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## A PUBLIC HEALTH APPROACH TO ADDRESSING HYPERPHOSPHATEMIA AMONG DIALYSIS PATIENTS

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## Abstract

Elevated serum phosphorus levels are a major source of morbidity and mortality for the 350,000 Americans receiving chronic dialysis treatment. Despite the widespread application of medical and behavioral interventions, the prevalence of hyperphosphatemia remains exceedingly high. At first glance, a public health perspective may seem inappropriate for addressing a disorder of mineral metabolism among patients receiving a life sustaining treatment. However, we analyzed this topic from a public health perspective and identified many opportunities to improve the management of hyperphosphatemia, including (a) media and cultural messages about food, (b) availability of appropriate foods and medications, (c) physical structures such as the location of products in grocery stores, and (d) social structures such as food labeling laws.

> Elevated serum phosphorus levels are a major source of morbidity and mortality for the 350,000 Americans receiving chronic dialysis treatment. Current approaches to managing hyperphosphatemia attempt to optimize dietary phosphorus intake, medication usage, and dialysis dose.[1,2] Despite the widespread application of these medical and behavioral interventions, the prevalence of hyperphosphatemia remains exceedingly high.[3–6]

> At first glance, a public health perspective may seem inappropriate for addressing a disorder of mineral metabolism among patients receiving a life sustaining treatment. However, we analyzed this topic from a public health perspective and identified many opportunities to improve the management of hyperphosphatemia. Specifically, we used a framework that focused on (a) media and cultural messages about food, (b) availability of appropriate foods and medications, (c) physical structures such as the location of products in grocery stores, and (d) social structures such as food labeling laws.[7] Developing interventions that address these

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contextual factors may not only reduce the burden of hyperphosphatemia among dialysis patients but also serve as a model for addressing other medical problems.

## Background and current approaches to managing hyperphosphatemia

Phosphorus is a major constituent of bone, is abundant in most tissues, and is involved in numerous metabolic processes. Because phosphorus is readily available in many foods, the kidneys must excrete large amounts of this mineral to maintain balance. Since dialysis patients have virtually no kidney function, phosphorus tends to accumulate.[8] Excess phosphorus forms complexes with calcium which deposit in blood vessels and other soft tissues.[9–11] Calcium-phosphorus deposition in the coronary arteries correlates with and likely contributes to the development of atherosclerotic cardiovascular disease.[12,13] Hyperphosphatemia appears to be a key dialysis-specific cardiovascular disease risk factor, and elevated phosphorus levels are independently associated with a 20–40% increased risk of both all-cause death and coronary disease death among dialysis patients.[3,14,15] Elevated phosphorus levels also stimulate parathyroid hormone which causes bone loss, decreased bone density, fibrosis, fractures, and bone pain.[16–18] In a recent study, a majority of long-term dialysis patients had evidence of severe bone disease.[3]

Several dietary and metabolic factors present among dialysis patients may contribute to hyperphosphatemia, including (a) excess intake of high phosphorus foods, (b) increased intestinal absorption of phosphorus, (c) inadequate removal of phosphorus by phosphorus binding medication, dialysis, and residual renal function, and (d) release of phosphorus from bone and tissue breakdown (Table 1). High intakes of foods naturally high in phosphorus, particularly meats, dairy products, whole grains, and nuts, may lead to elevated phosphorus levels. In addition, phosphorus-containing additives are frequently added to processed foods, particularly meats, cheeses, baked goods, and beverages.[19] Vitamin D analogs are administered to dialysis patients to suppress parathyroid hormone but can increase intestinal absorption of phosphorus.[20] Phosphorus binding medication attaches to dietary phosphorus and prevents intestinal absorption, but underprescription of or non-adherence with binders may impair the effectiveness of this approach.[21–23] An inadequate dose of dialysis or a lack of residual renal function will limit the removal of phosphorus from the body. Finally, release of phosphorus from bone and protein, as results from severe hyperparathyroidism, catabolism, and acidosis can increase serum phosphorus levels.[24–27]

Current approaches to managing hyperphosphatemia attempt to optimize dietary phosphorus intake, medication usage, and dialysis dose (Table 1).[1,2] Renal dietitians regularly counsel patients to limit dietary intake of phosphorus to 800–1000 mg/day while nephrologists monitor and optimize dialysis dose[1] Several new medications are also available, including vitamin D analogues and phosphorus binders that may have fewer adverse effects compared to older medications as well as calcimimetic medications that suppress parathyroid hormone levels. [20,25,28] An understanding of the pathophysiology of hyperphosphatemia, the widespread use of targeted medical and behavioral interventions, and the availability of newer medications should all be reasons for optimism. However, one-third to one-half of dialysis patients continue to have serum phosphorus concentrations above the 5.5 mg/dL (1.78 mmol/L) level recommended by practice guidelines.[1,3–6]

## Public health approach to understanding hyperphosphatemia

While current approaches to management of hyperphosphatemia focus on developing new medical treatments (e.g. vitamin D analogs), optimizing patient behavior (e.g. to limit dietary phosphorus intake), or optimizing provider behavior (e.g. to increase binder prescription), public health approaches would focus more on environmental factors (Table 2). Public health approaches acknowledge the importance of medical advances and behavioral interventions but

emphasize the interaction between human behavior and the environmental context in which it occurs.[7] These contextual factors include media and cultural messages, availability of health-related products, physical structures that influence the likelihood of health-related behavior, and social structures that facilitate or restrict health-related behavior.[29] Interventions based on an understanding of such contextual factors have been effective in addressing many health problems, most notably tobacco use in the United States. Mass media efforts to address tobacco use have included bans on television advertising of cigarettes, antismoking exhortations, and attacks on the tobacco products can be sold and by enforcing minimum age laws. Physical structural interventions have included proscriptions on smoking in many outdoor and indoor locations while social structural interventions have included taxing cigarettes to make them less affordable.[7] In the following paragraphs, we use this public health framework to analyze hyperphosphatemia and identify opportunities to improve its management.

Pervasive media and cultural messages encourage the consumption of foods containing high amounts of phosphorus. The food, beverage, and restaurant industry spends over \$11 billion annually on advertising.[30] Much of this advertising promotes foods that are high in phosphorus, particularly processed meats, soft drinks, and baked goods. Over the last two decades, the consumption of these products has increased dramatically in the general population.[31] By contrast, government efforts to encourage consumption of fruits and vegetables ("5 A Day" programs) have a budget that is 3 orders of magnitude smaller, or about \$10 million annually.[30] Moreover, American cultural preferences emphasize meat and dairy products as key components of breakfast, lunch, and dinner. As a result, the average American consumes more than five servings of meat and dairy products every day.[31]

The availability of products is a key determinant of nutrition behavior since readily available products are more likely to be purchased and consumed.[7] Processed meats, baked goods, and soft drinks are all readily available at large grocery stores, small convenience stores, sit-down restaurants, and fast food restaurants. Moreover, food portion sizes have increased considerably over the years, a phenomenon referred to as super-sizing. For example, McDonald's now offers hamburgers that contain 5 times more beef than the original size and soft drinks that are 6 times larger than the original size.[32] Alternative food choices that contain lower amounts of phosphorus may not be available at fast food restaurants or at small, inner-city convenience stores. Even when they are available, such products may be more expensive.[33,34] For example, fruits and vegetables are several times more expensive than other categories of foods on a cost per calorie basis.[35] The high cost of phosphorus binding medication, particularly newer drugs, may be another impediment to the management of hyperphosphatemia.[36]

Physical structures that influence dietary intake include the location of food stores, restaurants, farmer's markets, and vending machines, as well as the location of products within stores. Many dialysis patients have a low socioeconomic status or are members of minority groups. Previous research indicates that poor or minority neighborhoods generally have few or no large grocery stores but many fast food restaurants and convenience stores.[37,38] Moreover, even when grocery stores are present, the most visible locations in the stores tend to feature processed foods and soft drinks. This occurs both because these products are highly profitable for grocery stores and because food manufacturers make payments to stores, called slotting allowances, in exchange for shelf space in the most visible locations such as the ends of aisles.[39] It is perhaps not surprising that about half of dialysis patients consume more than the recommended amounts of phosphorus.[1,40,41]

Social structures include formal laws and policies, social supports, and social services. The Food and Drug Administration requires products to carry a nutrition facts label that lists the content of several nutrients that are important for dialysis patients to monitor, including

calories, fat, sodium, protein, and calcium. However, phosphorus content is not listed on these labels. This makes it nearly impossible for patients to know how much phosphorus they are ingesting, especially since phosphorus-containing additives are often added to enhance the flavor and stability of processed foods .[19] The phosphorus in these additives is more bioavailable than that in foods naturally high in phosphorus, and such additives can add 1000 mg to daily phosphorus intake depending on an individual's food choices.[42,43] In previous work, we found that one-fourth to one-half of dialysis patients need help with shopping or cooking. However, many patients don't have family members to help, and social services are often lacking in their communities.[44,45] This forces patients to rely on processed and junk food which tend to contain large amounts of phosphorus.

## Possible public health interventions

Unlike current approaches that target patient or provider behavior (Table 1), public health interventions target communities and populations (Table 2). Pervasive advertising of high phosphorus foods could be addressed by restricting or modifying advertising practices, as has been done in some European countries to limit the advertising of junk food to children.[46] Altering contextual factors such as food marketing may also help to modify societal preferences for specific foods over time.[7] For example, vigorous public marketing campaigns to promote fruits and vegetables may alter food preferences. The availability of high phosphorus foods could be reduced by taxing junk foods and by requiring larger sizes to be priced in a manner that is proportional to size, thereby eliminating the financial incentive to purchase super-sized portions.[47,48] Eliminating current subsidies for the constituents of junk and processed foods (grains, meats, sweeteners, dairy products) and subsidizing healthier alternatives may increase the availability of low phosphorus products.[49] Expanding health insurance coverage for medications and using Medicare's purchasing power to negotiate lower drug prices would help patients obtain phosphorus binding medication. Providing tax breaks for large grocery stores that locate in poor and minority neighborhoods and restricting junk food to less visible locations within stores would also improve the physical structures that influence dietary intake. Requiring phosphorus content on nutrition facts labels may encourage manufacturers to limit the use of phosphorus additives and may help patients to monitor and reduce their phosphorus intake. For example, many manufacturers have already eliminated or greatly reduced the trans fat content of their products in response to recently updated labeling guidelines.[50] We urge national organizations such as the National Kidney Foundation to lobby for labeling changes. Finally, expanding social services may help patients who need assistance with shopping or cooking.

Several issues must be considered in advocating for a public health approach to hyperphosphatemia among dialysis patients. First, is the number of dialysis patients large enough to warrant a public health approach? Public health approaches have traditionally targeted problems that are relevant to large segments of the population. The 350,000 American dialysis patients represent a relatively small proportion of the total population. However, end stage renal disease patients suffer from a disproportionate disease burden and account for about 7% of Medicare expenditures.[51] In addition, hyperphosphatemia may contribute to cardiovascular and bone disease among the 10 million Americans with moderate kidney disease.[2,52] Thus, a public health approach to addressing hyperphosphatemia may not only reduce the disease burden of dialysis patients but also benefit large numbers of individuals with less severe kidney disease.

Second, what will be the impact of such public health interventions on the general population? There is some evidence that the use of phosphorus-containing food additives may lower bone density and increase the likelihood of fractures among individuals with normal renal function. [53] Therefore, reducing phosphorus intake may reduce the prevalence of bone-related

problems among all Americans. In addition, many of the public health approaches we propose (Table 2) may have a beneficial effect on nutrition-related conditions in the general population. For example, reducing calorie and fat intake may reduce the prevalence of obesity, type II diabetes mellitus, and cardiovascular disease.

Third, is a public health approach feasible? While implementing public health interventions to address hyperphosphatemia may appear to be daunting, similar approaches have already been used to reduce tobacco use and are being actively considered to address the obesity epidemic. In fact, public health interventions to address hyperphosphatemia may be more successful if part of a larger, integrated campaign to tackle the contextual determinants of common health problems. Moreover, many food companies have succeeded economically by marketing low fat, organic, and/or low sodium products. Similar efforts to develop and market low phosphorus products may be both profitable for manufacturers and beneficial for individuals with renal disease.

Addressing upstream contributors to hyperphosphatemia doesn't mean abandoning efforts to optimize patient and provider behavior or to develop new medical treatments. It is likely that these medical and behavioral approaches will be more successful if accompanied by improvements in media and cultural messages, availability, physical structures, and social structures. Integrating medical/behavioral and public health approaches to reducing hyperphosphatemia may also serve as a model for addressing other medical problems.

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## Table 1

Medical and behavioral approach to hyperphosphatemia

Category	Mechanisms	Possible Medical/Behavioral Interventions
Intake	• Excess intake of phosphorus	Encourage dietary adherence
Absorption	<ul> <li>Vitamin D supplementation stimulates intestinal phosphorus absorption</li> </ul>	• Decrease dose or use less hyperphosphatemic vitamin D analog
Removal	<ul> <li>Underprescription of phosphorus-binder</li> </ul>	<ul> <li>Increase prescription of phosphorus-binder</li> </ul>
	<ul> <li>Non-adherence with phosphorus-binder</li> </ul>	<ul> <li>Encourage medication adherence</li> </ul>
	Inadequate dialysis dose	<ul> <li>Increase dialysis dose</li> </ul>
	<ul> <li>Lack of residual renal function</li> </ul>	<ul> <li>Increase dialysis dose</li> </ul>
Release	<ul> <li>Severe hyperparathyroidism</li> </ul>	<ul> <li>Medication to suppress parathyroid or surgical removal</li> </ul>
	High protein catabolic rate	<ul> <li>Ensure adequate caloric intake and address any underlying cause of catabolism</li> </ul>
	Acidosis	Administer bicarbonate

## Table 2

## Public health approach to hyperphosphatemia

Category	Mechanisms	Possible Public Health Interventions
Media and Cultural Messages	Advertising of high phosphorus foods	Restrict or modify advertising
5	<ul> <li>Cultural preference for meats, dairy products</li> </ul>	<ul> <li>Promote healthier diets</li> </ul>
Availability	<ul> <li>High phosphorus products readily available and super-sized</li> </ul>	• Tax or otherwise restrict junk food sales and super-sizing
	<ul> <li>Low phosphorus products less available and expensive</li> </ul>	<ul> <li>Subsidize healthier products, discontinue subsidies for junk foods</li> </ul>
	• High cost of phosphorus binders	• Expand health insurance coverage of medications, negotiate with drug companies for lower prices
Physical Structures	• Few large grocery stores in minority and poor neighborhoods	• Tax breaks for grocery stores in minority and poor neighborhoods
	<ul> <li>High phosphorus products in more visible locations within stores</li> </ul>	<ul> <li>Subsidize healthier products, restrict junk food to less visible locations</li> </ul>
Social Structures	<ul><li>Phosphorus content not on nutrition labels</li><li>Lack of help for shopping and cooking</li></ul>	<ul> <li>Require phosphorus content on labels</li> <li>Expand social supports and social services</li> </ul>