

# Serum Phosphorus Level and Pill Burden Are Inversely Associated With Adherence in Patients on Hemodialysis

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## Introduction

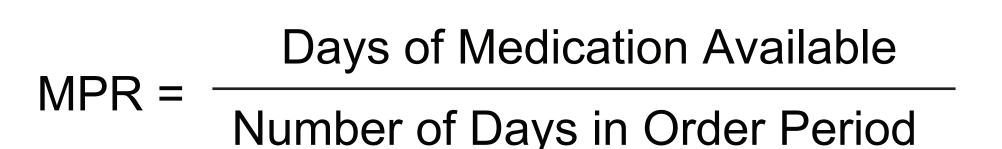
- Mineral and bone disorders are a serious problem among hemodialysis (HD) patients. Markers of mineral and bone disorders, including hyperphosphatemia, hypercalcemia, and secondary hyperparathyroidism, have been associated with increased risk of hospitalization and mortality. 2-4
- The National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF-KDOQI™) specifies that serum phosphorus levels should be maintained in the 3.5–5.5 mg/dL range through dietary restrictions and use of phosphate binder medications. However, only 41%–64% of dialysis patients are able to attain this target.<sup>5,6</sup>
- Phosphate binders pose a high pill burden, accounting for nearly half of the daily pill burden (median = 19 pills/day) for US HD patients. Higher pill burden may be associated with reduced adherence to treatment regimens and is associated with lower health-related quality of life.<sup>7,8</sup>
- Adherence can be estimated by medication possession ratio (MPR), defined as the proportion of time the patient has sufficient medication to take as prescribed.<sup>9,10</sup> Long gaps of time between refills will lower a patient's MPR.

## Objective

This retrospective, observational analysis assessed the association of phosphate binder pill burden with adherence (as measured by MPR), serum phosphorus levels, and serum phosphorus goal attainment in patients of a large dialysis organization (LDO) in the US.

## Methods

- Patients were ≥ 18 years old, Medicare recipients on phosphate binder monotherapy, receiving in-center HD ≥ 3 times per week, continuously enrolled in the LDO pharmacy management program. The study period was 1 January 2007 to 30 June 2011.
- Patients were excluded if they were receiving peritoneal dialysis, home HD, or nocturnal HD; were enrolled in the automatic refill system for phosphate binders; were receiving the powder or sachet formulation of sevelamer; or had serum phosphorus levels < 3.0 mg/dL.
- Patients were followed from first phosphate binder prescription fill for 1 year or until a censoring event occurred. Patients were censored on switching phosphate binder type, receiving prescriptions for multiple phosphate binders, enrolling in the automatic refill management system, having > 180 days between refills, having consecutive serum phosphorus levels < 3.0 mg/dL, discontinuing HD, or death.</li>
- MPR was defined as follows:



An MPR of 1.0 is optimal (most adherent) and MPR of 0 is worst (least adherent). Days medication available was calculated as (number of days of medication supplied in the period) - (number of days of medication left over at end of period).

- Outcome variables assessed were mean MPR, mean phosphorus level, and percentage of patients in phosphorus range (≤5.5 mg/dL). Mean MPR was stratified by pill burden, while mean phosphorus level and percent of patients in range were stratified by phosphate binder pill burden and MPR.
- Generalized Linear Models (GLM) were used to assess associations between strata and outcome variables.

## Results

- A total of 8,616 patients with order information in the pharmacy management program database were included in the analysis. Patient characteristics are presented in **Table 1**.
- MPR was calculated and stratified by patient pill burden (**Figure 1**). Overall, mean weighted MPR levels were low: from 0.51 in the group with the lowest pill burden (0-3 pills/day) to 0.42 in the group with the highest pill burden (> 15 pills/day). MPR was negatively associated with pill burden (p < 0.001).
- Mean serum phosphorus levels were also negatively associated with MPR (p<0.001, Figure 2).</li>
- WIthin most pill burden strata, lower MPR was associated with a higher mean phosphorus level (Figure 3A). However, within the > 6-9 and > 9-12 pills/day strata a non-linear pattern was observed with the middle range MPR associated with the lowest phosphorus concentration.
- Similarly, within most pill burden strata higher MPR was associated with a higher percentage of patients attaining phosphorus targets (**Figure 3B**). However, in the >6-9 and >9-12 pills/day strata a non-linear pattern was again observed, with the middle range MPR associated with the highest percentage of patients with phosphorus concentration ≤5.5 mg/dL.

#### Table 1: Patient Characteristics

	N	Mean ± SD
Total Patients (N)	8,616	
Age (years)		57.0 ± 14.3
	n	Percent
Gender (% male)	4,518	52.4%
Race/Ethnicity		
White	1,940	22.5%
Black	3,875	45.0%
Hispanic	2,199	25.5%
Asian	253	2.9%
Native American or Alaskan	64	0.7%
Native Hawaiian or Pacific Islander	87	1.0%
Primary Cause of End-Stage Renal Disease		
Diabetic Kidney Disease	3,785	44.1%
Hypertensive Kidney Disease	2,782	32.3%
Other/Unknown	1,847	21.4%
Polycystic Kidney Disease	192	2.2%

## Figure 1: Weighted MPR Stratified by Pill Burden

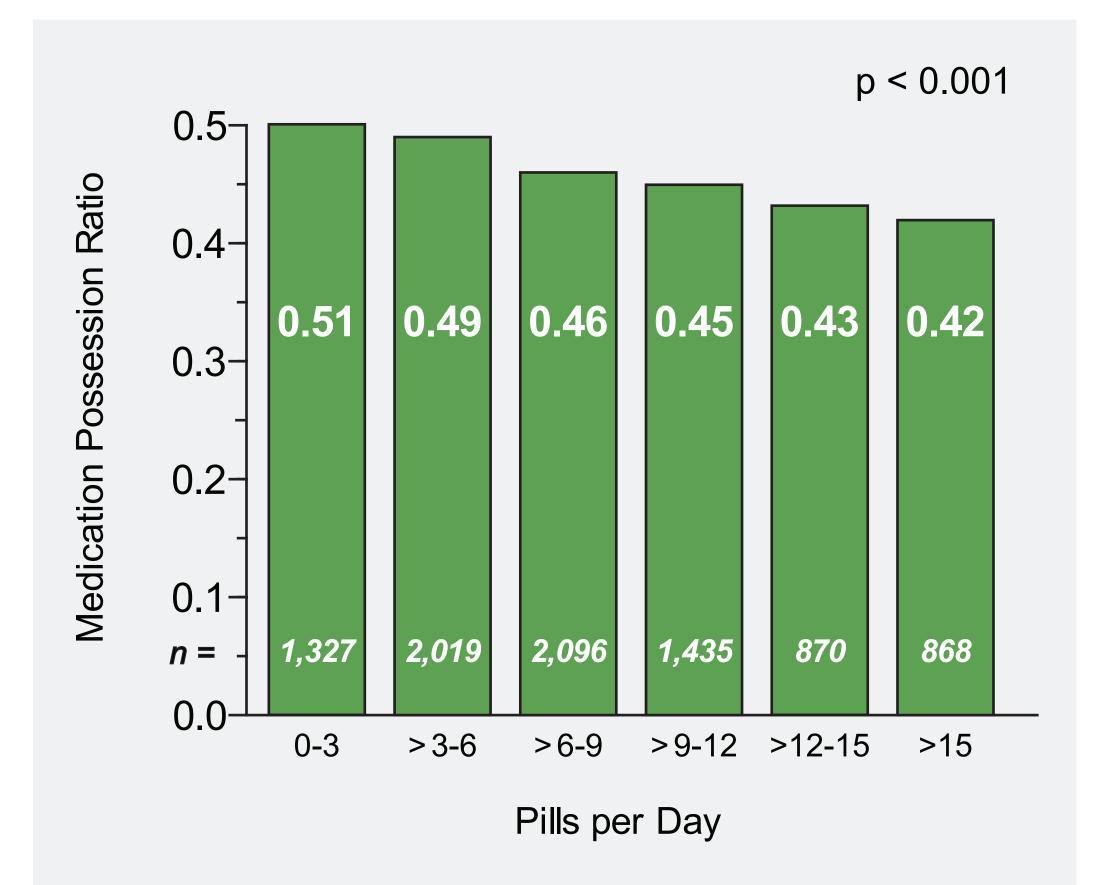


Figure 2: Mean Phosphorus Levels Stratified by MPR

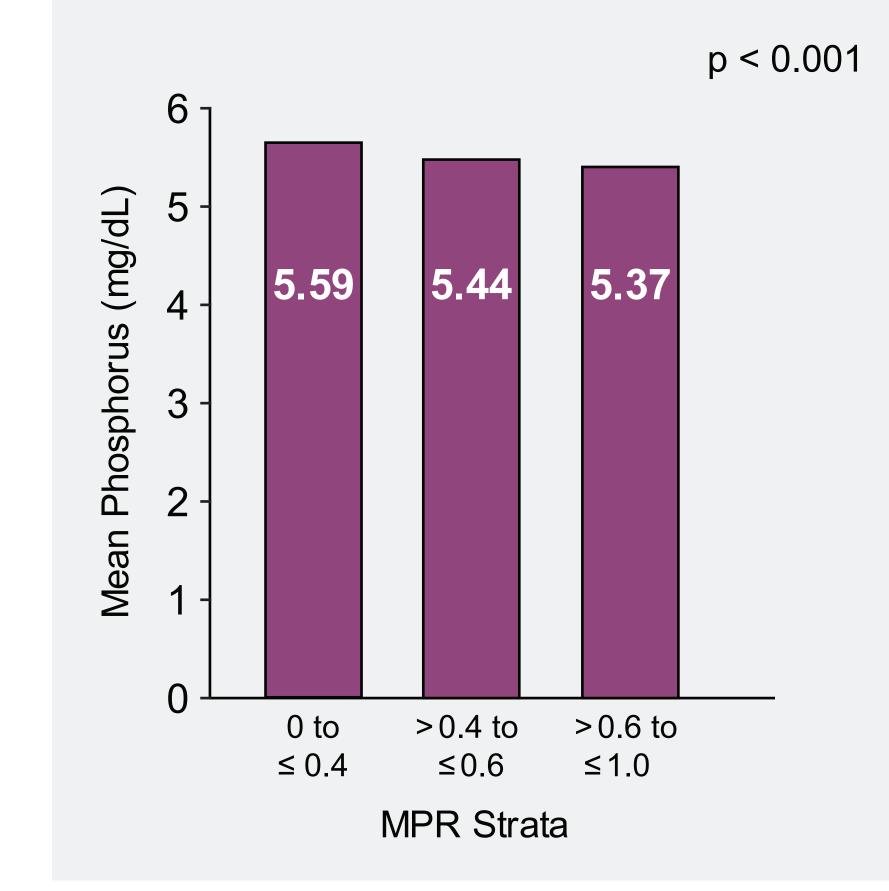
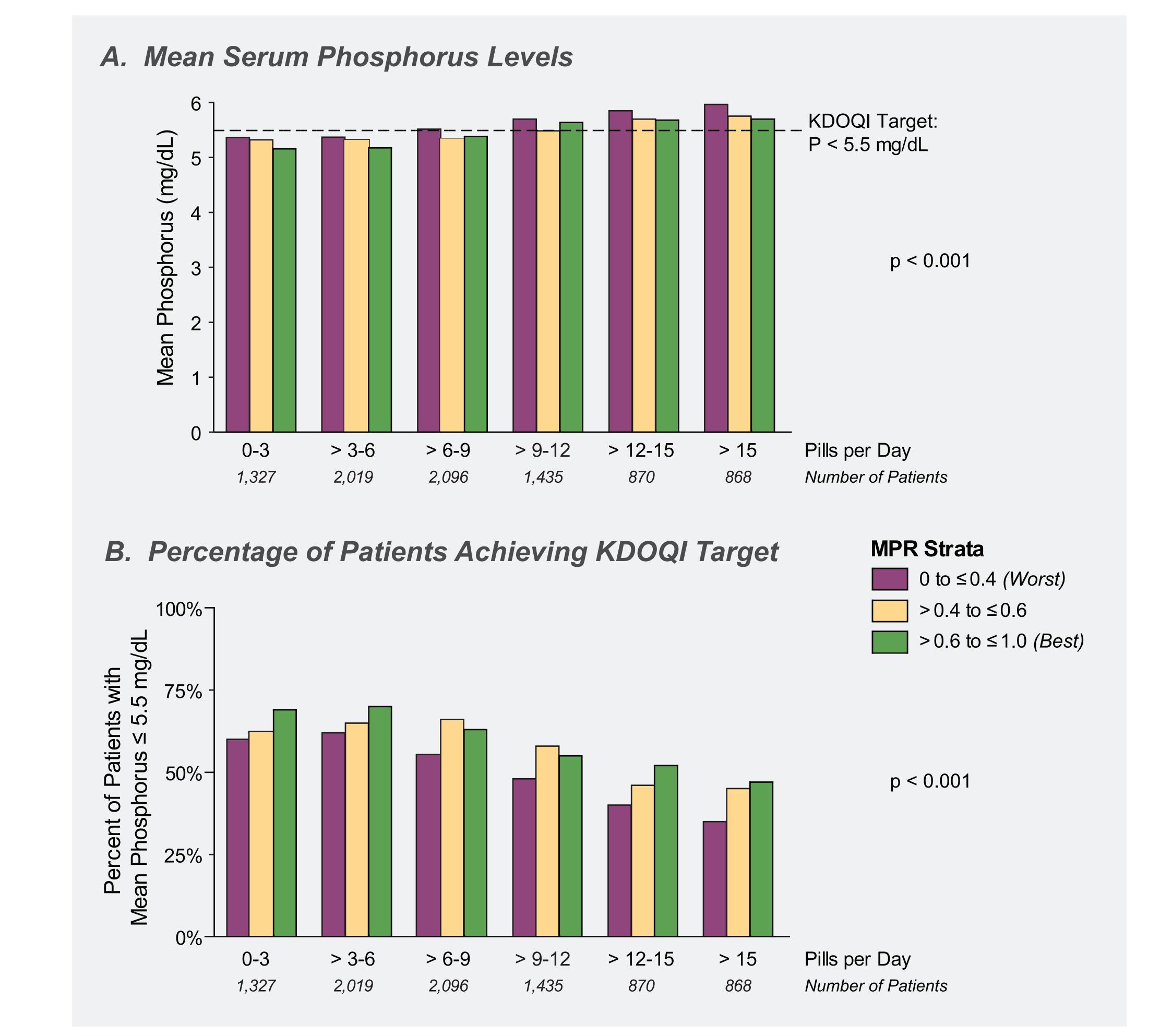


Figure 3: Mean Phosphorus Levels and Percentage of Patients with Phosphorus in Target Range by Pill Burden and MPR



## Conclusions

- Data on phosphate binder use from an LDO pharmacy management program show that overall MPR is low (0.42–0.51), and that MPR increases as pill burden decreases, supporting the hypothesis that lower pill burden is associated with higher adherence.
- Patients with higher MPR tended to have lower phosphorus laboratory values and were more likely to achieve KDOQI targets for serum phosphorus levels.
- Phosphate binders with lower pill burden may therefore help improve patient compliance and phosphorus control.

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