The Selenium and Vitamin E Cancer Prevention Trial (SELECT)

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Richard W. Peto, MD

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## USA, Canada, Puerto Rico

- 35.533 Männer
- Vitamin E (400 IU/d) und/oder Selen (200 µg/d) im Vergleich zu Placebo
- Vorzeitiger Studienabbruch nach 5,5 Jahren

V

TH

Eric

lan

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Joh

M.

Phy

Lori M. Minasian, MD

Leslie G. Ford, MD

Howard L. Parnes, MD

J. Michael Gaziano, MD, MPH

© 2011 American Medical Association

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# Beta-Carotin, Vitamine A, C, E, Selen

- Die Auswertung von 38 hochwertigen randomisiert-kontrollierten Studien, mittlere Dauer 3 Jahre, mit insgesamt etwa 52.000 Teilnehmern ergab einen Unterschied in der Sterberate von einem Prozentpunkt (1 von 100).

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# Beta-Carotin, Vitamine A, C, E, Selen

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**2012**

# **Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases (Review)**

Bjelakovic G, Nikolova D, Gluud LL, Simonetti RG, Gluud C





**2012**

**Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases (Review)**

Bjelakovic G, Nikolova D, Gluud LL, Simonetti RG, Gluud C



# Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases

Beta-Carotin, Vitamine A, C, E, Selen  
78 Studien (randomisiert-kontrolliert)  
296.707 Studienteilnehmer



## Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases

### **Authors' conclusions:**

We found no evidence to support antioxidant supplements for primary or secondary prevention.



## Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases

### **Authors' conclusions:**

Beta-carotene and vitamin E seem to increase mortality, and so may higher doses of vitamin A.



## Antioxidant supplements for prevention of mortality in healthy participants and patients with various diseases

### **Authors' conclusions:**

Antioxidant supplements need to be considered as medical products and should undergo sufficient evaluation before marketing.



# Methodisches Vorgehen

# Evidenz-basierte Medizin



*Institute for Quality and Efficiency in Health Care*

# Allgemeine Methoden

Version 4.0 vom 23.09.2011



# Evidenz-basierte Medizin

- Hilft durch qualitativ hochwertige wissenschaftliche Studien die Unsicherheit über Nutzen und Schaden bei medizinischen Entscheidungen zu vermindern.

# Definition Nutzen / Schaden

**IQWiG – Methoden 2011**

# Definition Patientennutzen

- Gemäß § 35b des SGB V sollen beim Patientennutzen insbesondere die Verbesserung des Gesundheitszustandes, eine Verkürzung der Krankheitsdauer, eine Verlängerung der Lebensdauer, eine Verringerung der Nebenwirkungen sowie eine Verbesserung der Lebensqualität angemessen berücksichtigt werden.

# Zielgrößen Patientennutzen

- Mortalität
- Morbidität (Beschwerden und Komplikationen)
- Gesundheitsbezogene Lebensqualität

# Keine Zielgrößen für Patientennutzen

- Vitaminspiegel
- Antioxidative Effekte
- Pathophysiologische Variablen
- Immunologische Variablen
- Bildgebende Verfahren
- .....

Die Fragestellung bestimmt  
den Studientyp

# Hypothesenbildung

- Grundlagenforschung
- Pathophysiologie
- Epidemiologie

# Nachweis von Wirksamkeit und Nutzen

- Randomisiert-kontrollierte verblindete Studien mit patientenrelevanten Zielgrößen



# Nachweis von Wirksamkeit und Nutzen

- Randomisiert-kontrollierte verblindete Studien mit patientenrelevanten Zielgrößen
- Systematische Reviews und Meta-Analysen von randomisiert-kontrollierten Studien

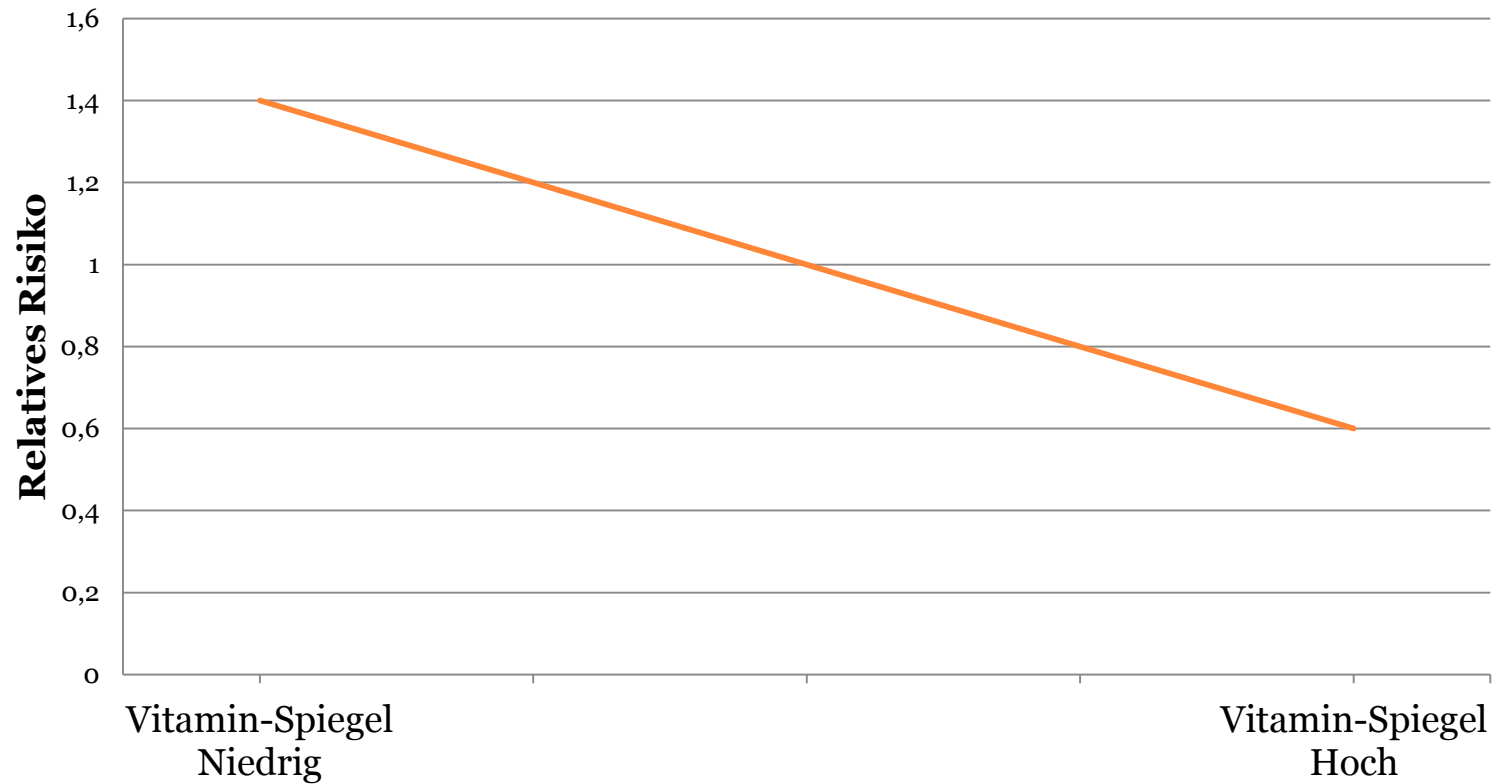
# Vitamine und Krankheit

- Laborexperimente
- Pathophysiologische Konzepte
- Klinische Beobachtungen
- Epidemiologische Analysen
- .....

# Vitaminspiegel erniedrigt bei

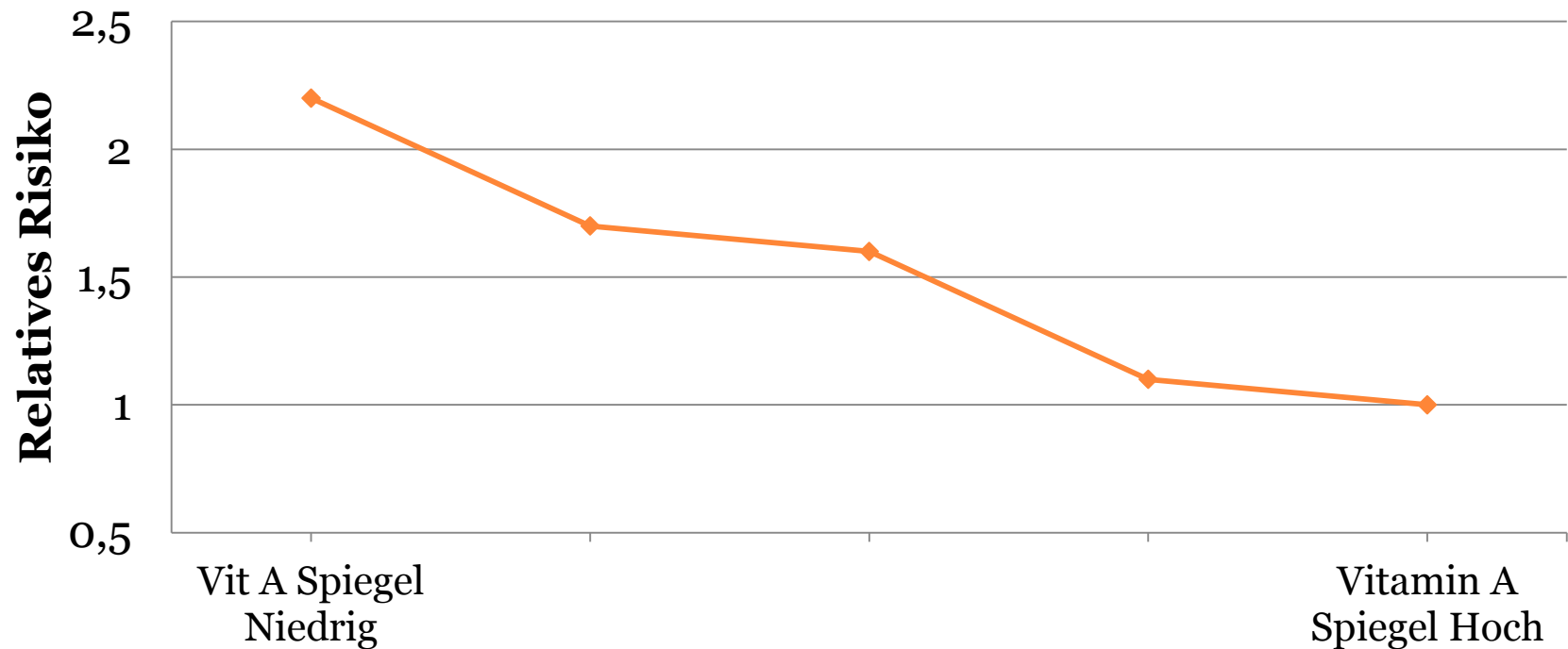
- Herzkreislauferkrankungen
- Krebs
- Infektionskrankheiten
- .....

# Zusammenhang zwischen Vitaminspiegel und Krankheitsrisiko



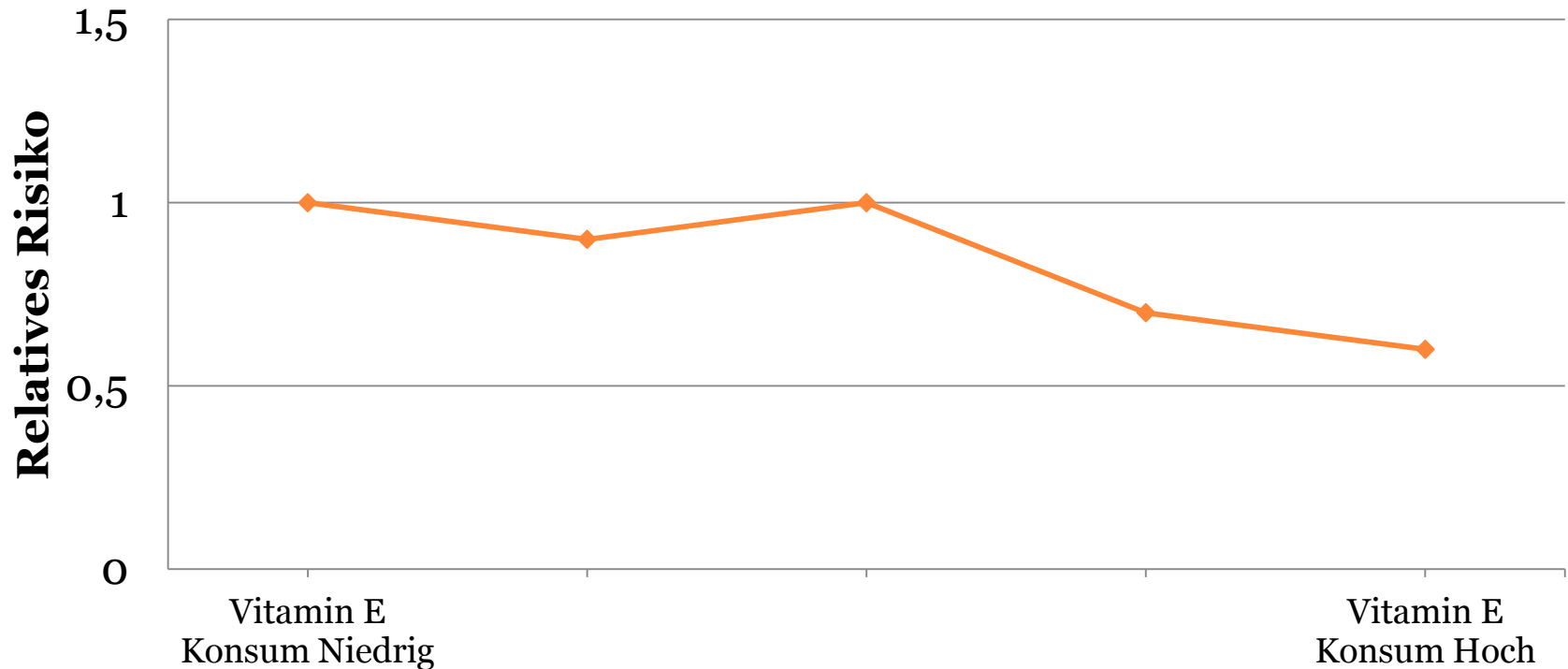
1981

## Relatives Risiko für Krebs in Abhängigkeit vom Vitamin A Spiegel



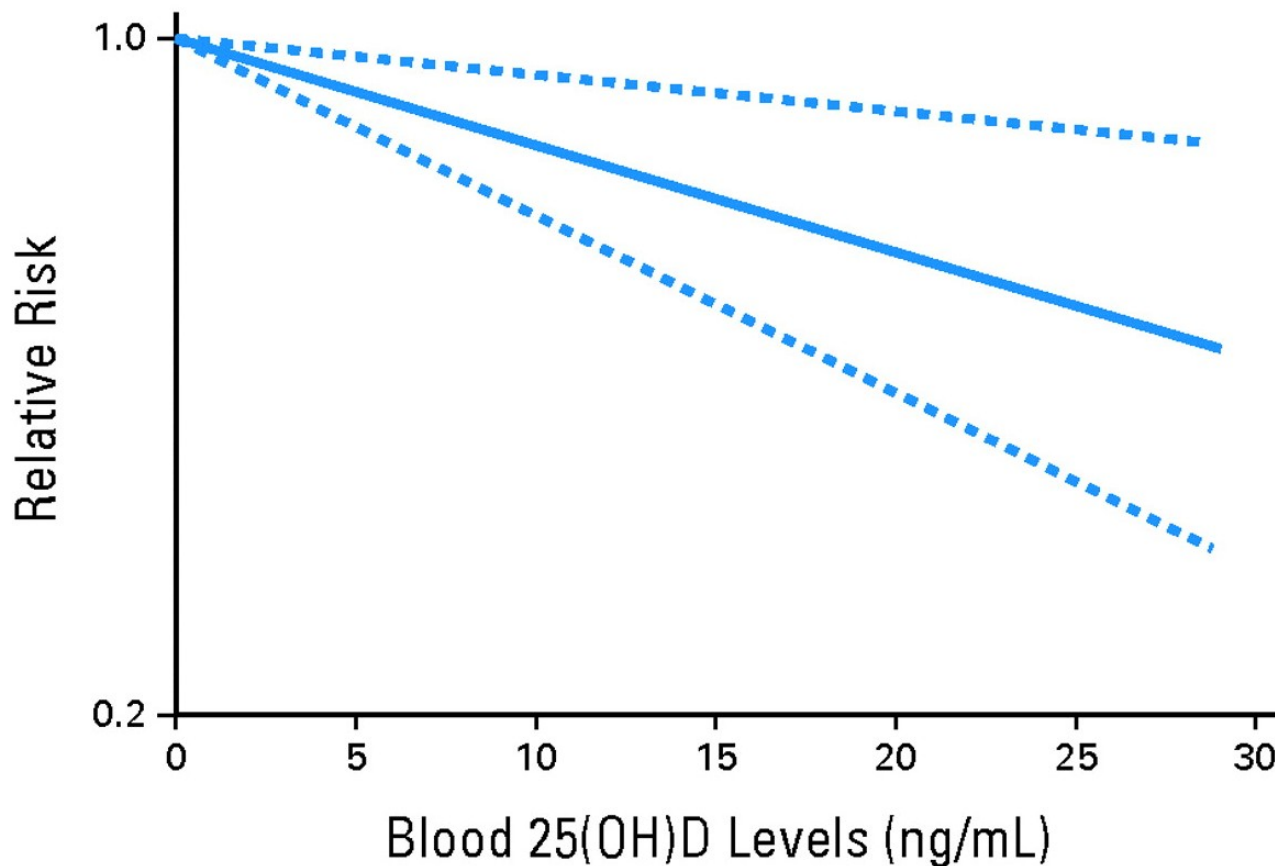
1993

## Relatives Risiko für Koronare Herzkrankheit und Vitamin E Konsum



2011

## Relatives Risiko für Darmkrebs und Vitamin D Spiegel



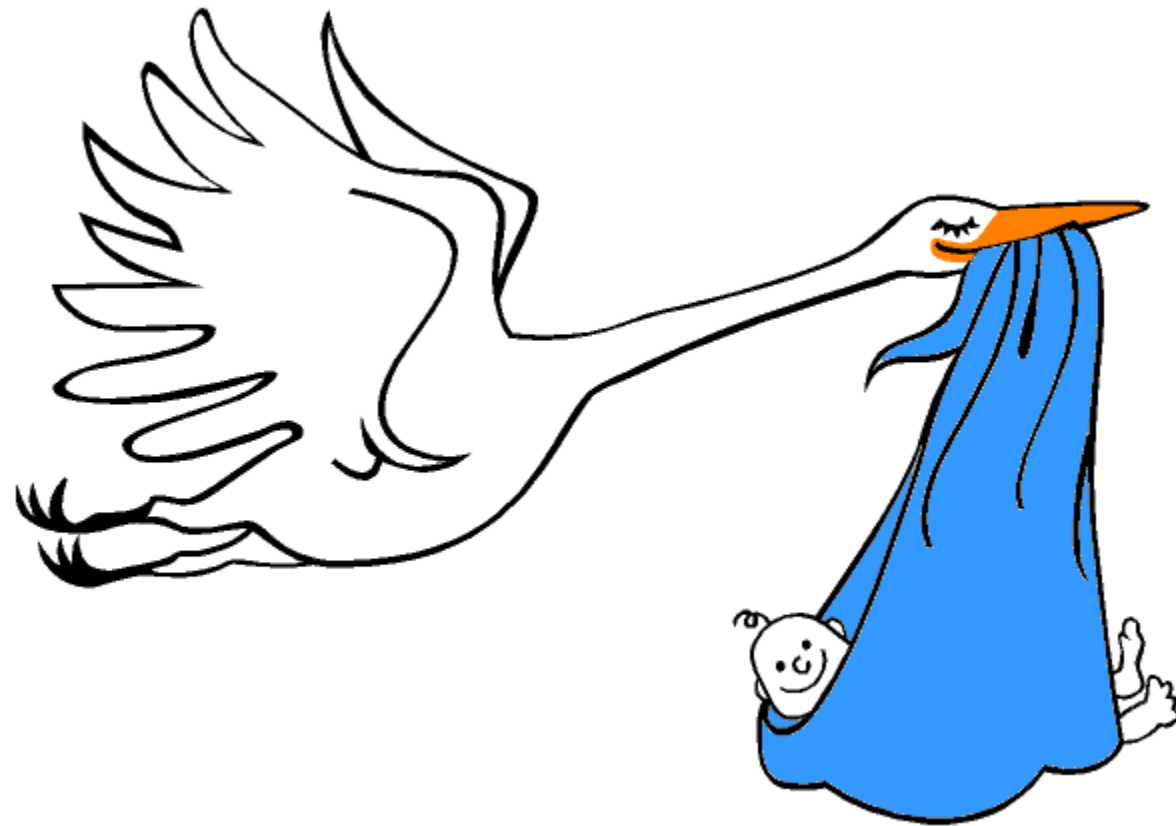
**Niedrige Vitaminspiegel:  
Krankheitsfolge oder  
Krankheitsursache?**



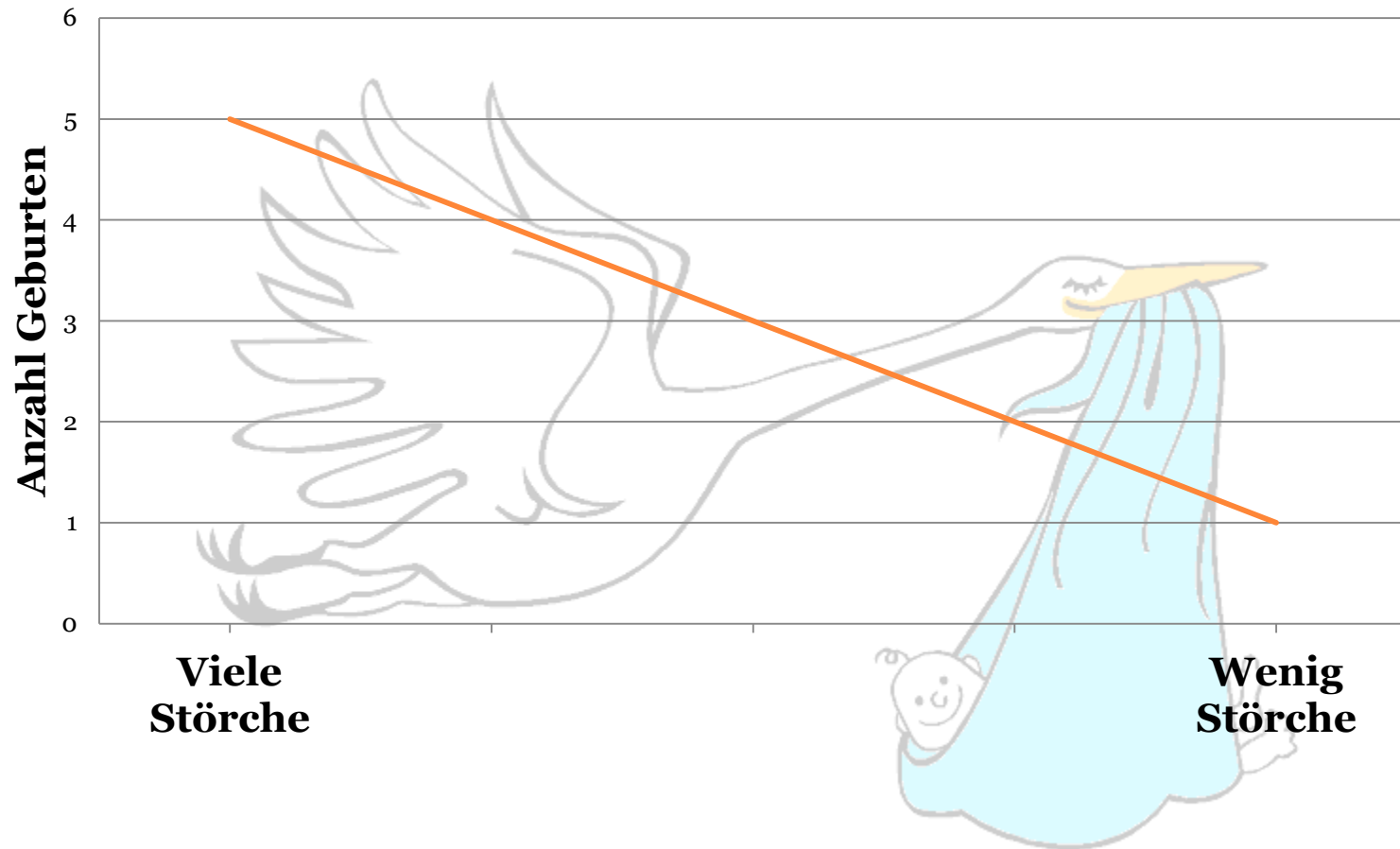
# Niedrige Vitaminspiegel:

K<sub>1</sub>

K<sub>2</sub>



# Zusammenhang zwischen Anzahl an Störchen und Geburten



# Nachweis von Wirksamkeit und Nutzen

- Randomisiert-kontrollierte verblindete Studien mit patientenrelevanten Zielgrößen
- Systematische Reviews und Meta-Analysen von randomisiert-kontrollierten Studien

# Qualität der Studien?

# BMJ

Laparoscopic colorectal surgery  
Maintaining weight loss in adults  
In search of beneficial drug reactions  
Gambling addiction: a patient's journey

3441-52 No 7838 ISSN 1759-2151  
7 January 2012 bmj.com

## Publication bias?

MISSING TRIAL DATA  
why we need the full picture



# BMJ

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Laparoscopic colorectal surgery  
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## MISSING TRIAL DATA

Why we need the full picture



# Beta-Carotin / Vitamin A

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# Beta-Carotin / Vitamin A und Lungenkrebs



# Beta-Carotin - Plausibilität für präventive Wirkung auf Lungenkrebs

- Es handelt sich um ein physiologisches Substrat.

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- Die antioxidative Wirkung des Beta-Carotins ist experimentell belegt und wird als wesentlich zur Vermeidung von Erkrankungen angesehen.

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- Die antioxidative Wirkung des Beta-Carotins ist experimentell belegt und wird als wesentlich zur Vermeidung von Erkrankungen angesehen.
- Durch orale Zufuhr lässt sich der Vitaminspiegel auf „normale“ Werte anheben.

The New England  
Journal of Medicine  
Society  
1994

# Randomisiert-kontrollierte, verblindete Studien

Volume 330

APRIL 14, 1994

Number 15

## THE EFFECT OF VITAMIN E AND BETA CAROTENE ON THE INCIDENCE OF LUNG CANCER AND OTHER CANCERS IN MALE SMOKERS

THE ALPHA-TOCOPHEROL, BETA CAROTENE CANCER PREVENTION STUDY GROUP\*

**Abstract Background.** Epidemiologic evidence indicates that diets high in carotenoid-rich fruits and vegetables, as well as high serum levels of vitamin E (alpha-tocopherol) and beta carotene, are associated with a reduced risk of lung cancer.

**Methods.** We performed a randomized, double-blind, placebo-controlled primary-prevention trial to determine whether daily supplementation with alpha-tocopherol, beta carotene, or both would reduce the incidence of

tene than among those who did not (change in incidence, 18 percent; 95 percent confidence interval, 3 to 36 percent). We found no evidence of an interaction between alpha-tocopherol and beta carotene with respect to the incidence of lung cancer. Fewer cases of prostate cancer were diagnosed among those who received alpha-tocopherol than among those who did not. Beta carotene had little or no effect on the incidence of cancer other than lung cancer. Alpha-tocopherol had no apparent effect on total

1994

# The New England Journal of Medicine

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# Beta-Carotin und Lungenkrebs

- 29.133 männliche Raucher aus Finnland
- 20 mg Beta-Carotin oder Placebo  
50 mg Vitamin E oder Vitamin E plus Beta-Carotin
- 5 bis 8 Jahre Studiendauer

The New England

# Zunahme statt Abnahme von Lungenkrebs

Journal of Medicine by the Massachusetts Medical Society

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- Unter Beta-Carotin nimmt Lungenkrebs um 18% zu, die Sterberate um 8%.

# Lungenkrebs

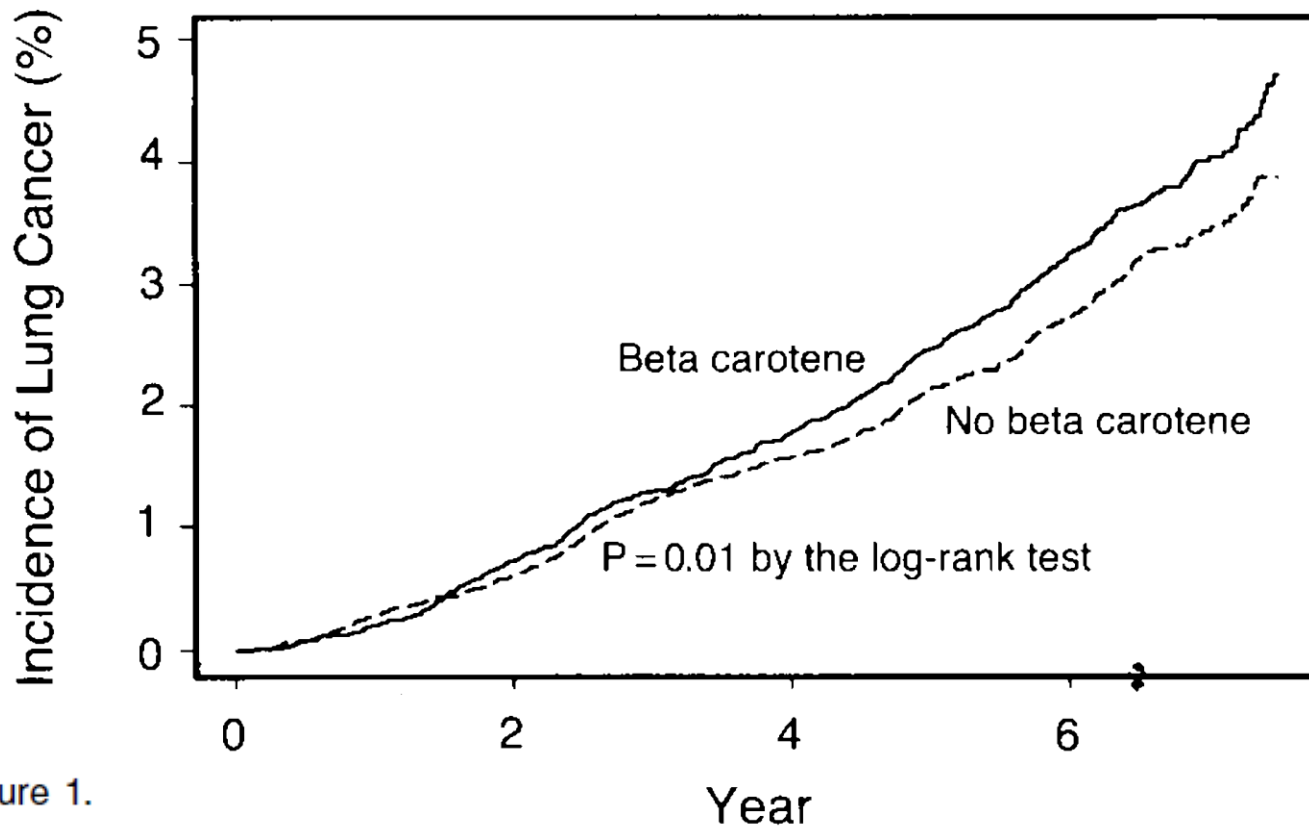


Figure 1.

## EFFECTS OF A COMBINATION OF BETA CAROTENE AND VITAMIN A ON LUNG CANCER AND CARDIOVASCULAR DISEASE

GILBERT S. OMENN, M.D., PH.D., GARY E. GOODMAN, M.D., M.S., MARK D. THORNQUIST, PH.D., JOHN BALMES, M.D., MARK R. CULLEN, M.D., ANDREW GLASS, M.D., JAMES P. KEOGH, M.D., FRANK L. MEYSKENS, JR., M.D., BARBARA VALANIS, DR.P.H., JAMES H. WILLIAMS, JR., M.D., SCOTT BARNHART, M.D., M.P.H., AND SAMUEL HAMMAR, M.D.\*

**Abstract** *Background.* Lung cancer and cardiovascular disease are major causes of death in the United States. It has been proposed that carotenoids and retinoids are agents that may prevent these disorders.

*Methods.* We conducted a multicenter, randomized, double-blind, placebo-controlled primary prevention trial — the Beta-Carotene and Retinol Efficacy Trial — involving a total of 18,314 smokers, former smokers, and workers exposed to asbestos. The effects of a combination of 30 mg of beta carotene per day and 25,000 IU of retinol (vitamin A) in the form of retinyl palmitate per day on the primary end point, the incidence of lung cancer, were compared with those of placebo

compared with the placebo group. There were no statistically significant differences in the risks of other types of cancer. In the active-treatment group, the relative risk of death from any cause was 1.17 (95 percent confidence interval, 1.03 to 1.33); of death from lung cancer, 1.46 (95 percent confidence interval, 1.07 to 2.00); and of death from cardiovascular disease, 1.26 (95 percent confidence interval, 0.99 to 1.61). On the basis of these findings, the randomized trial was stopped 21 months earlier than planned; follow-up will continue for another 5 years.

*Conclusions.* After an average of four years of supplementation, the combination of beta carotene and vitamin A had no benefit and may have had an adverse effect

# Beta-Carotin und Vitamin A zur Prävention von Lungenkrebs

- 18.314 Raucher und Asbestarbeiter, USA
- 30 mg of Beta-Carotin und 25.000 IU Vitamin A pro Tag
- Vergleich zu Placebo
- Vorzeitiger Studienabbruch nach 4 Jahren

EFFECTS OF A COMBINATION OF BETA CAROTENE AND VITAMIN A ON LUNG CANCER AND

# Zunahme statt Abnahme von Lungenkrebs und Sterberaten

GILBERT S. OMIEN, M.D., PH.D., GARY E. GOODMAN, M.D., M.S., MARK D. THORNQUIST, PH.D., JOHN BALMES, M.D., MARK R. CULLEN, M.D., ANDREW GIBBS, M.D., JAMES P. KEOGH, M.D., FRANK J. SHERIDAN, M.D., RICHARD P. MANNING, M.D., M.P.H., SCOTT BARNHART, M.D., M.P.H., AND SAMUEL HAMMAR, M.D.<sup>1,2</sup>

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*Conclusions.* After an average of four years of supplementation, the combination of beta carotene and vitamin A had no benefit and may have had an adverse effect

- Unter Beta-Carotin und Vitamin A steigt die Lungenkrebsrate um 28%, die Lungenkrebs-Sterblichkeit um 46% und die Gesamttodesrate um 17%.

# Lungenkrebs

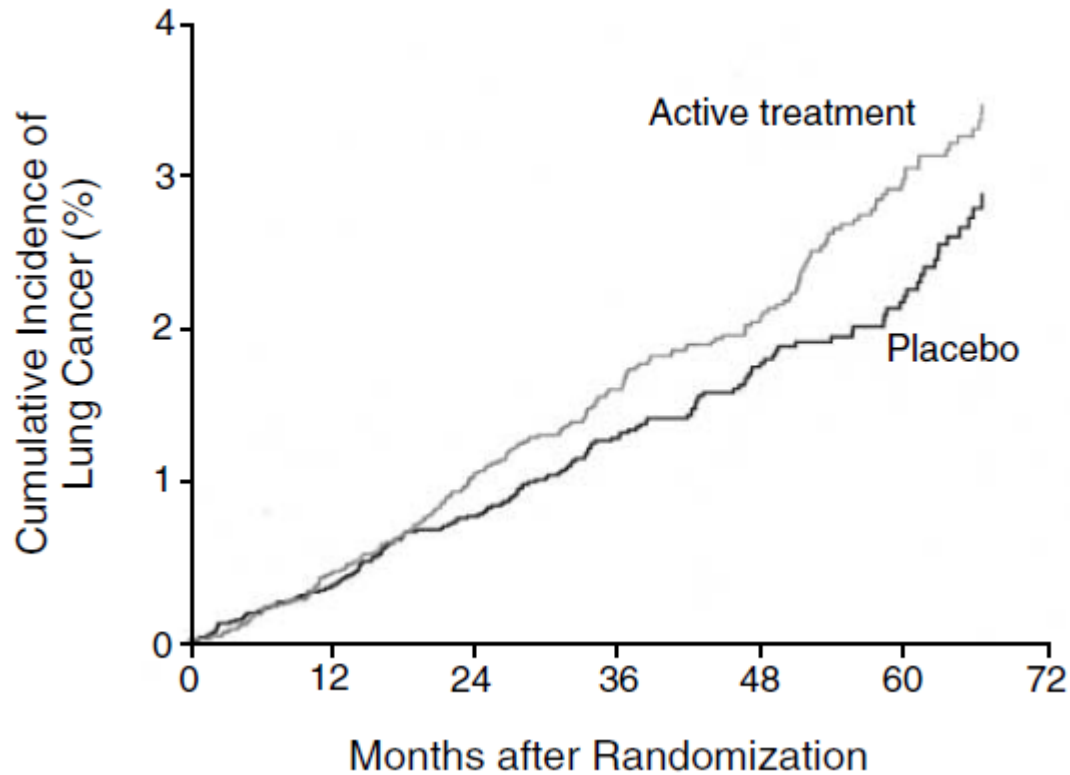


Figure 1.

# Sterberaten

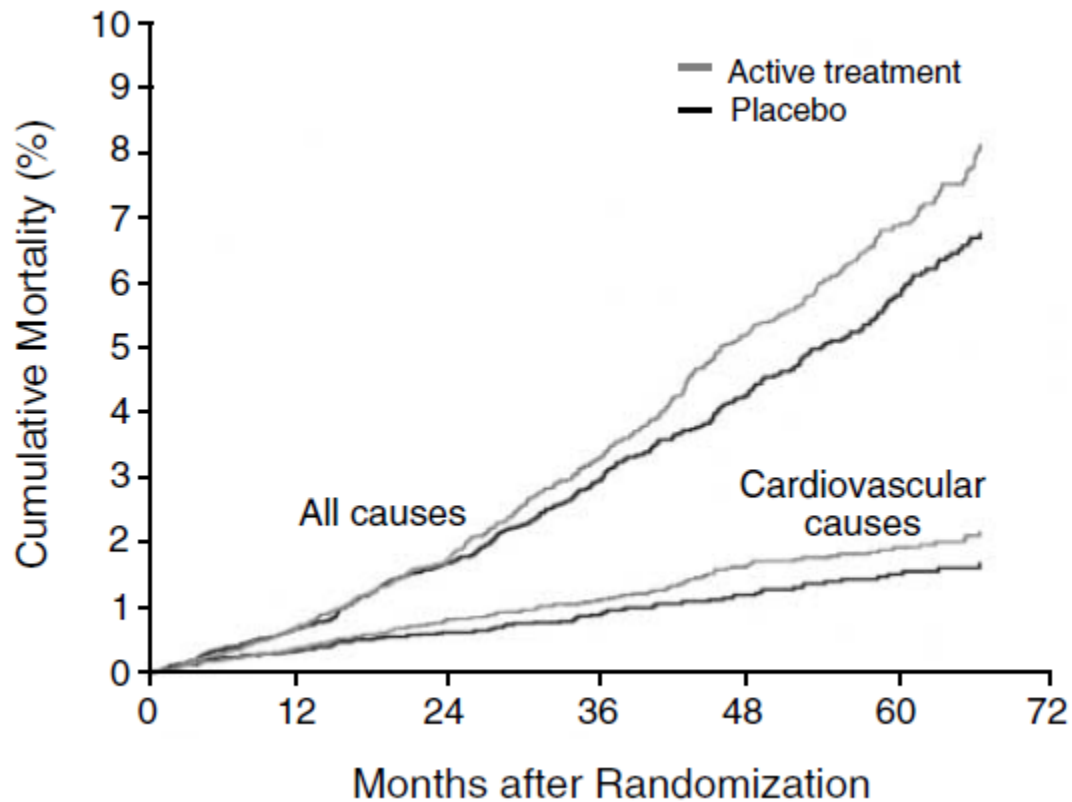


Figure 2.



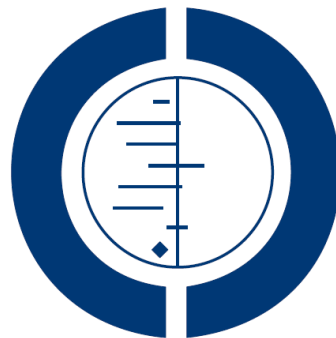
- Ein Schutz vor Herzleiden lässt sich ebenso wenig nachweisen: Das Risiko, als Raucher an Angina pectoris zu erkranken, scheint unter dem Provitamin eher zu steigen.

# Vitamin A bei Masern

**2011**

# **Vitamin A for treating measles in children (Review)**

Yang HM, Mao M, Wan C



**THE COCHRANE  
COLLABORATION®**

## Vitamin A for treating measles in children (Review)

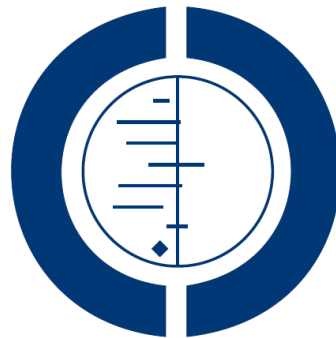
### **Authors' conclusions:**

No overall significant reduction in mortality with vitamin A therapy for children with measles was found.



# Vitamin A

- Conflicting evidence in neonates and children in low income countries.



THE COCHRANE  
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# Vitamin E

A decorative graphic consisting of a solid blue horizontal bar that spans the width of the page. Below this bar, on the right side, are several horizontal lines of varying lengths and colors (white and blue) that create a layered, stepped effect.

2005

REVIEW

## Meta-Analysis: High-Dosage Vitamin E Supplementation May Increase All-Cause Mortality

Edgar R. Miller III, MD, PhD; Roberto Pastor-Barriuso, PhD; Darshan Dalal, MD, MPH; Rudolph A. Riemersma, PhD, FRCPE; Lawrence J. Appel, MD, MPH; and Eliseo Guallar, MD, DrPH

**Background:** Experimental models and observational studies suggest that vitamin E supplementation may prevent cardiovascular disease and cancer. However, several trials of high-dosage vitamin E supplementation showed non-statistically significant increases in total mortality.

**Purpose:** To perform a meta-analysis of the dose-response relationship between vitamin E supplementation and total mortality by using data from randomized, controlled trials.

**Patients:** 135 967 participants in 19 clinical trials. Of these trials, 9 tested vitamin E alone and 10 tested vitamin E combined with other vitamins or minerals. The dosages of vitamin E ranged from

**Data Synthesis:** 9 of 11 trials testing high-dosage vitamin E ( $\geq 400$  IU/d) showed increased risk (risk difference  $> 0$ ) for all-cause mortality in comparisons of vitamin E versus control. The pooled all-cause mortality risk difference in high-dosage vitamin E trials was 39 per 10 000 persons (95% CI, 3 to 74 per 10 000 persons;  $P = 0.035$ ). For low-dosage vitamin E trials, the risk difference was  $-16$  per 10 000 persons (CI,  $-41$  to 10 per 10 000 persons;  $P > 0.2$ ). A dose-response analysis showed a statistically significant relationship between vitamin E dosage and all-cause mortality, with increased risk of dosages greater than 150 IU/d.

**Limitations:** High-dosage ( $\geq 400$  IU/d) trials were often small

# Vitamin E und Alzheimer



**2008**

# **Vitamin E for Alzheimer's disease and mild cognitive impairment (Review)**

Isaac MGEKN, Quinn R, Tabet N



**THE COCHRANE  
COLLABORATION®**

## Vitamin E for Alzheimer's disease and mild cognitive impairment (Review)

### **Conclusions:**

... There is no evidence of efficacy in the prevention or treatment ...



# Antioxidantien bei Chemo- oder Strahlentherapie

2008

COMMENTARY

---

## **Should Supplemental Antioxidant Administration Be Avoided During Chemotherapy and Radiation Therapy?**

Brian D. Lawenda, Kara M. Kelly, Elena J. Ladas, Stephen M. Sagar, Andrew Vickers, Jeffrey B. Blumberg

Despite nearly two decades of research investigating the use of dietary antioxidant supplementation during conventional chemotherapy and radiation therapy, controversy remains about the efficacy and safety of this complementary treatment. Several randomized clinical trials have demonstrated that the concurrent administration of antioxidants with chemotherapy or radiation therapy reduces treatment-related side effects. Some data indicate that antioxidants may protect tumor cells as well as healthy cells from oxidative damage generated by radiation therapy and some chemotherapeutic agents. However, other data suggest that antioxidants can protect normal tissues from chemotherapy- or radiation-induced damage without decreasing tumor control. We review some of the data regarding the putative benefits and potential risks of antioxidant supplementation concurrent with cytotoxic therapy. On the basis of our review of the published randomized clinical trials, we conclude that the use of supplemental antioxidants during chemotherapy and radiation therapy should be discouraged because of the possibility of tumor protection and reduced survival.

## Conclusions:

... the use of supplemental antioxidants during chemotherapy and radiation therapy should be discouraged because of the **possibility of tumor protection and reduced survival.**

# Antioxidantien bei Lebererkrankungen

**2011**

# **Antioxidant supplements for liver diseases (Review)**

Bjelakovic G, Gluud LL, Nikolova D, Bjelakovic M, Nagorni A, Gluud C



## Antioxidant supplements for liver diseases (Review)

### **Conclusions:**

... no evidence to support or refute antioxidant supplements in patients with liver disease.  
Antioxidant supplements **may increase liver enzyme activity.**





# Antioxidantien bei Zystischer Fibrose

**2010**

# **Antioxidant micronutrients for lung disease in cystic fibrosis (Review)**

Shamseer L, Adams D, Brown N, Johnson JA, Vohra S



Antioxidant micronutrients for lung disease in cystic fibrosis  
(Review)

**Authors' conclusions:**

... antioxidants appear to **decrease quality of life** and oxidative stress ...

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journal homepage: [www.elsevier.com/locate/free-radbiomed](http://www.elsevier.com/locate/free-radbiomed)

# Ist die „freie Radikale“ Theorie des Alterns falsch?

Review Article

Extending life span by increasing oxidative stress

Michael Ristow<sup>a,b,\*</sup>, Sebastian Schmeisser<sup>a</sup>

<sup>a</sup> Department of Human Nutrition, Institute of Nutrition, University of Jena, D-07743 Jena, Germany

<sup>b</sup> Department of Clinical Nutrition, German Institute of Human Nutrition Potsdam-Rehbrücke, D-14558 Nuthetal, Germany

## ARTICLE INFO

### Article history:

Received 6 February 2011

Revised 8 May 2011

Accepted 9 May 2011

## ABSTRACT

Various nutritional, behavioral, and pharmacological interventions have been previously shown to extend life span in diverse model organisms, including *Saccharomyces cerevisiae*, *Caenorhabditis elegans*, *Drosophila melanogaster*, mice, and rats, as well as possibly monkeys and humans. This review aims to summarize



Contents lists available at ScienceDirect

## Free Radical Biology & Medicine

journal homepage: [www.elsevier.com/locate/freeradbimed](http://www.elsevier.com/locate/freeradbimed)



Review Article

### Extending life span by increasing oxidative stress

Michael Ristow<sup>a,b,\*</sup>, Sebastian Schmeisser<sup>a</sup>

<sup>a</sup> Department of Human Nutrition, Institute of Nutrition, University of Jena, D-07743 Jena, Germany

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Various nutritional, behavioral, and pharmacological interventions have been previously shown to extend life span in diverse model organisms, including *Saccharomyces cerevisiae*, *Caenorhabditis elegans*, *Drosophila melanogaster*, mice, and rats, as well as possibly monkeys and humans. This review aims to summarize

# Folsäure und Vitamin B12

The title is positioned above a decorative graphic consisting of a solid blue horizontal bar. Below this bar, there are several white horizontal lines of varying lengths and thicknesses, creating a stepped, modern look.

# Folsäure und Vitamin B12

Herz-Kreislaufkrankungen



# Plausibilität

- Beobachtungsstudien zeigen eine Assoziation zwischen Homocysteinspiegel und Risiko für kardiovaskuläre Krankheiten.
- Orale Verabreichung von Folsäure und Vitamin B12 kann den Plasmaspiegel des Gesamt-Homocysteins senken.



# Mortality and Cardiovascular Events in Patients Treated With Homocysteine-Lowering B Vitamins After Coronary Angiography

## A Randomized Controlled Trial

Marta Ebbing, MD

Øyvind Bleie, MD, PhD

Per Magne Ueland, MD, PhD

Jan Erik Nordrehaug, MD, PhD

Dennis W. Nilsen, MD, PhD

Stein Emil Vollset, MD, DrPH

**Context** Observational studies have reported associations between circulating total homocysteine concentration and risk of cardiovascular disease. Oral administration of folic acid and vitamin B<sub>12</sub> can lower plasma total homocysteine levels.

**Objective** To assess the effect of treatment with folic acid and vitamin B<sub>12</sub> and the effect of treatment with vitamin B<sub>6</sub> as secondary prevention in patients with coronary artery disease or aortic valve stenosis.

**Design. Setting. and Participants** Randomized, double-blind controlled trial con-

## Intervention:

Folsäure 0,8 mg plus Vitamin B12 0,4 mg plus Vitamin B6 40 mg pro Tag;

Folsäure plus Vitamin B12;

Vitamin B6;

Placebo

folic acid and vitamin B<sub>12</sub> can lower plasma total homocysteine levels.

**Objective** To assess the effect of treatment with folic acid and vitamin B<sub>12</sub> and the effect of treatment with vitamin B<sub>6</sub> as secondary prevention in patients with coronary artery disease or aortic valve stenosis.

**Design, Setting, and Participants** Randomized, double-blind controlled trial con-

## Schlussfolgerungen:

... kein Effekt von Folsäure, Vitamin B12 oder Vitamin B6 auf kardiovaskuläre Erkrankungen oder Sterberaten ...

Marta  
Oyvind

Per Magne Ueland, MD, PhD

Jan Erik Nordrehaug, MD, PhD

Dennis W. Nilsen, MD, PhD

Stein Emil Vollset, MD, DrPH

folic acid and vitamin B<sub>12</sub> can lower plasma total homocysteine levels.

**Objective** To assess the effect of treatment with folic acid and vitamin B<sub>12</sub> and the effect of treatment with vitamin B<sub>6</sub> as secondary prevention in patients with coronary artery disease or aortic valve stenosis.

**Design, Setting, and Participants** Randomized, double-blind controlled trial con-

# Mortality and Cardiovascular Events Higher Dosierung nötig? in Patients Treated With Homocysteine-Lowering B Vitamins After Coronary Angiography A Randomized Controlled Trial

Marta Ebbing, MD

Oyvind Bleie, MD, PhD

Per Magne Ueland, MD, PhD

Jan Erik Nordrehaug, MD, PhD

Dennis W. Nilsen, MD, PhD

Stein Emil Vollset, MD, DrPH

**Context** Observational studies have reported associations between circulating total homocysteine concentration and risk of cardiovascular disease. Oral administration of folic acid and vitamin B<sub>12</sub> can lower plasma total homocysteine levels.

**Objective** To assess the effect of treatment with folic acid and vitamin B<sub>12</sub> and the effect of treatment with vitamin B<sub>6</sub> as secondary prevention in patients with coronary artery disease or aortic valve stenosis.

**Design, Setting, and Participants** Randomized, double-blind controlled trial con-

# Effects of Homocysteine-Lowering With Folic Acid Plus Vitamin B<sub>12</sub> vs Placebo on Mortality and Major Morbidity in Myocardial Infarction Survivors

## A Randomized Trial

Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine (SEARCH) Collaborative Group\*



OBSERVATIONAL STUDIES have consistently indi-

**Context** Blood homocysteine levels are positively associated with cardiovascular disease, but it is uncertain whether the association is causal.

**Objective** To assess the effects of reducing homocysteine levels with folic acid and vitamin B<sub>12</sub> on vascular and nonvascular outcomes.

**Design, Setting, and Patients** Double-blind randomized controlled trial of 12 064 survivors of myocardial infarction in secondary care hospitals in the United Kingdom between 1998 and 2008

# 12.064 Patienten nach Herzinfarkt United Kingdom, 1998-2008

Collaborative Group\*



OBSERVATIONAL STUDIES  
have consistently indi-

**Objective** To assess the effects of reducing homocysteine levels with folic acid and vitamin B<sub>12</sub> on vascular and nonvascular outcomes.

**Design, Setting, and Patients** Double-blind randomized controlled trial of 12 064 survivors of myocardial infarction in secondary care hospitals in the United Kingdom between 1998 and 2008

## Intervention:

Folsäure 2 mg plus Vitamin B12 1 mg pro Tag;  
Placebo

Study  
Ad  
and  
Collaborative Group\*



OBSERVATIONAL STUDIES  
have consistently indi-

**Objective** To assess the effects of reducing homocysteine levels with folic acid and vitamin B<sub>12</sub> on vascular and nonvascular outcomes.

**Design, Setting, and Patients** Double-blind randomized controlled trial of 12 064 survivors of myocardial infarction in secondary care hospitals in the United Kingdom between 1998 and 2008.

## Schlussfolgerungen:

Trotz anhaltender und substantieller Senkung des Homocysteinspiegels kein positiver Effekt auf vaskuläre Ereignisse

Study  
Ad  
and  
Collaborative Group\*



OBSERVATIONAL STUDIES  
have consistently indi-

**Objective** To assess the effects of reducing homocysteine levels with folic acid and vitamin B<sub>12</sub> on vascular and nonvascular outcomes.

**Design, Setting, and Patients** Double-blind randomized controlled trial of 12 064 survivors of myocardial infarction in secondary care hospitals in the United Kingdom between 1998 and 2008.



# Vitamin B

Nierenerkrankungen



2010

## Vascular Medicine

# B Vitamins and the Risk of Total Mortality and Cardiovascular Disease in End-Stage Renal Disease

### Results of a Randomized Controlled Trial

Judith Heinz, MSc; Siegfried Kropf, PhD; Ute Domröse, MD; Sabine Westphal, MD; Katrin Borucki, MD; Claus Luley, MD; Klaus H. Neumann, MD; Jutta Dierkes, PhD

**Background**—In observational studies, hyperhomocysteinemia has been found to be a risk factor for total mortality and cardiovascular events in patients with end-stage renal disease. These patients have grossly elevated homocysteine levels that can be lowered by supplementation with folic acid and vitamin B<sub>12</sub>. We conducted a randomized clinical trial with B vitamins to reduce homocysteine levels and therefore cardiovascular events and total mortality.

**Methods and Results**—This randomized, double-blind multicenter study was conducted in 33 dialysis centers in north and east Germany between July 2002 and July 2008. We randomly assigned 650 patients with end-stage renal disease who were undergoing hemodialysis to 2 postdialysis treatments: 5 mg folic acid, 50 µg vitamin B<sub>12</sub>, and 20 mg vitamin B<sub>6</sub> (active treatment) or 0.2 mg folic acid, 4 µg vitamin B<sub>12</sub>, and 1.0 mg vitamin B<sub>6</sub> (placebo) given 3 times per week for an average of 2 years. The primary outcome was total mortality; the secondary outcome was fatal and nonfatal cardiovascular events. The primary outcome occurred in 102 patients (31%) receiving the active treatment and in 92 (28%) receiving placebo (hazard ratio, 1.13; 95% confidence interval, 0.85 to 1.50; *P*=0.51). The secondary outcome occurred in 83 patients (25%) receiving the active treatment and in 98 (30%) receiving placebo (hazard ratio, 0.80; 95% confidence interval, 0.60 to 1.07; *P*=0.13).

**Conclusions**—Increased intake of folic acid, vitamin B<sub>12</sub>, and vitamin B<sub>6</sub> did not reduce total mortality and had no significant effect on the risk of cardiovascular events in patients with end-stage renal disease.

**Clinical Trial Registration**—URL: [www.anzctr.org.au](http://www.anzctr.org.au). Unique identifier: ACTRN12609000911291. URL: [www.cochrane-renal.org](http://www.cochrane-renal.org). Unique identifier: CRG010600027.

(*Circulation*. 2010;121:1432-1438.)

*Circulation*. 2010;121:1432-1438.

## Vascular Medicine

### B Vitamins and the Risk of Total Mortality and

#### **Schlussfolgerungen:**

... kein positiver Effekt auf vaskuläre Ereignisse oder Sterberaten ...

cardiovascular events. The primary outcome occurred in 102 patients (31%) receiving the active treatment and in 92 (28%) receiving placebo (hazard ratio, 1.13; 95% confidence interval, 0.85 to 1.50;  $P=0.51$ ). The secondary outcome occurred in 83 patients (25%) receiving the active treatment and in 98 (30%) receiving placebo (hazard ratio, 0.80; 95% confidence interval, 0.60 to 1.07;  $P=0.13$ ).

**Conclusions**—Increased intake of folic acid, vitamin B<sub>12</sub>, and vitamin B<sub>6</sub> did not reduce total mortality and had no significant effect on the risk of cardiovascular events in patients with end-stage renal disease.

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(*Circulation*. 2010;121:1432-1438.)

Höhere Dosierung nötig?

2010

ANNUAL CONTRIBUTION

# Effect of B-Vitamin Therapy on Progression of Diabetic Nephropathy

## A Randomized Controlled Trial

Andrew A. House, MD

Misha Eliasziw, PhD

Daniel C. Cattran, MD

David N. Churchill, MD

Matthew J. Oliver, MD

Adrian Fine, MD

George K. Dresser, MD

**Context** Hyperhomocysteinemia is frequently observed in patients with diabetic nephropathy. B-vitamin therapy (folic acid, vitamin B<sub>6</sub>, and vitamin B<sub>12</sub>) has been shown to lower the plasma concentration of homocysteine.

**Objective** To determine whether B-vitamin therapy can slow progression of diabetic nephropathy and prevent vascular complications.

**Design, Setting, and Participants** A multicenter, randomized, double-blind, placebo-controlled trial (Diabetic Intervention with Vitamins to Improve Nephropathy [DIVINE]) at 5 university medical centers in Canada conducted between May 2001 and July 2007 of 238 participants who had type 1 or 2 diabetes and a clinical diagnosis of diabetic

## Intervention:

Folsäure 2,5 mg plus Vitamin B12 1 mg plus Vitamin B6  
25 mg pro Tag;  
Placebo

Matthew J. Oliver, MD

Adrian Fine, MD

George K. Dresser, MD

diabetic nephropathy and prevent vascular complications.

**Design, Setting, and Participants** A multicenter, randomized, double-blind, placebo-controlled trial (Diabetic Intervention with Vitamins to Improve Nephropathy [DIVINE]) at 5 university medical centers in Canada conducted between May 2001 and July 2007 of 238 participants who had type 1 or 2 diabetes and a clinical diagnosis of diabetic

# Verschlechterung der Nierenfunktion und Zunahme statt Abnahme von Herz-Kreislaufkomplikationen

Andrew H. Williams, MD  
Misha Talbot, MD, PhD  
Daniel C. Gattran, MD  
David N. Churchill, MD  
Matthew J. Oliver, MD  
Adrian Fine, MD  
George K. Dresser, MD

**Effect:** B-vitamin therapy (thiamine, riboflavin, niacin, and pyridoxine) did not slow progression of diabetic nephropathy. B-vitamin therapy (thiamine, riboflavin, niacin, and pyridoxine) has been shown to lower the plasma concentration of homocysteine.

**Objective:** To determine whether B-vitamin therapy can slow progression of diabetic nephropathy and prevent vascular complications.

**Design, Setting, and Participants:** A multicenter, randomized, double-blind, placebo-controlled trial (Diabetic Intervention with Vitamins to Improve Nephropathy [DIVINE]) at 5 university medical centers in Canada conducted between May 2001 and July 2007 of 238 participants who had type 1 or 2 diabetes and a clinical diagnosis of diabetic

# Folsäure

Darmpolypen





# Folic Acid for the Prevention of Colorectal Adenomas

## A Randomized Clinical Trial

Bernard F. Cole, PhD

John A. Baron, MD

Robert S. Sandler, MD

Robert W. Haile, DrPh

Dennis J. Ahnen, MD

Robert S. Bresalier, MD

Gail McKeown-Eyssen, PhD

Robert W. Summers, MD

**Context** Laboratory and epidemiological data suggest that folic acid may have an antineoplastic effect in the large intestine.

**Objective** To assess the safety and efficacy of folic acid supplementation for preventing colorectal adenomas.

**Design, Setting, and Participants** A double-blind, placebo-controlled, 2-factor, phase 3, randomized clinical trial conducted at 9 clinical centers between July 6, 1994, and October 1, 2004. Participants included 1021 men and women with a recent history of colorectal adenomas and no previous invasive large intestine carcinoma.

**Intervention** Participants were randomly assigned in a 1:1 ratio to receive 1 mg/d of folic acid (n = 516) or placebo (n = 505), and were separately randomized to receive

## Schlussfolgerungen:

... kein präventiver Effekt ... **möglicherweise  
Zunahme von kolorektalen Neoplasien ...**

Bert...

John...

Rob...

Rob...

Den...

Robert S. Bresalier, MD

Gail McKeown-Eyssen, PhD

Robert W. Summers, MD

phase 3, randomized clinical trial conducted at 9 clinical centers between July 6, 1994, and October 1, 2004. Participants included 1021 men and women with a recent history of colorectal adenomas and no previous invasive large intestine carcinoma.

**Intervention** Participants were randomly assigned in a 1:1 ratio to receive 1 mg/d of folic acid (n = 516) or placebo (n = 505), and were separately randomized to receive

# Meta-Analysen

Folsäure, Vitamin B

2010

REVIEW ARTICLE

LESS IS MORE

# Effects of Lowering Homocysteine Levels With B Vitamins on Cardiovascular Disease, Cancer, and Cause-Specific Mortality

*Meta-analysis of 8 Randomized Trials Involving 37 485 Individuals*

Robert Clarke, FRCP; Jim Halsey, BSc; Sarah Lewington, DPhil; Eva Lonn, MD; Jane Armitage, FRCP; JoAnn E. Manson, MD, DrPH; Kaare H. Bønaa, MD; J. David Spence, MD; Ottar Nygård, MD; Rex Jamison, MD; J. Michael Gaziano, MD; Peter Guarino, PhD; Derrick Bennett, PhD; Fraz Mir, MD; Richard Peto, FRS; Rory Collins, FRCP; for the B-Vitamin Treatment Trialists' Collaboration

**E**levated plasma homocysteine levels have been associated with higher risks of cardiovascular disease, but the effects on disease rates of supplementation with folic acid to lower plasma homocysteine levels are uncertain. Individual participant data were obtained for a meta-analysis of 8 large, randomized, placebo-controlled trials of folic acid supplementation involving 37 485 individuals at increased risk of cardiovascular disease. The analy-

*Arch Intern Med. 2010;170(18):1622-1631*

LESS IS MORE

## Effects of Lowering Homocysteine Levels

### **Schlussfolgerungen:**

... kein Effekt auf Gesamtsterblichkeit,  
Herz-Kreislauf-Komplikationen oder  
Krebserkrankungen ...

Rob  
JoA  
J. M  
Ron

**L**ower plasma homocysteine levels are uncertain. Individual participant data were obtained for a meta-analysis of 8 large, randomized, placebo-controlled trials of folic acid supplementation involving 37 485 individuals at increased risk of cardiovascular disease. The analy-

# Vitamin D

Infektionskrankheiten



# Vitamin D

Prävention von Lungenentzündung bei Kindern

# Effect on the incidence of pneumonia of vitamin D supplementation by quarterly bolus dose to infants in Kabul: a randomised controlled superiority trial



Semira Manaseki-Holland, Zabihullah Maroof, Jane Bruce, M Zulf Mughal, Mohammad Isaq Masher, Zulfiqar A Bhutta, Gijs Walraven, Daniel Chandramohan

## Summary

**Background** Vitamin D has a role in regulating immune function, and its deficiency is a suggested risk factor for childhood pneumonia. Our aim was to assess whether oral supplementation of vitamin D<sub>3</sub> (cholecalciferol) will reduce the incidence and severity of pneumonia in a high-risk infant population.

**Methods** We did a randomised placebo-controlled trial to compare oral 100 000 IU (2.5 mg) vitamin D<sub>3</sub> with placebo given to children aged 1–11 months in Kabul, Afghanistan. Randomisation was by use of a computer-generated list.

*Lancet* 2012; 379: 1419–27

Published Online

April 10, 2012

DOI:10.1016/S0140-

6736(11)61650-4

See [Comment](#) page 1373



**2012**

Articles

## **Schlussfolgerungen:**

... keine Reduktion des Erstauftretens von  
Lungenentzündung ...

**Methods** We did a randomised placebo-controlled trial to compare oral 100 000 IU (2·5 mg) vitamin D<sub>3</sub> with placebo given to children aged 1–11 months in Kabul, Afghanistan. Randomisation was by use of a computer-generated list.

6736(11)61650-4

See Comment page 1373

2012

Articles

## Schlussfolgerungen:

... keine Reduktion des Erstauftretens von  
Lungenentzündung ...

... **mehrfache Lungenentzündungen häufiger  
unter Vitamin D Behandlung** ...

**Methods** We did a randomised placebo-controlled trial to compare oral 100 000 IU (2.5 mg) vitamin D<sub>3</sub> with placebo given to children aged 1–11 months in Kabul, Afghanistan. Randomisation was by use of a computer-generated list.

6736(11)61650-4

See Comment page 1373

# Vitamin D

Prävention von Darmkrebs



2011

Annals of Internal Medicine

REVIEW

# Vitamin D With or Without Calcium Supplementation for Prevention of Cancer and Fractures: An Updated Meta-analysis for the U.S. Preventive Services Task Force

Mei Chung, PhD, MPH; Jounghee Lee, PhD; Teruhiko Terasawa, MD, PhD; Joseph Lau, MD; and Thomas A. Trikalinos, MD, PhD

**Background:** Studies suggest that vitamin D supplementation may reduce cancer and fracture risks.

**Purpose:** To examine the benefits and harms of vitamin D with or without calcium supplementation on clinical outcomes of cancer and fractures in adults.

**Data Sources:** English-language studies identified from MEDLINE and the Cochrane Central Register of Controlled Trials through July 2011.

**Study Selection:** Randomized, controlled trials (RCTs), prospective

in blood 25-(OH)D concentration was associated with a 6% (95% CI, 3% to 9%) reduced risk for colorectal cancer but no statistically significant dose-response relationships for prostate and breast cancer. Random-effects model meta-analysis showed that combined vitamin D and calcium supplementation reduced fracture risk (pooled relative risk, 0.88 [CI, 0.78 to 0.99]) in older adults, but the effects differed according to study setting: institution (relative risk, 0.71 [CI, 0.57 to 0.89]) versus community-dwelling (relative risk, 0.89 [CI, 0.76 to 1.04]). One RCT showed adverse outcomes associated with supplementation, including increased risk for renal and urinary tract stones.

**Primary Funding Source:** Agency for Healthcare Research and Quality.

Vitamin D With or Without Calcium Supplementation for Prevention

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**Study Selection:** Randomized, controlled trials (RCTs), prospective

RCT showed adverse outcomes associated with supplementa-  
tion, including increased risk for renal and urinary tract stones.

**Schlussfolgerungen:**  
Die Evidenz ist nicht ausreichend zur Beurteilung von Nutzen und Schaden von Vitamin D Supplementen zur Krebsprävention.

**Primary Funding Source:** Agency for Healthcare Research and Quality.

# Vitamin D

Stürze



## The Effect of Vitamin D on Falls: A Systematic Review and Meta-Analysis

Mohammad Hassan Murad, Khalid B. Elamin, Nisrin O. Abu Elnour, Mohamed B. Elamin, Aziz A. Alkatib, Mitra M. Fatourechi, Jaime P. Almandoz, Rebecca J. Mullan, Melanie A. Lane, Hau Liu, Patricia J. Erwin, Donald D. Hensrud, and Victor M. Montori

Knowledge and Encounter Research Unit (M.H.M., N.O.A.E., M.B.E., A.A.A., M.M.F., J.P.A., R.J.M., M.A.L., P.J.E., V.M.M.), and Division of Preventive, Occupational, and Aerospace Medicine (M.H.M., D.D.H.), Mayo Clinic, Rochester, Minnesota 55905; Department of Medicine (K.B.E.), Case Western Reserve University, Metrohealth Medical Center, Cleveland, Ohio 44109; Division of Endocrinology, Diabetes, Metabolism, and Nutrition (V.M.M.), Mayo Clinic, Rochester, Minnesota 55905; and Division of Endocrinology and Metabolism (H.L.), Santa Clara Valley Medical Center, San Jose, California 95128

**Context:** Vitamin D affects bone and muscle health and likely reduces the risk of falls in the elderly.

**Objective:** The aim of this systematic review is to summarize the existing evidence on vitamin D use

- **Conclusions:** Vitamin D combined with calcium reduces the risk of falls. The reduction in studies without calcium co-administration did not reach statistical significance. The majority of the evidence is derived from trials enrolling elderly women.



# Vitamin D

Knochenbrüche



# Annual High-Dose Oral Vitamin D and Falls and Fractures in Older Women

## A Randomized Controlled Trial

Kerrie M. Sanders, PhD

Amanda L. Stuart, BappSc

Elizabeth J. Williamson, MA, PhD

Julie A. Simpson, PhD

Mark A. Kotowicz, MBBS, FRACP

Doris Young, MD, MBBS, FRACGP

**Context** Improving vitamin D status may be an important modifiable risk factor to reduce falls and fractures; however, adherence to daily supplementation is typically poor.

**Objective** To determine whether a single annual dose of 500 000 IU of cholecalciferol administered orally to older women in autumn or winter would improve adherence and reduce the risk of falls and fracture.

**Design, Setting, and Participants** A double-blind, placebo-controlled trial of 2256 community-dwelling women, aged 70 years or older, considered to be at high risk of

# Zunahme statt Abnahme von Stürzen und Frakturen

## Annual High-Dose Oral Vitamin D and Falls and Fractures in Older Women A Randomized Controlled Trial

Kerrie M. Sanders, PhD

Amanda L. Stuart, BappSc

Elizabeth J. Williamson, MA, PhD

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# Meta-Analysen

Vitamin D

2010

BMJ

RESEARCH

## Patient level pooled analysis of 68 500 patients from seven major vitamin D fracture trials in US and Europe

The DIPART (vitamin D Individual Patient Analysis of Randomized Trials) Group

Correspondence to: B Abrahamsen, Department of Internal Medicine and Endocrinology, Copenhagen University Hospital Gentofte, Niels Andersensvej 65, DK-2900 Hellerup, Denmark  
b.abrahamsen@physician.dk

Cite this as: *BMJ* 2010;340:b5463

### ABSTRACT

**Objectives** To identify participants' characteristics that influence the anti-fracture efficacy of vitamin D or vitamin D plus calcium with respect to any fracture, hip fracture, and clinical vertebral fracture and to assess the influence of dosing regimens and co-administration of calcium.

**Design** Individual patient data analysis using pooled data

particularly in residential and care homes. This may contribute to secondary hyperparathyroidism, bone loss, impaired neuromuscular function, and an increased risk of falls and fractures.<sup>5-8</sup> This provides the rationale for using vitamin D to prevent fractures in older people.

A large randomised controlled trial in women in

## Schlussfolgerungen:

... Vitamin D alleine verhindert keine Frakturen.  
Calcium in Kombination mit Vitamin D reduziert Frakturen ...

Correspondence:  
Department of  
and Endocrinology,  
University of  
Andersensvej 65, DK-2900  
Hellerup, Denmark  
b.abrahamsen@physician.dk

Cite this as: *BMJ* 2010;340:b5463

D plus calcium with respect to any fracture, hip fracture, and clinical vertebral fracture and to assess the influence of dosing regimens and co-administration of calcium.

Design Individual patient data analysis using pooled data

increased risk of falls and fractures.<sup>5,8</sup> This provides the rationale for using vitamin D to prevent fractures in older people.

A large randomised controlled trial in women in

2011

Annals of Internal Medicine

REVIEW

# Vitamin D With or Without Calcium Supplementation for Prevention of Cancer and Fractures: An Updated Meta-analysis for the U.S. Preventive Services Task Force

Mei Chung, PhD, MPH; Jounghee Lee, PhD; Teruhiko Terasawa, MD, PhD; Joseph Lau, MD; and Thomas A. Trikalinos, MD, PhD

**Background:** Studies suggest that vitamin D supplementation may reduce cancer and fracture risks.

**Purpose:** To examine the benefits and harms of vitamin D with or without calcium supplementation on clinical outcomes of cancer and fractures in adults.

**Data Sources:** English-language studies identified from MEDLINE and the Cochrane Central Register of Controlled Trials through July 2011.

**Study Selection:** Randomized, controlled trials (RCTs), prospective

in blood 25-(OH)D concentration was associated with a 6% (95% CI, 3% to 9%) reduced risk for colorectal cancer but no statistically significant dose-response relationships for prostate and breast cancer. Random-effects model meta-analysis showed that combined vitamin D and calcium supplementation reduced fracture risk (pooled relative risk, 0.88 [CI, 0.78 to 0.99]) in older adults, but the effects differed according to study setting: institution (relative risk, 0.71 [CI, 0.57 to 0.89]) versus community-dwelling (relative risk, 0.89 [CI, 0.76 to 1.04]). One RCT showed adverse outcomes associated with supplementation, including increased risk for renal and urinary tract stones.

**Primary Funding Source:** Agency for Healthcare Research and Quality.

Vitamin D With or Without Calcium Supplementation for Prevention

**Ergebnisse:**  
Vitamin D in Kombination mit Calcium kann Frakturen reduzieren. Kein Effekt bei Vitamin D alleine.  
Effekte vor allem bei Altenheimbewohnern.  
Optimale Dosierung und Behandlungsverfahren bleiben unklar.  
Das Risiko für Nieren- und Harnleitersteine nimmt zu.

**Study Selection:** Randomized, controlled trials (RCTs), prospective

**Primary Funding Source:** Agency for Healthcare Research and Quality.



# Calcium

Kardiovaskuläre Komplikationen

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# Meta-Analyse

Calcium

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## Effect of calcium supplements on risk of myocardial infarction and cardiovascular events: meta-analysis

Mark J Bolland, senior research fellow,<sup>1</sup> Alison Avenell, clinical senior lecturer,<sup>2</sup> John A Baron, professor,<sup>3</sup> Andrew Grey, associate professor,<sup>1</sup> Graeme S MacLennan, senior research fellow,<sup>2</sup> Greg D Gamble, research fellow,<sup>1</sup> Ian R Reid, professor<sup>1</sup>

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### ABSTRACT

**Objective** To investigate whether calcium supplements increase the risk of cardiovascular events.

**Design** Patient level and trial level meta-analyses.

### INTRODUCTION

Osteoporosis is a major cause of morbidity and mortality in older people.<sup>1</sup> Calcium supplements marginally reduce the risk of fracture,<sup>2,3</sup> and most guidelines

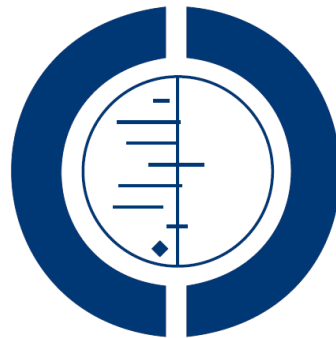
## Conclusions:

Calcium supplements (without coadministered vitamin D) are associated with an **increased risk of myocardial infarction ...**

**2011**

# Vitamin D supplementation for prevention of **mortality** in adults (Review)

Bjelakovic G, Glud LL, Nikolova D, Whitfield K, Wetterslev J, Simonetti RG, Bjelakovic M, Glud C



**THE COCHRANE  
COLLABORATION®**

## Vitamin D supplementation for prevention of mortality in

- 50 randomisiert-kontrollierte Studien  
94.148 Studienteilnehmer, meist ältere Frauen  
Behandlungsdauer durchschnittlich 2 Jahre



## Vitamin D supplementation for prevention of mortality in

- Relatives Risiko 0,97 (95% CI 0,94-1,00)

Bj

M,



## Vitamin D supplementation for prevention of mortality in

- Vitamin D alleine hat keinen Einfluss auf die Mortalität.

Bj

M,





## Vitamin D supplementation for prevention of mortality in

- Kein Effekt auf Krebserkrankungen

Bj

M,



# Multivitamine zur Prävention von Krebs und Herz-Kreislauf- Erkrankungen bei Frauen

2009

ORIGINAL INVESTIGATION

# Multivitamin Use and Risk of Cancer and Cardiovascular Disease in the Women's Health Initiative Cohorts

*Marian L. Neuhouser, PhD; Sylvia Wassertheil-Smoller, PhD; Cynthia Thomson, PhD, RD; Aaron Aragaki, MS; Garnet L. Anderson, PhD; JoAnn E. Manson, MD, DrPH; Ruth E. Patterson, PhD; Thomas E. Rohan, MD, PhD; Linda van Horn, MD, PhD; James M. Shikany, DrPH; Asha Thomas, PhD; Andrea LaCroix, PhD; Ross L. Prentice, PhD*

**Background:** Millions of postmenopausal women use multivitamins, often believing that supplements prevent chronic diseases such as cancer and cardiovascular disease (CVD). Therefore, we decided to examine associations between multivitamin use and risk of cancer, CVD, and mortality in postmenopausal women.

**Methods:** The study included 161 808 participants from the Women's Health Initiative clinical trials (N=68 132 in 3 overlapping trials of hormone therapy, dietary modifica-

nal, bladder, stomach, lung, or ovarian cancer; 8751 CVD events; and 9865 deaths were reported. Multivariate-adjusted analyses revealed no association of multivitamin use with risk of cancer (hazard ratio [HR], 0.98, and 95% confidence interval [CI], 0.91-1.05 for breast cancer; HR, 0.99, and 95% CI, 0.88-1.11 for colorectal cancer; HR, 1.05, and 95% CI, 0.90-1.21 for endometrial cancer; HR, 1.0, and 95% CI, 0.88-1.13 for lung cancer; and HR, 1.07, and 95% CI, 0.88-1.29 for ovarian cancer); CVD (HR, 0.96, and 95%

## Frauengesundheitsstudie (WHI Studie), USA

- 162.000 postmenopausale Frauen
- 8 Jahre Studiendauer

Multivitamin Use and Risk of Cancer and Mortality in Postmenopausal Women

**Background:** Multivitamin use is common among postmenopausal women, but little is known about associations between multivitamin use and risk of cancer, CVD, and mortality in postmenopausal women.

**Methods:** The study included 161 808 participants from the Women's Health Initiative clinical trials (N = 68 132 in 3 overlapping trials of hormone therapy, dietary modifica-

confidence interval [CI], 0.91-1.05 for breast cancer; HR, 0.99, and 95% CI, 0.88-1.11 for colorectal cancer; HR, 1.05, and 95% CI, 0.90-1.21 for endometrial cancer; HR, 1.0, and 95% CI, 0.88-1.13 for lung cancer; and HR, 1.07, and 95% CI, 0.88-1.29 for ovarian cancer); CVD (HR, 0.96, and 95%

## Conclusions:

... the study provided convincing evidence that multivitamin use has little or no influence on the risk of common cancers, CVD, or total mortality in postmenopausal women.

**Background:** Multivitamin use is common among postmenopausal women. There are conflicting data on associations between multivitamin use and risk of cancer, CVD, and mortality in postmenopausal women.

**Methods:** The study included 161 808 participants from the Women's Health Initiative clinical trials (N=68 132 in 3 overlapping trials of hormone therapy, dietary modifica-

confidence interval [CI], 0.91-1.05 for breast cancer; HR, 0.99, and 95% CI, 0.88-1.11 for colorectal cancer; HR, 1.05, and 95% CI, 0.90-1.21 for endometrial cancer; HR, 1.0, and 95% CI, 0.88-1.13 for lung cancer; and HR, 1.07, and 95% CI, 0.88-1.29 for ovarian cancer); CVD (HR, 0.96, and 95%

# Fazit

- Es gibt wenige medizinische Maßnahmen, die so umfassend untersucht wurden wie die Supplementierung mit Vitaminen.

# Fazit

- Die Supplementierung mit Vitaminen hat ein erhebliches Schadenspotenzial.
- Raucher und Menschen mit bereits bestehenden Erkrankungen scheinen besonders vulnerabel.
- Ein Nutzen ist selten nachweisbar.
- Vitaminspiegel sind nicht geeignet zur Beurteilung des Nutzens.

# Die gute Nachricht



# Die gute Nachricht

- We can do without it!