

# **Ernährung bei chronischer Nierenerkrankung (CKD)**



**Martin K. Kuhlmann**

**Vivantes Klinikum im Friedrichshain, Berlin**

**Martin.kuhlmann@vivantes.de**

***Heidelberger Nephrologisches Seminar***

***07-03-2024***

**Martin.kuhlmann@vivantes.de**

# Interessenkonflikte



- Keine Interessenkonflikte in Verbindung mit dem Thema
- Keine Erwähnung von Medikamenten

# Ernährungstherapie in der Nephrologie



- Niereninsuffizienz ist eine metabolische Erkrankung
- Vor der Entwicklung der Dialyse war eine diätetische Therapie die einzige Möglichkeit der (moderaten) Lebensverlängerung bei Niereninsuffizienz
- In der Bevölkerung sind Nierenerkrankungen und Diät immer noch eng miteinander verknüpft
- Nierenerkrankte sind daher empfänglich für Ernährungsempfehlungen

# Ernährungstherapie bei CKD

## Ziele

- **Progressionshemmung**
- **Hinauszögern der Dialyseeinleitung**
- **Reduktion kardiovaskulärer Morbidität und Mortalität**
- **Aufrechterhaltung eines guten Ernährungszustandes**

## Ernährungskonzepte

- **Eiweißrestriktion**
  - ✦ **Low Protein Diet**
  - ✦ **Very Low Protein Diet + Supplements**
- **Kochsalzrestriktion**
- **Pflanzen-basierte Ernährung**
  - ✦ **Mediterrane Kost**
  - ✦ **DASH-Diet**
  - ✦ **Vegetarische/vegane Ernährung**

# Eiweißzufuhr bei CKD

Diskussion kreist seit Jahrzehnten um die *Quantität* (g/kg KG/d) der Eiweißzufuhr

0,28 ~ 0,43  
0,55 ~ 0,60  
0,8 ~ 1,00  
0,6 ~ 0,80  
1,0 ~ 1,2

*Qualität* der Eiweiße bleibt in Empfehlungen meist unerwähnt

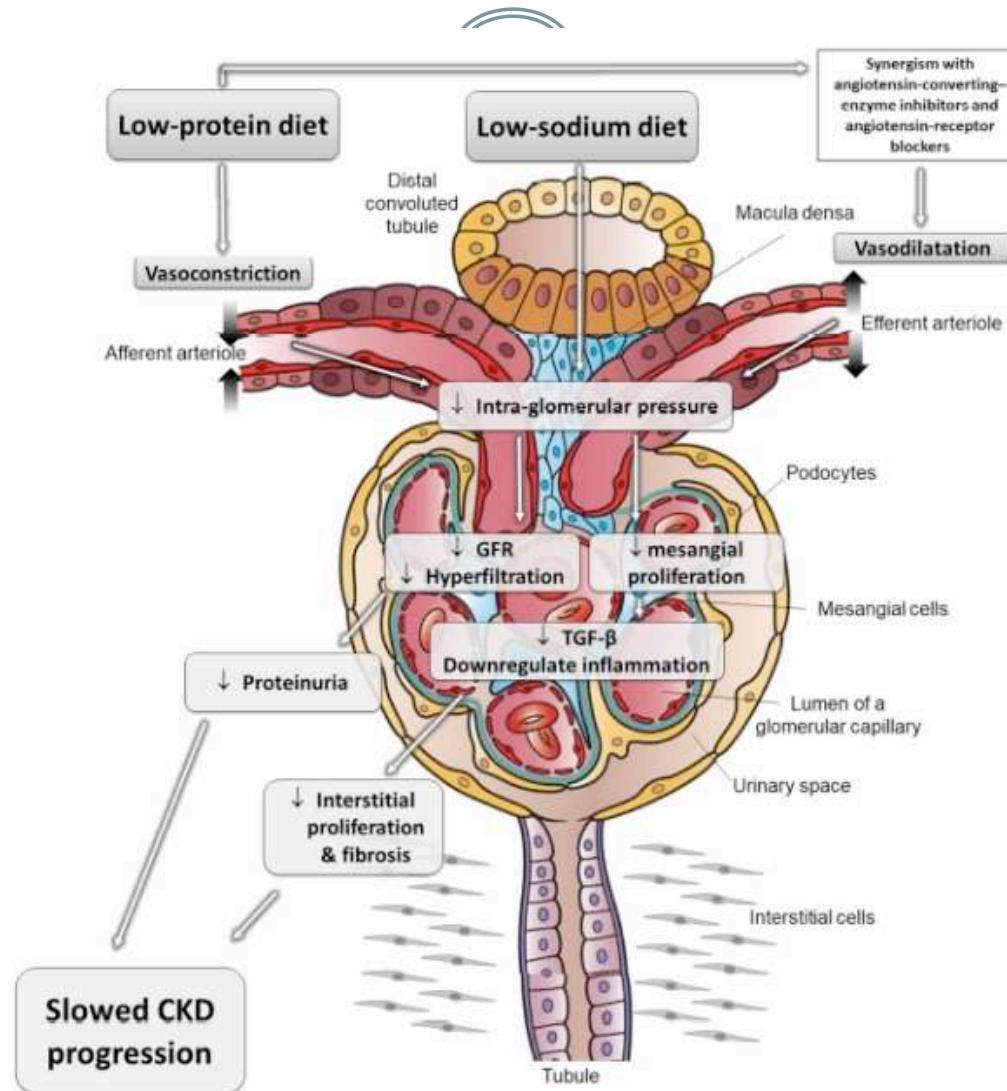


# Eiweißarme Diät – Definition



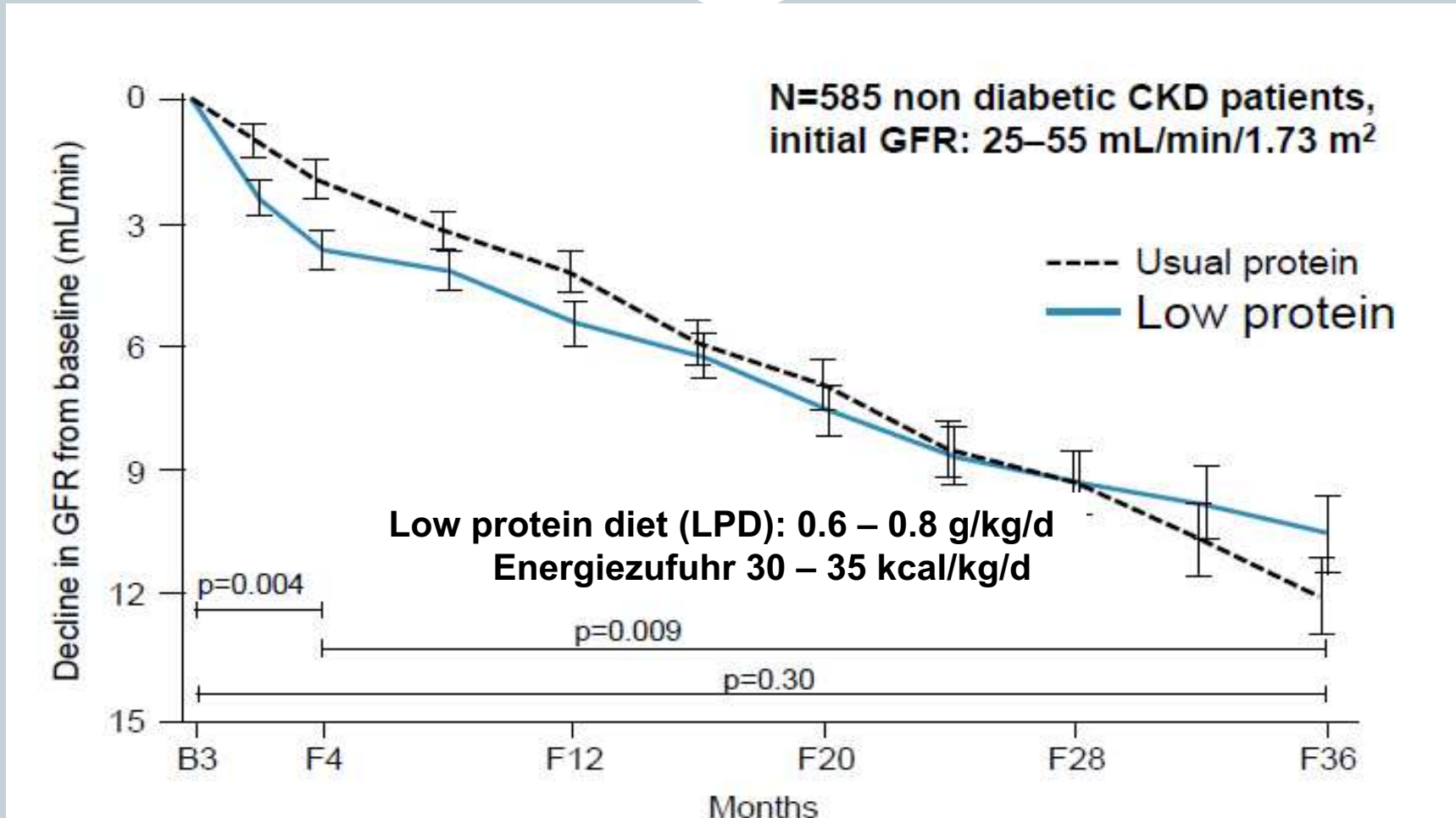
- Mittlere Eiweißzufuhr: 1.1 – 1.35 g/kg KG/d
- WHO-Empfehlung: 0.8 – 1.0 g/kg/d
- Mindestzufuhr für neutrale Stickstoffbilanz bei metabolischer Stabilität: 0.6 g/kg/d
  - Bei Energiezufuhr von 30-35 kcal/kg/d
- Low protein diet (LPD): 0.6 – 0.8 g/kg/d
  - Energiezufuhr 30 – 35 kcal/kg/d
- Very low protein diet (vLPD): 0.3 g/kg/d
  - vLPD muss supplementiert werden mit essentiellen Aminosäuren oder Ketosäuren

# LPD reduziert glomeruläre Hyperfiltration



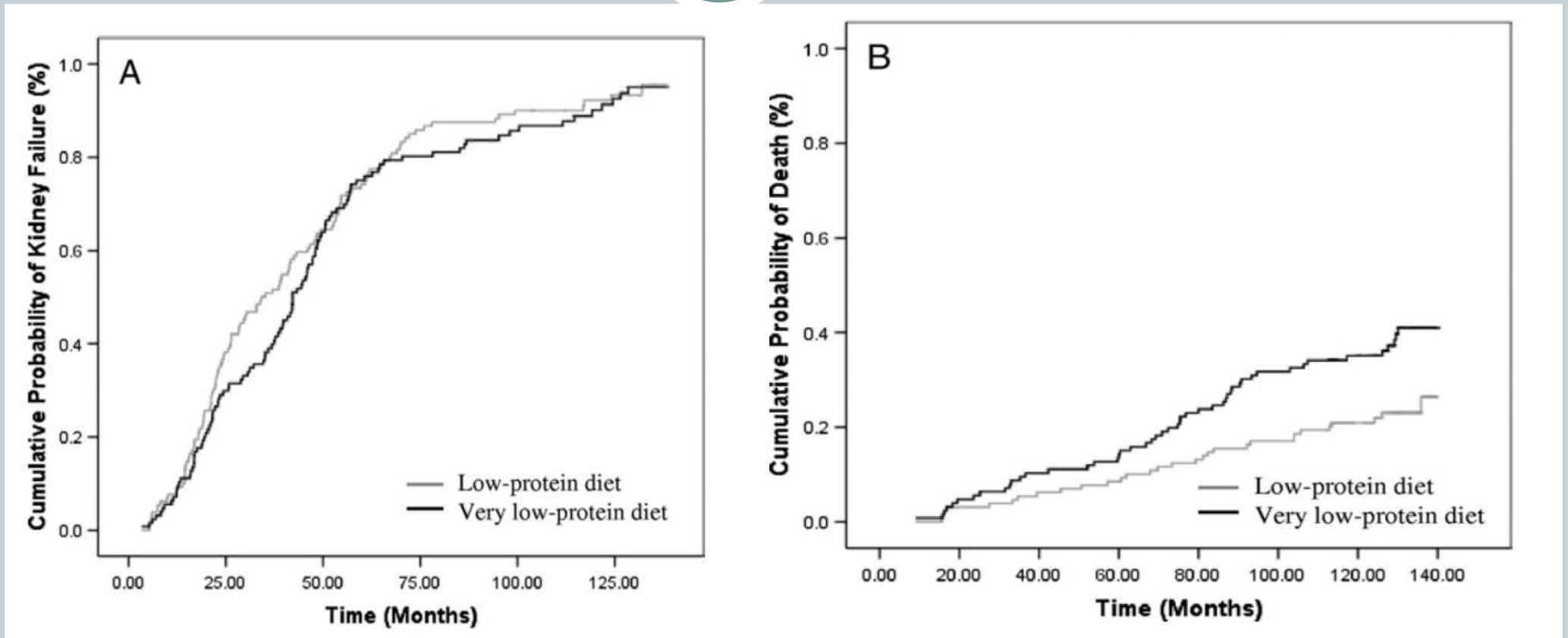


# MDRD-Studie: RCT zu Progressionshemmung durch diätetische Eiweißreduktion bei CKD





# vLPD: Langfristig gesteigerte Mortalität!



**Very low protein diet (vLPD): 0.3 g/kg/d + Ketoanaloga essentieller AS**

# Aktuelle KDIGO – Empfehlungen 2020

## KDOQI CLINICAL PRACTICE GUIDELINE FOR NUTRITION IN CKD: 2020 UPDATE

T. Alp Ikizler, Jerrilynn D. Burrowes, Laura D. Byham-Gray, Katrina L. Campbell, Juan-Jesus Carrero, Winnie Chan, Denis Fouque, Allon N. Friedman, Sana Ghaddar, D. Jordi Goldstein-Fuchs, George A. Kaysen, Joel D. Kopple, Daniel Teta, Angela Yee-Moon Wang, and Lilian Cuppari

Protein Restriction, CKD Patients Not on Dialysis and Without Diabetes

**3.0.1 In adults with CKD 3-5 who are metabolically stable, we recommend, under close clinical supervision, protein restriction with or without keto acid analogs, to reduce risk for end-stage kidney disease (ESKD)/death (1A) and improve quality of life (QoL) (2C):**

- a low-protein diet providing 0.55–0.60 g dietary protein/kg body weight/day, or
- a very low-protein diet providing 0.28–0.43 g dietary protein/kg body weight/day with additional keto acid/amino acid analogs to meet protein requirements (0.55–0.60 g/kg body weight/day)

4.1.1 Patients CKD G3-5D „at risk or with protein-energy-wasting“: Minimum 3 months trial of oral supplements

## CKD G3-5

- **Energie:** 25-35kcal/kg KG/d
- **Protein:** 0,55 - 0,60 g/kg KG/d  
*Low Protein Diet (LPD)*
- **ABER:** „metabolisch stabil“

## Ballaststoffe:

- *Mediterrane Kost (LDL)*
- **CKD G1-4:** viel Obst und Gemüse

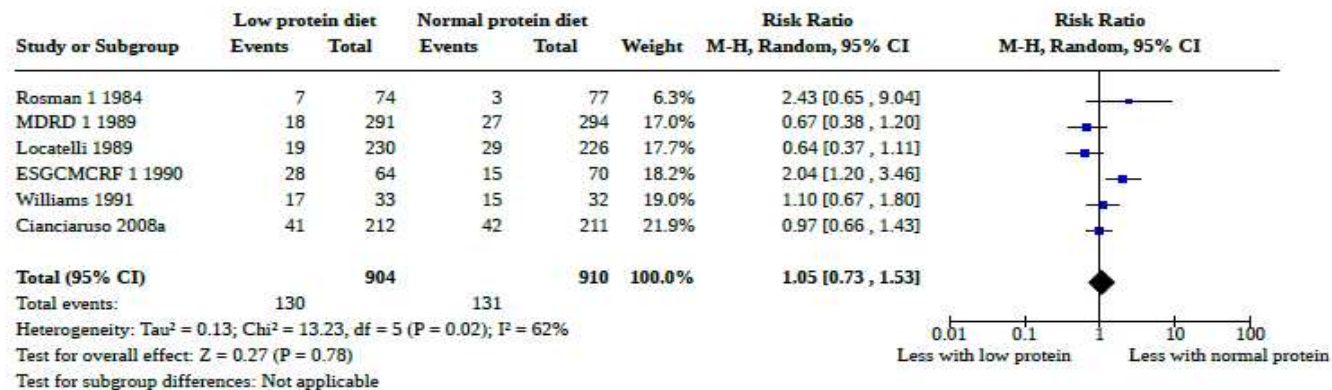
## CKD 5D

- **Protein:** 1-1,2g/kg KG/d
- **Bei PEW:** >1,2 g/kg KG/d

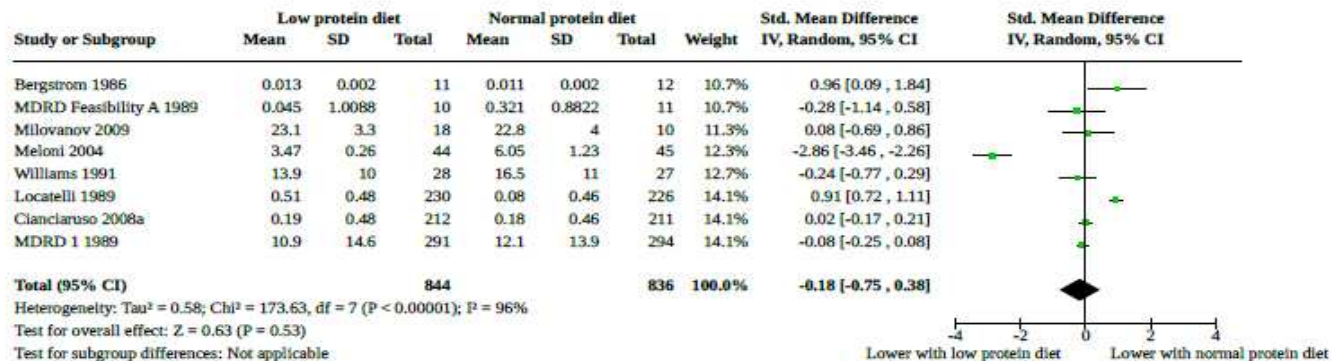
### Weak Recommendation (level 2 = we suggest)

Low (C) Our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect.

## Analysis 1.2. Comparison 1: Low protein diet versus normal protein diet, Outcome 2: ESKD



## Analysis 1.3. Comparison 1: Low protein diet versus normal protein diet, Outcome 3: End or change in GFR



- This review found that low protein diets (LPD) may make little difference to the number of people who progress to ESKD.
- Very low protein diets (VLPD) probably reduce the number of people with CKD 4 or 5, who progress to ESKD.
- LPD or VLPD probably do not influence death.
- There are limited data on adverse effects such as weight differences and protein energy wasting.
- There are no data on whether quality of life is impacted by difficulties in adhering to protein restriction.
- Studies evaluating the adverse effects and the impact on quality of life of dietary protein restriction are required before these dietary approaches can be recommended for widespread use.

# KDOQI 2020: LPD nur beim „metabolisch stabilen“ Patienten „metabolisch stabil“ =

Seite  
12

- keine aktive Inflammation oder Infektion
- kein Krankenhausaufenthalt in den vergangenen 14d
- kein unkontrollierter Diabetes Mellitus
- keine Tumorerkrankung
- keine Immunsuppression
- keine antibiotische Therapie
- kein Gewichtsverlust
- kein Untergewicht

nur für wenige Patienten sicher  
proteinarme Diät (0,6g/kg/d) - hohe  
Kalorienzufuhr (>30 Kcal/kg/d)  
(Risiko Mangelernährung)

„very low protein“ Diät (0,28-0,43 g/kg/d) nur  
unter Substitution von Ketoanaloga  
Erhalt Muskelmasse wichtig

# Potentielle Vorteile einer diätetischen Proteinrestriktion



- Verminderte glomeruläre Hyperfiltration

- **ABER:**
- **Proteinrestriktion hat**
- ***keinen Effekt* auf**
- **kardiovaskuläres Outcome**

Zufuhr gesättigter Fette aus tierischem Eiweiß

- Günstiger Effekt auf SBH (geringere Azidose)
- Besserung der Insulinresistenz (Urämietoxine?)



# Red Meat Intake and Risk of ESRD

Quan-Lan Jasmine Lew,<sup>\*</sup> Tazeen Hasan Jafar,<sup>†‡</sup> Hiromi Wai Ling Koh,<sup>§</sup> Aizhen Jin,<sup>||</sup>  
 Khuan Yew Chow,<sup>||</sup> Jian-Min Yuan,<sup>¶\*\*</sup> and Woon-Puay Koh<sup>†§</sup>

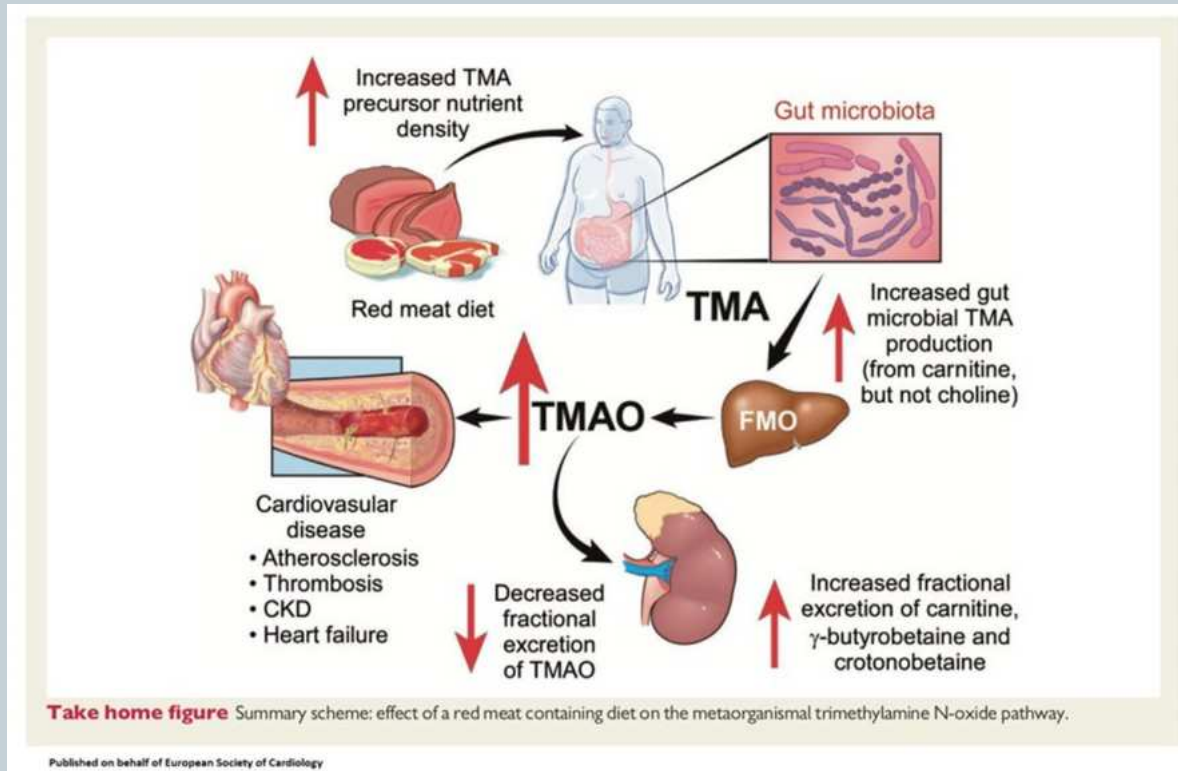
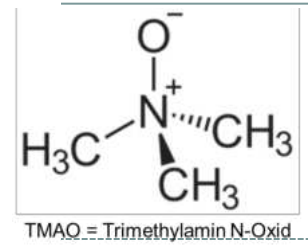
**Table 3.** Hazard ratios (95% CI) for risk of ESRD according to food sources of protein (n=60,198)

Food Sources of Protein (g/d)	Quartiles of Energy-Adjusted Food Intake				P for Trend <sup>a</sup>
	Q1	Q2	Q3	Q4	
<b>Red meat</b>					
Cases	194	220	267	270	
Person-years	236,141	236,256	230,243	230,006	
Multivariate model 1	1.00	1.11 (0.91–1.35)	1.39 (1.16–1.68)	1.47 (1.22–1.77)	<0.001
Multivariate model 2	1.00	1.01 (0.83–1.24)	1.29 (1.06–1.56)	1.36 (1.13–1.64)	<0.001
Multivariate model 3	1.00	1.03 (0.84–1.26)	1.32 (1.07–1.61)	1.40 (1.15–1.71)	<0.001
<b>Poultry</b>					
Cases	232	243	253	223	
Person-years	230,852	232,599	232,016	237,180	
Multivariate model 1	1.00	1.02 (0.85–1.22)	1.14 (0.95–1.36)	1.07 (0.89–1.29)	0.37
Multivariate model 2	1.00	0.92 (0.77–1.12)	1.04 (0.86–1.26)	0.99 (0.82–1.20)	0.77
Multivariate model 3	1.00	0.88 (0.72–1.06)	0.95 (0.78–1.16)	0.90 (0.74–1.09)	0.49
<b>Fish and shellfish</b>					
Cases	204	251	237	259	
Person-years	229,112	231,006	235,816	236,713	
Multivariate model 1	1.00	1.21 (1.01–1.46)	1.14 (0.94–1.37)	1.27 (1.06–1.53)	0.03
Multivariate model 2	1.00	1.16 (0.96–1.39)	1.06 (0.87–1.27)	1.12 (0.93–1.34)	0.44
Multivariate model 3	1.00	1.12 (0.93–1.35)	1.01 (0.84–1.23)	1.07 (0.89–1.30)	0.71



# The role of trimethylamine N-oxide as a mediator of cardiovascular complications in chronic kidney disease

James A.P. Tomlinson<sup>1,2</sup> and David C. Wheeler<sup>3</sup>



## Surprising Sources of TMAO

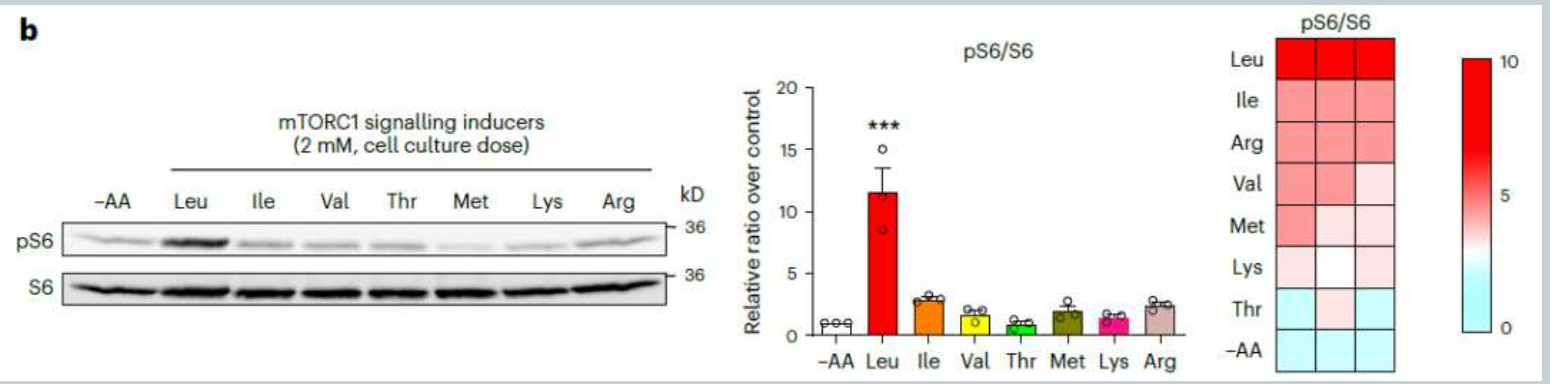
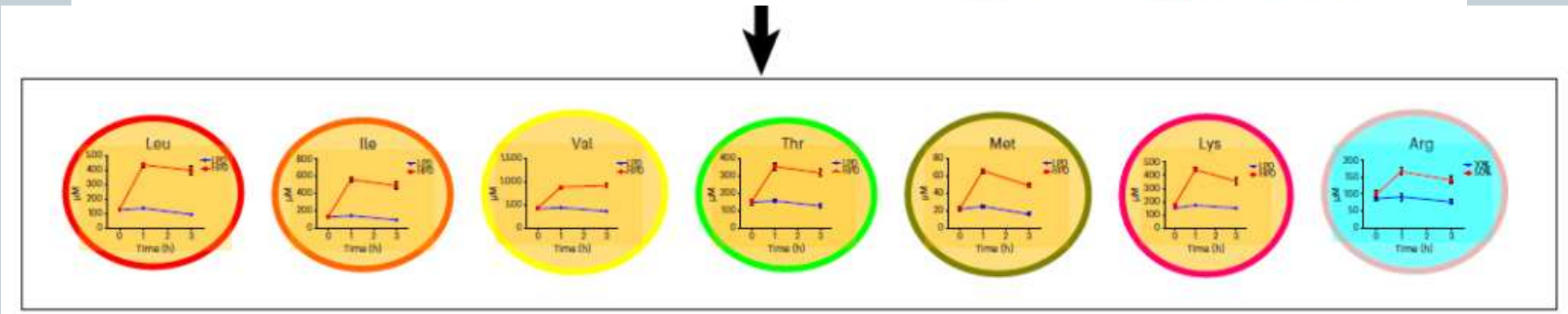
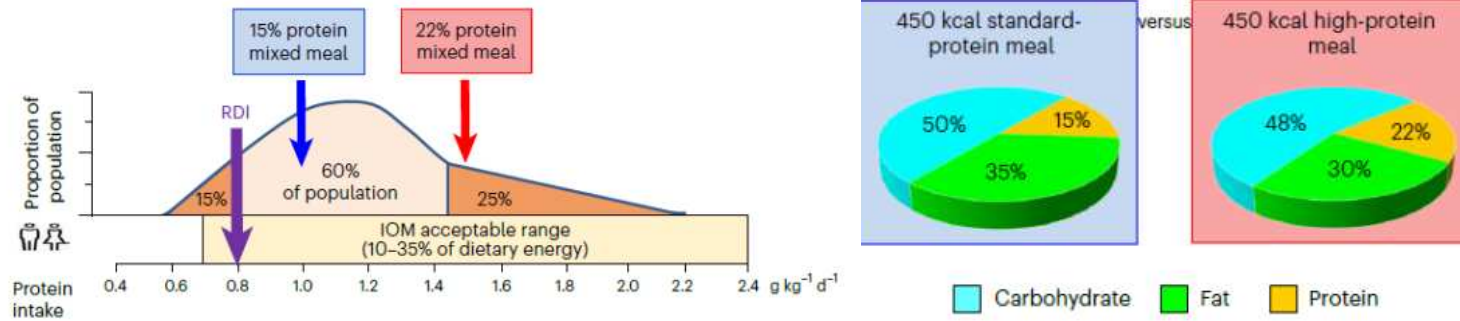
Animal products and dietary supplements are well-known sources of choline and L-carnitine, but the TMAO-precursors can also show up in these unexpected places:

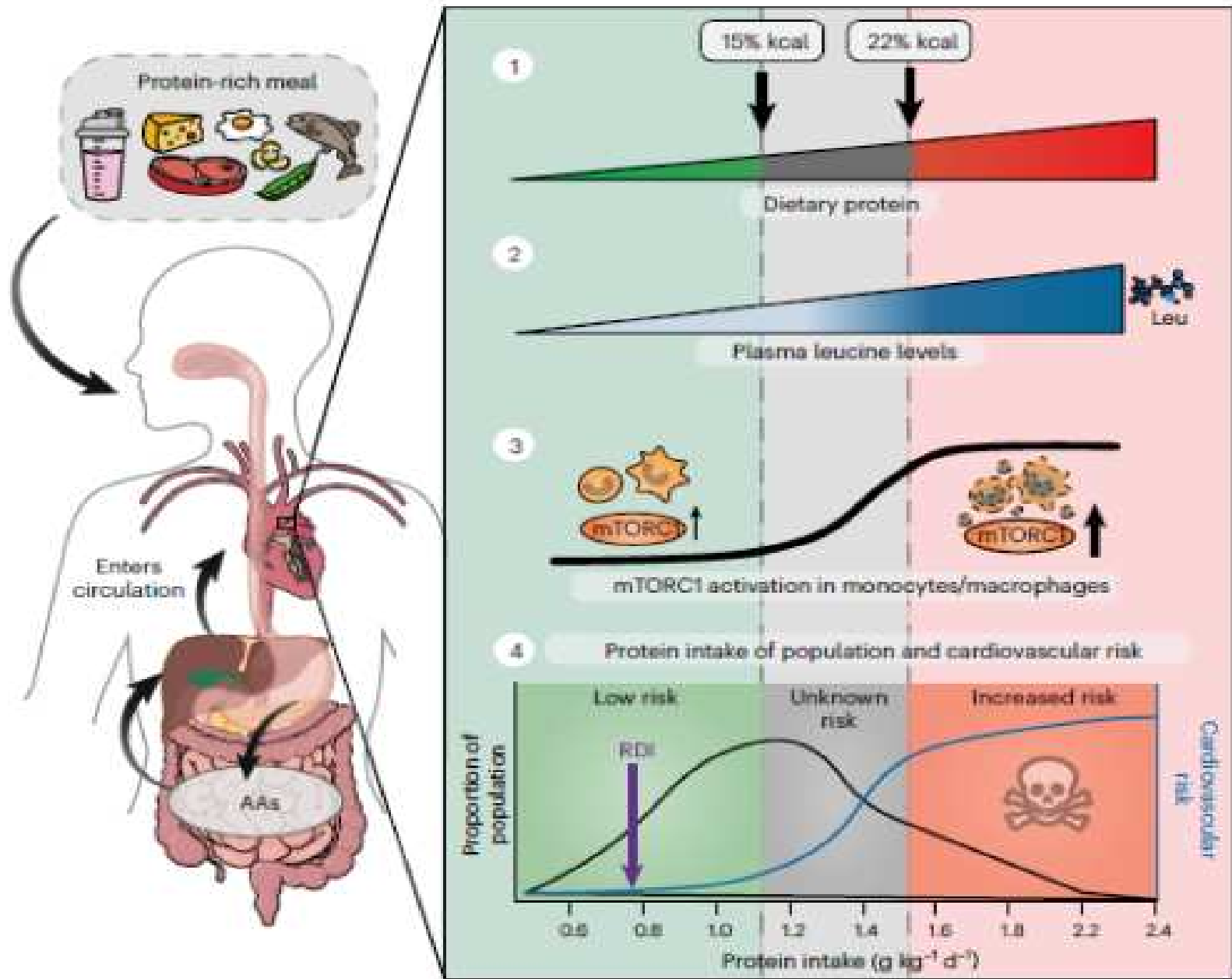
- Processed foods that contain phosphatidylcholine, also known as lecithin
- Energy drinks
- Protein supplementation products
- Some fruits and vegetables

FMO = Flavin Mono-oxygenase



# Identification of a leucine-mediated threshold effect governing macrophage mTOR signalling and cardiovascular risk

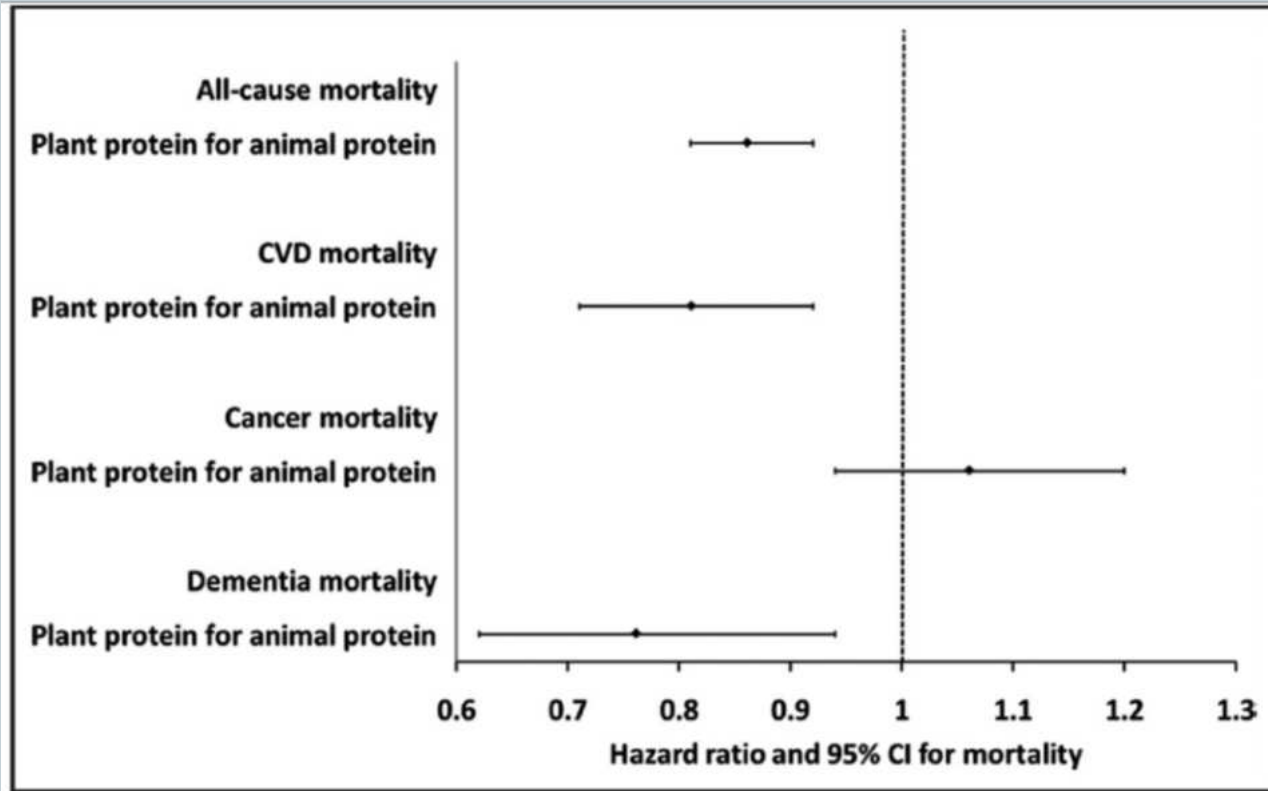




# Association of Major Dietary Protein Sources With All-Cause and Cause-Specific Mortality: Prospective Cohort Study

Yangbo Sun, MD, PhD; Buyun Liu, MD, PhD; Linda G. Snetselaar, PhD; Robert B. Wallace, MD;

**Figure 1.** Hazard ratios of all-cause and cause-specific mortality associated with replacement of 5% energy of animal protein with plant protein.



## CLINICAL PERSPECTIVE

### What Is New?

- Different dietary protein sources have varying associations with all-cause mortality, cardiovascular disease mortality, and dementia mortality.
- Higher plant protein intake and substitution of animal protein with plant protein were associated with lower risk of all-cause mortality, cardiovascular disease mortality, and dementia mortality.

### What Are the Clinical Implications?

- Our findings support the need for consideration of protein sources, in addition to the amount of protein intake, in future dietary guidelines.





# Pflanzen-basierte Ernährung



## Traditional Mediterranean Diet Meal Plan

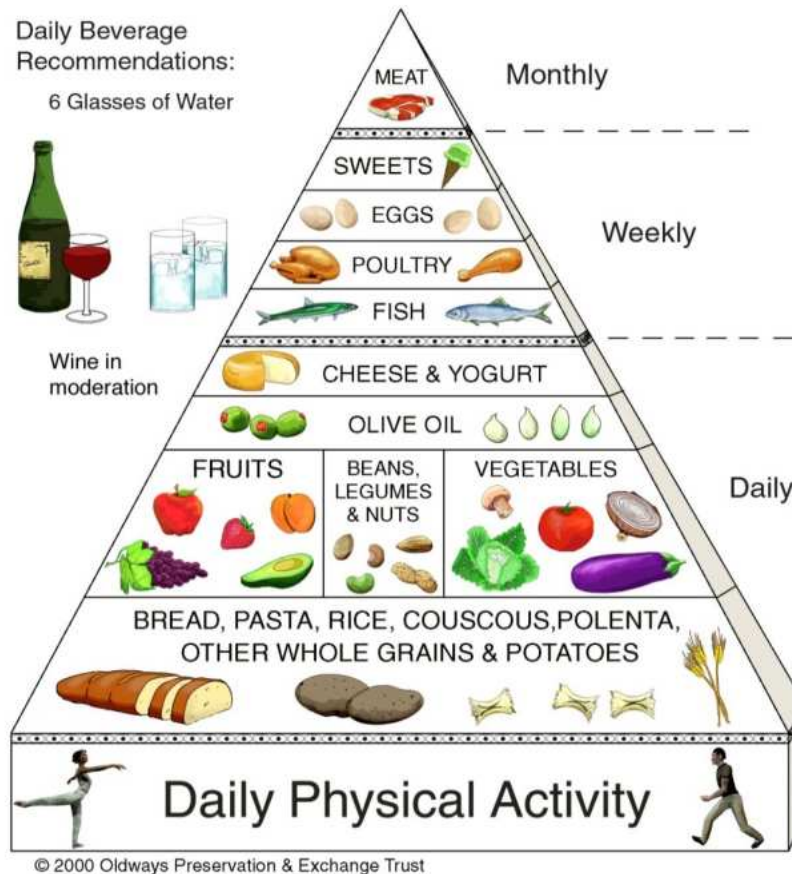


## The DASH Diet for Healthy Blood Pressure

Follow these DASH (Dietary Approaches to Stop Hypertension) guidelines for a healthier, more balanced diet



## The Traditional Healthy Mediterranean Diet Pyramid



- **Ungesättigte FS (Fisch, Olivenöl)**
- **Komplexe Kohlenhydrate (Hülsenfrüchte)**
- **Hoher Ballaststoffgehalt (Gemüse, Früchte)**
- **Hoher Gehalt an Vitamin B6, B12, C, E und Polyphenolen (Gemüse, Früchte, Cerealien, Olivenöl)**



# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

JUNE 26, 2003

VOL. 348 NO. 26

## Adherence to a Mediterranean Diet and Survival in a Greek Population

**Table 4.** Hazard Ratios for Death Associated with a Two-Point Increment in the Mediterranean-Diet Score.\*

Variable	No. of Deaths/ No. of Participants	Hazard Ratio for Death (95% CI)		
		Crude	Age- and Sex-Adjusted	Fully Adjusted
Death from any cause	275/22,043	0.74 (0.65–0.86)	0.79 (0.69–0.91)	0.75 (0.64–0.87)
Death from coronary heart disease	54/22,043	0.68 (0.50–0.94)	0.74 (0.54–1.02)	0.67 (0.47–0.94)
Death from cancer	97/22,043	0.81 (0.64–1.03)	0.85 (0.67–1.08)	0.76 (0.59–0.98)

**Mediterrane Diät senkt kardiovaskuläre Mortalität in  
Gesamtpopulation**

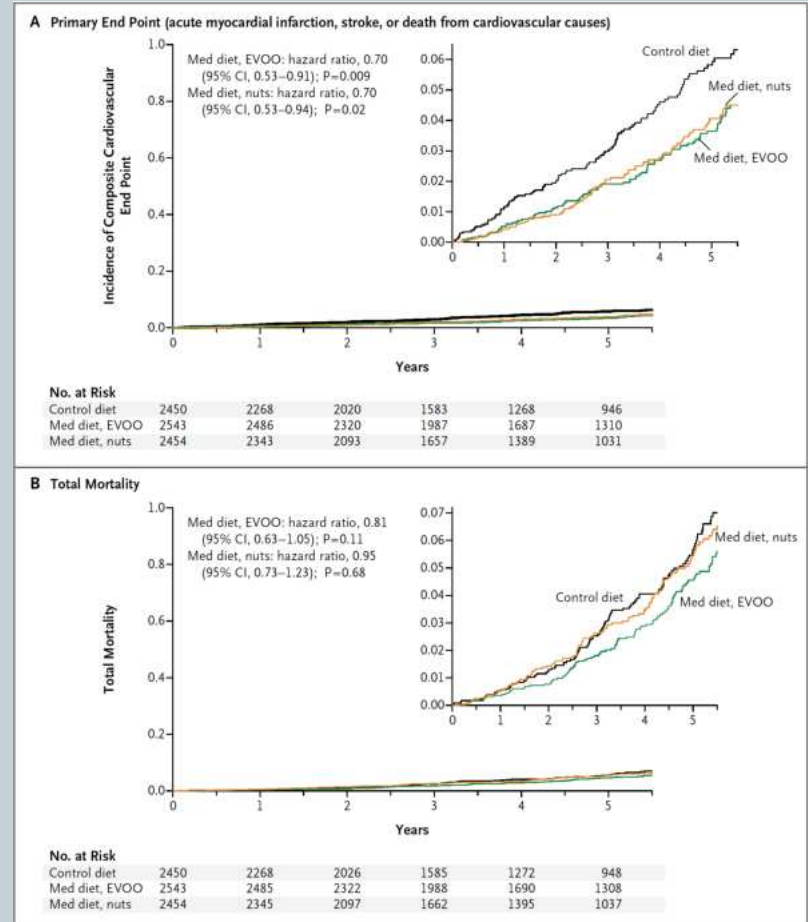
Primary Prevention of Cardiovascular Disease  
with a Mediterranean Diet

Ramón Estruch, M.D., Ph.D., Emilio Ros, M.D., Ph.D., Jordi Salas-Salvadó, M.D., Ph.D.,

- Multicenter RCT in Spain
- 7447 participants at high cardiovascular risk but free of cardiovascular disease
  - Mediterranean diet + extra-virgin olive oil (n = 2543)
  - Mediterranean diet + mixed nuts (n = 2454)
  - Fat reduced control diet (n = 2450)
- After interim analysis the trial was stopped (median FU of 4.8 yrs)

**CONCLUSIONS**

Among persons at high cardiovascular risk, a Mediterranean diet supplemented with extra-virgin olive oil or nuts reduced the incidence of major cardiovascular events. (Funded by the Spanish government's Instituto de Salud Carlos III and others; Controlled-Trials.com number, ISRCTN35739639.)





# Association Between Plant and Animal Protein Intake and Overall and Cause-Specific Mortality

Jiaqi Huang, PhD; Linda M. Liao, PhD, MPH; Stephanie J. Weinstein, PhD; Rashmi Sinha, PhD; Barry I. Graubard, PhD; Demetrius Albanes, MD

**DESIGN, SETTING, AND PARTICIPANTS** This prospective cohort study analyzed data from 416 104 men and women in the US National Institutes of Health–AARP Diet and Health Study from 1995 to 2011. Data were analyzed from October 2018 through April 2020.

Figure. Risk of Overall Mortality Associated With Intake of Plant Protein According to Subgroups Among 237 036 Men and 179 068 Women

Subgroup	Men HR (95% CI)	Is increased mortality	P for interaction
Age at baseline, y			
<60	0.93 (0.90-0.96)		<.001 <sup>a</sup>
60-65	0.95 (0.92-0.98)		
≥65	0.97 (0.95-0.99)		
Smoking status			
Never	0.97 (0.94-1.00)		.009
Former	0.96 (0.94-0.98)		
Current	0.94 (0.91-0.97)		
Diabetes			
No	0.96 (0.94-0.97)		.006
Yes	0.93 (0.90-0.97)		
BMI			
<18.5	1.10 (0.96-1.27)		<.001 <sup>a</sup>
18.5 to <25	0.94 (0.91-0.96)		
25 to <30	0.96 (0.94-0.99)		
30 to <35	0.95 (0.92-0.99)		
≥35	0.99 (0.93-1.05)		
Alcoholic drinks/d			
≤1	0.97 (0.96-0.99)		
>1 to 3	0.93 (0.89-0.97)		
>3	0.89 (0.85-0.93)		.006

## Key Points

**Question** Does an association exist between dietary protein choice, particularly from various food sources, and long-term overall mortality or cause-specific mortality in the US population?

**Findings** In this cohort of 237 036 men and 179 068 women with 16 years of observation and nearly 78 000 deaths, greater intake of plant protein was significantly associated with lower overall mortality and cardiovascular disease mortality independent of several other risk factors.

**Meaning** This study provides evidence for public health recommendations regarding dietary modifications in choice of protein sources that may promote health and longevity.





# Plant-Based Diets and Incident CKD and Kidney Function

Hyunju Kim,<sup>1,2</sup> Laura E. Caulfield,<sup>1</sup> Vanessa Garcia-Larsen,<sup>1</sup> Lyn M. Steffen,<sup>3</sup> Morgan E. Grams,<sup>2,4</sup> Josef Coresh,<sup>2,4</sup> and Casey M. Rebholz<sup>2,4</sup>

**Design, setting, participants, & measurements** Analyses were conducted in a sample of 14,686 middle-aged adults enrolled in the Atherosclerosis Risk in Communities study. Diets were characterized using four plant-based diet indices. In the overall plant-based diet index, all plant foods were positively scored; in the healthy plant-based diet index, only healthful plant foods were positively scored; in the provegetarian diet, selected plant foods were positively scored. In the less healthy plant-based diet index, only less healthful plant foods were positively scored. All indices negatively scored animal foods. We used Cox proportional hazards models to study the association with incident CKD and linear mixed models to examine decline in eGFR, adjusting for confounders.

**Results** During a median follow-up of 24 years, 4343 incident CKD cases occurred. Higher adherence to a healthy plant-based diet (HR comparing quintile 5 versus quintile 1 [ $HR_{Q5 \text{ versus } Q1}$ ], 0.86; 95% confidence interval [95% CI], 0.78 to 0.96;  $P$  for trend = 0.001) and a provegetarian diet ( $HR_{Q5 \text{ versus } Q1}$ , 0.90; 95% CI, 0.82 to 0.99;  $P$  for trend = 0.03) were associated with a lower risk of CKD, whereas higher adherence to a less healthy plant-based diet ( $HR_{Q5 \text{ versus } Q1}$ , 1.11; 95% CI, 1.01 to 1.21;  $P$  for trend = 0.04) was associated with an elevated risk. Higher adherence to an overall plant-based diet and a healthy plant-based diet was associated with slower eGFR decline. The proportion of CKD attributable to lower adherence to healthy plant-based diets was 4.1% (95% CI, 0.6% to 8.3%).

**Conclusions** Higher adherence to healthy plant-based diets and a vegetarian diet was associated with favorable kidney disease outcomes.

# Healthy Dietary Patterns and Risk of Mortality and ESRD in CKD: A Meta-Analysis of Cohort Studies

Jaimon T. Kelly,\* Suetonia C. Palmer,<sup>†</sup> Shu Ning Wai,\* Marinella Ruospo,<sup>‡§</sup> Juan-Jesus Carrero,<sup>||</sup> Katrina L. Campbell,\* and Giovanni F. M. Strippoli<sup>§¶\*\*</sup>

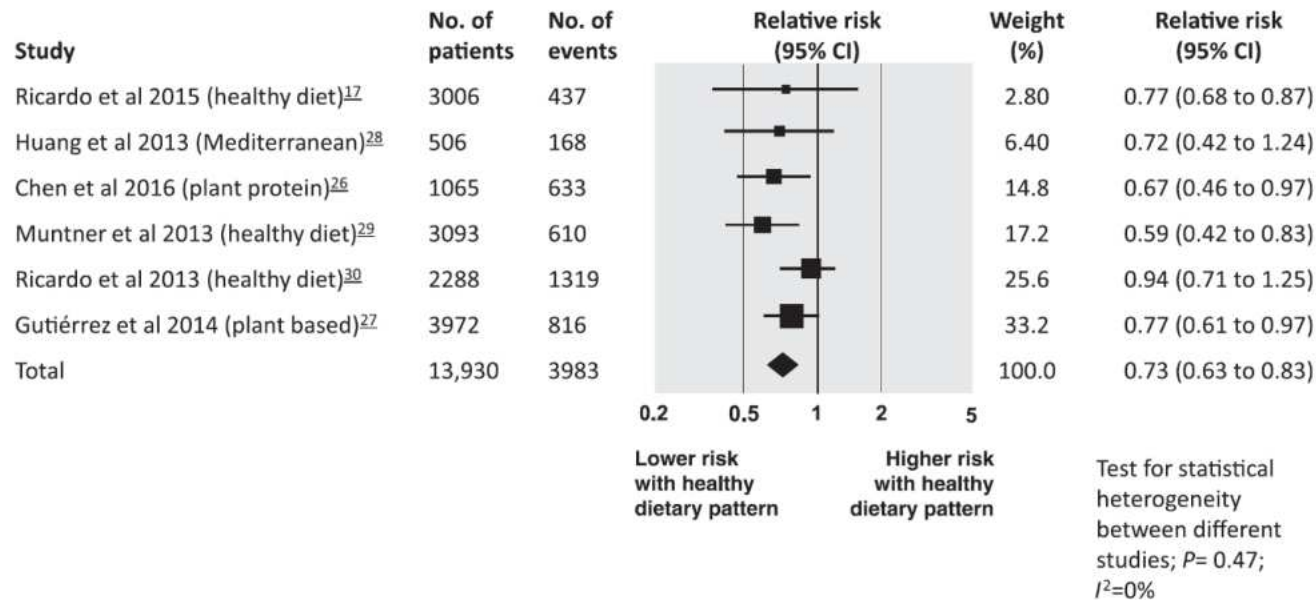


Figure 2. | Risk of all-cause mortality associated with healthy dietary patterns among adults with CKD. 95% CI, 95% confidence interval.

**Conclusions** Healthy dietary patterns are associated with lower mortality in people with kidney disease. Interventions to support adherence to increased fruit and vegetable, fish, legume, whole grain, and fiber intake, and reduced red meat, sodium, and refined sugar intake could be effective tools to lower mortality in people with kidney disease.



# Ballaststoffreiche Ernährung assoziiert mit weniger Inflammation und niedrigerer Mortalität bei CKD-Patienten

- Empfohlene Ballaststoffaufnahme: 30g/Tag<sup>1</sup>
- CKD-Patienten: im Schnitt nur 15g/d<sup>2,3</sup>
- Obst, Gemüse, Vollkorn wichtige Quellen
- Mehr Ballaststoffe = weniger Inflammation (CRP↓)<sup>2,3</sup>
- Mehr Ballaststoffe = niedrigere Mortalität bei CKD<sup>2,3</sup>
- Fermentierbare Ballaststoffe → kurzkettige Fettsäuren (SCFA)
- Nicht-fermentierbare Ballaststoffe → kürzere Darmpassagezeit, höheres Stuhlvolumen

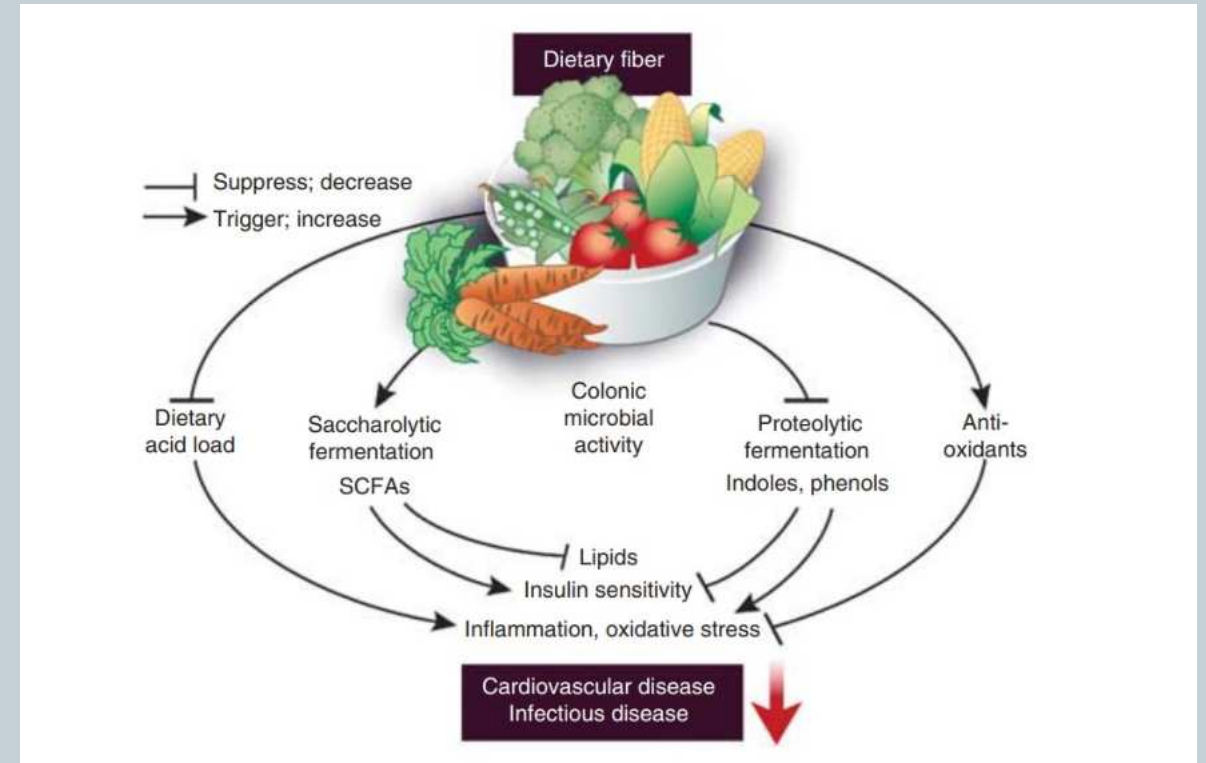


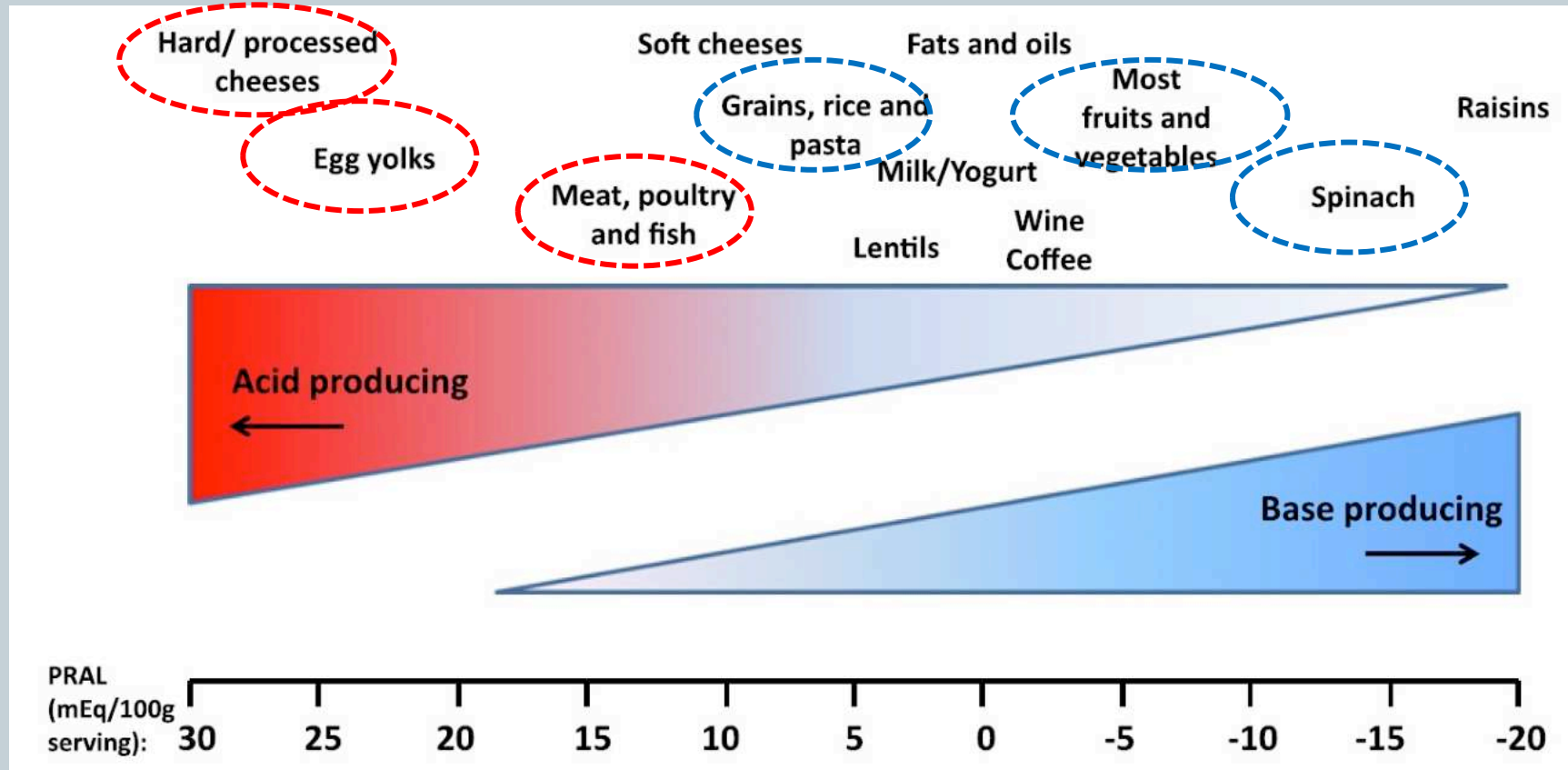
Abbildung aus<sup>3</sup>

1 <https://www.dge.de/gesunde-ernaehrung/dge-ernaehrungsempfehlungen/>

2 Krishnamurthy, V. M., et al. (2012). "High dietary fiber intake is associated with decreased inflammation and all-cause mortality in patients with chronic kidney disease." *Kidney Int* 81(3): 300-306.

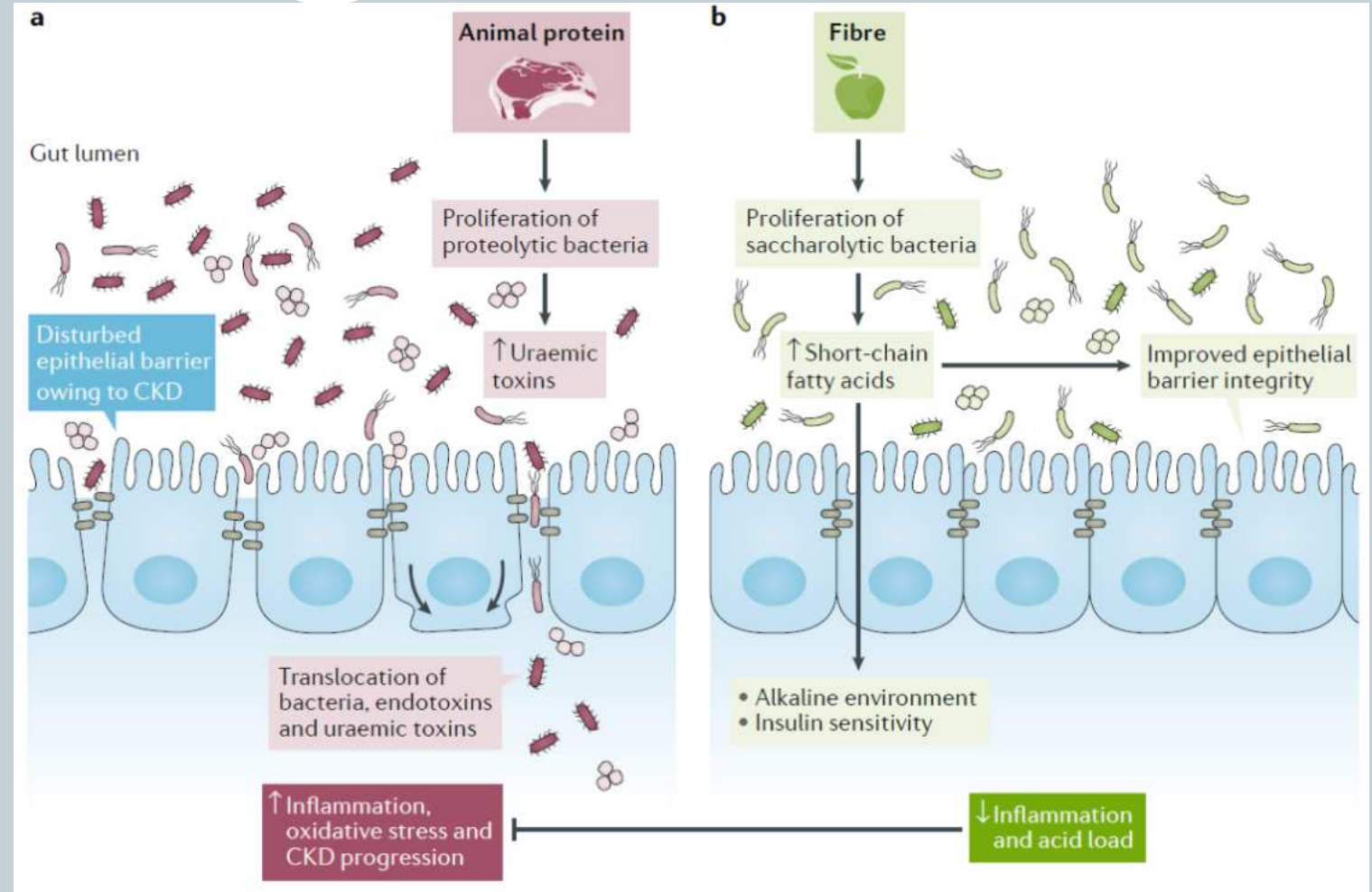
3 Evenepoel, P. and B. K. Meijers (2012). "Dietary fiber and protein: nutritional therapy in chronic kidney disease and beyond." *Kidney Int* 81(3): 227-229.

# Pflanzen-basierte Kost verringert die endogene Säurebelastung



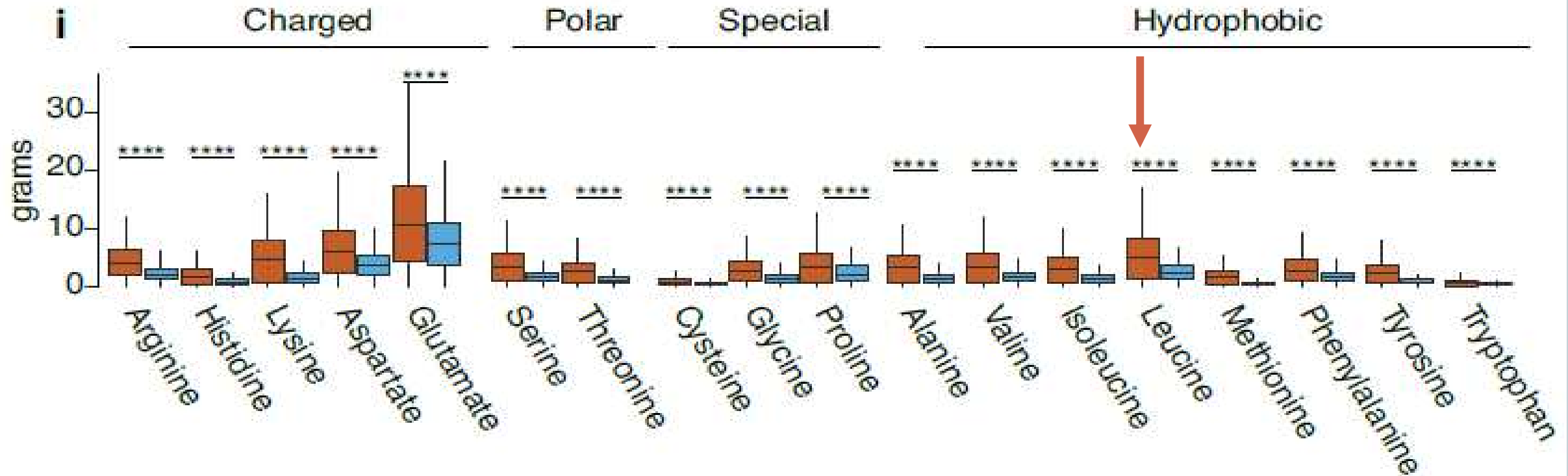
# Ballaststoffe stimulieren das Darm-Microbiom zur Produktion von anti-inflammatorischen Substanzen und weniger Urämietoxinen

- **Urämietoxine** entstehen im Darm durch bakteriellen Abbau von Proteinen (**proteolytische Bakterien**)
- bei CKD vermehrt wg. Malabsorption = mehr Protein im Colon
- Urämietoxine (u.a. TMAO, P-cresyl-sulfat, Indoxylsulfat) fördern Atherosklerose und endotheliale Dysfunktion → höheres kardiovaskuläres Risiko
- **Kurzkettenige Fettsäuren** entstehen durch mikrobielle Fermentation von Ballaststoffen (**symbiotische Saccharolytische Bakterien**) → Integrität Darmepithel
- Pflanzliche Proteine = immer gemeinsam mit Ballaststoffen



# Effect of a plant-based, low-fat diet versus an animal-based, ketogenic diet on ad libitum energy intake

Kevin D. Hall<sup>1</sup>✉, Juen Guo<sup>1</sup>, Amber B. Courville<sup>1</sup>, James Boring<sup>2</sup>, Robert Brychta<sup>1</sup>,





# Risikostratifizierung bei CKD

		CKD-assoziiertes kardiovaskuläres* und renales** Risiko (KDIGO 2012)		Albuminurie-Kategorien Albumin/Kreatinin-Quotient i. U. mg/g Kreatinin		
				A1	A2	A3
				< 30	30 - 300	> 300
GFR-Kategorien ml/min/1,73 m <sup>2</sup>	G1	> 90	niedrig	moderat	hoch	
	G2	60 - 89	niedrig	moderat	hoch	
	G3a	45 - 59	moderat	hoch	sehr hoch	
	G3b	30 - 44	hoch	sehr hoch	sehr hoch	
	G4	15 - 29	sehr hoch	sehr hoch	sehr hoch	
	G5	< 15	sehr hoch	sehr hoch	sehr hoch	

\*Kardiovaskuläre Mortalität, Gesamtmortalität

\*\*Progression der Niereninsuffizienz, Dialysepflicht

# Nutrition in CKD by KDIGO Risk Categories



Cardiovascular and Renal Risk	<i>low</i>	<i>moderately increased</i>	<i>high</i>	<i>very high</i>
CKD-Stages	G1A1, G2A1	G1A2, G2A2, G3aA1	G1A3, G2A3, G3aA2, G3bA1	G3aA3, G3bA2/A3, G4Ax, G5Ax
Fraction of CKD-Population <sup>§</sup>	63,1%	23.6%	8,2%	5,1%
Protein Intake	No protein restriction 0,8 - 1,2 g/kg ibw*/d adjusted for physical activity level	No protein restriction 0,8 - 1,2 g/kg ibw*/d adjusted for physical activity level	Moderate protein restriction 0,6 - 0,8 g/kg ibw/d monitor nutritional status	0,6 - 1,0 g/kg ibw/d cave: risk of malnutrition with inadequate protein intake
Energy Intake	25 - 35 kcal/kg ibw/d adjusted for physical activity level	25 - 35 kcal/kg ibw/d adjusted for physical activity level	30 - 35 kcal/kg ibw/d adjusted for physical activity level	30 - 35 kcal/kg ibw/d adjusted for physical activity level
Alkali	No need for substitution	No need for substitution	Plant-based protein as alkali source	Plant-based protein HCO <sub>3</sub> <sup>-</sup> -substitution in acidotic pts.
Nutritional concept	Plant-based nutrition	Plant-based nutrition	Plant-based nutrition	Plant-based nutrition + regular dietary counseling














§Rheinberger M, Jung B, Segiet T et al. Poor risk factor control in outpatients with diabetes mellitus type 2 in Germany: The DIAbetes COHoRte (DIACORE) study. PLoS ONE 2019; 14(3): e0213157

**Vielen Dank für die Aufmerksamkeit**
















**Vielen Dank für die Aufmerksamkeit**

## Analysis 1.2. Comparison 1: CKD stage, Outcome 2: Systolic blood pressure

Study or Subgroup	Low salt			High salt			Weight	Mean Difference	
	Mean [mm Hg]	SD [mm Hg]	Total	Mean [mm Hg]	SD [mm Hg]	Total		IV, Random, 95% CI [mm Hg]	IV, Random, 95% CI [mm Hg]
<b>1.2.1 CKD</b>									
Ruilope 1992a	146.1	20.2	14	148	21.2	14	1.4%	-1.90 [-17.24, 13.44]	
Mulhauser 1996	-1.7	8.3132	8	3.2	6.9376	8	4.3%	-4.90 [-12.40, 2.60]	
DUAAAL 2011	123	16.3975	52	134	16.3975	52	5.3%	-11.00 [-17.30, -4.70]	
Saran 2017	137	15.7468	49	147.8	15.7468	49	5.3%	-10.80 [-17.04, -4.56]	
Vogt 2008	137	11.9197	33	143	11.9197	33	5.8%	-6.00 [-11.75, -0.25]	
Konishi 2001	115	11.2	38	121.6	13.1	38	6.1%	-6.60 [-12.08, -1.12]	
VIRTUE-CKD 2016	123	12	43	129	14	44	6.1%	-6.00 [-11.48, -0.52]	
LowSALT CKD 2012	144.9	8.2285	20	154.6	8.2285	20	6.6%	-9.70 [-14.80, -4.60]	
Kwakernaak 2014	141	10.4869	45	147	10.4869	45	7.6%	-6.00 [-10.33, -1.67]	
ESPECIAL 2014	-1.7	14.6	119	-0.6	15.1	126	8.4%	-1.10 [-4.62, 2.62]	
ESMO 2017	125	9.8	67	127	10.1	71	9.0%	-2.00 [-5.32, 1.32]	
de Brito-Ashurst 2013	-8.6	5.2977	25	-0.6	5.2977	23	9.5%	-8.00 [-11.00, -5.00]	
<b>Subtotal (95% CI)</b>			<b>513</b>			<b>523</b>	<b>75.5%</b>	<b>-6.10 [-8.11, -4.08]</b>	







Heterogeneity: Tau<sup>2</sup> = 5.51; Chi<sup>2</sup> = 20.96, df = 11 (P = 0.03); I<sup>2</sup> = 48%  
Test for overall effect: Z = 5.93 (P < 0.00001)

## Analysis 1.3. Comparison 1: CKD stage, Outcome 3: Diastolic blood pressure

Study or Subgroup	Low salt			High salt			Weight	Mean Difference	
	Mean [mm Hg]	SD [mm Hg]	Total	Mean [mm Hg]	SD [mm Hg]	Total		IV, Random, 95% CI [mm Hg]	IV, Random, 95% CI [mm Hg]
<b>1.3.1 CKD</b>									
Ruilope 1992a	90.3	11.3	14	90.1	12.1	14	1.0%	0.20 [-8.47, 8.87]	
Mulhauser 1996	-3.1	3.2894	8	2.2	4.7846	8	4.1%	-5.30 [-9.32, -1.28]	
DUAAAL 2011	73	10.4348	52	80	10.4348	52	4.1%	-7.00 [-11.01, -2.99]	
Konishi 2001	75	8	38	79	9	38	4.5%	-4.00 [-7.83, -0.17]	
Saran 2017	70.8	7.4201	47	77	7.4201	47	6.6%	-6.20 [-9.20, -3.20]	
VIRTUE-CKD 2016	74	7.0049	43	77	7.0049	44	6.8%	-3.00 [-5.94, -0.06]	
Vogt 2008	83	6.093	33	86	6.093	33	6.8%	-3.00 [-5.94, -0.06]	
ESPECIAL 2014	73.6	10.7768	119	76	10.7768	126	7.7%	-2.40 [-5.10, 0.30]	
LowSALT CKD 2012	79.4	4.0336	20	83.3	4.0336	20	8.6%	-3.90 [-6.40, -1.40]	
Kwakernaak 2014	78.6	5.8084	45	82	5.8084	45	9.1%	-3.40 [-5.80, -1.00]	
ESMO 2017	74	6.5	67	76	6.7	71	10.1%	-2.00 [-4.20, 0.20]	
de Brito-Ashurst 2013	-4	4.4	25	-1	2.1	23	11.9%	-3.00 [-4.93, -1.07]	
<b>Subtotal (95% CI)</b>			<b>511</b>			<b>521</b>	<b>81.3%</b>	<b>-3.47 [-4.28, -2.65]</b>	

Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 10.57, df = 11 (P = 0.48); I<sup>2</sup> = 0%  
Test for overall effect: Z = 8.30 (P < 0.00001)

## Analysis 1.5. Comparison 1: CKD stage, Outcome 5: Albuminuria [ln mg/d]

Study or Subgroup	MD	SE	Weight	Mean Difference	
				IV, Random, 95% CI	IV, Random, 95% CI
<b>1.5.1 CKD</b>					
Saran 2017	-0.2	0.2551	7.1%	-0.20 [-0.70, 0.30]	
ESPECIAL 2014	-0.43	0.158224	15.5%	-0.43 [-0.74, -0.12]	
Kwakernaak 2014	-0.5447	0.1379	18.9%	-0.54 [-0.81, -0.27]	
VIRTUE-CKD 2016	-0.293	0.1376	18.9%	-0.29 [-0.56, -0.02]	
LowSALT CKD 2012	-0.5798769	0.0798343	34.3%	-0.58 [-0.74, -0.42]	
<b>Subtotal (95% CI)</b>			<b>94.8%</b>	<b>-0.47 [-0.60, -0.34]</b>	

Heterogeneity: Tau<sup>2</sup> = 0.00; Chi<sup>2</sup> = 4.91, df = 4 (P = 0.30); I<sup>2</sup> = 19%  
Test for overall effect: Z = 7.17 (P < 0.00001)

- High certainty evidence that salt reduction reduced blood pressure in people with CKD, and albuminuria in people with earlier stage CKD in the short-term.
- If such reductions could be maintained long-term, this effect may translate to clinically significant reductions in CKD progression and cardiovascular events.
- Research into the long-term effects of sodium-restricted diet for people with CKD is warranted.

# Nutrition in CKD by KDIGO Risk Categories

	KDIGO Risk-Category I	KDIGO Risk-Category II	KDIGO Risk-Category III	KDIGO Risk-Category IV
Cardiovascular and Renal Risk	<i>low</i>	<i>moderately increased</i>	<i>high</i>	<i>very high</i>
CKD-Stages	G1A1, G2A1	G1A2, G2A2, G3aA1	G1A3, G2A3, G3aA2, G3bA1	G3aA3, G3bA2/A3, G4Ax, G5Ax
Fraction of CKD-Population <sup>§</sup>	63,1%	23.6%	8,2%	5,1%
Protein Intake	No protein restriction 0,8 - 1,2 g/kg ibw*/d adjusted for physical activity level	No protein restriction 0,8 - 1,2 g/kg ibw*/d adjusted for physical activity level	Moderate protein restriction 0,6 - 0,8 g/kg ibw/d monitor nutritional status	0,6 - 1,0 g/kg ibw/d cave: risk of malnutrition with inadequate protein intake
Energy Intake	25 - 35 kcal/kg ibw/d adjusted for physical activity level	25 - 35 kcal/kg ibw/d adjusted for physical activity level	30 - 35 kcal/kg ibw/d adjusted for physical activity level	30 - 35 kcal/kg ibw/d adjusted for physical activity level
Sodium/Salt	In pts w/arterial hypertension < 3-4 g Na <sup>+</sup> /d, < 6-8 g salt/d	< 2-3 g Na <sup>+</sup> /d, < 5-6 g salt/d	< 2-3 g Na <sup>+</sup> /d, < 5-6 g salt/d	< 2 g Na <sup>+</sup> /d, < 5 g salt/d
Potassium	No restriction	No restriction	Rarely K <sup>+</sup> -restriction	Dietary K <sup>+</sup> -restriction or potassium binders in pts with increased risk for hyperkalemia
Calcium	1000 - 2000 mg/d	1000 - 2000 mg/d	1000 mg/d, maximum 1500 mg/d	1000 mg/d, maximum 1500 mg/d avoid Ca <sup>++</sup> -containing phosphate binders
Phosphate	No restriction	10 - 15 mg/kg bw/d	10 - 15 mg/kg bw/d avoid phosphate containing food additives	10 - 15 mg/kg bw/d avoid PO-containing food additives consider phosphate binders
Vitamines	No special requirements	No special requirements	Substitution for specific hypovitaminosis	Substitution in malnutrition and/or specific hypovitaminosis
Fluid intake	No restriction no minimum requirement	No restriction no minimum requirement	Dependent on volume status and comorbidities	Dependent on volume status, comorbidities and RRF
Alkali	No need for substitution	No need for substitution	Plant-based protein as alkali source	Plant-based protein HCO <sub>3</sub> <sup>-</sup> -substitution in acidotic pts.
Nutritional concept	Mediterranean Diet	Mediterranean Diet	Mediterranean Diet	Mediterranean Diet + regular dietary counseling

§Rheinberger M, Jung B, Segiet T et al. Poor risk factor control in outpatients with diabetes mellitus type 2 in Germany: The DIAbetes COhoRtE (DIACORE) study. PLoS ONE 2019; 14(3): e0213157