

Plant-Based Diets in Dialysis

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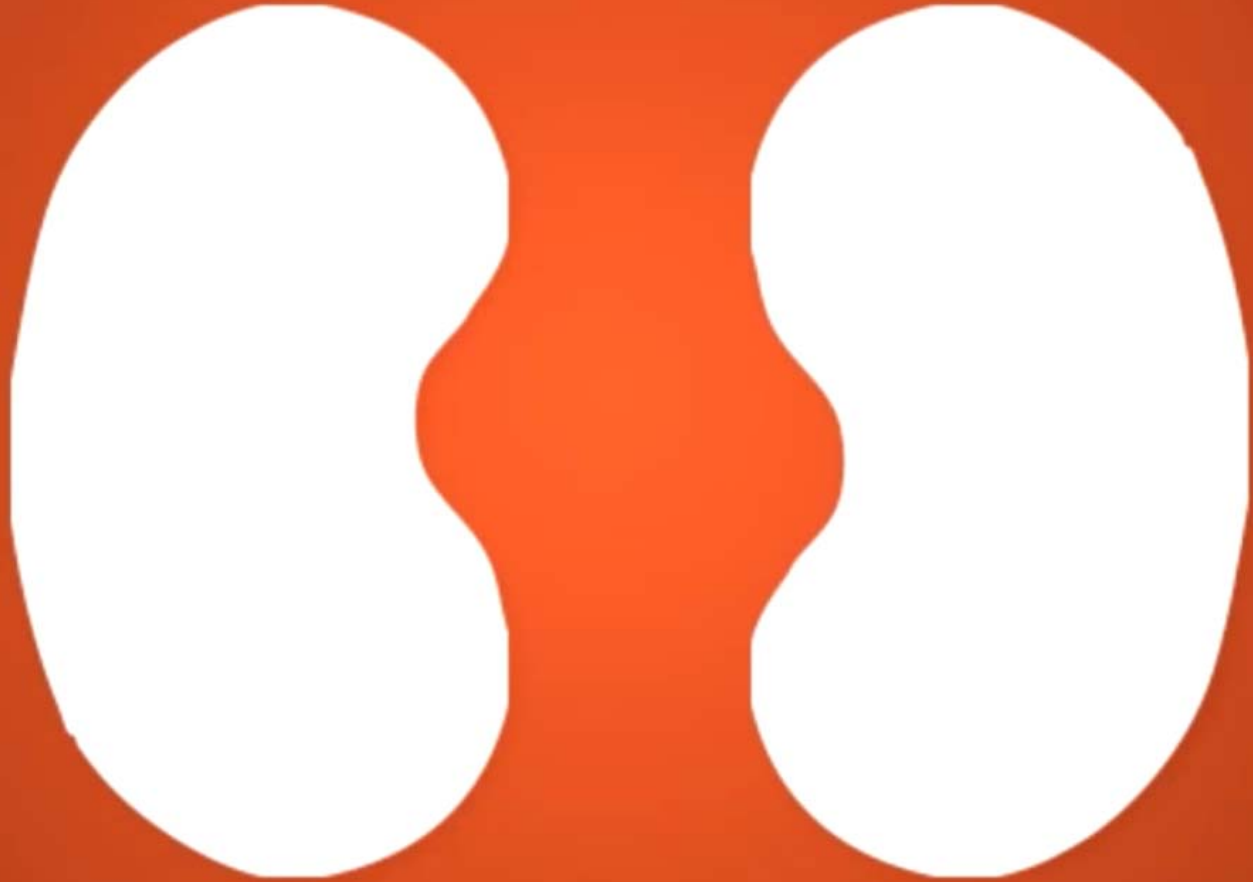
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None



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*Studies in dialysis are limited; relevant CKD studies may be mentioned

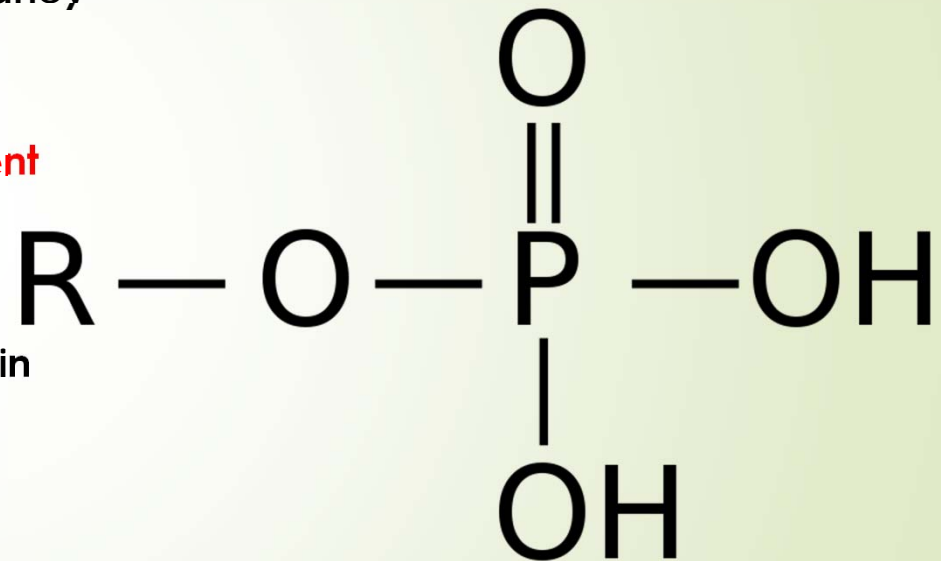


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Hyperphosphatemia

Hyperphosphatemia

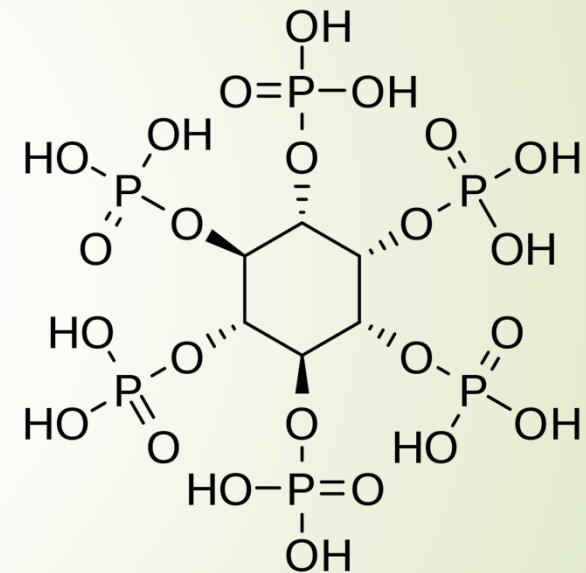
- ▶ Phosphate levels rise in advanced kidney disease
- ▶ Hyperphosphatemia is an **independent** risk factor for mortality in CKD and dialysis patients¹
- ▶ Phosphate restriction recommended in patients with CKD
 - ▶ Although adherence is difficult
 - ▶ **Phosphate content not disclosed on nutrition labels!**



¹Kestenbaum, Bryan, et al. "Serum phosphate levels and mortality risk among people with chronic kidney disease." *Journal of the American Society of Nephrology* 16.2 (2005): 520-528

Dietary Sources of Phosphate

- ▶ Plant-based proteins actually have more phosphorus than animal-based proteins
 - ▶ However, **plant-based phosphate is mostly bound as phytates**
 - ▶ Phytates are the storage form of phosphorus in plants
 - ▶ **Phosphorus in phytate form is not absorbable because humans lack the enzyme phytase**



“Rule of Thirds”

Source	Serving	Phosphorus, mg	Phosphorus-Protein Ratio, mg/g	Gastrointestinal Absorption, %
Organic				
Animal protein				
Milk, skim	8 ounces	247	29	40 to 60
Yogurt, plain nonfat	8 ounces	385	27	40 to 60
Cheese, mozzarella; part skim	1 ounces	131	20	40 to 60
Egg	1 large	86	14	40 to 60
Beef (cooked)	3 ounces*	173	7	40 to 60
Chicken	3 ounces	155	8	40 to 60
Turkey	3 ounces	173	8	40 to 60
Fish, halibut	3 ounces	242	9.3	40 to 60
Fish, salmon	3 ounces	282	13.4	40 to 60
Vegetarian protein†				
Bread, whole wheat	1 slice	57	Varies	10 to 30
Bread, enriched white	1 slice	25	Varies	10 to 30
Almonds	12 ounces	134	23	10 to 30
Peanuts	1 ounce	107	15	10 to 30
Lentils (cooked)	Half a cup	178	20	10 to 30
Chocolate	1.4 ounces	142 to 216	27	10 to 30
Inorganic (additives and preservatives)‡				
Carbonated cola drink	12 ounces	40	Not Applicable	80 to 100

*A 3-ounce serving is about the size of a deck of cards.

†Phytate leads to less absorbability.

‡Inorganic phosphorous may comprise 50% or more of daily dietary phosphorus load.

Noori N, Sims JJ, Kopple JD, et al: Organic and inorganic dietary phosphorus and its management in chronic kidney disease. Iranian Journal of Kidney Diseases 4(2):89, 2010

Improved Phosphate Control with Plant-Based Diets in Humans

- ▶ Human study of 8 patients with III/IV CKD
- ▶ Cross-over study lasting one week
- ▶ Compared vegetarian and meat diets with equivalent phosphate content
- ▶ Those on vegetarian diet had **lower plasma phosphorus**

Moe, Sharon M., et al. "Vegetarian compared with meat dietary protein source and phosphorus homeostasis in chronic kidney disease." *Clinical Journal of the American Society of Nephrology* 6.2 (2011): 257-264.

Overall Study Design:

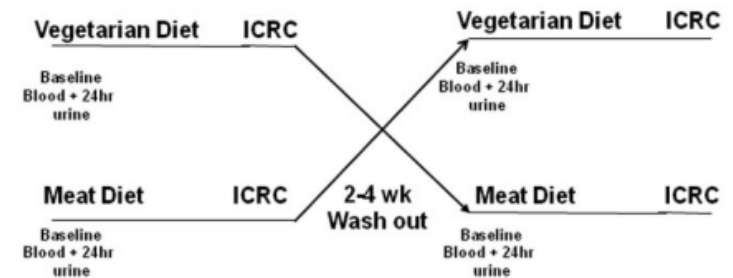


Table 2. Blood and urine measurements after 1 week of diet as outpatient

	Before Meat (casein) Diet	After Meat (casein) Diet	Before Vegetarian (grain) Diet	After Vegetarian (grain) Diet	P (paired t test) ^a
Average daily phosphorus intake (mg/day)		810 ± 27		795 ± 51	NS
Plasma phosphorus (mg/dl)	3.5 ± 0.6	3.7 ± 0.6	3.5 ± 0.6	3.2 ± 0.5	0.02
Plasma intact PTH (pg/ml)	58 ± 31	46 ± 29	58 ± 39	56 ± 30	0.002
Plasma FGF23 (pg/ml)	72 ± 39	101 ± 83	84 ± 65	61 ± 35	0.008
Plasma calcium (mg/dl)	9.2 ± 0.4	9.4 ± 0.7	9.3 ± 0.4	9.1 ± 0.3	NS
Creatinine clearance (ml/min)	47 ± 16	47 ± 16	43 ± 11	44 ± 16	NS
Urine 24-hour calcium excretion (mg/24 h)	66 ± 69	77 ± 48	60 ± 59	71 ± 43	NS
Urine 24-hour phosphorus excretion (mg/24 h)	836 ± 187	583 ± 216	778 ± 190	416 ± 233	0.07
Urine 24-hour FePhosph (%)	38.0 ± 6.2	23.9 ± 5.1	38.2 ± 11.5	20.9 ± 9.9	NS

^aBy paired t test comparing results at end (after) each 7-day controlled diet study period drawn at the same time (8:00 p.m.). Results are mean ± SD. The before values are shown to demonstrate what the patients ate on their own during the before-study and washout periods and to demonstrate no carryover effect.

Caveat to Phosphate Bioavailability from Plants

- ▶ Although humans lack phytase (which digests phytate)...
- ▶ Phytate can be broken loose with industrial processing ($> 140\text{ }^{\circ}\text{C}$)¹
 - ▶ Processed foods
 - ▶ Baked bread
- ▶ Not all plant foods are created equally
- ▶ Phytate cannot be broken down by home cooking (up to $100\text{ }^{\circ}\text{C}$)



¹ Moorthi. *Dietary Phosphorus: Health, Nutrition, and Regulatory Aspects*. CRC Press, 2017. 235-246.

Serum Phosphate Levels in Dialysis

- ▶ Cross-sectional study of dialysis patients
- ▶ 19 vegetarian and 299 non-veg
- ▶ Serum phosphate levels were significantly lower in those who were vegetarian

Table 5 Electrolyte and parathyroid hormone of non-vegetarian (non-Veg) and vegetarian (Veg) haemodialysis patients

	Non-Veg	Veg
K (mEq/L)	4.8 ± 0.12	5.0 ± 0.2
Ca (mg/dL)	10.7 ± 1.0	9.1 ± 0.3
P (mg/dL)*	4.8 ± 0.1	4.1 ± 0.2
iPTH (pg/mL)**	239.2 ± 32.1	111.0 ± 25.9
Alkaline phosphatase (IU/L)	117.5 ± 6.9	105.2 ± 8.8

* $P < 0.05$; ** $P < 0.01$. iPTH, intact parathyroid hormone.

Fiber

Mortality, Uremic Toxins, and Constipation

Mortality

Mortality in Kidney Disease

- Kidney disease is extremely deadly
- Those with kidney disease are 16 to 40 times more likely to die than to progress to kidney failure¹
- Those with kidney failure don't fair any better
 - 5-year survival rate is 42%²
 - This is worse than early stage lung cancer

¹ <https://report.nih.gov/nihfactsheets/ViewFactSheet.aspx?csid=34>

² https://www.usrds.org/2018/view/v2_05.aspx

For those with kidney failure who wait for a transplant...death comes sooner

5.3 Adjusted survival by treatment modality and incident cohort year (year of ESRD onset)

	3 months (%)	12 months (%)	24 months (%)	36 months (%)	60 months (%)
Hemodialysis					
2003	91.0	74.8	61.8	51.4	36.6
2005	91.2	75.4	62.7	53.0	38.6
2007	91.6	76.3	64.2	54.6	40.0
2009	91.8	77.5	65.7	56.2	41.6
2011	92.1	78.3	66.8	57.4	42.0

- ▶ A transplant can't come soon enough..
- ▶ **Only 42% of patients with kidney failure on dialysis are alive after five years (on average)**
- ▶ By comparison, the five-year survival rate for localized lung cancer is 56%

Plant-Based Diets in **CKD & Mortality**

Article

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

Jaimon T. Kelly,* Suetonia C. Palmer,[†] Shu Ning Wai,* Marinella Ruospo,^{‡§} Juan-Jesus Carrero,^{||} Katrina L. Campbell,* and Giovanni F. M. Strippoli^{§***}

Abstract

Background and objectives Patients with CKD are advised to follow dietary recommendations that restrict individual nutrients. Emerging evidence indicates overall eating patterns may better predict clinical outcomes, however, current data on dietary patterns in kidney disease are limited.

Design, setting, participants, & measurements This systematic review aimed to evaluate the association between dietary patterns and mortality or ESRD among adults with CKD. Medline, Embase, and reference lists were systematically searched up to November 24, 2015 by two independent review authors. Eligible studies were longitudinal cohort studies reporting the association of dietary patterns with mortality, cardiovascular events, or ESRD.

Results A total of seven studies involving 15,285 participants were included. Healthy dietary patterns were generally higher in fruit and vegetables, fish, legumes, cereals, whole grains, and fiber, and lower in red meat, salt, and refined sugars. In six studies, healthy dietary patterns were consistently associated with lower mortality (3983 events; adjusted relative risk, 0.73; 95% confidence interval, 0.63 to 0.83; risk difference of 46 fewer (29–63

- Meta-Analysis of 6 prospective cohort studies including nearly 14,000 adults with CKD
- Eating a healthy dietary pattern associated with a lower risk of mortality (**adjusted relative risk 0.73, 95% CI 0.63-0.83**)
- **More fruits, vegetables, fish, legumes, cereals, whole grains, fiber AND less red meat, salt, and refined sugars**

Fruits and Vegetables in ESRD & Mortality

Article

Fruit and Vegetable Intake and Mortality in Adults undergoing Maintenance Hemodialysis

Valeria M. Saglimbene,^{1,2} Germaine Wong,^{1,3,4} Marinella Ruospo,² Suetonia C. Palmer,⁵ Vanessa Garcia-Larsen,⁶ Patrizia Natale,^{2,7} Armando Teixeira-Pinto,^{1,3} Katrina L. Campbell,⁸ Juan-Jesus Carrero,⁹ Peter Stenvinkel,¹⁰ Letizia Gargano,² Angelo M. Murgu,² David W. Johnson,^{11,12} Marcello Tonelli,¹³ Rubén Gelfman,² Eduardo Celia,² Tevrik Ecdar,² Amparo G. Bemat,² Domingo Del Castillo,² Delia Timofte,² Marietta Török,² Anna Bednarek-Skublewska,^{2,14} Jan Duława,^{2,15} Paul Stroumza,² Susanne Hoischen,² Martin Hansis,² Elisabeth Fabricius,² Paolo Felaco,¹⁶ Charlotta Wollheim,² Jürgen Hegbrant,² Jonathan C. Craig,¹⁷ and Giovanni F.M. Strippoli^{1,2,7,18}

Abstract

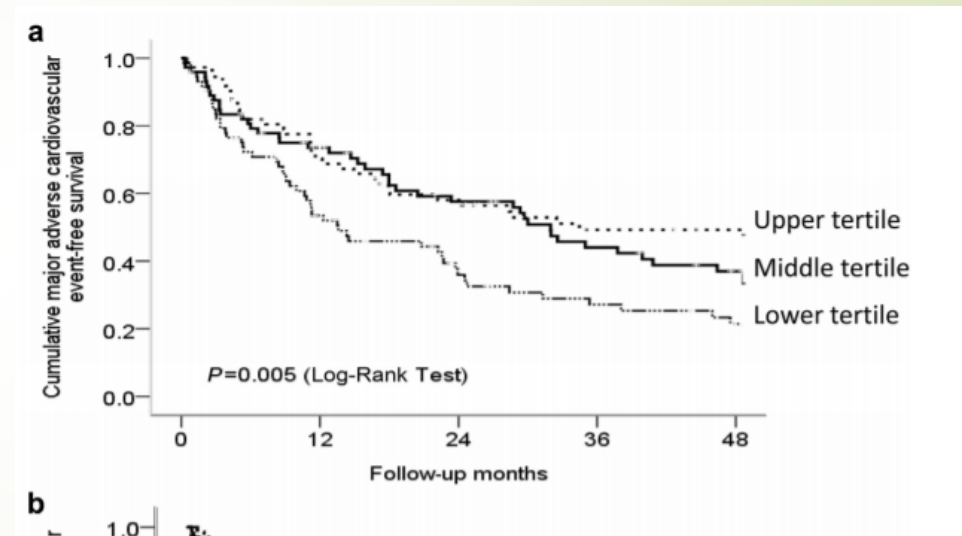
Background and objectives Higher fruit and vegetable intake is associated with lower cardiovascular and all-cause mortality in the general population. It is unclear whether this association occurs in patients on hemodialysis, in whom high fruit and vegetable intake is generally discouraged because of a potential risk of hyperkalemia. We aimed to evaluate the association between fruit and vegetable intake and mortality in hemodialysis.

Design, setting, participants, & measurements Fruit and vegetable intake was ascertained by the Global Allergy and Asthma European Network food frequency questionnaire within the Dietary Intake, Death and Hospitalization in Adults with ESKD Treated with Hemodialysis study, a multinational cohort study of 9757 adults on hemodialysis, of whom 8078 (83%) had analyzable dietary data. Adjusted Cox regression analyses clustered by country were conducted to evaluate the association between tertiles of fruit and vegetable intake with all-cause

- Prospective study from DIET-HD cohort involving 11 countries in Europe and South America
- Approx. 8,000 people followed for a median of 2.7 years
- Fruit and Vegetable (F+V) intake and mortality were measured
- **Median number of servings was 8 per week**
- **Only 4% consumed 4 servings per day (the recommended minimum)**
- Compared with the lowest tertile of servings per week, those in the **highest tertile were associated with a lower risk of all-cause mortality (HR 0.80, 95% CI 0.71 – 0.91) and non-CV mortality (HR 0.77, 95% CI 0.66 – 0.91)**

Fiber Associated with Reduced MACE in Dialysis

- ▶ Prospective study with 4 years follow-up
- ▶ 219 patients on dialysis in Hong Kong
- ▶ Every 1 g/day higher fiber intake was associated with a 11% lower risk of MACE
 - ▶ Also lower markers of inflammation and lower ventricular hypertrophy



Fiber Associated with Reduced Mortality in Peritoneal Dialysis

Table 3. Outcomes among peritoneal dialysis (PD) patients (n 881)
(Medians and interquartile ranges; number of events and event rate/100 person-years)

Outcomes	Tertile of time-averaged fibre intake								P
	Total		Low (< 6.2 g/d)		Middle (6.2–8.3 g/d)		High (> 8.3 g/d)		
	No. of events	Event rate/100 person-years	No. of events	Event rate/100 person-years	No. of events	Event rate/100 person-years	No. of events	Event rate/100 person-years	
Follow-up (months)									
Median	45.0		33.0*		47		54.0‡		< 0.001
Interquartile range	21.5, 74.0		17.0, 62.0		22.0, 75.0		25.8, 81.0		
Death	434	11.52	186*	18.08	148†	11.00	100‡	7.17	< 0.001
Cardiovascular events§	178	4.72	68	6.61	67	4.98	43	3.08	0.138
Infection	107	2.84	41	3.99	37	2.75	29	2.08	0.279
Transfer to haemodialysis	164	4.35	45	4.38	53	3.94	66	4.73	0.554
PD-related infection	95	2.52	23	2.24	34	2.53	38	2.73	0.378
Renal transplantation	114	3.03	25	2.43	35†	2.60	54‡	3.87	0.031

* P < 0.05 low-tertile group compared with middle-tertile group.

† P < 0.05 middle-tertile group compared with high-tertile group.

‡ P < 0.05 high-tertile group compared with low-tertile group.

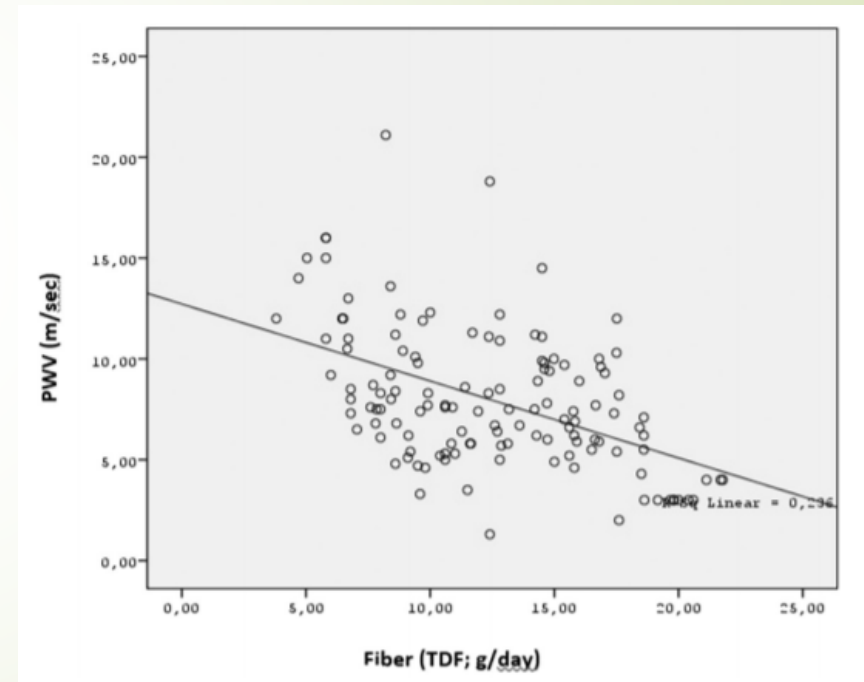
§ Cardiovascular events include cardiovascular events, cerebrovascular events and sudden death.

- A long-term (12 year) prospective cohort study of patients on peritoneal dialysis (n = 881)
- Independent association between fiber intake and all-cause mortality
- **Each 1 gram per day increase in fiber intake correlated with a 13% reduction in all-cause mortality**

Xu, Xiao, et al. "Dietary fibre and mortality risk in patients on peritoneal dialysis." *British Journal of Nutrition* 122.9 (2019): 996-1005.

Fiber Reduces Traditional CVD Risk Factors in Dialysis

- ▶ 128 patients on maintenance hemodialysis
- ▶ Dietary fiber level was independently correlated with advanced glycation end products ($r^2 = 0.164$, $P = 0.017$) and C-reactive protein levels ($r^2 = 0.238$, $P = 0.01$)
- ▶ Increased dietary fiber was also associated with less arterial stiffness (as measured by pulse wave velocity)



Fiber Reduces Traditional CVD Risk Factors in Dialysis

- ▶ 124 hemodialysis patients randomized to either 10 g/d, 20 g/d of fiber or placebo for 6 weeks
- ▶ Compared to placebo, fiber supplemented patients had lower
 - ▶ Total Cholesterol
 - ▶ LDL Cholesterol
 - ▶ Inflammatory makers (TNF- α , IL-6, IL-8 and CRP)

Table 3

Lipid profiles of the subjects in the study (Mean \pm SD)

Parameters	Group A		Group B		Group control	
	Before	After	Before	After	Before	After
TG (mmol/L)	2.6 \pm 1.5	2.5 \pm 1.4	2.6 \pm 1.6	2.6 \pm 1.5	2.6 \pm 1.5	2.5 \pm 1.4
TC (mmol/L)	4.8 \pm 1.3	4.3 \pm 1.1 ^{a,b}	4.8 \pm 1.2	4.2 \pm 1.3 ^{a,b}	4.8 \pm 1.2	4.8 \pm 1.2
LDL (mmol/L)	2.6 \pm 0.5	2.1 \pm 0.3 ^{a,b}	2.7 \pm 0.3	2.2 \pm 0.3 ^{a,b}	2.6 \pm 0.4	2.5 \pm 0.3
HDL (mmol/L)	1.3 \pm 0.4	1.4 \pm 0.5	1.4 \pm 0.6	1.4 \pm 0.7	1.3 \pm 0.5	1.3 \pm 0.5
TC:HDL ratio	3.6 \pm 0.4	3.0 \pm 0.3 ^{a,b}	3.4 \pm 0.4	2.9 \pm 0.4 ^{a,b}	3.3 \pm 0.4	3.5 \pm 0.4

^a $P < 0.05$ vs. before value within the group;

^b $P < 0.05$ vs. after value with control group.

Polyphenol-Rich Interventions Reduced CVD Risk Factors

- Polyphenols are only found in plants
- Systematic review and meta-analysis of 12 studies
- Polyphenol-rich interventions improved
 - Diastolic blood pressure
 - Triglycerides
 - Myeloperoxidase (marker of oxidative stress)

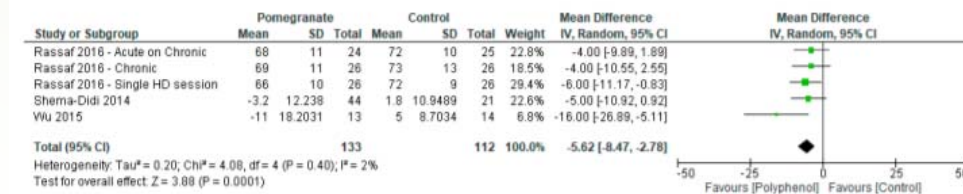


Figure 3. Forest plot of polyphenol-rich interventions on diastolic blood pressure.

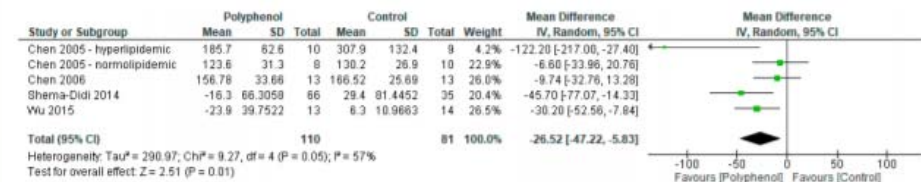


Figure 6. Forest plot of polyphenol-rich interventions on triglyceride levels.

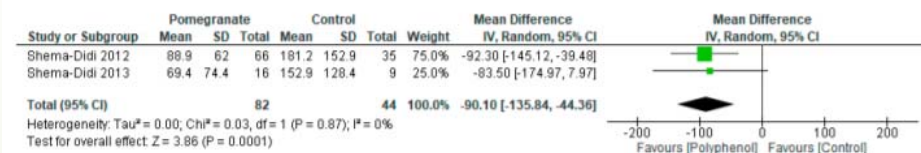


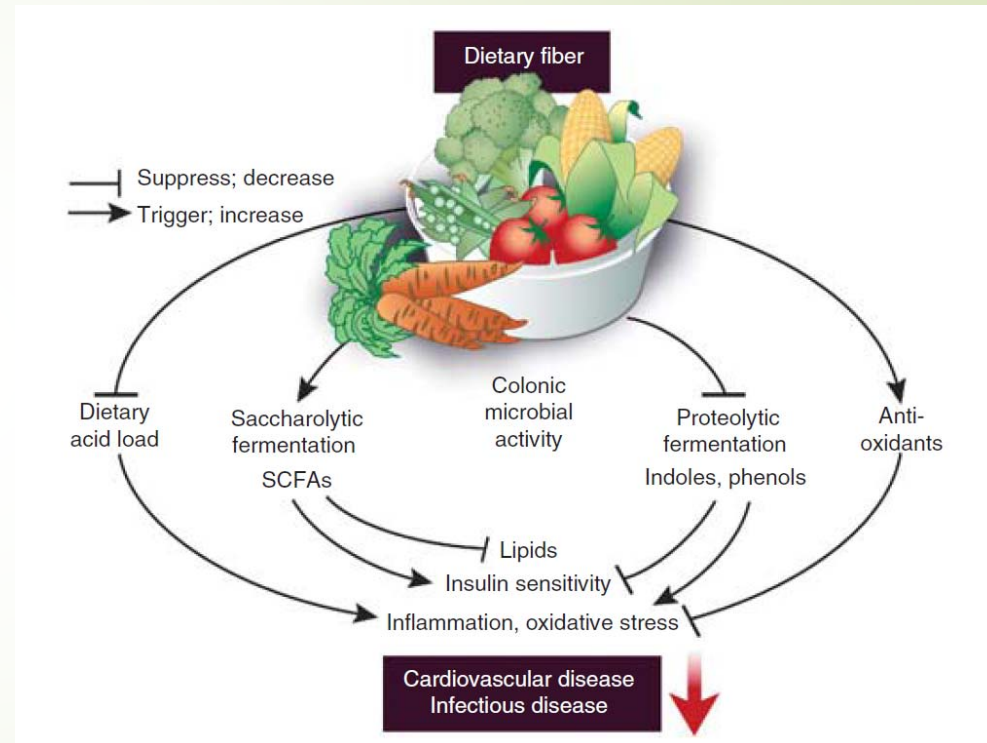
Figure 2. Forest plot of polyphenol-rich interventions on myeloperoxidase.

Marx, Wolfgang, et al. "The effect of polyphenol-rich interventions on cardiovascular risk factors in haemodialysis: A systematic review and meta-analysis." *Nutrients* 9.12 (2017): 1345.

Uremic Toxins

Fiber in Kidney Failure

- ▶ Dietary fiber was used as a treatment for kidney failure 30 years ago because it reduced blood levels of nitrogenous waste (urea)¹
- ▶ Fiber intake has been associated with reduced mortality and cardiovascular disease in CKD^{2,3}
- ▶ In one study, every extra 1 gram of fiber was associated with an 11% reduction in cardiovascular events³



¹ Rose et al. *Uro & Nephron*. 2019; 6(3): 555-687

² Evenepoel. *Kidney International* 81.3 (2012): 227-229.

³ Wang. *Kidney International Reports* 4.6 (2019): 814-823.

Image: Reference 2

Uremic Toxins Reduced in Vegetarian Diets

The Production of p-Cresol Sulfate and Indoxyl Sulfate in Vegetarians Versus Omnivores

Kajal P. Patel,* Frank J.-G. Luo,* Natalie S. Plummer,* Thomas H. Hostetter,[†] and Timothy W. Meyer*

Summary

Background and objectives The uremic solutes p-cresol sulfate (PCS) and indoxyl sulfate (IS) are generated by colon bacteria acting on food components that escape absorption in the small bowel. The production of these potentially toxic compounds may thus be influenced by diet. This study examined whether production of PCS and IS is different in vegetarians and omnivores.

Design, setting, participants, & measurements The production of PCS and IS was assessed by measuring their urinary excretion rates in participants with normal kidney function. Studies were carried out in 15 vegetarians and 11 individuals consuming an unrestricted diet. Participants recorded food intake over 4 days and collected urine over the final 2 days of each of two study periods, which were 1 month apart.

*Department of Medicine, Palo Alto VA Health Care System, Stanford University, Palo Alto, California; and [†]Department of Medicine, Case Western University School of Medicine, Columbus, Ohio

Dietary protein-fiber ratio associates with circulating levels of indoxyl sulfate and p-cresyl sulfate in chronic kidney disease patients

M. Rossi[✉], D.W. Johnson, H. Xu, J.J. Carrero, E. Pascoe, C. French, K.L. Campbell

PlumX Metrics

DOI: <http://dx.doi.org/10.1016/j.numecd.2015.03.015> |  CrossMark

 Article Info



Uremic Toxins Reduced in Vegetarian Diets

Indoxyl sulfate and p cresyl sulfate are protein-bound uremic toxins

- ▶ Reduced (by 50%) in those on hemodiafiltration eating vegetarian diets¹
- ▶ Possible mechanisms:
 - ▶ Alterations in gut microbiome
 - ▶ Increased frequency of bowel movements
 - ▶ Inherent differences in proteins

¹Kandouz, Sakina, et al. "Reduced protein bound uraemic toxins in vegetarian kidney failure patients treated by haemodiafiltration." *Hemodialysis International* 20.4 (2016): 610-617.

Image: Ibid.

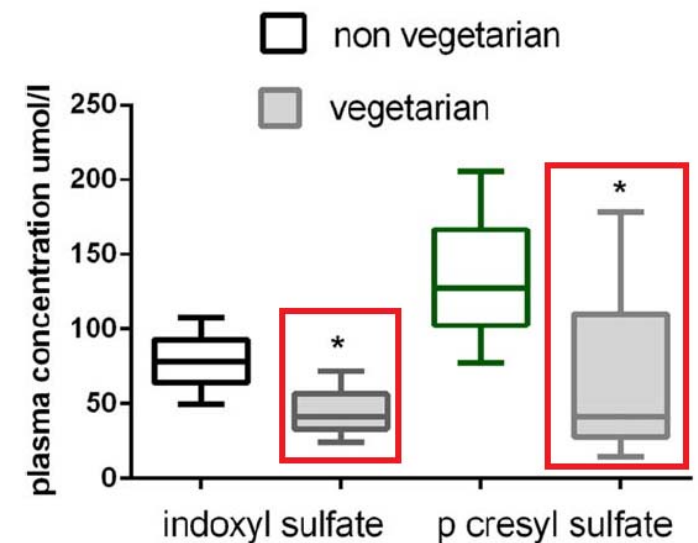


Figure 1 Plasma concentrations of indoxyl sulfate and p cresyl sulfate in non-vegetarian and vegetarian patients. Results expressed as median (interquartile range). *P < 0.05 vs. non-vegetarian.

Plant Foods & Uremic Toxins

- ▶ Recurrent signal in the literature
- ▶ Cross-sectional study of 22 patients on hemodialysis¹
- ▶ Higher adherence to a **plant-based diet index (PDI)** was associated with **lower indoxyl sulfate levels**
 - ▶ A **healthy PDI** was associated with **lower indoxyl sulfate** levels compared to an **unhealthy PDI**
- ▶ Animal fats, sweets and desserts were associated with bacteria linked to higher **indoxyl sulfate** and **p-cresyl sulfate** concentrations
- ▶ **Indoxyl sulfate** has been shown to predict not only need for **dialysis** but also **cardiovascular disease**

¹ Stanford et al. Associations Among Plant-Based Diet Quality, Uremic Toxins, and Gut Microbiota Profile in Adults Undergoing Hemodialysis Therapy. *Journal of Renal Nutrition* 2020.

² Lin, Cheng-Jui, et al. "Indoxyl sulfate predicts cardiovascular disease and renal function deterioration in advanced chronic kidney disease." *Archives of Medical Research* 43.6 (2012): 451-456.

Effect of Increasing Dietary Fiber on Uremic Toxins in Hemodialysis

- ▶ Randomized controlled trial of 56 patients on hemodialysis
- ▶ An increase in fiber intake was shown to significantly reduce plasma levels of indoxyl sulfate by 17% ($p = 0.04$) and non-significantly reduced plasma levels of p-cresol by 8% ($p = 0.63$)

Effect of Increasing Dietary Fiber on Plasma Levels of Colon-Derived Solutes in Hemodialysis Patients

Tammy L. Sirich,* Natalie S. Plummer,* Christopher D. Gardner,* Thomas H. Hostetter,[†] and Timothy W. Meyer*

Abstract

Background and objectives Numerous uremic solutes are derived from the action of colon microbes. Two such solutes, indoxyl sulfate and p-cresol sulfate, have been associated with adverse outcomes in renal failure. This study tested whether increasing dietary fiber in the form of resistant starch would lower the plasma levels of these solutes in patients on hemodialysis.

Design, setting, participants, & measurements Fifty-six patients on maintenance hemodialysis were randomly assigned to receive supplements containing resistant starch ($n=28$) or control starch ($n=28$) daily for 6 weeks in a study conducted between October 2010 and May 2013. Of these, 40 patients (20 in each group) completed the study and were included in the final analysis. Plasma indoxyl sulfate and p-cresol sulfate levels were measured at baseline and week 6.

Results Increasing dietary fiber for 6 weeks significantly reduced the unbound, free plasma level of indoxyl sulfate (median -29% [25th percentile, -56, -12] for fiber versus -0.4% [-20, 34] for control,

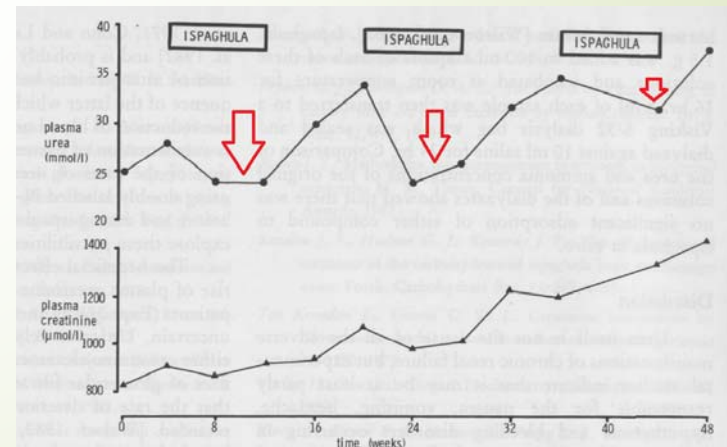
Single Arm Trial of Psyllium Demonstrated Urea Reduction

- 9 patients with a mean creatinine clearance of 8.2 ml/min
- Given "ispaghula" husk (psyllium) 3.5 g BID for 8 weeks
- Demonstrated
 - 17% reduction in urea after 4 weeks
 - 19% reduction in urea after 8 weeks
- 4 patients discontinued psyllium after a week due to flatulence and "a sensation of fullness"

Table 2 Effect of ispaghula (7 g/d for 8 weeks [weeks 4–11 inclusive]) on plasma urea and creatinine concentrations and their rates of change (d urea/dt and d creatinine/dt) in uremic patients (Expt 2). Means \pm SEM are shown.

Time (weeks)	0	4	8 ⁵	12 ⁵	16
No. of patients	9	9	9	9	8
urea (mmoles/l)	32 \pm 2	38 \pm 3 ¹	32 \pm 3 ²	31 \pm 3 ²	37 \pm 4 ³
d urea/dt (mmoles/l/mth)	–	+6 \pm 3	–6 \pm 2 ²	–1 \pm 2 ²	+7 \pm 2 ^{3,4}
creatinine (μ moles/l)	794 \pm 76	893 \pm 97 ¹	838 \pm 107	869 \pm 111	893 \pm 111 ^{1,3}
d creatinine/dt (μ moles/l/mth)	–	+99 \pm 32	–55 \pm 38 ²	+31 \pm 23	+99 \pm 32 ⁴

¹P <0.05 from 0 weeks; ²P <0.05 from 4 weeks; ³P <0.05 from 12 weeks; ⁴P <0.01 from weeks 4–11 inclusive; ⁵ samples taken after 4 and



FAMOUS KIDNEYS



BILLY THE KIDNEY



NICOLE KIDNEY



HELLO KIDNEY



JOHN F. KIDNEY



THE KIDNEY AND I



KIDNEY ROCK



Common Concerns with Plant-Based Diets in Dialysis

Potassium and Protein

Potassium

Plant-Based Foods, Potassium, and ESRD

- ▶ Historically, plant-based foods have been excluded from “renal diets” due to their potassium content
- ▶ However, recent research suggests that this risk may be overstated
- ▶ Factors mitigating a rise in serum potassium in ESRD with plant-based foods:
 - ▶ **Fiber** – Leads to larger and more frequent bowel movements, leading to potassium loss
 - ▶ **Colonic Secretion of Potassium** – In CKD, **up to 80% of dietary potassium can be secreted into the colon!**
 - ▶ **Intracellular Movement of Potassium** – Due to improved insulin sensitivity and natural alkali found in foods
 - ▶ **Bioavailability** (next slide)

Bioavailability of Potassium in Plant Foods is Less than Animal Foods

- ▶ Cells of plants and animals differ
- ▶ Plants have cell walls; animals do not
- ▶ Plant cell walls are difficult to digest
 - ▶ Potassium is generally found inside cell-walls
- ▶ Potassium in plants is no more than 60% in unprocessed fruits and vegetables

PRACTICAL ASPECTS

Potassium Additives and Bioavailability: Are We Missing Something in Hyperkalemia Management?

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Kelly Picard, BSC, RD

Hyperkalemia and hyperphosphatemia are common metabolic disturbances in chronic kidney disease. Management may include instructions on a low-potassium or low-phosphorus diet, respectively. Low-phosphorus diet teaching includes information on phosphorus additives in addition to naturally occurring phosphorus food sources. Phosphorus additives are known to be more bioavailable compared with naturally occurring phosphorus. The concentration of phosphorus can also be much higher in processed foods compared with whole foods. Similar considerations may also be needed for dietary potassium teaching. The use of potassium additives

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August 2008; 59(5): 438-450

informa
healthcare

An investigation into the bioaccessibility of potassium in unprocessed fruits and vegetables

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Case Reports of Hyperkalemia with Plant-Based Foods

European Journal of Clinical Nutrition
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REVIEW ARTICLE

Review of case reports on hyperkalemia induced by dietary intake: not restricted to chronic kidney disease patients

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Abstract

Hyperkalemia is a metabolic disturbance of the potassium balance that can cause potentially fatal cardiac arrhythmias. Kidney dysfunction and renin–angiotensin–aldosterone system inhibiting drugs are notorious for their tendency to induce hyperkalemia by decreasing the excretion of potassium. The role of dietary potassium intake in inducing hyperkalemia is less clear. We review and analyze the common presentation, laboratory, and electrocardiogram (ECG) findings and therapeutic options associated with dietary-induced hyperkalemia, and find evidence for hyperkalemia development in non-renal

Most of the case reports are attributed to juices, sauces, and dried fruit – not unprocessed plant foods

Table 1 Overview of case reports of patients without underlying CKD/AKI (upper part) and with or non-specified CKD/AKI (lower part)

Author	Year	Origin of paper	Subjects	Cause	Age (sex)	CKD/AKI
<i>Without underlying CKD/AKI</i>						
Berk et al. [21]	2004	USA	1	Orange juice	66 (F)	No
Bosse et al. [22]	2011	USA	1	Potassium supplements	56 (F)	No
Briggs et al. [23]	2014	USA	1	Potassium supplements	44 (F)	No
Browning et al. [24]	1981	UK	1	Potassium citrate mix	83 (F)	No
Corbacioglu et al. [25]	2012	Turkey	1	Bananas	44 (F)	No
Epperly [26]	1987	USA	1	Baby food, fruit juices, and liquid supplements	80 (M)	No
Hoyt [27]	1986	USA	1	Salt substitute	70 (F)	No
Illingworth et al. [17]	1980	UK	1	40 slow potassium tablets	26 (M)	No
John et al. [28]	2011	Lebanon	2	Salt substitute, potassium supplements, sport nutritional drinks	65 (M); 35 (M)	Both: no
Kallen et al. [29]	1976	USA	1	Salt substitute	8 months (M)	No
Lisenbee et al. [30]	2012	USA	1	Potassium supplements	38 (M)	No
Pavletic [31]	2011	USA	1	Dried fruits	36 (F)	No
Restucio [18]	1992	USA	1	Salt substitute	53 (M)	No
Rusyniak et al. [32]	2013	USA	1	Cream of tartar	16 (M)	No
Schim Van Der Loeff et al. [33]	1988	Netherlands	1	Salt substitute	29 (F)	No
Wetli et al. [19]	1978	USA	1	Potassium chloride	2 months (M)	No
<i>With underlying CKD/AKI, or unknown/not specified</i>						
Belknap [34]	1991	USA	1	Blackstrap molasses	67 (M)	Yes
Berrebi et al. [35]	2009	France	1	Fruit ingestion	57 (M)	Yes
Cheng et al. [36]	2005	Taiwan	1	Raw coconut juice	38 (M)	Yes
Corbacioglu et al. [25]	2012	Turkey	1	Apricot	58 (F)	Yes
Doorenbos et al. [37]	2003	Netherlands	1	Salt substitute	74 (F)	Yes
Fan et al. [38]	1996	USA	1	Orange juice	50 (M)	Yes
Gelfand et al. [39]	1975	USA	5	Geophagia	45 (M); 33 (M); 65 (F); 44 (F); 59 (F)	All: yes
Hakimian et al. [40]	2014	USA	1	Coconut water	42 (M)	Yes
Javed et al. [6]	2007	USA	1	Orange juice	51 (M)	Yes
Jones [41]	2004	USA	1	Tomato juice	68 (M)	Yes
Lamid et al. [42]	1978	USA	1	Tomato soup	62 (M)	Unknown
Leo et al. [43]	2011	Malaysia	1	Durian fruit	48 (F)	Yes
Mueller et al. [44]	2000	USA	1	Noni juice	?? (M)	Yes
Nagasaki et al. [8]	2005	Japan	1	Gerson therapy	52 (M)	Yes
Ray et al. [45]	1999	UK	2	Salt substitute and high potassium diet	67 (M); 64 (M)	Yes/Not specified
Rusyniak et al. [32]	2013	USA	1	Cream of tartar	32 (M)	Yes
Tazoe et al. [46]	2007	Japan	1	Bananas	15 (F)	Unknown
Wang [47]	1996	China	1	Bananas, peaches	23 (F)	Yes
Williams et al. [48]	2001	USA	1	Apple juice	70 (M)	Yes
Yap et al. [49]	1976	USA	2	Salt substitute	76 (M); 74 (M)	Both: Not specified
Yip et al. [50]	2012	China	1	Salt substitute	57 (F)	Yes

Got Hyperkalemia?

Editorial

Does an Apple (or Many) Each Day, Keep Mortality Away?

Ranjani N. Moorthi

Clin J Am Soc Nephrol 14: 180–181, 2019. doi: <https://doi.org/10.2215/CJN.15001218>

In this issue of the *Clinical Journal of the American Society of Nephrology*, Saglimbene *et al.* (1) highlight the importance of fruit and vegetable intake in 9757 patients undergoing from this study demonstrate that it is dramatically lower in those on hemodialysis compared with the general population. As the authors point out, patients

The inadvertent consequence of this avoidance is that they fail to derive benefits from fruits and vegetables such as the antioxidants, fiber, and other benefits. Despite this recommendation, there is actually little data to support that eating fruits and vegetables increases serum potassium.

Summary of Evidence Showing **Nearly** No Increase in Potassium with Plant-Based Diets

Name	Quantity of Plants Consumed	Size	Duration/Type	Increase in Potassium?	Stage of CKD	Comment
Goraya Kidney Int 2012	Typically 2 to 4 cups	199	30 days Controlled trial	No	I/II	
Goraya Kidney Int 2014	2 to 4 cups	108	3 years RCT	No	III	
Tyson CKJ 2016	DASH diet	10	2 weeks Controlled trial	No	III	
Moorthi AJN 2014	70% plant protein	13	4 weeks Controlled trial	No but	III/IV	1 patient with type IV RTA
Barsotti Nephron 1996	Vegetarian diet	37	3 months Controlled trial	No	III-V	14 months data on K not reported
Goraya CJASN 2013	2 to 4 cups	76	1 year RCT	No	IV	
Wu Nephrology 2011	Vegetarian diet	19	Cross-sectional	No	HD	
St-Jules J Ren Nutr 2016	Increasing K+ intake	140	Cross-sectional	No	HD	No correlation b/w serum K+ & dietary K
Saglimbene JASN 2019	Median 8 servings F+V/week	8078	Prospective observational (median 2.8 years)	No	HD	
Gonzalez Ortiz NDT 2020	Plant-based diet score	150	Prospective (1 year)	No	HD	

The One Patient with Hyperkalemia (with a known Type IV RTA)

“There were a total of 2 incidences of potassium of 5.8 mEq/l and both these measures were in the same subject, with a known type IV RTA, which required modifying the plant protein source from raw edamame (482 mg of potassium/100 g) the highest potassium content among all plant sources (National Database for Standard Reference: USDA Release 26) to fried tofu.”¹

¹Moorthi, Ranjani N. *American Journal of Nephrology* 40.6 (2014): 582-591.

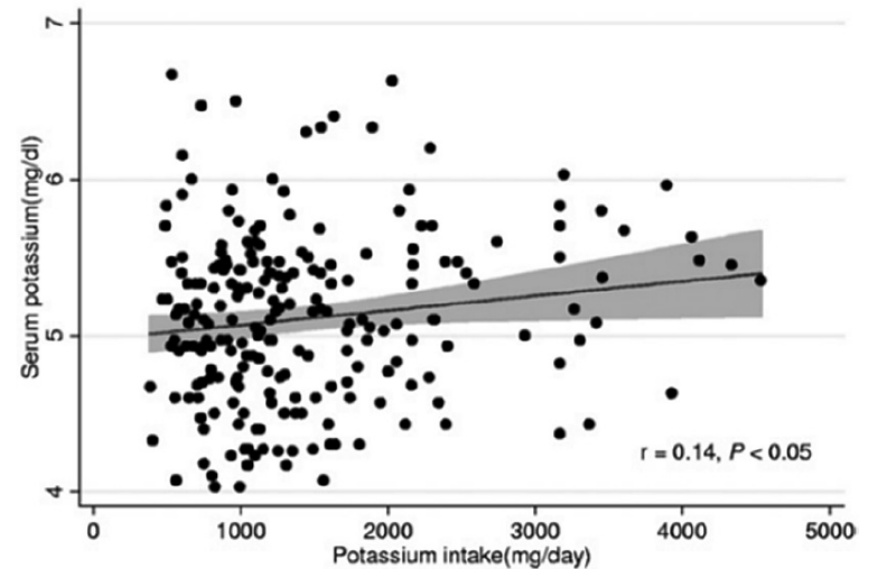
Foods with the Most Potassium

NDB_No	Description	Weight(g)	Measure	Potassium, K (mg) Per Measure
19304	Molasses	337.0	1.0 cup	4934
11432	Radishes, oriental, dried	116.0	1.0 cup	4053
11382	Potatoes, mashed, dehydrated, granules with milk, dry form	200.0	1.0 cup	3696
16049	Beans, white, mature seeds, raw	202.0	1.0 cup	3626
16108	Soybeans, mature seeds, raw	186.0	1.0 cup	3342
16045	Beans, small white, mature seeds, raw	215.0	1.0 cup	3315
19355	Syrups, sorghum	330.0	1.0 cup	3300
12005	Seeds, breadnut tree seeds, dried	160.0	1.0 cup	3218
16040	Beans, pink, mature seeds, raw	210.0	1.0 cup	3074
16071	Lima beans, large, mature seeds, raw	178.0	1.0 cup	3069
16119	Soy meal, defatted, raw	122.0	1.0 cup	3038
01115	Whey, sweet, dried	145.0	1.0 cup	3016
16014	Beans, black, mature seeds, raw	194.0	1.0 cup	2877

USDA Food Composition Database. <https://ndb.nal.usda.gov/ndb/search/list?home=true>. Accessed 5/8/19.

(Almost) No Association Between Dietary Potassium & Serum Potassium Pre-Dialysis

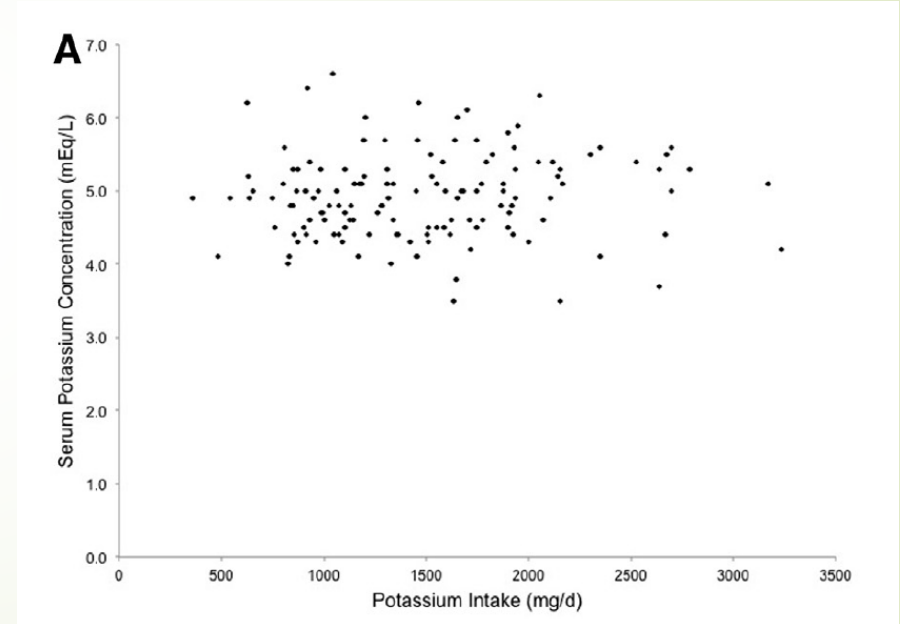
- ▶ Secondary analysis of 224 patients on dialysis in the Nutritional and Inflammatory Evaluation in Dialysis
- ▶ Only 2% of the variance in quarterly mean predialysis serum potassium
- ▶ Based on this data, increasing dietary potassium 9-fold – from 500 mg to 4500 mg per day, would be expected to increase serum potassium by only 0.4 mEq/L



Noori, Nazanin, et al. "Dietary potassium intake and mortality in long-term hemodialysis patients." *American journal of kidney diseases* 56.2 (2010): 338-347.

No Association Between Dietary Potassium & Serum Potassium Pre-Dialysis

- 140 HD patients in the BalanceWise Study
- “No significant correlations were found between [serum potassium] and either absolute reported potassium intake ($r = 0.06, P = 0.50$) or potassium density ($r = -0.003, P = 0.97$;)”



St-Jules, David E., David S. Goldfarb, and Mary Ann Sevick. "Nutrient non-equivalence: Does restricting high-potassium plant foods help to prevent hyperkalemia in hemodialysis patients?." *Journal of Renal Nutrition* 26.5 (2016): 282-287.

Not all potassium sources are the same

REVIEW ARTICLE

CPE Nutrient Non-equivalence: Does Restricting High-Potassium Plant Foods Help to Prevent Hyperkalemia in Hemodialysis Patients? CrossMark

David E. St-Jules, RD, PhD, David S. Goldfarb, MD,† and Mary Ann Sevick, ScD, RN**

Hemodialysis patients are often advised to limit their intake of high-potassium foods to help manage hyperkalemia. However, the benefits of this practice are entirely theoretical and not supported by rigorous randomized controlled trials. The hypothesis that potassium restriction is useful is based on the assumption that different sources of dietary potassium are therapeutically equivalent. In fact, animal and plant sources of potassium may differ in their potential to contribute to hyperkalemia. In this commentary, we summarize the historical research basis for limiting high-potassium foods. Ultimately, we conclude that this approach is not evidence-based and may actually present harm to patients. However, given the uncertainty arising from the paucity of conclusive data, we agree that until the appropriate intervention studies are conducted, practitioners should continue to advise restriction of high-potassium foods.

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Fiber Increases Fecal Potassium Excretion

- ▶ Single patient study
- ▶ Patient was on dialysis and given 3.5 g twice a day of ispaghula (psyllium) for 11 weeks
- ▶ Researchers noted a 32% increase in fecal potassium excretion

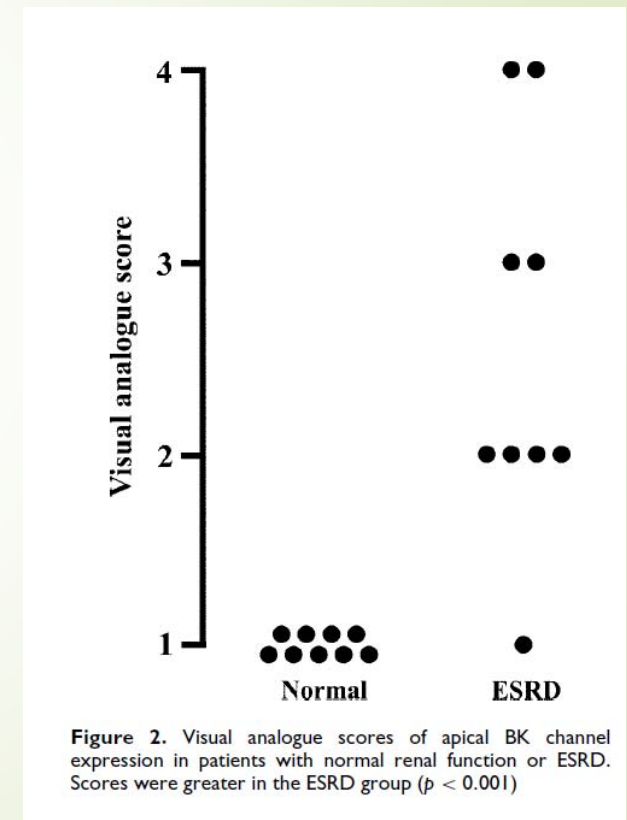
Table 3 Effect of ispaghula (7 g/d for 11 weeks) on faecal excretion of nitrogen, potassium, calcium, magnesium and phosphate in a single uraemic patient on a strictly controlled diet. The results of the 2 consecutive 4-day collection periods before and during ispaghula supplementation are shown.

	Diet alone	Diet and ispaghula	Mean change
N(g/d)	1.2, 1.1	1.8, 1.4	+30%
K (mmoles/d)	15.5, 12.4	20.8, 16.2	+32%
Ca(mmoles/d)	14.9, 15.7	18.4, 15.5	+10%
Mg(mmoles/d)	1.7, 1.6	2.2, 1.9	+22%
P(mmoles/d)	14.7, 12.9	15.6, 11.1	- 3%

Colonic Potassium Excretion Increased in Patients with ESRD

- ▶ Compared to patients with normal renal function, rectal K secretion is **nearly 3x higher in patients with ESRD**
- ▶ Colonic potassium excretion appears to be an active process mediated by an upregulation of **high-conductance (BK) apical K⁺ channels in surface colonic epithelial cells**

Mathialahan et al. Enhanced large intestinal potassium permeability in end-stage renal disease. *Journal of Pathology* (2005) 206: 46-51.



Protein

Do hemodialysis patients get enough protein on a plant-based diet?

- ▶ HD patients recommended to get **1.0-1.2 g/kg/day**
- ▶ Two studies of vegetarians on hemodialysis showed protein intake of **1.2-1.25 g/kg/day** without compromise^{1,2}
- ▶ Unclear from studies if their diets were modified in any way (versus eating ad lib) or supplemented with protein-containing foods

¹Wu T, Chang C, Hsu W, et al. Nutritional status of vegetarians on maintenance haemodialysis. *Nephrology*. 2011;16(6):582-587.

²Kandouz S, Mohamed AS, Zheng Y, Sandeman S, Davenport A. Reduced protein bound uraemic toxins in vegetarian kidney failure patients treated by haemodiafiltration. *Hemodialysis International*. 2016;20(4):610-617.

NEPHROLOGY

Nephrology 16 (2011) 582-587

Original Article

Nutritional status of vegetarians on maintenance haemodialysis

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Hemodialysis International 2016; 20:610-617

Nutrition

Reduced protein bound uraemic toxins in vegetarian kidney failure patients treated by haemodiafiltration

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A Variety of Plant-Foods Provide Adequate Protein with Typical Consumption

PRACTICAL ASPECTS

Adequacy of Plant-Based Proteins in Chronic Kidney Disease

Shivam Joshi, MD, Sanjeev Shah, MD,* and Kamyar Kalantar-Zadeh, MD†*

Concerns regarding protein and amino acid deficiencies with plant-based proteins have precluded their use in chronic kidney disease (CKD) patients. Many of these concerns were debunked years ago, but recommendations persist regarding the use of “high-biological value” (animal-based) proteins in CKD patients, which may contribute to worsening of other parameters such as blood pressure, metabolic acidosis, and hyperphosphatemia. Plant-based proteins are sufficient in meeting both quantity and quality requirements. Those eating primarily plant-based diets have been observed to consume approximately 1.0 g/kg/day of protein, or more. CKD patients have been seen to consume 0.7-0.9 g/kg/day of mostly plant-based protein without any negative effects. Furthermore, those substituting animal-based proteins for plant-based proteins have shown reductions in severity of hypertension, hyperphosphatemia, and meta-

It is important to note that amino acid deficiency is possible in those who are eating a restrictive diet limited to one or two food sources, creating a situation such that attaining the RDA for an amino acid may exceed the number of servings than is humanly possible. A stark example of this can be illustrated by the low tryptophan content of an apple. A medium-sized (100 g) apple contains 1 mg of tryptophan.¹⁸ Based on the RDA for tryptophan (5 mg/kg/day), a 70-kg person would need on average 350 mg of tryptophan per day.⁴ To meet this, a person eating a diet exclusively of apples would need to eat 350 apples daily to meet the RDA for tryptophan, which is not possible in a real-world scenario.

Less Protein But Better Nutritional Status?

- 150 patients on dialysis followed prospectively for a year
- 3-day food record every 3 months & characterized by a **healthy plant-based diet score**
- Those with a higher plant-based diet score had a **higher risk of low protein intake (< 1.1 g/kg/d OR 1.11, 95% CI 1.04-1.19)**
 - Intake was **0.9 g/kg/d** in moderate & high groups

- However, those with a higher plant-based diet score also had a **lower malnutrition inflammation score (aka better nutritional status)**
- Diet still wasn't healthy!
 - Overall low intake of legumes, fruits, and vegetables!

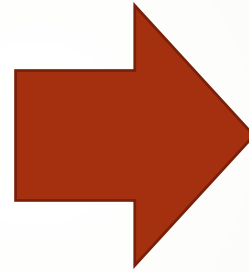
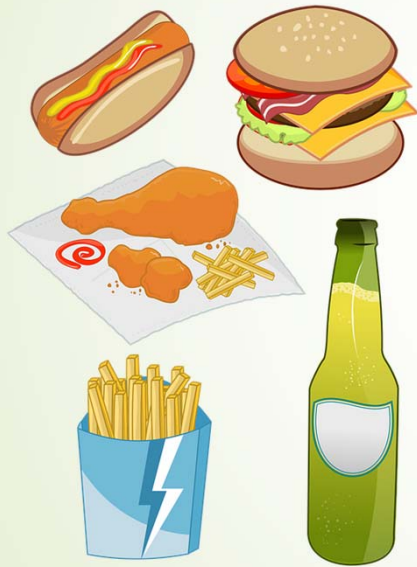
Table 3. Food nutrients and group servings according to increasing tertiles of the HPDS

Variable	Low adherence (n = 43)	Moderate adherence (n = 53)	High adherence (n = 54)	P-value for trend
Nutrient intake				
Energy (kcal/g/day)	25 (19-30)	21 (17-27)	23 (17-26)	0.06
Total protein (g/kg/day)	1.1 (0.8-1.3)	0.9 (0.8-1.1)	0.9 (0.7-1.1)	<0.01
Animal protein (g/day)	46 (5-64)	37 (27-49)	29 (21-40)	<0.01
Plant protein (g/day)	19 (16-24)	21 (16-25)	23 (18-30)	<0.01
Fat (% of energy)	32 (27-38)	29 (23-33)	26 (21-31)	<0.01
Carbohydrates (% of energy)	51 (44-55)	56 (52-60)	59 (54-65)	<0.01
Fibre (g/1000kcal/day)	7 (5-10)	9 (7-11)	12 (10-14)	<0.01
Potassium (mg/1000 kcal/day)	993 (885-1166)	1039 (839-1418)	1094 (913-1308)	0.11
Phosphorus (mg/1000 kcal/day)	325 (264-434)	322 (269-469)	340 (253-449)	0.9
Food groups (servings per 1000 kcal/day)				
Cereals	4.4 (3.5-5.4)	5.1 (4.5-6.1)	6.3 (5.3-7.0)	<0.01
Fruit	0.7 (0.4-1.2)	1.1 (0.5-2.0)	1.4 (1.1-1.9)	<0.01
Vegetable	0.9 (0.6-1.5)	1.2 (0.8-1.9)	1.8 (1.1-2.7)	0.01
Legumes	0.0 (0.0-0.2)	0 (0-0.2)	0.16 (0.0-0.3)	0.01
Sugar	1.8 (1.2-2.7)	1.0 (0.4-1.9)	0.4 (0.0-0.9)	<0.01
Meat	4.0 (2.9-4.5)	3.3 (2.6-4.6)	2.8 (2.2-3.9)	<0.01
Fat	2.3 (1.6-3.6)	2.1 (1.4-3.2)	1.8 (1.2-2.7)	<0.05
Milk	0.3 (0-0.6)	0.2 (0-0.6)	0.0 (0.0-0.14)	<0.01

González-Ortiz et al. Nutritional status, hyperkalaemia and attainment of energy/protein intake targets in haemodialysis patients following plant-based diets: a longitudinal cohort study. *Nephrology Dialysis Transplantation*. Oct 6, 2020.

Concluding Thoughts

“An ounce of prevention...”





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- 

Thank You!

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Questions?

