Plant-based protein intake and the risk of CKD

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Disclosure

- I have received consulting fees from Otsuka and Vertex in my role as a national leader. I also serve as a site principal investigator for clinical trials sponsored by Apellis, Novartis, Boehringer Ingelheim, Travere, Chinook, Alexion, Biogen, ADARx, CSL Behring, Walden Biosciences, and Arrowhead. Additionally, I receive compensation for my role as an Associate Editor of the *Clinical Journal of the American Society of Nephrology.*

- **I have no actual or potential conflict of interest in relation to this lecture/presentation.**

Outline

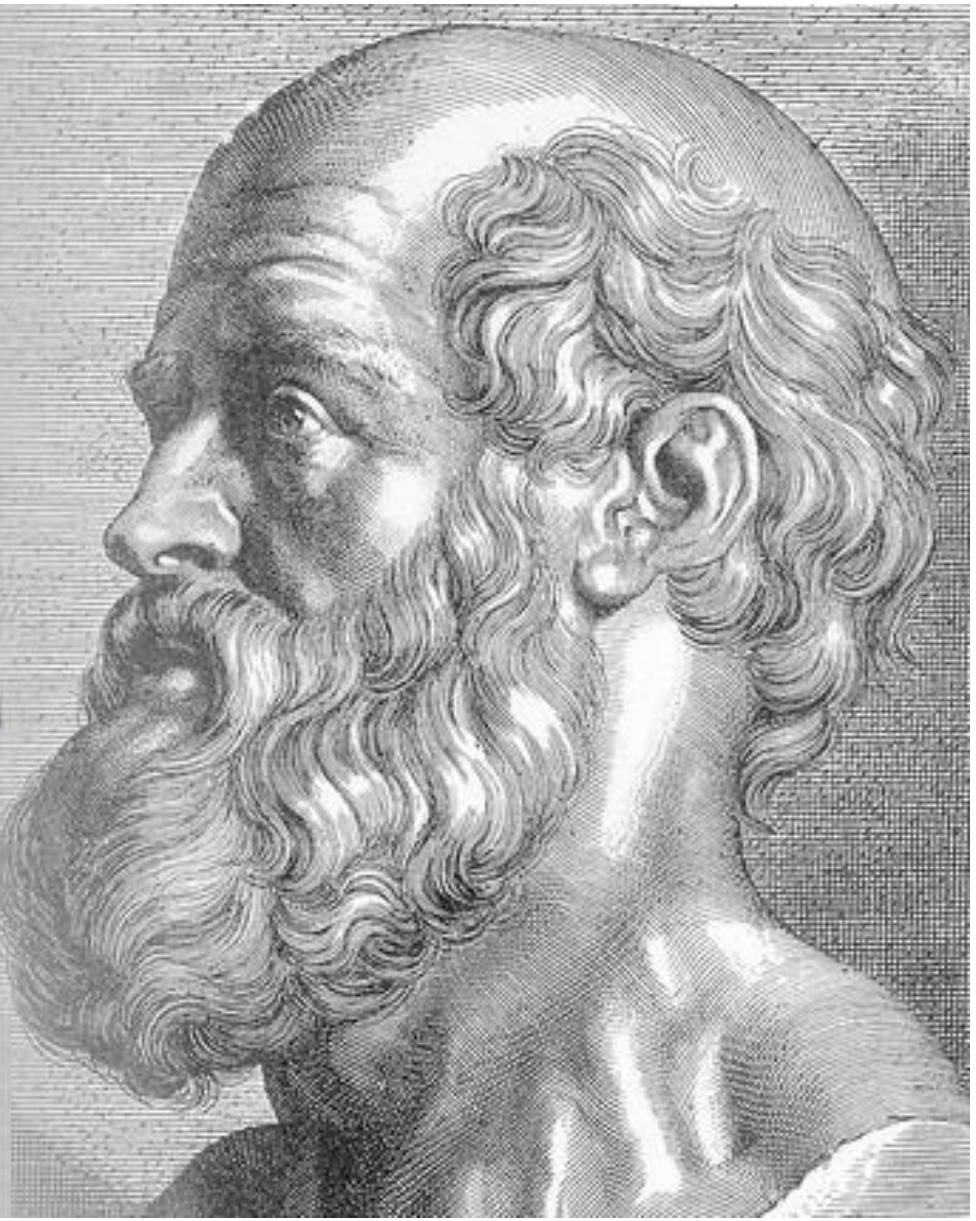
- Historical context: diet as medicine
- Diet and cardiovascular and kidney health
- Role of protein source: plant vs. animal

  - Our study on plant protein and CKD/Mechanistic insights and clinical implications

- Where do current guidelines stand?
- Summary

LET FOOD BE THY MEDICINE, AND MEDICINE BE THY FOOD.

HIPPOCRATES



RCT Evidence: The MDRD Study

The New England
Journal of Medicine

Volume 330 MARCH 31, 1994 Number 13

THE EFFECTS OF DIETARY PROTEIN RESTRICTION AND BLOOD-PRESSURE CONTROL ON THE PROGRESSION OF CHRONIC RENAL DISEASE

SAULO KLAHR, M.D., ANDREW S. LEVEY, M.D., GERALD J. BECK, PH.D., ARLENE W. CAGGIULA, PH.D., LAWRENCE HUNSICKER, M.D., JOHN W. KUSEK, PH.D., AND GARY STRIKER, M.D., FOR THE MODIFICATION OF DIET IN RENAL DISEASE STUDY GROUP*

Effect of a Very Low-Protein Diet on Outcomes: Long-term Follow-up of the Modification of Diet in Renal Disease (MDRD) Study

Vandana Menon, MD, PhD,[1] Joel D. Kopple, MD,[2] Xuelei Wang, MS,[3] Gerald J. Beck, PhD,[3] Allan J. Collins, MD,[4] John W. Kusek, PhD,[5] Tom Greene, PhD,[6] Andrew S. Levey, MD,[1] and Mark J. Sarnak, MD, MS[1]

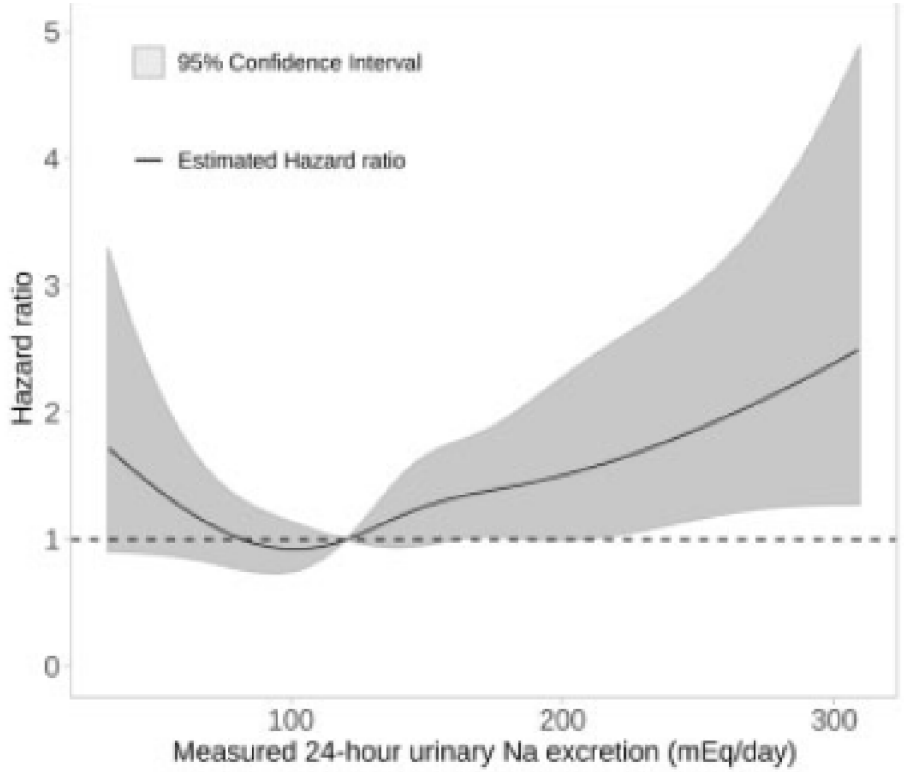
Am J Kidney Dis 53:208-217

- Landmark trial on protein restriction and CKD progression.
- Found no significant benefit in primary analysis (NEJM 1994).
- Later follow-ups showed modest benefit (AJKD 2009).
- Still forms the basis of modern guideline recommendations.

Nephrol Dial Transplant (2021) 36: 512–519
doi: 10.1093/ndt/gfaa107
Advance Access publication 24 June 2020

ndt
Nephrology Dialysis Transplantation

Measured sodium excretion is associated with CKD progression: results from the KNOW-CKD study

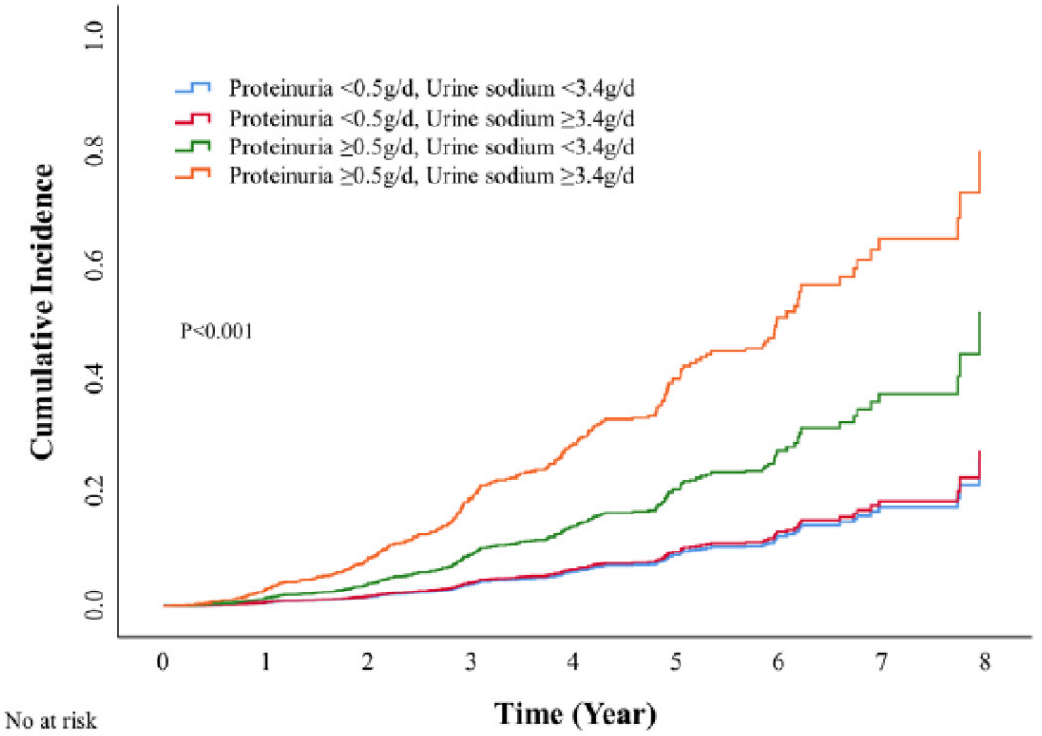


KI REPORTS
KIReports.org
CLINICAL RESEARCH

Proteinuria Modifies the Relationship Between Urinary Sodium Excretion and Adverse Kidney Outcomes: Findings From KNOW-CKD

Check for updates

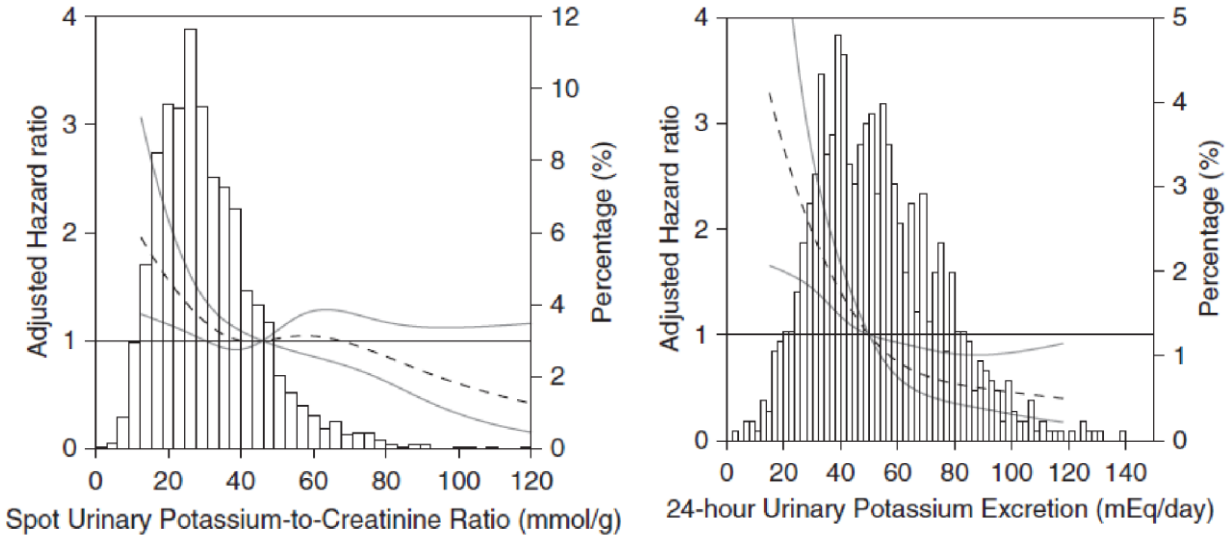
Hyo Jeong Kim[1,2], Chan-Young Jung[1,3], Hyung Woo Kim[1], Jung Tak Park[1], Tae-Hyun Yoo[1], Shin-Wook Kang[1], Sue K. Park[4,5,6], Yeong Hoon Kim[7], Su Ah Sung[8], Young Youl Hyun[9], Kook-Hwan Oh[10] and Seung Hyeok Han[1]



Clin J Am Soc Nephrol 14: 330–340, 2019.

Urinary Potassium Excretion and Progression of CKD

Hyung Woo Kim,[1] Jung Tak Park,[1] Tae-Hyun Yoo,[1] Joongyub Lee,[2] Wookyung Chung,[3] Kyu-Beck Lee,[4] Dong-Wan Chae,[5] Curie Ahn,[5] Shin-Wook Kang,[1] Kyu Hun Choi,[1] and Seung Hyeok Han,[1] on behalf of the KNOW-CKD Study Investigators



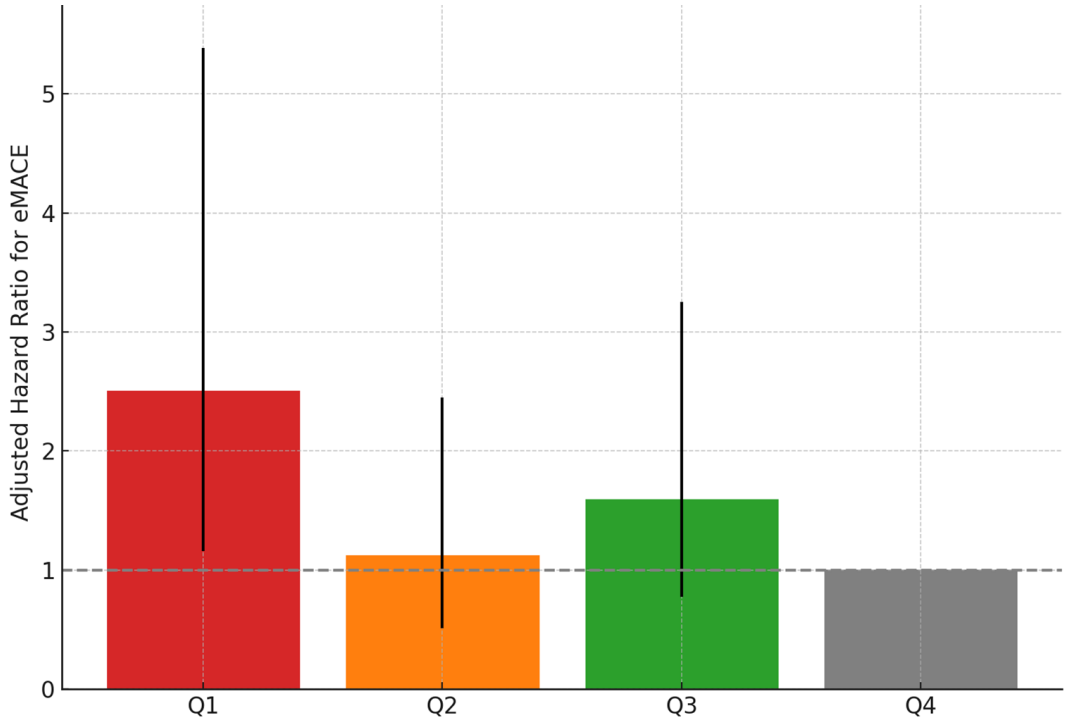
nutrients

MDPI

Article

Association of Urinary Potassium Excretion with Blood Pressure Variability and Cardiovascular Outcomes in Patients with Pre-Dialysis Chronic Kidney Disease

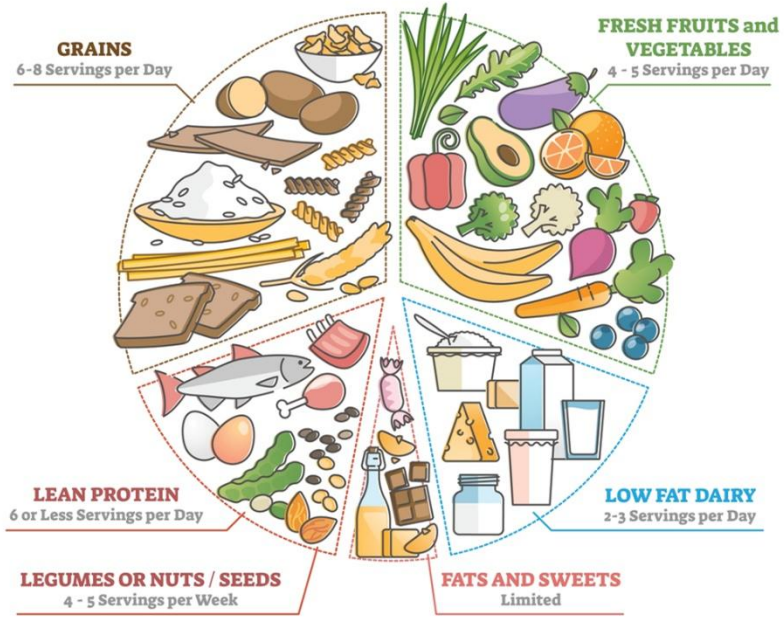
Sang Heon Suh [1], Su Hyun Song [1], Tae Ryom Oh [1], Hong Sang Choi [1], Chang Seong Kim [1], Eun Hui Bae [1], Kook-Hwan Oh [2], Joongyub Lee [3], Seung Hyeok Han [4], Yeong Hoon Kim [5], Dong-Wan Chae [6], Seong Kwon Ma [1,*], Soo Wan Kim [1,*] and on behalf of the Korean Cohort Study for Outcomes in Patients with Chronic Kidney Disease (KNOW-CKD) Investigators [†]



Can Diet Prevent Cardio-Metabolic Kidney Disease?

DASH-Style Diet

- High in fruits, vegetables, whole grains
- Rich in potassium, magnesium, calcium
- Low in sodium, red/processed meat, and added sugars
- Moderate intake of dairy and plant protein sources



Mediterranean Diet

- Daily plant-based intake: fruits, vegetables, whole grains, legumes, nuts
- Primary fat: extra-virgin olive oil
- Moderate fish, poultry, eggs, dairy (especially cheese/yogurt)
- Red/processed meat and sweets consumed rarely

In Reality, We Have Few RCTs on Diet and CKM Prevention

- Sustained adherence to dietary patterns is challenging
- Blinding is not feasible — participants know what they're eating
- Complex interventions (entire diets vs. single nutrients or pills)
- Expensive and resource-intensive to provide meals or coaching
- Long follow-up needed for hard outcomes like CKD, CVD, or diabetes
- Ethical/practical concerns with long-term restrictive diets

Lifestyle Intervention and CVD Prevention: Lessons from the Look AHEAD Trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Cardiovascular Effects of Intensive Lifestyle Intervention in Type 2 Diabetes

The Look AHEAD Research Group*

NEJM 2013

Baseline

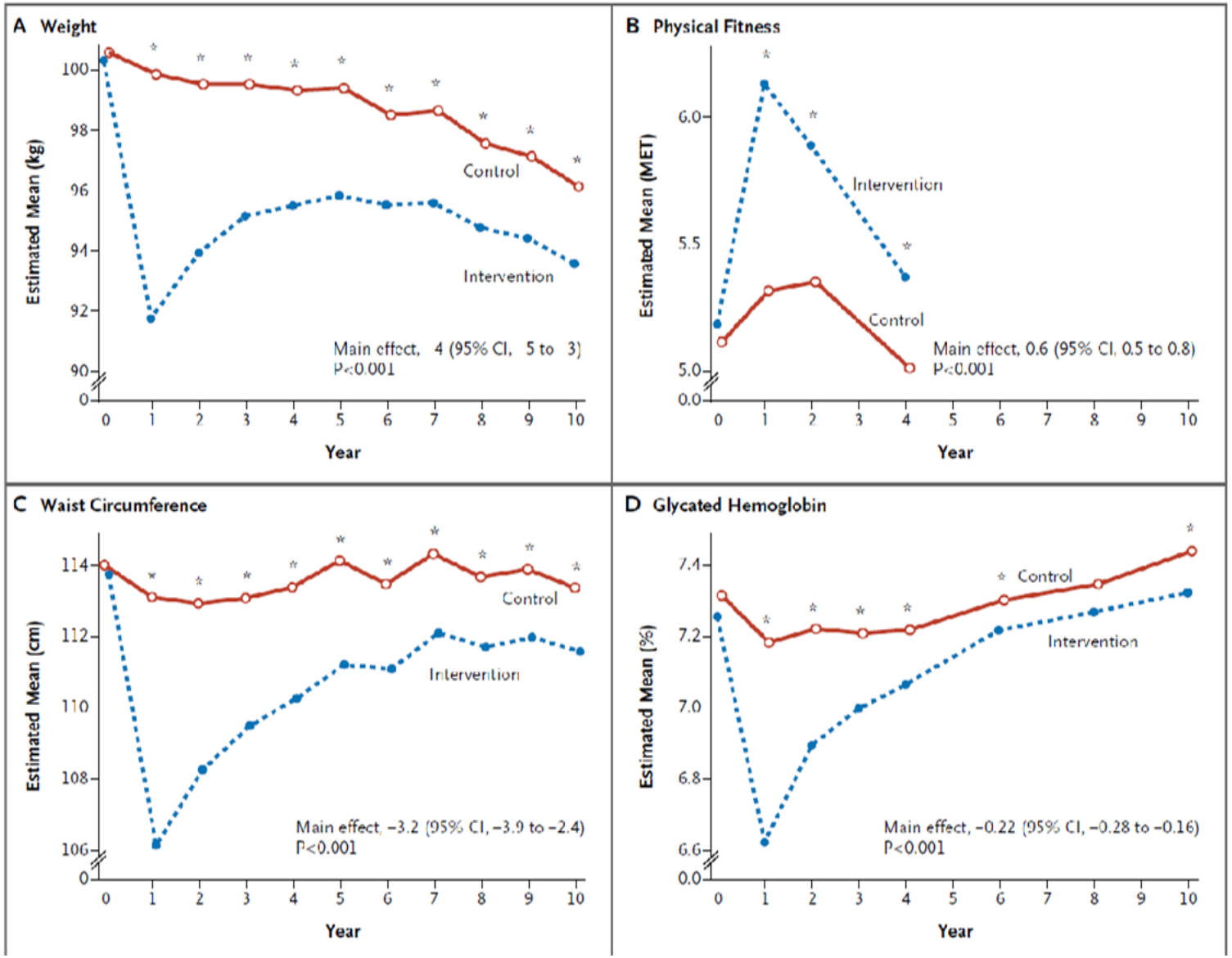
5145 overweight or obese patients with T2DM

Bwt: 101 kg

BMI: 36 kg/m2

The median duration of DM: 5 years,

Patients with a history of CVD: 14%



Role of Diet on Primary CVD Prevention

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Primary Prevention of Cardiovascular Disease with a Mediterranean Diet Supplemented with Extra-Virgin Olive Oil or Nuts

R. Estruch, E. Ros, J. Salas-Salvadó, M.-I. Covas, D. Corella, F. Arós, E. Gómez-Gracia, V. Ruiz-Gutiérrez, M. Fiol, J. Lapetra, R.M. Lamuela-Raventos, L. Serra-Majem, X. Pintó, J. Basora, M.A. Muñoz, J.V. Sorlí, J.A. Martínez, M. Fitó, A. Gea, M.A. Hernán, and M.A. Martínez-González, for the PREDIMED Study Investigators*

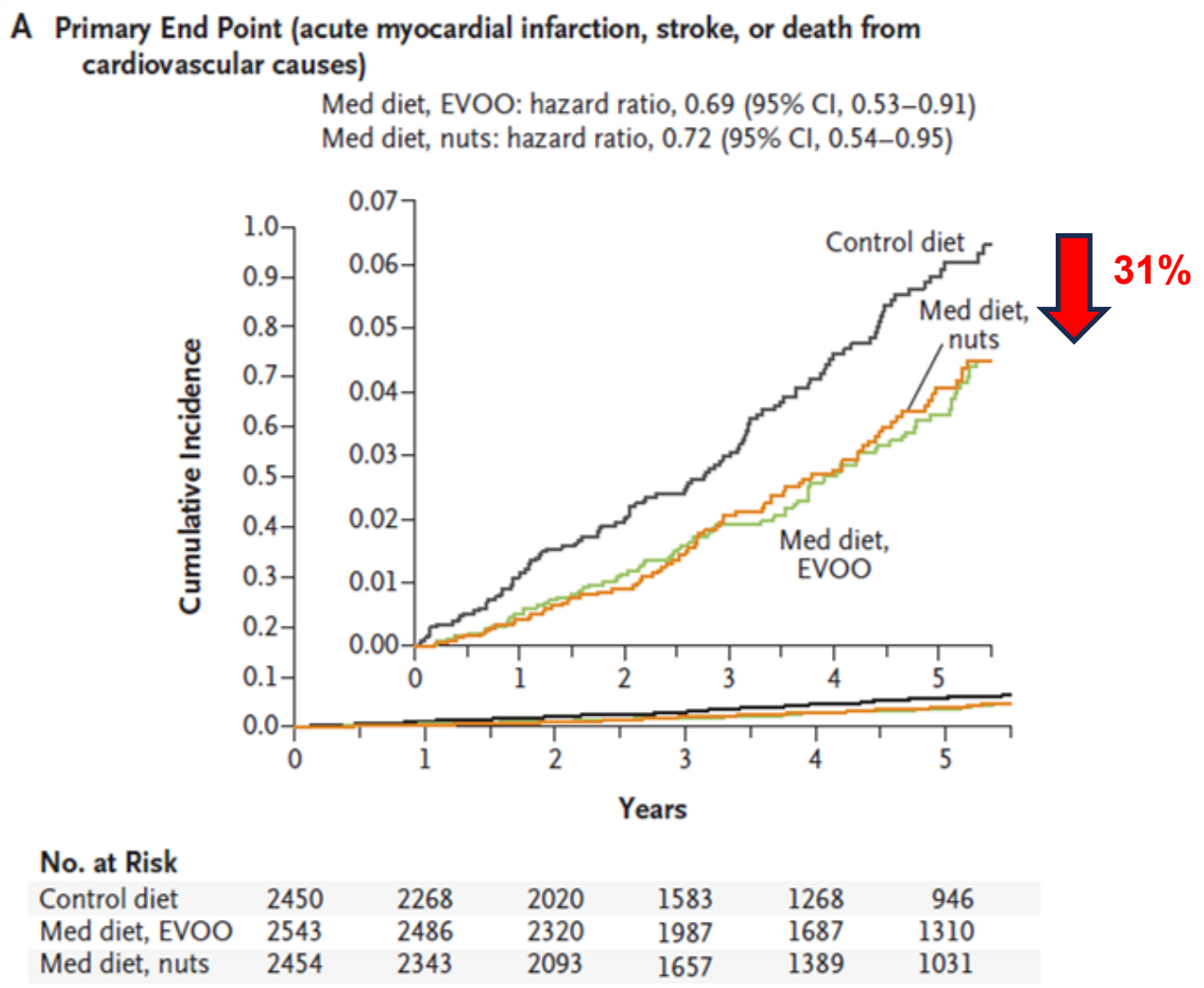
Baseline

7447 individuals at high risk of CVD

but without a history of CVD

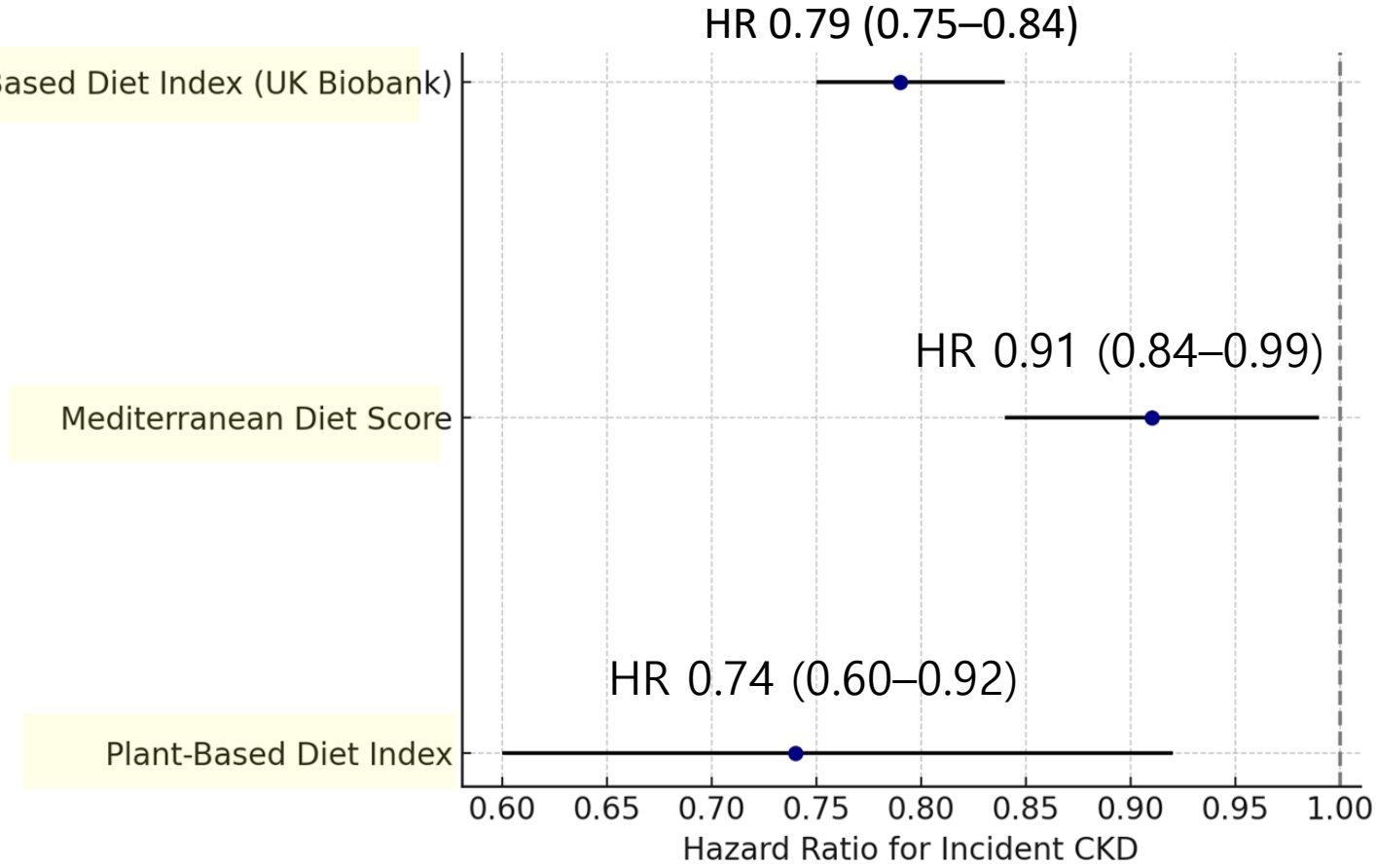
BMI: 30 kg/m2

Patients with a history of T2DM: 50%



Can Diet Prevent CKD? Evidence from Observational Studies

- **Few large RCTs** have tested diet for primary CKD prevention; Evidence comes from large prospective cohorts
- Diet quality matters: more plant-based, whole foods, less sodium and animal protein



BMC Public Health. 2025; Nephrology 2020; J Ren Nutri 2024

MAYO CLINIC PROCEEDINGS

ORIGINAL ARTICLE

Association Between Mediterranean Lifestyle and Lower Risk of Chronic Kidney Disease: A Population-Based Prospective Study

Hyo Jeong Kim, MD; Hee Byung Koh, MD; Chan-Young Jung, MD, PhD; Hyung Woo Kim, MD; Jung Tak Park, MD, PhD; Tae Ik Chang, MD, PhD; Tae-Hyun Yoo, MD, PhD; Shin-Wook Kang, MD, PhD; and Seung Hyeok Han, MD, PhD

Mayo Clin Proc. ■ XXX 2025;

Methods

Cohort

1 UK Biobank cohort
Participants with no history of CKD

Exposure

1 Quartiles of MEDLIFE index
MEDLIFE index is comprised of 3 blocks
2 Block 1: Mediterranean diet
Block 2: Dietary habits
Block 3: Physical activity, rest, social habits, conviviality

Outcome

1 Incident CKD

Results

Inverse graded relationship between MEDLIFE index and incident CKD

MEDLIFE index	HR (95% CI)
1-point increase	0.94 (0.93-0.95)
Quartile 1	Reference
Quartile 2	0.80 (0.74-0.87)
Quartile 3	0.76 (0.70-0.82)
Quartile 4	0.65 (0.59-0.72)

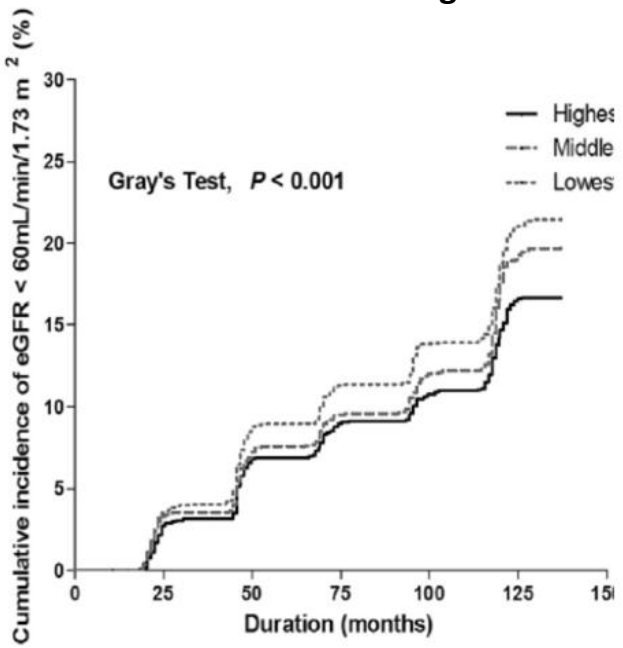
A 1-point increase in each block was associated with a decreased risk of incident CKD.

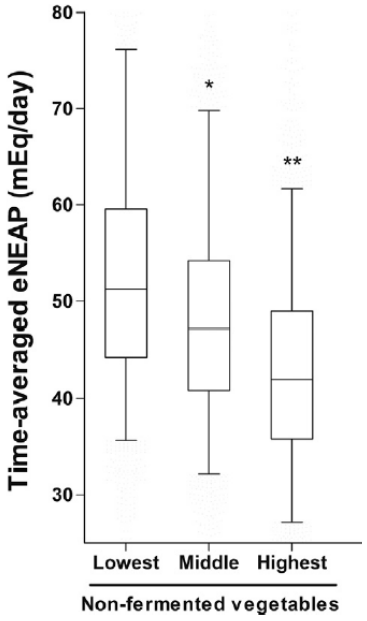
Block 1	Block 2	Block 3
0.95 (0.94-0.97)	0.92 (0.89-0.95)	0.90 (0.87-0.92)

A Diet Rich in Vegetables and Fruit and Incident CKD: A Community-Based Prospective Cohort Study

Jong Hyun Jhee, Youn Kyung Kee, Jung Tak Park, Tae-Ik Chang, Ea Wha Kang, Tae-Hyun Yoo, Shin-Wook Kang, and Seung Hyeok Han

Non-fermented vegetables





What About Protein Source?

- Protein quality and source may influence CKD risk
- Animal protein intake associated with kidney hyperfiltration and eGFR decline
- Plant protein associated with better metabolic and acid–base profiles
- Few studies have evaluated plant protein intake and incident CKD

Original Investigation

AJKD

AJKD Vol 82 | Iss 6 | December 2023

Association of Plant Protein Intake With Risk of Incident CKD: A UK Biobank Study

Ga Young Heo, Hee Byung Koh, Hyo Jeong Kim, Kyung Won Kim, Chan Young Jung, Hyung Woo Kim, Tae Ik Chang, Jung Tak Park, Tae-Hyun Yoo, Shin-Wook Kang, and Seung Hyeok Han

- **Aim of this study**:
- To examine the association between plant protein intake and the risk of developing CKD

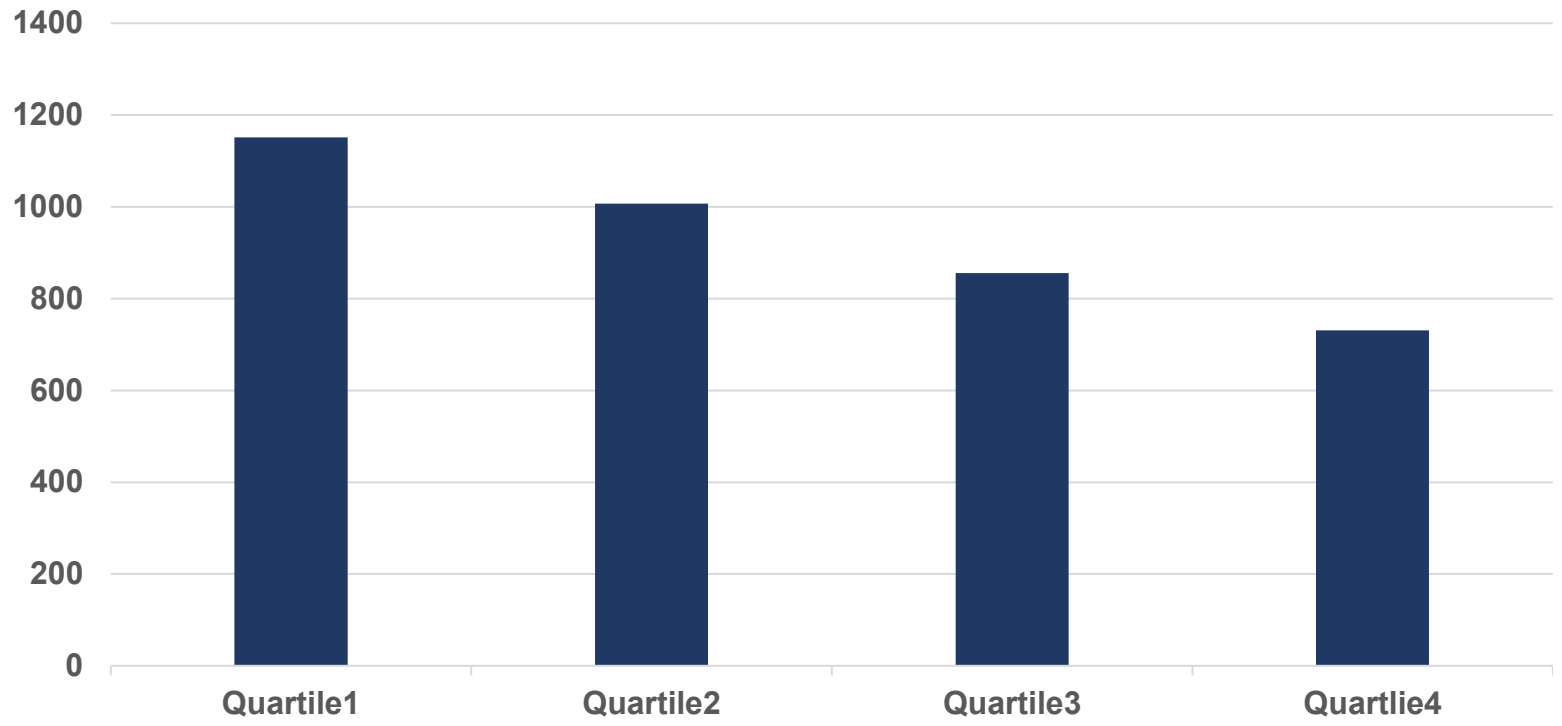
- **Study Population**:
- UK Biobank cohort (n = 117,809)
- Adults aged 40–69 years
- Free of CKD at baseline
- Median follow-up: 9.9 years

- **Methods**:
- Dietary intake assessed using Oxford WebQ 24-hour recall
- Plant protein intake (% of total protein energy) calculated
- Participants categorized into quartiles of plant protein intake

- **Study Outcome: Incident CKD**
- ICD-10–defined CKD
- eGFR-based CKD based on linked primary care records

Outcome Events

- During the median follow-up period of 9.9 years, 3745 (3.2%) incident CKD occurred with an incidence rate of 3.2 per 1000 person-years.



Plant protein intake with incident CKD (ICD-10 codes)

Incident CKD	Unadjusted		Adjusted	
	HR (95% CI)	P value	HR (95% CI)	P value
Plant protein intake				
Quartile				
<0.27 g/kg/day	1.00 (Reference)	-	1.00 (Reference)	-
≥0.27 and <0.35 g/kg/day	0.87 (0.80 - 0.95)	0.002	0.90 (0.82 - 0.99)	0.02
≥0.35 and <0.46 g/kg/day	0.74 (0.68 - 0.81)	<0.001	0.83 (0.75 - 0.92)	<0.001
≥0.46 g/kg/day	0.63 (0.57 - 0.69)	<0.001	**0.82 (0.73 - 0.93)**	0.002
Continuous				
per 0.1 g/kg/day increase	0.90 (0.88 - 0.92)	<0.001	**0.96 (0.93 - 0.99)**	0.01

Plant protein intake with incident CKD (eGFR-based CKD)

Incident CKD (strictly defined) : subcohort (N = 37,995)	Unadjusted		Adjusted	
	HR (95% CI)	P value	HR (95% CI)	P value
Plant protein intake				
Quartile				
<0.27 g/kg/day	1.00 (Reference)	-	1.00 (Reference)	-
≥0.27 and <0.35 g/kg/day	0.92 (0.83 - 1.02)	0.1	0.90 (0.81 - 1.00)	0.06
≥0.35 and <0.46 g/kg/day	0.73 (0.66 - 0.81)	<0.001	0.77 (0.68 - 0.86)	<0.001
≥0.46 g/kg/day	0.65 (0.58 - 0.72)	<0.001	**0.75 (0.66 - 0.87)**	<0.001
Continuous				
per 0.1 g/kg/day increase	0.90 (0.88 - 0.92)	<0.001	**0.96 (0.93 - 0.99)**	0.03

Sensitivity analysis

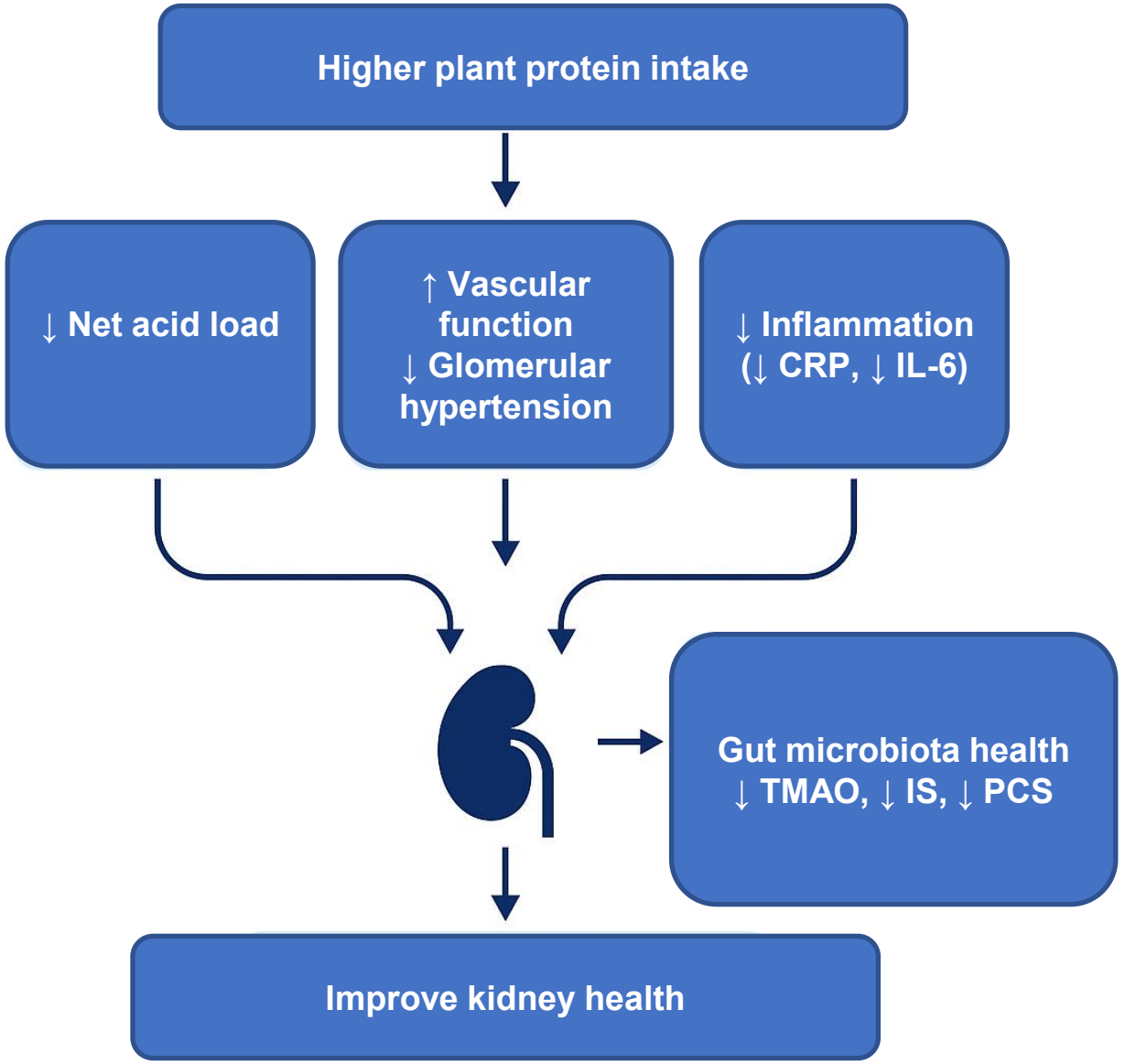
- Time-varying plant protein intake with incident CKD among the participants who conducted two or more dietary assessments

Incident CKD	Unadjusted		Adjusted	
	HR (95% CI)	P value	HR (95% CI)	P value
Time-varying plant protein intake				
Quartile				
<0.27 g/kg/day	1.00 (Reference)	-	1.00 (Reference)	-
≥0.27 and <0.35 g/kg/day	0.86 (0.77 - 0.95)	0.005	0.86 (0.77 - 0.95)	0.005
≥0.35 and <0.46 g/kg/day	0.71 (0.63 - 0.80)	<0.001	0.71 (0.63 - 0.80)	<0.001
≥0.46 g/kg/day	0.60 (0.53 - 0.68)	<0.001	**0.60 (0.53 - 0.68)**	<0.001
Continuous				
per 0.1 g/kg/day increase	0.88 (0.85 - 0.90)	<0.001	**0.88 (0.85 - 0.90)**	<0.001

Correlations between plant protein intake and parameters

Variables	Correlation coefficient	P value
Systolic blood pressure, mmHg (−)	-0.09	<0.001
Diastolic blood pressure, mmHg (−)	-0.14	<0.001
BMI, kg/m^2 (−)	-0.37	<0.001
Physical activity, MET-min/week (+)	0.08	<0.001
LDL-C, mg/dL (−)	-0.07	<0.001
HDL-C, mg/dL (+)	0.12	<0.001
Triglyceride, mg/dL (−)	-0.11	<0.001
hs-CRP, mg/L (−)	-0.10	<0.001

Mechanistic Insights Supporting Plant Protein and Kidney Health



Cautionary Notes: Nutritional Adequacy of Plant-Based Protein

- **Not all proteins are created equal:**
- **Animal proteins** have **higher biologic value** (complete amino acid profile, higher digestibility)
- **Plant proteins** often lack one or more essential amino acids (e.g., lysine in grains, methionine in legumes)
- Protein Digestibility-Corrected Amino Acid Score (**PDCAAS**) is generally higher for animal protein

- **How much is needed?** To meet equivalent protein quality:
- Need ~**25–30% more** plant protein by weight
- Example: 100 g of cooked beef provides ~30 g of high-quality protein.
- 175–200 g of cooked lentils (which provide ~18 g of protein per cup)
- That's about 1.5 to 2 cups of cooked lentils
- Or roughly 2.5–3 servings, where 1 serving = ½ cup cooked legumes (~100 g)

- **Mitigation strategies:**
- Combine complementary plant proteins (e.g., grains + legumes)
- Include diverse, minimally processed plant foods
- Ensure adequate caloric intake to avoid protein-energy wasting

Where Do The Guideline Stand?

Protein intake

3.1.13: We suggest lowering protein intake to 0.8 g/kg/day in adults with diabetes (*2C*) or without diabetes (*2B*) and GFR <30 ml/min/ 1.73 m^2 (GFR categories G4-G5), with appropriate education.

3.1.14: We suggest avoiding high protein intake (>1.3 g/kg/day) in adults with CKD at risk of progression. (*2C*)

KDIGO

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 BW/day) Protein Restriction, CKD Patients Not on Dialysis and With Diabetes

3.0.2 In the adult with CKD 3-5 and who has diabetes, it is reasonable to prescribe, under close clinical supervision, a dietary protein intake of 0.6 - 0.8 g/kg body weight per day to maintain a stable nutritional status and optimize glycemic control (OPINION)

KDOQI

Statement on Protein Type

- 3.2.1 In adults with CKD 1-5D (1B) or posttransplantation (OPINION), there is **insufficient evidence to recommend a particular protein type (plant vs animal)** in terms of the effects on nutritional status, calcium or phosphorus levels, or the blood lipid profile.

Mediterranean Diet

- 3.3.1 In adults with CKD 1-5 not on dialysis or posttransplantation, with or without dyslipidemia, we suggest that prescribing a Mediterranean Diet may improve lipid profiles (2C).

Fruits and Vegetables

- 3.3.2 In adults with CKD 1-4, we suggest that prescribing increased fruit and vegetable intake may decrease body weight, blood pressure, and net acid production (NEAP) (2C).

Summary

- Diet is a modifiable determinant of CKD and cardiovascular risk, but RCT evidence remains limited, especially for CKD prevention.
- Plant-forward dietary patterns (DASH, Mediterranean) are associated with lower risk of CKD and improved cardiometabolic health.
- In our UK Biobank study, higher plant protein intake was independently associated with a lower risk of incident CKD, with a clear dose–response trend.
- These findings are supported by mechanistic studies (e.g., lower acid load, better BP, lipid, and inflammation profiles).
- Current guidelines are cautious on protein type, but increasingly acknowledge the benefits of plant-based dietary patterns in CKD care.


Thank
you