

Original Research Article

Open Access

# Phosphate Binder Compliance Study in Patients with End-Stage Kidney Disease

Kathleen M Hill Gallant<sup>1</sup>, Douglas Jermasek<sup>2</sup>, Brooks Oppenheimer<sup>3</sup>, Sheila Doss<sup>4</sup>

<sup>1</sup>University of Minnesota-Twin Cities, St. Paul, MN, USA

<sup>2</sup>Unicyclic Therapeutics, Inc., Los Altos, CA, USA

<sup>3</sup>Reason Research, Philadelphia, PA, USA

<sup>4</sup>American Nephrology Nurses Association, Pitman, NJ, USA

## Article Info

### Article Notes

Received: June 03, 2024

Accepted: August 20, 2025

### \*Correspondence:

\*Dr. Kathleen M Hill Gallant, University of Minnesota-Twin Cities, St. Paul, MN, USA; Email: hillkm@umn.edu.

©2025 Hill Gallant KM. This article is distributed under the terms of the Creative Commons Attribution 4.0 International License.

### Key words:

End-stage kidney disease

Hyperphosphatemia

Phosphate binders

Oxylanthanum carbonate

Pill burden

Hemodialysis

## Abstract

**Introduction:** ~600k US end-stage kidney disease patients undergo dialysis, and >43% have serum phosphorus >5.5mg/dL, increasing bone disorder and mortality. Recent studies report phosphate binder (PB) non-adherence rates up to 78%.

**Objective:** Understanding patient perspectives on PB therapy challenges to improve adherence and outcomes.

**Methods:** 20-minute online survey was conducted (2/15-5/16/24) with patients from the National Kidney Foundation email list. Eligibility: on dialysis (in-center or home), ≥40 years old, using ≥1 phosphate management treatment, and insured. The survey assessed patient perspectives on daily pill burden, PB-related challenges, non-adherence drivers, and impact of PB attributes on compliance.

**Results:** 200 patients surveyed. PBs had the highest daily pill requirements (4.8 pills/day) vs. diabetes, high cholesterol, high blood pressure, and depression medications (1.2-2.6 pills or injections/day). Among non-compliant group (≤80% compliant), 58% rated taking PBs as directed as “extremely important,” vs. 67%-100% for other medications. PB non-compliance was ~3-fold higher vs. other medications (37% of patients vs. 12-18%,  $p \leq 0.05$ ). Self-reported non-compliant patients were 2.6-times more likely to report uncontrolled phosphate levels. Among 126 patients with <100% compliance, top barriers were forgetting to take PBs, too many pills, and large pill size. Patients were 4- and 2-times more likely to be compliant with fewer and smaller pills, respectively.

**Conclusion:** PBs had the highest pill burden and lowest compliance. Pill number and size were two of the top barriers. Patients preferred regimens with fewer, smaller pills. Reducing pill burden and enhancing the perceived importance of phosphate control may improve adherence and phosphate management.

## Plain Language Summary

Of the approximately 600,000 US patients undergoing dialysis,<sup>1</sup> over 43% have elevated serum phosphate concentrations,<sup>2</sup> which is associated with negative health outcomes and increased risk of death.<sup>1</sup> Phosphate binders are used to decrease phosphate concentrations. However, many patients do not take phosphate binders according to the prescribed dosing instructions, which decreases effectiveness. We conducted an online survey to gain a better understanding of patient perspectives on challenges related to phosphate binder therapy. Overall, phosphate binders have the highest number of pills per day (~5), and patients also saw phosphate binders as less

important than their other medications such as diabetes, high blood pressure, and high cholesterol. Two of the key barriers to taking phosphate binders as instructed were the high number and large size of pills. Addressing these barriers may improve adherence to phosphate binders.

## Introduction

Of the approximately 600,000 US patients with end-stage kidney disease (ESKD) undergoing dialysis,<sup>1</sup> over 43% have serum phosphate >5.5 mg/dL,<sup>2</sup> which is associated with increased mineral bone disorder and risk of death.<sup>1</sup> The development of hyperphosphatemia (serum phosphate concentrations >4.5 mg/dL) is associated with significant pathophysiology and increased mortality risk, including an associated elevated risk of cardiovascular disease,<sup>3</sup> and an estimated 23% increased mortality risk in CKD patients for each 1 mg/dL increase in serum phosphate.<sup>4</sup> Therefore, there is an unmet need for strategies that achieve and maintain target serum concentrations in patients with ESKD.

Despite a multifaceted approach to phosphate control, including restricting dietary phosphorus intake, enhancing phosphate elimination with dialysis, and use of phosphate binders, management of hyperphosphatemia remains unsuccessful in many patients.<sup>5</sup> One contributor to unsuccessful hyperphosphatemia management is poor adherence to prescribed phosphate binder dosing instructions. Recent studies report phosphate binder (PB) non-adherence rates up to 78%.<sup>6</sup> Low adherence is attributed to pharmacological characteristics including perceived side effects and intake inconvenience, such as taste, number and size of pills, and having to take with meals.<sup>6</sup> Additionally, phosphate binders are the single largest contributor to the daily pill burden in patients on dialysis, accounting for ~50% of total daily pills.<sup>7</sup>

It should be acknowledged that there is some controversy around whether phosphate binder use has beneficial effects on relevant clinical outcomes. For example, although the Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend lowering elevated phosphate levels toward the normal range, they also state that “trial data demonstrating that treatments that lower serum phosphate will improve patient-centered outcomes are still lacking, and therefore the strength of this recommendation remains weak”.<sup>8</sup> Additionally, a network analysis of randomized trials concluded that “There is currently no evidence that phosphate-binder treatment reduces mortality compared to placebo in adults with CKD.”<sup>9</sup> However, the authors acknowledged that their results were limited by high risks of reporting bias among included studies and short study durations (median of 6 months).<sup>9</sup> In contrast, observational studies provide evidence for survival benefits with phosphate

binder therapy. Indeed, the KDIGO guidelines highlight three large cohort studies that support improved survival and better nutritional status with phosphate binder use: a 3-year follow-up, multi-center study of 6,797 patients found that, in an adjusted multivariate analysis, patients prescribed phosphate-binding agents showed a 29 and 22% lower all-cause and cardiovascular mortality risk, respectively;<sup>10</sup> a 1-year study of 10,044 patients found that “treatment with phosphorus binders is independently associated with improved survival among incident hemodialysis patients”;<sup>11</sup> and a study of 23,898 patients from 12 countries (using DOPPS data from 1996-2008) found that patients prescribed phosphate binders had 25% lower mortality (adjusted HR=0.75, 95% CI 0.68-0.83) and phosphate binder prescriptions were associated with better nutritional status (e.g., higher values for serum creatinine, albumin, normalized protein catabolic rate).<sup>12</sup>

Understanding patient perspectives on challenges related to phosphate binder therapy is critical for improving adherence and phosphate management. In this prospective, internet-based study, we aimed to assess the perspectives of patients with ESKD on daily pill burden across diagnosed medical conditions, the perceived importance of taking medications as directed, compliance with medication regimen, and top barriers to phosphate binder compliance.

## Methods

A 20-minute online survey was conducted between February 15 and May 16, 2024 in patients recruited entirely from the National Kidney Foundation (NKF) email list. Patients were screened for the following inclusion criteria: currently receiving dialysis (either in-center or at home), at least 40 years of age, currently using at least one treatment to manage phosphate levels, and having active health insurance coverage. Patients not meeting all these criteria were excluded from participating. All participants were recruited exclusively via NKF’s database. Survey participants were compensated for their time in order to reduce nonresponse bias.

The survey assessed patient perspectives on their current daily pill burden across all medical conditions, challenges and preferences around phosphate binders, factors driving non-adherence, and the impact of various phosphate binder attributes on compliance. Demographic data (e.g., age and sex) were gathered. As this study was conducted exclusively via an online survey, no further clinical data (e.g., serum phosphate, blood pressure, eGFR, hemoglobin, urine protein) were collected.

All responses were manually reviewed by Reason Research to ensure data quality following ISO 20252:2019 protocols for survey research. Data were analyzed using SPSS v22, applying a hierarchical Bayesian choice-based conjoint

**Table 1.** Dialysis Patient Research Demographics Table – All Patients (n=200)

Category	Measures	Values
<b>Age (Years)</b>	Mean	63
	Median (Q <sub>1</sub> -Q <sub>3</sub> )	63 (56-71)
<b>Gender (%)</b>	Males	52
	White	57
<b>Race/Ethnicity (%)</b>	Black	26
	Latinx	10
	Asian	4
	Others	4
	Renvela/Renagel (sevelamer carbonate)	47
<b>Current Treatments (%)</b>	PhosLo/Phoslyra (calcium acetate)	21
	Velphoro (sucroferric oxyhydroxide)	16
	TUMS (calcium carbonate)	13
	Auryxia (ferric citrate)	8
	Fosrenol (lanthanum carbonate)	5
	XPHOZAH (tenapanor)	1

Category	Measures	Values
<b>Medical Conditions Diagnosed<sup>1</sup> (%)</b>	Chronic kidney disease	100
	High blood pressure	68
	Iron deficiency anemia	36
	Diabetes	32
	High cholesterol	27
	Depression	14
	Parkinson's Disease	0
	None of the above	0
<b>Community Type (%)</b>	Suburban	53
	Urban	27
	Rural	21
<b>Location/Region (USA) (%)</b>	South	38
	West	25
	Northeast	19
	Northwest	18
	US Territory	1

<sup>1</sup>Patients could report multiple medical conditions

model via Sawtooth Software. An example choice task is shown in Exhibit A, whereby the size of the hypothetical pills was shown on-screen to ensure “small” and “large” had the same meaning to all patients (Supplementary Figure 1). Statistical significance was evaluated using two-tailed t-tests and  $\alpha = 0.05$  with Bonferroni correction.

## Results

### Demographics

200 patients were surveyed. Their mean age was 63 years, and the majority were male (52%) and White (57%) (Table 1). The most commonly used phosphate binder was sevelamer carbonate (47%), followed by calcium acetate (21%) and sucroferric oxyhydroxide (16%). Co-morbid medical conditions self-reported were high blood pressure (68%), iron deficiency anemia (36%), diabetes (32%), high cholesterol (27%), and depression (14%).

### Pill Burden Across Diseases

Phosphate medications required significantly more pills or injections compared to all other surveyed conditions. 45% of patients required six or more phosphate binders

daily. In contrast, only 9%, 6%, and 2% of patients needed six or more pills or injections per day for high blood pressure, diabetes, and high cholesterol, respectively. No patients needed six or more daily pills or injections to treat depression (Figure 1a). Phosphate binders had the highest daily pill requirements (4.8 pills/day) compared to other medications for diabetes, high cholesterol, high blood pressure, and depression (ranging from 1.2-2.6 pills or injections/day) (Figure 1b).

### Perceived Importance of Taking Medication as Directed

The perceived importance of taking phosphate binders as directed was among the lowest of medications for surveyed conditions, with 79% rating taking phosphate binders as directed as “extremely important”, compared to 72%, 81%, 90% and 92% for high cholesterol, depression, high blood pressure, and diabetes respectively (Figure 1b). Within the non-compliant group ( $\leq 80\%$  self-reported compliance), 58% rated taking phosphate binders as directed as “extremely important,” compared to 67%, 80%, 94%, and 100% for high cholesterol, depression, high blood pressure, and diabetes medications, respectively (Figure 1c).

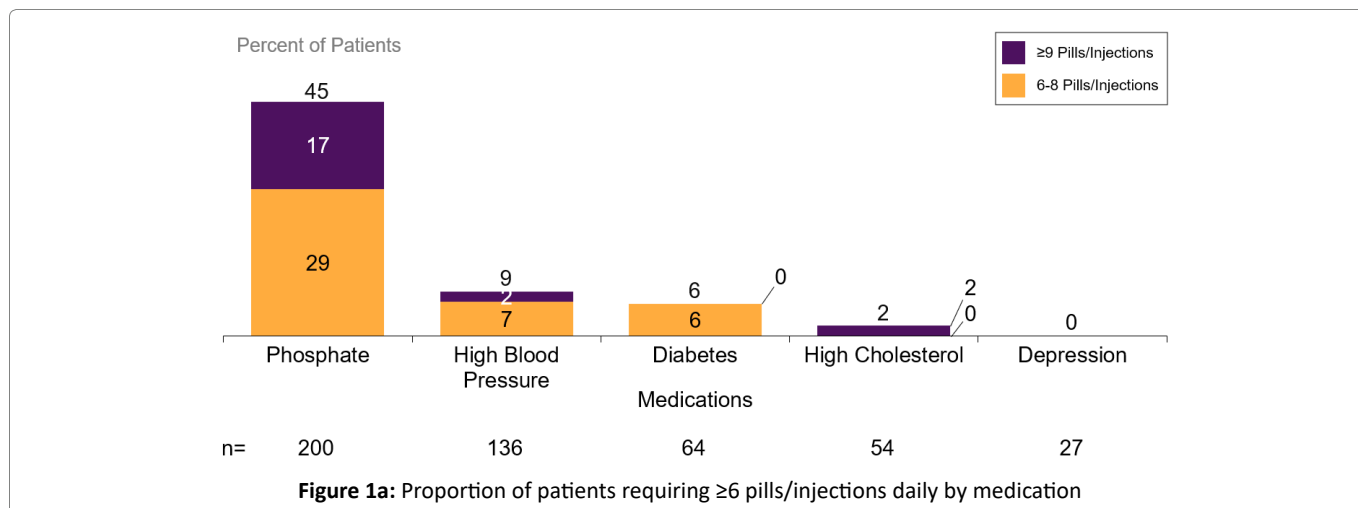


Figure 1a: Proportion of patients requiring ≥6 pills/injections daily by medication

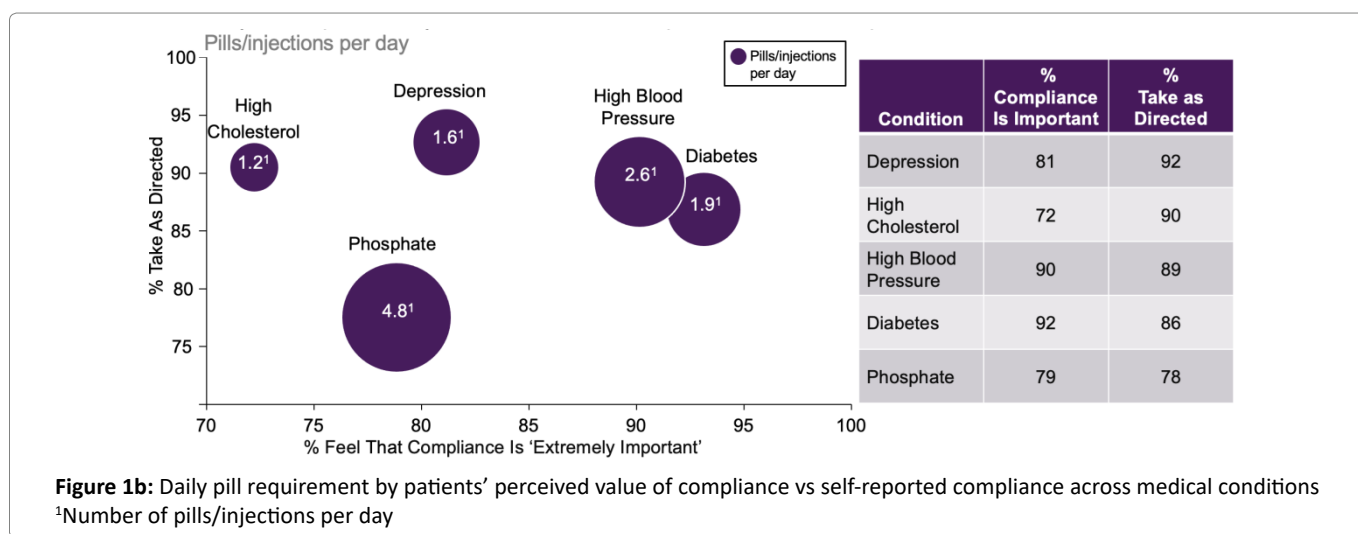


Figure 1b: Daily pill requirement by patients' perceived value of compliance vs self-reported compliance across medical conditions  
<sup>1</sup>Number of pills/injections per day

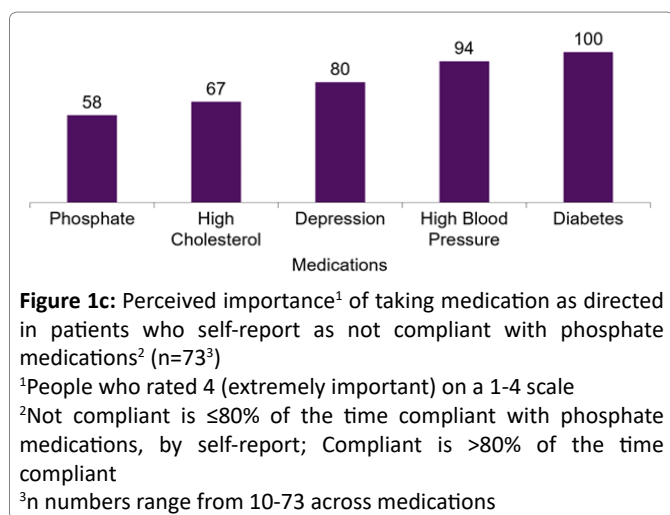


Figure 1c: Perceived importance<sup>1</sup> of taking medication as directed in patients who self-report as not compliant with phosphate medications<sup>2</sup> (n=73<sup>3</sup>)

<sup>1</sup>People who rated 4 (extremely important) on a 1-4 scale  
<sup>2</sup>Not compliant is ≤80% of the time compliant with phosphate medications, by self-report; Compliant is >80% of the time compliant  
<sup>3</sup>n numbers range from 10-73 across medications

### Compliance with Medication Regimen

Of all medications surveyed, compliance was the lowest for phosphate binders, with 78% of patients self-reporting taking them as directed, compared to 86%, 89%, 90%, and 92% for diabetes, high blood pressure, high

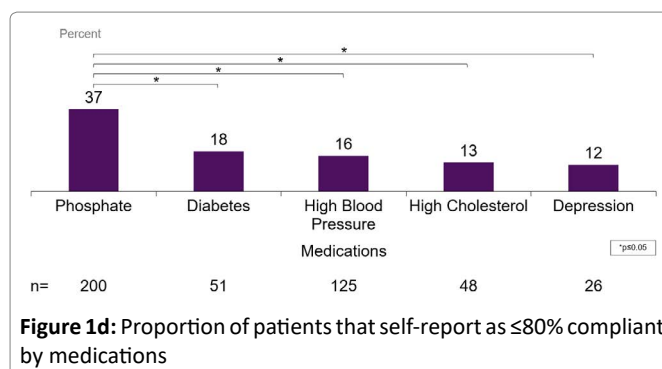
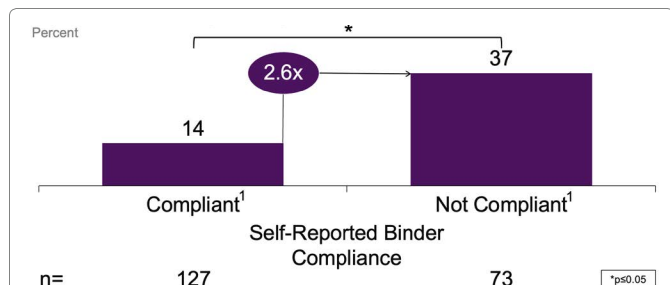


Figure 1d: Proportion of patients that self-report as ≤80% compliant by medications

cholesterol, and depression respectively (Figure 1b). The proportion of patients non-compliant (≤80% self-reported compliance) to phosphate binders is approximately 3-fold higher compared to other medications (37% vs. 12-18%, p≤0.05 for all) (Figure 1d). Self-reported non-compliant patients are 2.6-times more likely to also report that their phosphate levels are not under control (Figure 2a). Self-reported compliance was 1.3-times higher (95% vs 75%) for patients who reported that their phosphate was 'controlled' vs 'not controlled' (Figure 2b).

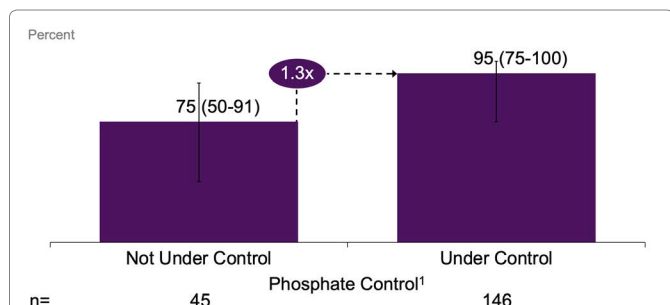
### Barriers to Phosphate Medication Compliance

Based on responses from 126 patients with <100% self-reported compliance, forgetting to take phosphate binders, too many pills, and large size of pills are the top three reported barriers to taking phosphate binder medication (Figure 3a). Other barriers included difficulty carrying



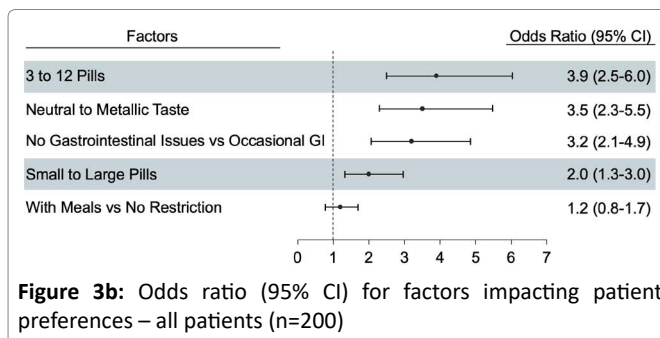
**Figure 2a:** Proportion of patients self-reported phosphate levels not under control

<sup>1</sup>Compliant is self-report >80% of the time compliant with phosphate medications; Not compliant is ≤80% of the time compliant



**Figure 2b:** Median (Q<sub>1</sub>-Q<sub>3</sub>) percent of time phosphate medication was taken as directed<sup>1</sup> by self-reported phosphate control<sup>1</sup>

<sup>1</sup>Percent of time phosphate medication was taken as directed and phosphate control, as self-reported by patients

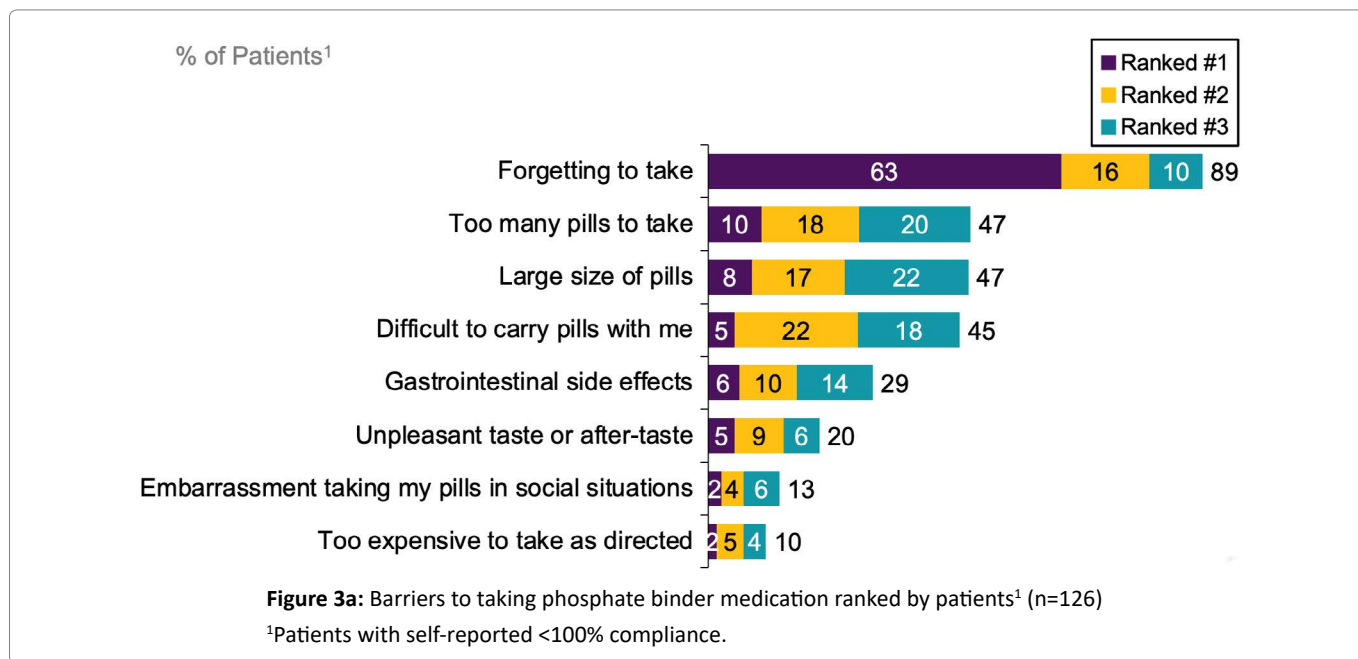


**Figure 3b:** Odds ratio (95% CI) for factors impacting patient preferences – all patients (n=200)

pills outside patients’ home, GI side effects, and unpleasant taste or after-taste. Patients are 4- and 2-times more likely to be compliant with fewer and smaller pills, respectively (Figure 3b).

### Discussion

The goal of phosphate management for patients with chronic kidney disease (CKD) or ESKD is to achieve normal phosphate levels of 3 to 4.5 mg/dL,<sup>13</sup> per KDIGO recommendations.<sup>8</sup> Several large observational studies found that phosphate binders are associated with decreased mortality (all-cause<sup>10-12</sup> and cardiovascular<sup>10</sup>) and improved nutritional status.<sup>12</sup> However, despite widespread phosphate binder treatment, a large proportion of patients on dialysis have phosphate concentrations over 5.5 mg/dL,<sup>5</sup> which highlights the current deficiencies in phosphate management. By systematically identifying and quantifying patient-reported barriers, our research highlights critical gaps in current treatment strategies. These findings are crucial as they provide actionable insights that can inform the development of more patient-friendly phosphate binders, improve adherence, and lead to better phosphate control and clinical outcomes.



**Figure 3a:** Barriers to taking phosphate binder medication ranked by patients<sup>1</sup> (n=126)

<sup>1</sup>Patients with self-reported <100% compliance.

Our data suggest that reducing pill size and the number of daily pills may improve phosphate binder compliance, as patients were found to be 4x more likely to adhere to regimens with fewer pills and 2x more likely with smaller pills. Consequently, identifying a phosphate binder that combines high phosphate binding capacity with good intake convenience may improve adherence and patient quality of life related to pill burden. Investigational therapies, such as oxylanthanum carbonate, which requires fewer and smaller pills that can be swallowed whole without chewing, may address phosphate binder compliance issues seen with current binders.

Additionally, increasing patient education on the importance of preventing hyperphosphatemia may also increase compliance by addressing current patient perceptions that taking phosphate binders is not important or less important compared to medications for other conditions. Education should stress that hyperphosphatemia may have negative effects, e.g., increased cardiovascular risk, even though patients may not immediately experience any negative effects after not taking phosphate binders as directed. However, scant randomized trial evidence for benefits of phosphate binders on patient-centered clinical outcomes remains a valid concern that may lessen the perceived importance of phosphate binders compared with other medications by clinicians as well as patients, particularly in light of the high pill burden of phosphate binders. Thus, further clinical trial evidence on the effects of phosphate binders and phosphate control on clinical outcomes is needed.

While this study offers important insights, there are several limitations to consider. First, patients were recruited solely from the NKF database, which may introduce sampling bias, as these patients may be more engaged in their care, more compliant, and potentially skewed towards younger, more educated, or wealthier demographics due to the online nature of the survey. The study relied on self-reported data, which may introduce bias or inaccuracies in patient responses regarding compliance and phosphate control. Recall bias may also affect the accuracy of these responses, as patients may not accurately remember or report their past behaviors. Additionally, the survey was conducted via the internet, which may limit its generalizability, as it may not fully represent the broader population of dialysis patients, particularly those with limited access to technology. Another potential limitation is the self-fulfilling prophecy where patients with good phosphate control may be praised for compliance, regardless of their actual adherence, while those with poor phosphate control may be assumed to be non-compliant. Furthermore, this study focused on patient perceptions of compliance and did not collect biochemical (e.g., serum phosphate

concentrations) or clinical outcome data (e.g., survival). Future studies should aim to corroborate these findings with real-world clinical data and explore the long-term impact of reduced pill burden on phosphate control.

Increasing medication adherence to phosphate binders is critical for their efficacy in improving phosphate control. The insights gained from this study can inform the design and development of more patient-centric treatments that address common compliance barriers, such as pill burden and size. Survey results also highlight the need for stronger patient education on the potential adverse effects of hyperphosphatemia and why consistently taking phosphate binders as directed is important. By making phosphate binders easier to take and improving patient understanding and awareness of their importance, healthcare providers may be able to improve adherence.

## Conclusions

These survey findings highlight significant challenges in achieving patient compliance with phosphate binder therapy. Phosphate binders had the highest pill burden and lowest compliance rate, further reinforcing the need to address these barriers. Among patients with  $\leq 80\%$  self-reported compliance, phosphate binders were perceived as less important compared to other medications, a trend not observed with other treatments. Additionally, self-reported non-compliance was strongly associated with self-reported inadequate phosphate control, with self-reported non-compliant patients being 2.6 times more likely to report uncontrolled phosphate levels. The excessive number and size of phosphate binder pills emerged as two of the top barriers to consistent medication use, from both the simple stated and conjoint-derived perspective. In simulated scenarios, patients were more likely to prefer medication regimens with fewer and smaller pills, underscoring the impact of pill burden on compliance. Strategies to reduce pill burden and enhance the perceived importance of phosphate control may be critical in improving adherence and possibly phosphate management in this population.

## Statements

### Statement of Ethics

This study was conducted in accordance with the Declaration of Helsinki. Survey participants have given their written Informed consent prior to participating in the survey. The survey study protocol was reviewed, approved, and conducted by the National Kidney Foundation's committee.

### Conflict of Interest Statement

D.J. is an employee of Unicycive Therapeutics, Inc. K.H., D.J., and B.O. have no conflicts to disclose.

## Funding Sources

The study was funded by the National Kidney Foundation through an educational grant from Unicycive Therapeutics, Inc.

## Author Contributions

K.H.: Conceptualization, Methodology, Writing – review & editing

D.J.: Conceptualization, Methodology, Writing – review & editing

B.O.: Methodology, Data curation, Formal analysis, Writing – review & editing

S.D.: Conceptualization, Methodology, Writing – review & editing

## Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request. Restrictions apply to the availability of data generated or analyzed during this study to preserve patient confidentiality or because they were used under license. The corresponding author will on request detail the restrictions and any conditions under which access to some data may be provided.

## Acknowledgements



Editorial support was provided by Xelay Acumen Group, Inc. (funded by Unicycive Therapeutics, Inc.).

## References

1. 2020 USRDS Annual Data Report: Epidemiology of kidney disease in the United States. Bethesda, MD2020.

2. Monitor DP. Serum phosphorus (3 month average), categories. Published 2021. Accessed.
3. Hruska KA, Mathew S, Lund R, et al. Hyperphosphatemia of chronic kidney disease. *Kidney Int.* 2008; 74(2): 148-157.
4. Kestenbaum B, Sampson JN, Rudser KD, et al. Serum phosphate levels and mortality risk among people with chronic kidney disease. *J Am Soc Nephrol.* 2005; 16(2): 520-528.
5. Serum phosphorus (most recent), categories. DOPPS Practice Monitor. [https://www.dopps.org/DPM-HD/Files/phosphmgdl\\_c\\_overallTAB.htm](https://www.dopps.org/DPM-HD/Files/phosphmgdl_c_overallTAB.htm). Published 2023. Accessed October 9, 2023.
6. Van Camp YP, Vrijens B, Abraham I, et al. Adherence to phosphate binders in hemodialysis patients: prevalence and determinants. *J Nephrol.* 2014; 27(6): 673-679.
7. Chiu YW, Teitelbaum I, Misra M, et al. Pill burden, adherence, hyperphosphatemia, and quality of life in maintenance dialysis patients. *Clin J Am Soc Nephrol.* 2009; 4(6): 1089-1096.
8. 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.* 2017; 7(1): 1-59.
9. Palmer SC, Gardner S, Tonelli M, et al. Phosphate-Binding Agents in Adults With CKD: A Network Meta-analysis of Randomized Trials. *Am J Kidney Dis.* 2016; 68(5): 691-702.
10. Cannata-Andía JB, Fernández-Martín JL, Locatelli F, et al. Use of phosphate-binding agents is associated with a lower risk of mortality. *Kidney Int.* 2013; 84(5): 998-1008.
11. Isakova T, Gutiérrez OM, Chang Y, et al. Phosphorus binders and survival on hemodialysis. *J Am Soc Nephrol.* 2009; 20(2): 388-396.
12. Lopes AA, Tong L, Thumma J, et al. Phosphate binder use and mortality among hemodialysis patients in the Dialysis Outcomes and Practice Patterns Study (DOPPS): evaluation of possible confounding by nutritional status. *Am J Kidney Dis.* 2012; 60(1): 90-101.
13. Suki WN, Moore LW. Phosphorus Regulation in Chronic Kidney Disease. *Methodist Debaquey Cardiovasc J.* 2016; 12(4 Suppl): 6-9.

**Supplementary Figure 1: Scenario Example: Choosing Between Hypotheticals**

	<b>A</b>		<b>B</b>	
<b>Number of Pills per Day and Size</b>				
<b>Chew/Swallow</b>	Must swallow whole with water (cannot be crushed)		Must chew, neutral taste	
<b>Time of Day</b>	Must be taken with meals		Take with or without food	
<b>Gastrointestinal Side Effects</b>	Occasional constipation		None	
<b>Option to Be Selected</b>	Much easier to take A as directed	Slightly easier to take A as directed	Slightly easier to take B as directed	Much easier to take B as directed