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‘Phos’tering a clear message: the evolution of dietary phosphorus management in chronic kidney disease

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Abstract

Phosphorus is a vital nutrient, but disturbances in phosphorus homeostasis are central to chronic kidney disease-mineral and bone disorder. To minimize disturbances, traditional dietary guidance focused on a numerical phosphorus target leading to the exclusion of many healthy foods and implementation challenges. Contemporary phosphorus guidance focuses on dietary source, avoiding additives, and emphasizing low-phosphorus bioaccessibility foods, leading to a more liberal approach. Additional work is needed to demonstrate the efficacy of these contemporary approaches and understand the influence of specific foods, processing, and cooking methods. Unfortunately, patient education using traditional and contemporary strategies may give mixed messages, particularly related to plant-based foods. Thus, greater clarity on the effects of specific foods and dietary patterns may improve phosphorus education. This review aims to discuss the evolution of dietary phosphorus management while highlighting areas for future research that can help move the field towards stronger evidence-based guidance to prevent and treat hyperphosphatemia.

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Introduction

Phosphorus is the second most abundant mineral in the body, with vital functions including structure (e.g., bone hydroxyapatite, cell membranes), cell signaling, and energy metabolism. Loss of kidney function in chronic kidney disease (CKD) is associated with disturbances in phosphorus homeostasis, which is a central component of CKD-mineral and bone disorder (CKD-MBD). CKD-MBD is a systemic disorder of biochemical abnormalities of mineral metabolism, bone alterations, and vascular calcification, leading to greater risk of fractures, cardiovascular events, and mortality.[1] The actions of phosphaturic hormones fibroblast growth factor-23 (FGF23) and parathyroid hormone (PTH) typically prevent hyperphosphatemia until late stages of CKD, when the actions of these hormones are no longer sufficient to maintain phosphorus homeostasis.[1] However, elevated FGF23 and PTH are not benign compensations, as both hormones have detrimental cardiovascular effects,[2,3] and high PTH contributes to bone loss.[4] Moreover, greater all-cause and cardiovascular mortality are observed with higher serum phosphorus levels even within the normal reference range, not only in patients with CKD,[5] but also the general population.[6] Therefore, while CKD-MBD clinical guidelines call for phosphorus lowering interventions for hyperphosphatemia and/or hyperparathyroidism, there is considerable interest in phosphorus lowering earlier in the disease to slow or prevent CKD-MBD.[1]

Serum phosphorus is affected by a complex interplay between the gut, bone, and kidneys. In people with normal kidney function, the kidneys efficiently maintain phosphorus homeostasis and balance by increasing urinary phosphorus excretion in response to increased dietary and/or serum phosphorus loads.[7] For people with kidney failure, dialysis is the main strategy to reduce hyperphosphatemia.[8] However, the removal of phosphorus by dialysis is not sufficient to prevent hyperphosphatemia and additional approaches are necessary, including phosphate binders[9] and limiting dietary phosphorus intake. But, even with implementation of all three of these strategies, many patients continue to have serum phosphorus levels above the recommended level of 5.5 mg/dL (1.8 mmol/L).[5] Importantly, bone metabolism (not just dietary intake and renal excretion) also affects serum phosphorus, where both high and low bone turnover can lead to elevated serum phosphorus (i.e., excess phosphorus released from bone with high turnover, and inadequate phosphorus uptake into bone mineral with low turnover/adynamic bone disease).[4]

Limiting dietary phosphorus is challenging due to its widespread availability in the food supply.[10] Furthermore, high-protein foods are also some of the richest phosphorus sources, putting goals to increase protein and reduce phosphorus intakes at odds for patients receiving dialysis.[11] Traditional dietary guidance for limiting phosphorus intake focused on avoiding foods high in total phosphorus, promoting the intake of low phosphorus-to-protein ratio foods, and prioritizing animal over plant sources of protein.[12] More recent strategies involve a shift in focus to phosphorus bioaccessibility (i.e., the amount of a nutrient that is accessible for digestion) and bioavailability (i.e., the amount of a nutrient that is absorbed, reaches circulation, and is available for use by the body). These strategies include limiting highly-bioaccessible phosphorus-containing food additives, prioritizing plant (lower bioaccessibility) over animal (higher bioaccessibility) protein, and optimizing cooking techniques to reduce phosphorus or to avoid methods that increase phosphorus

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bioaccessibility. The contradictions that exist between these traditional and emerging strategies can create confusion on the appropriate foods and dietary patterns for people with CKD.[13] This review aims to discuss the evolution of dietary phosphorus management while highlighting areas for future research that can help move the field towards stronger evidence-based nutrition guidance to prevent and treat hyperphosphatemia.

The Evolution of Dietary Phosphorus Management

Although many early diets for patients with CKD were low in phosphorus (reviewed previously[14]), the focus on reducing dietary phosphorus intake in CKD accelerated in the 1970s. At the time, cadaver studies showed that people with kidney failure had renal calcium deposition.[15] Animal experiments demonstrated that a low-phosphorus diet could prevent renal calcification and the subsequent increase in inflammation and fibrosis leading to a decline in kidney function.[16] Further experimental and clinical studies showed that a low-phosphorus diet prevented secondary hyperparathyroidism and hyperphosphatemia associated with CKD.[17]

However, much of the early evidence for dietary phosphorus restriction was in the context of low-protein diets. Kopple and Coburn[18] performed metabolic studies in eight individuals with CKD that were prescribed 20 and 40 g/day protein, with phosphorus intake of 564 ± 38 mg/day and 789 ± 43 mg/day, respectively. Serum phosphorus declined after both diets, but phosphorus balance was lower in the diet with 20 g/day protein compared to the 40 g/d diet (96 ± 44 vs. +64 ± 58 mg/day). Similarly, Barsotti et al.[19] studied the effects of a low-protein/lowphosphorus diet compared with a standard protein/phosphorus diet and found that the lowprotein/low-phosphorus diet attenuated kidney function decline, lowered serum phosphorus, and improved secondary hyperparathyroidism. In a *post hoc* analysis of the Modification of Diet in Renal Disease (MDRD) study, compared to a usual protein intake of 1.3 g/kg/d, low-protein and very-low protein diets (0.57 and 0.28 g/kg/d protein, respectively) led to a reduction in urinary phosphorus and a marginally, albeit significant, lower serum phosphorus.[20]

These early studies and others suggested that following a low-protein diet with reduced phosphorus content could help with phosphorus management and may delay kidney function decline. As such, an 800–1000 mg/d phosphorus recommendation became a foundational part of the nutritional guidelines in CKD for individuals in stage 3–5 with serum phosphorus or PTH above a target level.[21] These early diets, characterized by general phosphorus restriction, were difficult to follow. One challenge in adhering to these diets was that food sources of protein, which are often high in phosphorus, were likely to be restricted, potentially increasing the risk of developing protein-energy wasting in people on dialysis.[11] Furthermore, with an overall phosphorus restriction, some food groups were avoided despite their nutrient density, including whole grains, nuts, seeds, legumes, and dairy. This resulted in a highly restrictive diet that limited staple foods commonly consumed in many cultures.

More recent versions of CKD-MBD guidelines have become less restrictive, focusing on trends in biochemistries rather than distinct target values, and treatment goals of lowering serum phosphorus towards the normal range with use of dietary phosphorus restriction,

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phosphate binders, and/or dialysis as applicable.[22–24] Furthermore, recent research has advanced the idea of the need to identify the *hidden* sources of phosphorus (i.e., phosphorus-containing additives) in the food supply. These reports highlighted that: 1) phosphorus intake in Western diets is higher than recommendations, 2) phosphorus-containing additives are abundant in manufactured foods, 3) most databases do not account for the added sources of phosphorus, and 4) this may represent a critical problem for people with CKD.[25,26] Limiting phosphorus-containing additives by educating people on how to read food labels and avoiding these additives was shown to be effective in lowering serum phosphorus by 0.6 mg/dL in people on hemodialysis.[27] Therefore, recent guidelines have also shifted towards considering the phosphorus source when educating people on how to achieve a lower dietary phosphorus intake.[23,24]

Approaches for the Implementation of Dietary Phosphorus Management

Along with changes in guidance to dietary phosphorus, there have also been various approaches developed to help patients and clinicians implement these dietary recommendations (Table 1). Each of the approaches has strengths and weaknesses, but due to differing focuses can create conflicting messages related to specific foods, food groups, or patterns.

Phosphorus Richness vs. Density

The traditional low-phosphorus diet was developed by grouping foods based on their crude phosphorus richness (mg/serving). However, this “per-serving” approach failed to account that total dietary phosphorus intake (mg/day) is more dependent on phosphorus density (mg/kcal), as overall phosphorus intake is regulated based on energy, not servings. The distinction between phosphorus richness and density brings in the concept of energy density (kcal/serving), which may be more useful in clinical practice. Similar foods that differ in energy density (e.g., skim milk (84 kcal/Cup) vs. whole milk (149 kcal/Cup)) can have similar phosphorus richness (263 mg/Cup vs. 251 mg/Cup), while differing as much as two-fold in phosphorus density (315 mg/100 kcal vs. 168 mg/100 kcal). Additionally, certain phosphorus-rich foods that had been restricted on a high-phosphorus diet such as nuts and seeds, are lower in phosphorus density.

Phosphorus-to-Protein Ratio

Since dietary protein intake is important for the management of CKD and prevention of protein-energy wasting particularly once on dialysis treatment, the phosphorus-to-protein ratio is another commonly used approach. Tables with dietary total phosphorus-to-protein ratio have been published widely.[28] Foods with a higher phosphorus-to-protein ratio have been associated with increased risk of mortality in people on maintenance hemodialysis.[29] However, total phosphorus is often listed without reflecting the differences in bioaccessibility, leading to the potential limitation of some food groups, such as whole grains, nuts, seeds, and legumes, potentially losing sight of the overall diet quality.

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Phosphorus Bioaccessibility

It is often cited that animal sources of phosphorus have a bioaccessibility of 40–60% (higher if meat products are enhanced with phosphorus-containing additives), plant sources <50% bioaccessibility, as a majority of the phosphorus is phytate-bound, and finally inorganic sources (i.e., phosphorus-containing additives) >90% (Figure 1).[28] However, it is important to consider the difference between phosphorus bioavailability and bioaccessibility, as mentioned above, to clear some of the confusion and emphasize the critical need for research. While most of the literature refers to the term "bioavailability," the data presented is usually that of "bioaccessibility." Karp et al.[30,31] compared the *in vitro* digestibility (i.e., bioaccessibility) of meat, milk products, plant foods, and beverages. The plant foods explored had the lowest bioaccessibility compared to animal-based foods, processed foods, and beverages, with important variability particularly among plant-based foods. While humans do not express phytase to release the phytate-bound phosphorus, food manufacturers may add phytase in cereals and grain processing. Similarly, cooking, soaking, and fermenting can enhance the amount of bioaccessible phosphorus.[31] While it is likely that foods with higher bioaccessibility lead to higher bioavailability, there is limited data and this is almost certainly not a linear correlation.[32,33]

Moreover, while differences in phosphorus bioaccessibility have been welcomed by the kidney nutrition community, implementation in nutrition education materials has been slow and inconsistent, leading to confusion in people with CKD.[13,34] For example, materials with food lists may still restrict whole grains, legumes, and nuts. Therefore, efforts to improve nutritional education materials for clinicians and patients are needed.

Protein Source

There is considerable interest in plant-based diets in CKD due to several proposed benefits including higher dietary fiber and phytonutrients, lower dietary acid load, and benefits to the gastrointestinal microbiota and cardiovascular disease.[35] For CKD-MBD, the benefits of consuming plant-based vs. animal-based food sources potentially include a lower phosphorus load due to lower bioaccessibility. In a cross-over trial in people with CKD, a 7-day diet with plant-based vs. animal-based protein sources led to lower serum phosphorus and FGF23.[32] Similarly, a 70% plant-protein intervention for one month led to lower urinary phosphorus.[36] However, the current guidelines do not recommend a specific type of protein source due to insufficient evidence. Therefore, research into protein source for hyperphosphatemia management is needed.

Protein-free Foods

Protein-free foods, mainly bread, pasta, and snacks are available mostly in the European Union, but also in other regions including Asia.[37] These products are processed so that the protein (and phosphorus) is removed or lowered, making them an attractive alternative to regular food products, particularly when low-protein diets are recommended. However, availability and cost are important barriers for their use.[37]

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Phosphatemic Index

Another recently studied concept is the phosphatemic index. Similar to the glycemic index, the phosphatemic index measures the effect that foods and meals have on blood phosphorus levels, reflecting phosphorus bioavailability.[33] When healthy participants consumed meals with a low-phosphatemic index for five days, fasting intact PTH and intact FGF-23, but not serum phosphorus, were reduced.[33] However, the phosphatemic index, like the glycemic index, does not account for differences in phosphorus per serving or relative to energy, nor the underlying severity of CKD-MBD. Future studies should assess the phosphatemic index, and potentially the phosphatemic load, in individuals with CKD to determine if it is a useful educational or research tool.

Culinary Techniques for Reducing Phosphorus

Cooking and processing methods can also influence both the amount and bioaccessibility of phosphorus in foods. For example, soaking has been shown to reduce the amount of phosphorus in foods including legumes, vegetables, cereals, and grains, as well as some animal-based foods.[38] Wet-cooking methods and slicing meat have been shown to reduce phosphorus while maintaining protein content.[39]

However, in addition to the quantity of phosphorus present, processing techniques can also influence phosphorus bioaccessibility. In plants, especially cereals and grains, legumes, seeds, and nuts, phosphorus comes largely from phytate. Phytate is mostly indigestible due to the lack of phytase in the small intestine of humans and has limited accessibility due to its likelihood to chelate with other minerals. Processing techniques such as treatment with phytase, soaking, boiling (>140°C) for prolonged periods of time, fermenting, or germinating may increase the release of phosphorus from phytate and increase the proportion of phosphorus containing compounds less likely to chelate, potentially making the remaining phosphorus more bioaccessible for absorption.[40,41]

While culinary techniques including food processing are a potential tool to lower the phosphorus load from the diet, there is sparse data in this area, particularly as it relates to phosphorus bioavailability. Some culinary methods may both lower the overall quantity and increase the accessibility of phosphorus. Therefore, improving our understanding of the net effect of changes in phosphorus quantity, composition, bioaccessibility, and especially bioavailability when food is processed would improve guidance about controlling phosphorus intake.

Food Label Education

A major barrier to effective phosphorus management is that phosphorus is not currently included on the nutrition facts label in the US and other countries, compared to other micronutrients of interest in CKD, such as potassium, sodium, calcium, and iron.[42] As such, food manufacturers are not required to quantify and report the amount of phosphorus included in their products. Additionally, phosphorus-containing additives are widespread in the food supply due to their major food-enhancing benefits.[25] The US Department of Agriculture continuously tests manufactured products for a variety of nutrients, including total phosphorus (i.e., without distinguishing between naturally-occurring vs.

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added phosphorus). However, the proportion of manufactured foods analyzed remains a small portion of the products available in the food supply. An additional limitation is the possible variability even within food categories and manufactured foods with different ingredients. Because of these limitations, nutrition education has been focused on a qualitative recommendation to avoid foods with phosphorus-containing additives (e.g., avoiding ingredients with PHOS or E number in Europe, Australia, and New Zealand) and educating on modified ingredients that can also include added phosphorus (e.g., modified corn starch – an organic phosphorus-containing additives).

The Future of Dietary Phosphorus Management

Despite our increased phosphorus management knowledge (Table 1), there is ample room for innovation from a food, phosphorus physiology, and patient outcomes perspective (Table 2). For example, processed and ultraprocessed foods are major sources of phosphate additives which can be difficult to quantify. Opportunities exist to improve quantification of these additives, awareness, and to limit their use in the food supply. Furthermore, the amount and composition of phosphorus in foods and beverages is variable and can be influenced by growing conditions, processing, and culinary techniques.[42] Expanding our knowledge of how these factors influence bioaccessibility and bioavailability could help clinicians clarify points of disagreement about specific foods or food groups.

Recent studies with the sodium-hydrogen exchanger-3 (NHE3) inhibitor, tenapanor, have highlighted the importance of paracellular intestinal phosphorus absorption.[43] NHE3 inhibition blocks sodium absorption causing conformational changes in the tight junction proteins, leading to a lower phosphorus paracellular diffusion.[43] Focusing on paracellular absorption has physiological relevance, particularly at high-phosphorus consumption levels. While still not FDA approved for hyperphosphatemia, changes in phosphorus management with the addition of this pharmacological agent may be possible in the future. While this reflects an important step in understanding phosphorus physiology, more studies are needed to explore the nuances of intestinal phosphorus absorption in people with CKD. Research on individual-level characteristics that may enhance or limit phosphorus absorption, and the effect of the endogenous microbial phytase, binders, probiotics, synbiotics, and fiber on phosphorus absorption may also be helpful. Recently, it was shown that individuals with CKD 3a and b as well as matched controls had similar intestinal phosphorus absorption using radiolabeled ^{33}P despite different serum levels of 1,25-dihydroxy vitamin D.[44] This technique offers unique opportunities to broaden our understanding of intestinal phosphorus absorption.[45]

Finally, dietary phosphorus management is complex and needs further patient-centered research. While the association of hyperphosphatemia and poor clinical outcomes has been reported extensively, the effect of treatments to lower serum phosphorus on hard outcomes has been inconsistent. Ongoing pragmatic trials (HiLo- NCT04095039 and PHOSPHATE-a NCT03573089) are underway to study if tight phosphorus control vs. liberalized management is better for hard and patient-centered outcomes. Furthermore, the practice of providing generic education materials containing lists of foods high and low in phosphorus can be overly simplistic, overly restrictive, and often does not consider

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competing nutritional requirements. Despite good intentions and support from the kidney nutrition community, educational materials currently available may also provide conflicting messages, partly due to sparse and incomplete data on bioaccessibility of food products.[13,34] Individualized assessment and tailored nutrition counselling is more likely to be effective in reducing phosphorus intake and should be encouraged. Advances in technology including social media, mobile applications, and telehealth offer the potential to incorporate advancing knowledge on phosphate additives, physiology, source, and food processing to help make phosphorus management more patient-centered and encourage self-management.[46,47] Expanding our ability to optimally incorporate these tools into practice will be an important area to advance kidney nutrition.

Conclusions

Phosphorus is a vital nutrient, but when kidney function declines it becomes challenging to manage due to its ubiquitous nature in our food supply. Over time, dietary education aimed at preventing and treating hyperphosphatemia has shifted from focusing primarily on the numerical quantity of phosphorus to considering other factors that may influence phosphorus load. This shift has created inconsistent messaging that can be confusing and frustrating for individuals with CKD. Therefore, it is imperative that clinicians and people with CKD work together to promote a clear message on dietary phosphorus management appropriate for the stage of CKD that takes into consideration an individual's goals, culture, social, and dietary preferences as well as overall diet quality.

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References

1. Kidney Disease: Improving Global Outcomes CKDMBDUWG. KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). Kidney Int Suppl (2011). Jul 2017;7(1):1–59. doi:10.1016/j.kisu.2017.04.001 [PubMed: 30675420]
2. Faul C, Amaral AP, Oskouei B, et al. FGF23 induces left ventricular hypertrophy. J Clin Invest. Nov 2011;121(11):4393–408. doi:10.1172/JCI46122 [PubMed: 21985788]
3. Lishmanov A, Dorairajan S, Pak Y, Chaudhary K, Chockalingam A. Elevated serum parathyroid hormone is a cardiovascular risk factor in moderate chronic kidney disease. Int Urol Nephrol. Apr 2012;44(2):541–7. doi:10.1007/s11255-010-9897-2 [PubMed: 21327525]

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

4. Martin KJ, Gonzalez EA. Metabolic bone disease in chronic kidney disease. J Am Soc Nephrol. Mar 2007;18(3):875–85. doi:10.1681/ASN.2006070771 [PubMed: 17251386]

5. Kestenbaum B, Sampson JN, Rudser KD, et al. Serum phosphate levels and mortality risk among people with chronic kidney disease. J Am Soc Nephrol. Feb 2005;16(2):520–8. doi:10.1681/ASN.2004070602 [PubMed: 15615819]

6. Dhingra R, Sullivan LM, Fox CS, et al. Relations of serum phosphorus and calcium levels to the incidence of cardiovascular disease in the community. Arch Intern Med. May 14 2007;167(9):879–85. doi:10.1001/archinte.167.9.879 [PubMed: 17502528]

7. Scanni R, vonRotz M, Jehle S, Hulter HN, Krapf R. The human response to acute enteral and parenteral phosphate loads. J Am Soc Nephrol. Dec 2014;25(12):2730–9. doi:10.1681/ASN.2013101076 [PubMed: 24854273]

8. Kuhlmann MK. Phosphate elimination in modalities of hemodialysis and peritoneal dialysis. Blood Purif. 2010;29(2):137–44. doi:10.1159/000245640 [PubMed: 20093819]

9. Doshi SM, Wish JB. Past, Present, and Future of Phosphate Management. Kidney Int Rep. Apr 2022;7(4):688–698. doi:10.1016/j.ekir.2022.01.1055 [PubMed: 35497793]

10. McClure ST, Chang AR, Selvin E, Rebholz CM, Appel LJ. Dietary Sources of Phosphorus among Adults in the United States: Results from NHANES 2001–2014. Nutrients. Jan 30 2017;9(2)doi:10.3390/nu9020095

11. Shinaberger CS, Greenland S, Kopple JD, et al. Is controlling phosphorus by decreasing dietary protein intake beneficial or harmful in persons with chronic kidney disease? Am J Clin Nutr. Dec 2008;88(6):1511–8. doi:10.3945/ajcn.2008.26665 [PubMed: 19064510]

12. Clinical practice guidelines for nutrition in chronic renal failure. K/DOQI, National Kidney Foundation. Am J Kidney Dis. Jun 2000;35(6 Suppl 2):S17–S104. doi:10.1053/ajkd.2000.v35.aajkd03517 [PubMed: 10895784]

13. Begum MM, Biruete A, Kistler BM, St-Jules D, Meade A. 154: A SYSTEMATIC REVIEW OF ONLINE MATERIALS ON DIETARY MANAGEMENT OF HYPERPHOSPHATEMIA IN PEOPLE WITH CHRONIC KIDNEY DISEASE. Am J Kidney Dis. 79(4):S47.

14. Hensley MK. Historical Perspective of Nutrition in Kidney Disease. In: Byham-Gray LD, Chertow GM, Burrowes JD, eds. Nutrition in Kidney Disease. Humana Press; 2008:17–33.

15. Kuzela DC, Huffer WE, Conger JD, Winter SD, Hammond WS. Soft tissue calcification in chronic dialysis patients. Am J Pathol. Feb 1977;86(2):403–24. [PubMed: 836675]

16. Ibels LS, Alfrey AC, Haut L, Huffer WE. Preservation of function in experimental renal disease by dietary restriction of phosphate. N Engl J Med. Jan 19 1978;298(3):122–6. doi:10.1056/NEJM197801192980302 [PubMed: 619240]

17. Slatopolsky E, Caglar S, Gradowska L, Canterbury J, Reiss E, Bricker NS. On the prevention of secondary hyperparathyroidism in experimental chronic renal disease using “proportional reduction” of dietary phosphorus intake. Kidney Int. Sep 1972;2(3):147–51. doi:10.1038/ki.1972.84 [PubMed: 4669450]

18. Kopple JD, Coburn JW. Metabolic studies of low protein diets in uremia. II. Calcium, phosphorus and magnesium. Medicine (Baltimore). Nov 1973;52(6):597–607. doi:10.1097/00005792-197311000-00005 [PubMed: 4748593]

19. Barsotti G, Morelli E, Giannoni A, Guiducci A, Lupetti S, Giovannetti S. Restricted phosphorus and nitrogen intake to slow the progression of chronic renal failure: a controlled trial. Kidney Int Suppl. Dec 1983;16:S278–84. [PubMed: 6376918]

20. Newsome B, Ix JH, Tighiouart H, et al. Effect of protein restriction on serum and urine phosphate in the modification of diet in renal disease (MDRD) study. Am J Kidney Dis. Jun 2013;61(6):1045–6. doi:10.1053/j.ajkd.2013.01.007 [PubMed: 23415016]

21. National Kidney F. K/DOQI clinical practice guidelines for bone metabolism and disease in chronic kidney disease. Am J Kidney Dis. Oct 2003;42(4 Suppl 3):S1–201. [PubMed: 14520607]

22. Kidney Disease: Improving Global Outcomes CKDMBDWG. KDIGO clinical practice guideline for the diagnosis, evaluation, prevention, and treatment of Chronic Kidney Disease-Mineral and Bone Disorder (CKD-MBD). Kidney Int Suppl. Aug 2009;(113):S1–130. doi:10.1038/ki.2009.188

23. Ketteler M, Block GA, Evenepoel P, et al. Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease-Mineral and Bone Disorder: Synopsis of the Kidney Disease: Improving

Author Manuscript Author Manuscript Author Manuscript Author Manuscript

Global Outcomes 2017 Clinical Practice Guideline Update. Annals of internal medicine. Mar 20 2018;168(6):422–430. doi:10.7326/M172640 [PubMed: 29459980]

24. Ikizler TA, Burrowes JD, Byham-Gray LD, et al. KDOQI Clinical Practice Guideline for Nutrition in CKD: 2020 Update. Am J Kidney Dis. Sep 2020;76(3S1):S1–S107. doi:10.1053/j.ajkd.2020.05.006 [PubMed: 32829751]
25. Uribarri J, Calvo MS. Hidden sources of phosphorus in the typical American diet: does it matter in nephrology? Semin Dial. May-Jun 2003;16(3):186–8. doi:10.1046/j.1525-139x.2003.16037.x [PubMed: 12753675]
26. Calvo MS, Moshfegh AJ, Tucker KL. Assessing the health impact of phosphorus in the food supply: issues and considerations. Adv Nutr. Jan 1 2014;5(1):104–13. doi:10.3945/an.113.004861 [PubMed: 24425729]
27. Sullivan C, Sayre SS, Leon JB, et al. Effect of food additives on hyperphosphatemia among patients with end-stage renal disease: a randomized controlled trial. JAMA. Feb 11 2009;301(6):629–35. doi:10.1001/jama.2009.96 [PubMed: 19211470]
28. Kalantar-Zadeh K, Gutekunst L, Mehrotra R, et al. Understanding sources of dietary phosphorus in the treatment of patients with chronic kidney disease. Clin J Am Soc Nephrol. Mar 2010;5(3):519–30. doi:10.2215/CJN.06080809 [PubMed: 20093346]
29. Noori N, Kalantar-Zadeh K, Kovesdy CP, Bross R, Benner D, Kopple JD. Association of dietary phosphorus intake and phosphorus to protein ratio with mortality in hemodialysis patients. Clin J Am Soc Nephrol. Apr 2010;5(4):683–92. doi:10.2215/CJN.08601209 [PubMed: 20185606]
30. Karp H, Ekholm P, Kemi V, Hirvonen T, Lamberg-Allardt C. Differences among total and in vitro digestible phosphorus content of meat and milk products. J Ren Nutr. May 2012;22(3):344–9. doi:10.1053/j.jrn.2011.07.004 [PubMed: 21978846]
31. Karp H, Ekholm P, Kemi V, et al. Differences among total and in vitro digestible phosphorus content of plant foods and beverages. J Ren Nutr. Jul 2012;22(4):416–22. doi:10.1053/j.jrn.2011.04.004 [PubMed: 21741857]
32. Moe SM, Zidehsarai MP, Chambers MA, et al. Vegetarian compared with meat dietary protein source and phosphorus homeostasis in chronic kidney disease. Clin J Am Soc Nephrol. Feb 2011;6(2):257–64. doi:10.2215/CJN.05040610 [PubMed: 21183586]
33. Narasaki Y, Yamasaki M, Matsuura S, et al. Phosphatemic Index Is a Novel Evaluation Tool for Dietary Phosphorus Load: A Whole-Foods Approach. J Ren Nutr. Nov 2020;30(6):493–502. doi:10.1053/j.jrn.2020.02.005 [PubMed: 32778471]
34. Picard K, Razcon-Echeagaray A, Griffiths M, Mager D, Richard C. Currently available handouts for low phosphorus diets in chronic kidney disease continue to restrict plant proteins and minimally processed dairy products. J Ren Nutr. Apr 22 2022;doi:10.1053/j.jrn.2022.04.002
35. Carrero JJ, Gonzalez-Ortiz A, Avesani CM, et al. Plant-based diets to manage the risks and complications of chronic kidney disease. Nat Rev Nephrol. Jun 11 2020;doi:10.1038/s41581-020-0297-2
36. Moorthi RN, Armstrong CL, Janda K, Ponsler-Sipes K, Asplin JR, Moe SM. The effect of a diet containing 70% protein from plants on mineral metabolism and musculoskeletal health in chronic kidney disease. Am J Nephrol. 2014;40(6):582–91. doi:10.1159/000371498 [PubMed: 25613675]
37. D'Alessandro C, Rossi A, Innocenti M, et al. Dietary protein restriction for renal patients: don't forget protein-free foods. J Ren Nutr. Sep 2013;23(5):367–71. doi:10.1053/j.jrn.2012.12.006 [PubMed: 23434390]
38. Vahia de Abreu DB, Picard K, Simas Torres Klein MR, Marino Gadas O, Richard C, Barreto Silva MI. Soaking to reduce potassium and phosphorus content of foods. J Ren Nutr. Jul 5 2022;doi:10.1053/j.jrn.2022.06.010
39. Ando S, Sakuma M, Morimoto Y, Arai H. The Effect of Various Boiling Conditions on Reduction of Phosphorus and Protein in Meat. J Ren Nutr. Nov 2015;25(6):504–9. doi:10.1053/j.jrn.2015.05.005 [PubMed: 26163744]
40. Schlemmer U, Frolich W, Prieto RM, Grases F. Phytate in foods and significance for humans: food sources, intake, processing, bioavailability, protective role and analysis. Mol Nutr Food Res. Sep 2009;53 Suppl 2:S330–75. doi:10.1002/mnfr.200900099 [PubMed: 19774556]

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41. Morris E, Hill D. Inositol Phosphate Content of Selected Dry Beans, Peas, and Lentils, Raw and Cooked. JOURNAL OF FOOD COMPOSITION AND ANALYSIS. 1996;9(1):2–12.

42. Calvo MS, Uribarri J. Perspective: Plant-based Whole-Grain Foods for Chronic Kidney Disease: The Phytate-Phosphorus Conundrum. Adv Nutr. Jun 30 2021;doi:10.1093/advances/nmab066

43. King AJ, Siegel M, He Y, et al. Inhibition of sodium/hydrogen exchanger 3 in the gastrointestinal tract by tenapanor reduces paracellular phosphate permeability. Sci Transl Med. Aug 29 2018;10(456)doi:10.1126/scitranslmed.aam6474

44. Stremke ER, Wiese GN, Moe SM, Wastney ME, Moorthi RN, Hill Gallant KM. Intestinal Phosphorus Absorption in Moderate CKD and Healthy Adults Determined Using a Radioisotopic Tracer. J Am Soc Nephrol. Aug 2021;32(8):2057–2069. doi:10.1681/ASN.2020091340 [PubMed: 34244325]

45. Hill Gallant KM, Vorland CJ. Intestinal phosphorus absorption: recent findings in translational and clinical research. Curr Opin Nephrol Hypertens. Jul 1 2021;30(4):404–410. doi:10.1097/MNH.0000000000000719 [PubMed: 34027902]

46. Biruete A, Kistler BM, Kalantar-Zadeh K, Moore LW. Kidney Nutrition in the Era of Social Media: Bridging the Gap of Nutrition Education and Kidney Health Literacy by Leveraging Resources of Social Networking. J Ren Nutr. Sep 13 2022;doi:10.1053/j.jrn.2022.09.002

47. St-Jules DE, Hu L, Woolf K, et al. An Evaluation of Alternative Technology-Supported Counseling Approaches to Promote Multiple Lifestyle Behavior Changes in Patients With Type 2 Diabetes and Chronic Kidney Disease. J Ren Nutr. Jun 22 2022;doi:10.1053/j.jrn.2022.05.006

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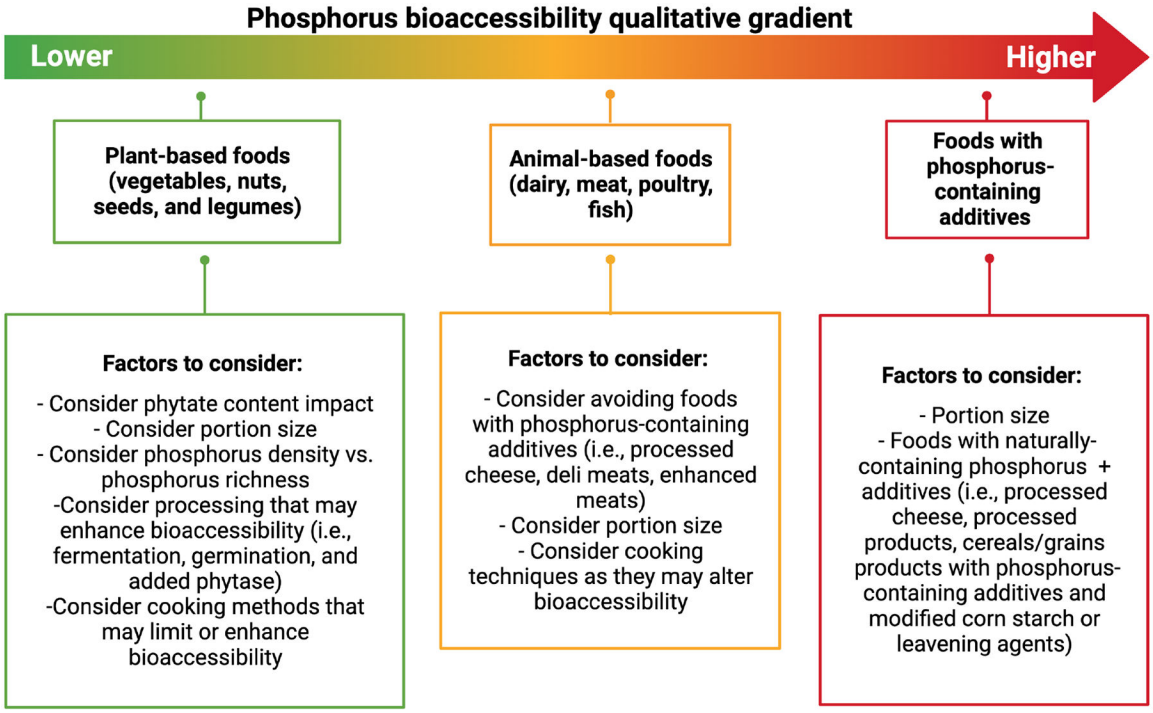

Figure 1: Phosphorus bioaccessibility qualitative gradient.

Foods can be qualitatively classified as having lower phosphorus bioaccessibility (i.e., plant-based foods), moderate phosphorus bioaccessibility (i.e., animal-based foods), and higher phosphorus bioaccessibility (i.e., foods with phosphorus-containing additives). However, within phosphorus bioaccessibility categories there are factors that may limit or enhance phosphorus bioaccessibility that should be considered.

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Table 1.

Advantages and Disadvantages of the Available Approaches for the Implementation of Dietary Phosphorus Management

Technique (Description)	Advantages	Disadvantages/Limitations
Phosphorus richness vs. density Classify foods based on total phosphorus richness (mg/serving, traditional approach) vs. density (mg/kcal, adds that intake is regulated based on energy).	✓ Exemplifies foods in the same food category may have important variation (i.e., skim vs. whole milk). ✓ Traditionally phosphorus-rich foods have low phosphorus density (i.e., nuts and seeds).	✘ Does not take into consideration phosphorus bioaccessibility.
Phosphorus-to-protein ratio Classifies foods based on the phosphorus-to-protein ratio [often <10–12 mg/g]	✓ Prioritizes foods that provide protein over phosphorus content, particularly relevant for dialysis patients.	✘ Most tables do not take into consideration phosphorus bioaccessibility. ✘ Tends to limit plant-based foods, including whole grains, nuts, seeds, legumes, and dairy.
Phosphorus bioaccessibility Classifies foods as based on food bioaccessibility (plant-based sources <50% bioaccessible, animal-based sources 40–60% bioaccessible, and phosphorus-containing additives >90%)	✓ Promotes the consumption of plant-based foods due to the phytate-bound phosphorus. ✓ Better represents the bioaccessible fraction of dietary phosphorus, which may be clinically relevant. ✓ Promotes liberalization of diet to incorporate plant-based foods.	✘ Based on *in vitro* digestibility studies. ✘ Relation to bioavailability is unclear. ✘ Does not take into consideration the amount of phosphorus.
Protein source Prioritizes plant-based sources of protein based on bioaccessibility and other nutrient content	✓ Prioritizes intake of plant-based vs. animal- based sources of protein. ✓ Short-term clinical trials suggest that plant-based vs. animal-based foods beneficially impact phosphorus homeostasis.	✘ Limited long-term data. ✘ Lack of understanding about definition of plant- based diets may lead to over-restriction of some protein sources.
Protein-free foods	✓ Alternatives to regular foods (e.g., bread, pasta, and snacks) useful with low-protein diets.	✘ Cost ✘ Limited availability
Phosphatemic index Measures the impact of foods on postprandial blood phosphorus levels	✓ May have potential to be used like glycemic index with additional research.	✘ Data is limited to single pilot study of healthy adults. ✘ Unclear the interindividual variability on the phosphatemic response. ✘ Does not account for phosphorus content of foods.
Culinary techniques for reducing food phosphorus content Focuses on techniques that alter quantity and/or bioaccesibility of phosphorus in food	✓ Can be widely applied to a variety of foods, allowing patients to maintain relatively normal intakes. ✓ Wet-cooking methods reduce the production of advanced glycation end-products. ✓ Also leaches other minerals that may be harmful.	✘ Requires time and resources, including control of preparation of foods. ✘ May reduce palatability of some foods. ✘ May lose beneficial nutrients.
Food Label Education Qualitative education on limiting foods with phosphorus-containing additives (by avoiding ingredients	✓ Has been shown clinically to be an effective technique to reduce serum phosphorus in patients on hemodialysis.	✘ Phosphorus amount is not included in the Nutrition Facts Label.

Technique (Description)	Advantages	Disadvantages/Limitations
with PHOS or E numbers) and modified ingredients		✘ There may be variability within food categories and ingredients.

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Table 2.

Research Priorities on the Dietary Management of Hyperphosphatemia

What is the impact of food characteristics, processing, and culinary techniques on phosphorus homeostasis and phosphorus balance?
What is the impact of foods and meals with various phosphorus bioaccessibility on phosphorus homeostasis and phosphorus balance?
What are the individual-level factors that may enhance or limit phosphorus absorption?
How does endogenous microbial phytase impact phosphorus absorption and overall phosphorus balance?
What is the impact of tight phosphorus control vs. liberalized management on hard and patient-centered outcomes?
What is the impact of tight vs. liberalized management on overall dietary patterns in people CKD?