

# Patient Perspectives: The Effects of Contemporary Phosphorus Management on Quality of Life

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## Article Info

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## Abstract

Effective regulation of phosphate levels is essential for managing the health of the nearly 600,000 dialysis patients in the United States, over 43% of whom exceed the recommended serum phosphate target of 5.5 mg/dL. Current phosphate binders present significant challenges, including large pills that are hard to swallow, pills that require thorough chewing, which may be difficult for patients with impaired dentition, frequent dosing, gastrointestinal adverse effects, and the need to take them while in public, which can lead to non-adherence and reduced social eating. Coupled with stringent dietary restrictions, confusion over administration timing, and high medication cost, these factors severely compromise patients' quality of life. Addressing these barriers requires a comprehensive strategy: clinicians must recognize the difficulties faced by patients, bridge knowledge gaps regarding dietary phosphorus, and explore novel therapies that reduce pill size and burden without sacrificing efficacy. By mitigating these challenges, healthcare providers can enhance treatment experiences, strengthen patient-clinician relationships, and ultimately improve overall quality of life for dialysis patients. With a focus on patients' perspectives, this review highlights the critical need for patient-centered approaches in phosphate management to ensure better clinical outcomes and patient satisfaction.

## Practitioner Points

For patients, the challenges of phosphate binder therapy (e.g., large pill size, high pill number, difficulties with taking binders in public) may lead to non-adherence, which may in turn lead to poor clinical outcomes.

Patients may not have convenient access to grocery stores that stock healthy low-phosphate foods, forcing them to travel long distances, pay for expensive grocery delivery services, or abandon dietary phosphate control.

Clinicians should communicate and ensure that patients understand the timing of taking pills and that behaviors inconsistent with phosphate management strategies may lead to negative health outcomes, including increased cardiovascular risk.

## Introduction

The regulation of phosphate levels is a crucial part of disease management for the nearly 600,000 United States patients with kidney failure requiring dialysis.<sup>1</sup> More than 43% of these individuals have serum phosphate levels over the recommended target of 5.5 mg/dL.<sup>2</sup> The large proportion of patients with elevated phosphate, or hyperphosphatemia, is alarming because this condition is associated

with increased mortality risk. In fact, Kestenbaum et al. found that each 1 mg/dL increase in serum phosphate was associated with an estimated 23% increased mortality risk in patients with chronic kidney disease (CKD).<sup>3</sup> Thus, vigorous control of hyperphosphatemia is needed to improve patient survival.

Some characteristics of currently available phosphate binders (e.g., large binder size, binders must be chewed before ingestion, high pill number, and gastrointestinal [GI] adverse effects) negatively impact the patient experience, which likely contributes to decreased patient adherence and treatment efficacy. A study of phosphate binder adherence reported that 20% of patients experienced intake challenge, mainly related to binder tablet size.<sup>4</sup> A separate study of reasons for phosphate binder discontinuation found that, of patients who discontinued treatment due to “not tolerating” binders, 48% and 8% cited GI upset and an inability to chew or swallow the pill, respectively.<sup>5</sup> Additionally, Chiu et al. reported that patients on dialysis ingested a median of nine phosphate binder tablets daily and that only 38% of them were adherent to therapy.<sup>6</sup> Thus, strategies to decrease binder size, increase ease of administration, reduce GI adverse effects, and lower pill burden may increase patient adherence and quality of life, thereby improving serum phosphate control and clinical outcomes.

Emerging treatment approaches for hyperphosphatemia address the limitations of current phosphate binders and may welcome new choices for CKD patients. One recently approved treatment is tenapanor, a minimally systemically absorbed inhibitor of intestinal sodium/hydrogen exchanger 3 (NHE3) that is used as an add-on therapy for patients whose serum phosphate is not adequately controlled with phosphate binders.<sup>7</sup> Tenapanor pills are much smaller than phosphate binder pills and are taken twice daily, while phosphate binders must be taken with every meal to bind ingested phosphate. However, the tenapanor prescribing information includes a warning that “patients may experience severe diarrhea,” and diarrhea was the most common adverse effect in the combined clinical trials (reported 43-53% of patients).<sup>8</sup> Thus, GI adverse effects associated with tenapanor may decrease adherence. Another emerging investigational new drug is oxylanthanum carbonate, a novel nanotechnology product that combines lanthanum, which has the highest binding capacity vs other phosphate binders, with a smaller pill size and is swallowed whole with water rather than chewed. However, it has not yet been approved by the FDA. Compared to currently available phosphate binders, oxylanthanum carbonate had a 3- to 4-fold lower daily dose volume (~2.3 cm<sup>3</sup>).<sup>9</sup>

This review explores the challenges of phosphate management therapies, particularly focusing on phosphate binders, and incorporates quotes from four patients,

including two patient authors (M.L. and A.B.). The subsection for each challenge is structured as a descriptive paragraph followed by corresponding quotes from patients that represent their experiences. By highlighting the firsthand experiences of CKD patients, we shed light on the real-world barriers they face in managing hyperphosphatemia and emphasize the urgent need for solutions that improve adherence and overall well-being.

## Nonadherence in Taking Phosphate Binders

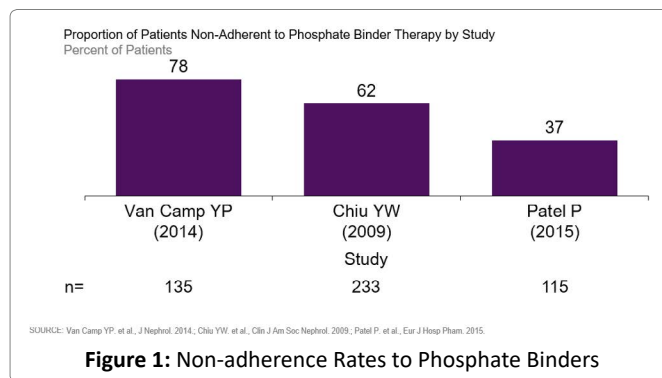
Nonadherence to phosphate binders is a well-documented challenge that likely contributes to widespread above-target serum phosphate levels. One systematic review of 34 studies reported phosphate binder non-adherence rates ranging from 22 to 74%, with a mean non-adherence rate of 51%.<sup>10</sup> A separate study found that 37% of patients were non-adherent to phosphate binder treatment on a daily basis or when eating meals away from home (Figure 1), and 43% had above serum phosphate target levels.<sup>11</sup> In this study, 87% of patients reported forgetting to take the binders as the reason for non-adherence and 28% found the phosphate binder containers too difficult to transport when leaving the house.<sup>11</sup> In another study, only 38% of the participants were adherent to their prescribed phosphate binder therapy, while 20% took less than 40% of their prescribed medications.<sup>6</sup> It was observed that adherence decreased significantly when the daily pill burden exceeded 12 pills, which had a direct relationship with higher serum phosphorus levels, emphasizing pill burden as a key factor in adherence.<sup>6</sup>

In an average month, there may be 100 opportunities for non-adherence to phosphate binders (three meals per day and 10 snacks per month). As mean phosphate levels have been shown to be lower in adherent vs. non-adherent patients,<sup>4</sup> a phosphate binder option that improves adherence may also improve serum phosphate control.

## Challenges with Characteristics of Phosphate Binders

### Large Phosphate Binder Pill Size

Phosphate binders must be taken with meals or snacks three or more times a day, and often include multiple



binders at each meal. Different pill types also have specific challenges. In one study, the most common phosphate binders discontinued by patients because they were unable to swallow the binders or had difficulty chewing were, lanthanum carbonate (49%), sevelamer (36%), and calcium acetate (14%).<sup>5</sup> (Box 1) Capsules and tablets are hard to swallow due to their large size, Therefore, patients may require multiple attempts to ingest the pills. This may not only cause physical discomfort for the patient but also anxiety at having to repeat the uncomfortable process multiple times every day. The daily dose volume of phosphate binders was calculated to be between ~4.0–9.7 cm<sup>3</sup> (Figure 2).<sup>9</sup> However, oxylanthanum carbonate total daily dose volume was 2.3 cm<sup>3</sup>, which is ~2-4x smaller compared to other phosphate binders.<sup>9</sup> Chewable binders can also be particularly problematic for patients with dentition issues and can impair their ability to effectively use binders that require thorough chewing.<sup>12</sup> Phosphate binders that can be cut or crushed, such as sucroferric oxyhydroxide,<sup>13</sup> can help overcome chewing difficulties for patients with impaired dentition. However, chewable binders may have an undesirable taste or chalky sensation and might still be difficult to swallow.

### High Number of Phosphate Binders Pills

Dialysis patients have one of the highest reported

daily pill burdens in any chronic disease state, and phosphate binders are the single largest contributor, accounting for ~50% of total daily pills.<sup>6</sup> (Figure 3). The mean number of phosphate binders patients must take each day is 11 pills.<sup>6,10</sup> The median daily pill burden by phosphate binder type was nine for sevelamer monotherapy, nine for calcium monotherapy, six for lanthanum carbonate monotherapy, and 13 for combination therapy.<sup>6</sup> Dialysis patients with a phosphate binder pill burden exceeding six pills have been found to report lower mental component scores,<sup>14</sup> indicating that a higher pill burden adversely impacts mental health and overall quality of life. Patients frequently express frustration over this burden, stating that the number of pills complicates their daily routines and affects their willingness to adhere to the treatment regimen. (Box 2) Finally, binder dosage depends on dietary phosphate ingestion, and the quantity of required binders increases with increased phosphate intake.

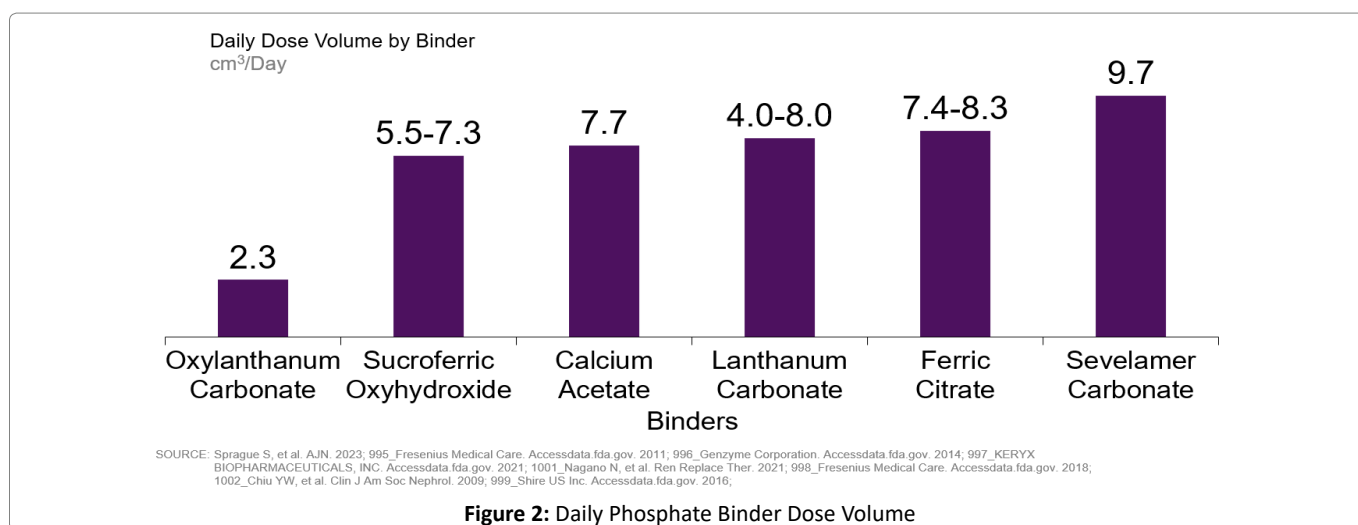
### Gastrointestinal Adverse Effects

Phosphate binders often cause adverse GI effects, which may contribute to decrease adherence. Gastrointestinal adverse events were observed in 45%, 34%, and 56% of clinical trial patients taking sucroferric oxyhydroxide,<sup>15</sup> sevelamer,<sup>15</sup> and lanthanum carbonate,<sup>16</sup> respectively. The specific GI adverse event of nausea was

#### Box 1

##### Patient Quotes on Large Phosphate Binder Pill Size

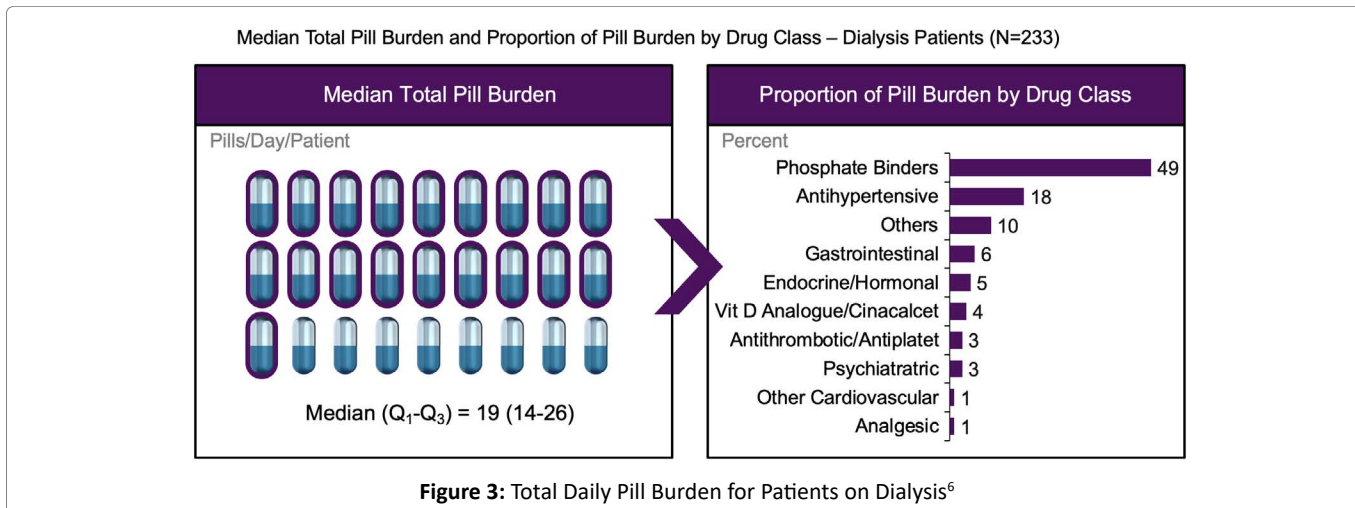
- “The pills are very large, like the size of horse pills. I can't actually swallow them. It's awkward to pull the pills out at a restaurant, use the bottom of my water glass to crush and grind the pill, try to sweep up the powder pieces into my hand to put into my mouth, and then use the water to drink and swallow whatever powder I was able to get into my mouth.”
- “Because the pills are too big, I can only fit enough for 1 meal in my pill box. I commute an hour every day for work and help take care of my nieces and nephew on the weekend so going back home to refill my pill box isn't really an option. When I run out of pills to take, I have to choose between skipping a dose or skipping a meal.”
- “If phosphate binder pills were smaller, I could just take them with the rest of my medication. Instead, I have to carry them in a separate container and make sure I have at least two glasses of water available whenever I eat. The pill size and amount of liquid I need to swallow them makes taking these binders not just physically uncomfortable but totally impractical when I'm out and about.”



**Box 2**

**Patient Quotes on High Phosphate Binder Pill Burden**

- “One pill a day would be heavenly. Anything to alleviate the dread I feel at having to choke down so many huge pills three times a day.”
- “My daily binder prescription doesn’t even fit in a standard pill box so I have to carry them in an Altoids tin. Every time I hear them rattling around in my purse, I get stressed out thinking about the next time I’ll have to chew up all those pills.”
- “I eat 5 meals a day so I have to calculate how many binders to take with each meal. It’s such a pain and I forget all the time, so I probably only take less than half the binders I’m supposed to.”



reported in 7%, 11%, and 26% of patients treated with sucroferric oxyhydroxide,<sup>15</sup> sevelamer,<sup>15</sup> and lanthanum carbonate,<sup>17</sup> respectively. An analysis of reasons for phosphate binder discontinuation found that, of the 11% of patients who discontinued treatment due to an inability to tolerate the medication, 48% specifically cited GI upset.<sup>4</sup>

**Social Challenges with Phosphate Binders**

**Public Consumption of Medication**

The requirement to take phosphate binders with each meal poses a unique challenge for patients, as they are often compelled to ingest these medications in public spaces. Given that individuals may not consume all their meals at home, it becomes imperative for them to carry an ample supply of binders and take them in various social settings. This necessitates the constant mindfulness of patients to not only remember

their medication but also carry a conspicuous pillbox, potentially subjecting them to the social discomfort of medication consumption in the presence of others, including strangers. Additionally, patients may skip a dose or take it at the wrong time because they do not feel comfortable interrupting a social event or occasion to go get their medications. (Box 3)

**Impact on Social Occasions**

Taking phosphate binders during social gatherings can cause discomfort and embarrassment for patients. (Box 4) The need for binders may affect patients’ participation in social occasions, for example, some patients may be hesitant to eat in public if they do not have their medications available. Additionally, the necessity of taking these binders in front of friends and family can create feelings of unease.

**Box 3**

**Patient Quotes on Public Consumption of Medication**

- “When I go out to eat, I often forget to take the binders from my car into the restaurant. I feel so awkward asking the valet to bring my car back, getting my pills, and then going back to my table to take the pills, so I usually just skip a dose. The problem is I travel a lot for work and eat out up to five days a week. You can imagine that the missed doses start to really add up.”
- “There’s no graceful way to take my binders when I’m at a restaurant. If I put them in my pocket, I either forget they’re there or have to explain what they are and why I need them when I pull them out. If I put them on the table at the beginning of the meal so that I don’t forget, I feel bad for making everyone stare at a bottle of pills.”
- “On a usual afternoon, I may arrive a little late to a friend’s house. They offer to take me to dinner in their car. I do not want to interrupt and hold everyone up by going to my car to pick up the emergency pill set, so I justify it by thinking this is only time this week that I will not take the pills with a meal, I will pick the right foods, and will take the pills right after I come back while the food is still digesting. At this point, the slippery slope of compromised compliance starts.”



## Potential Social Isolation

These inconveniences, whether real or perceived, may contribute to patients opting out of social events altogether or choosing to skip doses to avoid the associated challenges. The psychological impact of managing phosphate binder intake in public spaces raises concerns about the potential social isolation experienced by patients dealing with this aspect of their medical regimen. (Box 5)

## Challenges in Timing of Phosphate Binder Administration

The complexities surrounding the timing of phosphate binder administration can significantly impact patient adherence to their treatment regimen. (Box 6) All phosphate binders should be taken with meals to increase their efficiency.<sup>18</sup> If the patients forget to take the phosphate binder dose with a meal, they should take it within 30

### Box 4

#### Patient Quotes on Social Occasions

- "I don't want to take pills with friends and family watching, especially if there are children there, because it reminds everyone that I'm 'sick.' Typically, I step aside, excuse myself to the restroom, and discreetly take my pills to avoid any questions."
- "If I do take my binders while other people are around, I feel compelled to give them a long explanation of why I need to take handfuls of pills every time I eat. It's so exhausting, frustrating, and embarrassing to have to repeat myself every time I meet a new person."

### Box 5

#### Patient Quotes on Potential Social Isolation

- "When you have guests over, you really don't want a pill bottle on the table and you probably don't want pills on your dessert plate. To be honest, most of the time I end up just skipping that dose but then I'm stressed about not taking my medication. Sometimes I feel like it's easier to not have people over at all to avoid the situation."

### Box 6

#### Patient Quotes on Timing of Phosphate Binder Administration

- "I often get really confused when to take the binders because the situation can vary and plans constantly change. I often feel confused about whether the binders can be taken before meals, and if so, how long before the meal is okay? Or if it can also be taken after the meal, how long after the meal is okay?"
- "Sometimes I'm unable to take the pill during the meal, forget, or don't have my pills with me. Then it takes time to travel home, but if there's traffic and it takes longer to get home, then I'm not sure if I should still take the pill or not."

minutes. If this time window passes, they should skip the dose.<sup>19</sup> The timing of administration instructions can be confusing and challenging for patients. Patients sometimes do not know what is the right time to take their pills. This may lead to skipping doses or taking pills at the wrong time, which may lead to inadequate control of serum phosphorus levels. Additionally, CKD patients often take numerous other medications alongside phosphate binders, which increases the complexity of managing multiple medication dosing schedules.<sup>20</sup> All phosphate binders interact with certain other medications, which limits how closely together they can be taken. As a result, patients are required to adhere to strict medication timing not only to optimize the efficacy of phosphate binders but also to prevent potential reduction in the effectiveness of concurrent medications. For example, many immunosuppressants (cyclosporine, tacrolimus, and mycophenolate mofetil) should be taken one hour before or three hours after the administration of sevelamer to avoid reducing their efficacy and preventing potential adverse interactions.<sup>20</sup> However, if patients are instructed to take multiple medications "with meals", they may become very confused when to take each, leading to improper or missed doses. The need for careful timing and coordination can create significant management challenges, especially in patients with complex regimens, potentially leading to non-adherence and suboptimal treatment outcomes.

## Challenges with High Cost of Phosphate Binders

The high cost of phosphate binders is likely a barrier to adherence, particularly in low-income patients. An analysis found that the adjusted odds of receiving a phosphate binder was higher for low-income subsidy patients, and that low-income subsidy patients were more likely than non-low-income subsidy patients to receive prescriptions for more expensive brand name phosphate binders.<sup>21</sup> Thus, low-income patients may struggle with the cost for these brand name phosphate binders, leading to increased stress, reduced sleep quality, taking lower than prescribed doses to save money, or skipping doses altogether. Patients on fixed incomes may be forced to choose between various medications or even between paying for their medications and paying for living expenses e.g., rent and/or food.<sup>22</sup>

## Dietary Restrictions

Over the past several decades, the use of phosphate food additives has surged, significantly increasing dietary phosphate intake, especially in patients with CKD and end-stage kidney disease (ESKD). Between 2013 and 2022, the prevalence of severe hyperphosphatemia (serum phosphate levels >6.5 mg/dL) among hemodialysis patients increased by 50%,<sup>23</sup> even with new medications and high-efficiency dialyzers available. This indicates that, while

nonadherence may contribute to hyperphosphatemia, it is also compounded by factors like increased phosphate additives in the food supply.

The first step in controlling serum phosphate is limiting dietary intake, as recommended by the KDOQI Clinical Practice Guidelines for Nutrition in CKD.<sup>24</sup> However, in practice, adherence to these dietary restrictions can be challenging. Many patients struggle with the practicalities of preparing separate, phosphate-restricted meals for themselves while also cooking for other household members, which can be both costly and time-consuming. Furthermore, patients may not have easy access to grocery stores that offer healthy, low-phosphate food options. This lack of accessibility forces them to travel long distances, pay for expensive delivery services, or give up entirely on maintaining a phosphate-restricted diet. The situation is further complicated by the absence of detailed nutritional information on food labels, making it difficult for patients to accurately track their phosphate intake. Moreover, the perception that adhering to a low-phosphate diet will reduce their quality of life often discourages patients, as they feel restricted from enjoying favorite foods or participating in social activities that involve shared meals with family and friends. (Box 7)

An additional challenge in maintaining a low-phosphate diet is the widespread presence of “hidden” phosphate additives in the food supply, along with the phosphate content in medications commonly prescribed to patients with end-stage renal disease (ESRD). Since food labels are not required to disclose phosphate additives, patients on restricted diets unknowingly consume large amounts of “hidden” phosphates. A study of 2,394 grocery items found that 44% of the best-selling products contained phosphorus additives.<sup>25</sup> Meals comprised mostly of these products contained 736 mg more phosphorus per day compared to additive-free meals, which were also more expensive.<sup>25</sup> Phosphate additives were particularly prevalent in packaged meat (65%) and yogurt (51%)—foods that are often recommended to ESRD patients to ensure adequate protein intake. Furthermore, phosphate content in medications can also contribute significantly to dietary phosphorus intake. Sawin et al. calculated that the median daily dose of the top five medications prescribed to dialysis patients contributed an additional 428 mg of phosphorus per day.<sup>26</sup>

This combination of “hidden” phosphates in food, unavoidable phosphate content in medications, and the

limited phosphate-binding capacity of phosphate binders makes hyperphosphatemia an ongoing challenge for many dialysis patients.

### Education Gap in Phosphate Binder Usage

Effective patient education on the importance of serum phosphate control and its impact on cardiovascular health is crucial, as it may help improve adherence to prescribed phosphate binders. The leading cause of death among CKD patients with estimated glomerular filtration rate <60 ml/min is cardiovascular disease.<sup>27</sup> Reduced glomerular filtration rate causes elevated serum phosphate levels.<sup>28</sup> Therefore, hyperphosphatemia is associated with increased cardiovascular risk and mortality in (CKD).<sup>29</sup> High serum phosphate levels caused by reduced kidney function results in several cardiovascular conditions such as hypertension, vascular calcification, cardiac valvular calcification, atherosclerosis, and left ventricular hypertrophy. Although the link between elevated serum phosphate and increased cardiovascular risk has been established,<sup>30</sup> nutritional knowledge for phosphorus is lower compared to other nutrients (e.g., protein, sodium, potassium), even in patients with hyperphosphatemia or those on phosphate binders. Clinicians, dietitians and other healthcare providers should communicate and ensure that patients understand that inadequate serum phosphate control (e.g., not taking phosphate binders as prescribed) may lead to negative health outcomes, including increased cardiovascular risk.

If clinicians (including physicians, nurses, dietitians, etc.) do not perform patient-centered actions, such as providing sufficient education on the negative impact of hyperphosphatemia, the phosphate binder landscape, and when binders must be taken, patients may be harmed. First, if patients do not understand why achieving and maintaining low phosphate is important, they may be less likely to adhere to dietary restrictions and phosphate binders. Moreover, patients who are not taught about the range of phosphate binders available and the differences between them (e.g., iron- vs. calcium-based) may choose a binder that is not well-suited to their needs (e.g., insurance, swallowing ability, dentition) and preferences (e.g., lifestyle and social habits), thus potentially negatively impacting adherence and clinical outcomes. Finally, if patients are not taught about proper phosphate binder administration, they may negate the efficacy of phosphate binders by not taking enough or taking them at the wrong time. (Box 8)

#### Box 7

##### Patient Quotes on Dietary Restrictions

- "How do I know which foods have high phosphate! The chart I got from the dialysis center only lists ten foods so 90% of the time I need to look up whatever I'm eating. It's exhausting."
- "I used to religiously follow the rule of no high phosphate diet, but it was so boring and depressing eating the same foods every day, and I like to experiment."

#### Box 8

##### Patient Quotes on Phosphate Binder Education

- “I’ve been on dialysis for two years and I’m still confused about serum phosphate control. I know the prescribing information says to take binders with every meal but do I really need to take them with every meal or just the meals that have phosphorus?”
- “It’s news to me that there are so many different types of phosphate binders. When I got my prescription for lanthanum carbonate, someone at the dialysis center gave me a 5-minute talk about taking them and that was it. Then last week I was chatting with another patient during dialysis and she said she was on binders with iron in them and that she only has to take 3 with each meal. I’ve been dealing with 4 or 5! I wish someone had explained all the options and considered my preferences.”

### Suboptimal Efficacy of Phosphate Binders Erodes the Patient-Clinician Relationship

Suboptimal phosphate binder efficacy can damage the patient-clinician relationship. Consistent adherence to phosphate medications and low phosphate diets along with access to low phosphate foods in the context of normal daily activities is still extremely challenging with currently available medications and support systems. Patients may feel that clinicians blame them for the lack of phosphate control, even when they follow dosing instructions, and are ashamed that they are not being “good patients.” Patients may also feel frustrated with clinicians because they perceive that they are not receiving adequate education, resources, care, and support. These negative emotions may lead patients to distrust clinicians.

### Implications for Clinical Practice

Strategies to help overcome phosphate management barriers include robust patient education, support and visual aids from dietitians, and the future introduction of novel serum phosphate control therapies. Patient education (e.g., on avoiding foods with phosphorus additives) has been shown to improve serum phosphate control. Involving patients in discussions about the different types of phosphate binders and their unique characteristics is vital for helping them select the most appropriate option, which can lead to improved adherence and satisfaction. Patients may also benefit from dietitian support and the use of visual aids that make it easier to identify low-phosphate foods. Finally, novel serum phosphate control therapies that decrease pill size and/or pill burden while maintaining efficacy would likely improve clinical outcomes, patient quality of life, and the patient-clinician relationship.

### Conclusions

It is vital for clinicians to consider the perspective of patients requiring dialysis who have elevated serum phosphate. For patients, the challenges of phosphate binders (e.g., large pill size, difficulties with thorough chewing due to impaired dentition, high pill number, GI adverse effects, difficulties with taking binders in public, confusion regarding correct timing of phosphate binder administration, high medication cost) may lead to nonadherence, which may in turn lead to poor clinical outcomes. Sticking to recommended dietary restrictions is

also difficult, expensive, and confusing. Both the challenges of phosphate binders and the difficulty of complying with dietary restrictions negatively impact patient quality of life and may erode the patient/clinician relationship. Recognizing the difficulties that patients with elevated serum phosphate must contend with every day is the first step toward improving the treatment experience and potentially achieving better outcomes.

### Author Contributions

AB helped to draft manuscript, read, and approved the final manuscript. ML helped to draft manuscript, read, and approved the final manuscript.

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### Conflict of Interest

Authors have no conflict of interest to disclose.

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