Simplified phosphorus kinetic modeling: predicting changes in predialysis serum phosphorus concentration after altering the hemodialysis prescription

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**Abstract**

**Background.** The KDIGO work group recommends increasing dialytic phosphorus removal in Stage 5D chronic kidney disease patients with persistent hyperphosphatemia; however, optimal prescriptions to enhance phosphorus removal by hemodialysis (HD) therapies have not yet been established. This study evaluated whether phosphorus kinetic modeling based on a pseudo one-compartment model could provide practical clinical guidance for predicting changes in predialysis serum phosphorus concentration after altering the HD prescription.

**Methods.** Patient-specific phosphorus kinetic parameters determined from thrice weekly HD treatments on 774 patients in the HEMO Study were used to predict changes in predialysis serum phosphorus concentration after altering the HD prescription from thrice weekly to short daily and long nocturnal HD therapies. The effect of changes in the oral phosphorus binder prescription on predicted changes in the predialysis serum phosphorus concentration was also illustrated using the concept of equivalent phosphorus binder dose.

**Results.** Decreases in predialysis serum phosphorus concentration from thrice weekly HD to short daily and long nocturnal HD therapies demonstrated strong associations with the predialysis serum phosphorus concentration during thrice weekly HD that were relatively independent of patient-specific phosphorus kinetic parameters. Thus, the percent decrease in predialysis serum phosphorus concentration was approximately the same among patients for a given alteration in the HD prescription. Both increased weekly treatment time and frequency resulted in a reduction in the predialysis serum phosphorus concentration; however, the effect of treatment time was more influential. Simultaneous reduction in the effective phosphorus binder dose blunted the decrease in the predialysis serum phosphorus concentration.

**Conclusions.** This study demonstrated that a simplified form of phosphorus kinetic modeling based on a pseudo one-compartment model can provide practical clinical guidance for predicting changes in predialysis serum phosphorus concentration after altering the HD prescription. Prospective validation of this approach in future studies is warranted.

**Keywords:** hemodialysis, kinetic modeling, mobilization, phosphate, phosphorus

**Introduction**

Conventional thrice weekly hemodialysis (HD) or hemodiafiltration therapies are unable to maintain the serum phosphorus concentration within the normal range in a large fraction of Stage 5D (G5 GFR category [1]) chronic kidney disease (CKD) patients despite the liberal prescription of oral phosphorus binders [2–12]. The KDIGO guidelines recommend increasing dialytic phosphorus removal in the treatment of Stage 5 CKD patients with persistent hyperphosphatemia [13]; however, optimal prescriptions to enhance dialytic phosphorus removal have not yet been established. Generally, HD treatments applied more frequently than thrice weekly without increasing the weekly treatment time result in only modest reductions in serum phosphorus concentrations [14]. Instead, longer weekly treatment times are necessary to achieve substantial increases in dialytic phosphorus removal [15–19], and some therapy prescriptions can require the addition of...
phosphate salts to the dialysis solution to prevent hypophosphatemia [20]. Regrettably, a quantitative approach for prescribing HD therapies to target predialysis serum phosphorus concentrations is lacking. Indeed, the Frequent Hemodialysis Network (FHN) group has recently concluded, based on their extensive investigation of mineral metabolism during frequent HD therapies [21], that the ‘optimum frequency and session length for hemodialysis patients with hyperphosphatemia remain to be determined’. One potential approach for determining such prescriptions would be the use of phosphorus kinetic modeling.

We have recently described a novel pseudo one-compartment model for describing phosphorus kinetics [22] and have demonstrated that it can describe intradialysis and postdialysis phosphorus kinetics during a variety of extracorporeal modalities [23–25]. This kinetic model is a simplified two-compartment model where phosphorus is directly removed by HD, for example, from an accessible, central compartment, and phosphorus is mobilized into that compartment during HD from a very large inaccessible, peripheral compartment. The model is advantageous because its mathematical description is simple and it only requires the identification of two kinetic parameters, the phosphorus mobilization clearance from the peripheral to the central compartment and the phosphorus central distribution volume. Nonetheless, conventional use of such a model to quantitatively predict the effect of changes in the HD prescription on the predialysis serum phosphorus concentration requires prior determination of patient-specific phosphorus kinetic parameters [26].

In this report, phosphorus kinetic modeling based on a pseudo one-compartment model is used to predict changes in predialysis serum phosphorus concentration after altering the HD prescription from conventional thrice weekly therapy based on phosphorus kinetic parameters determined from 774 patients in the HEMO study [25]. It is further demonstrated that the predicted changes in predialysis serum phosphorus concentration can be made with a limited loss of accuracy without the need for prior determination of phosphorus kinetic parameters. Such an approach can also account for changes in the oral phosphorus binder prescription using the concept of phosphate binder equivalent dose [27], also called the equivalent phosphorus binder dose (EPBD) [21].

**Materials and Methods**

This study used phosphorus kinetic modeling based on a pseudo one-compartment model to predict changes in predialysis serum phosphorus concentration after altering the HD prescription following considerations of phosphorus mass balance over a weekly interval [26]. In these examples, it was assumed that HD treatments are performed symmetrically during the week, there is no residual kidney function and the net phosphorus generation rate or G (dietary intake minus intestinal phosphorus absorption) is constant throughout the week. The assumption of symmetrically performed treatments simplifies the calculations but neglects differences in the predialysis serum phosphorus concentration and the ultrafiltration rate during different days of the week as is typical during HD. The initial thrice weekly HD prescription is defined by the following measurable parameters: (i) predialysis serum phosphorus concentration; (ii) dialyzer phosphorus clearance; (iii) treatment frequency (thrice weekly); (iv) treatment time per session and (iv) ultrafiltration rate during the treatment. From those parameters and knowledge of phosphorus kinetic parameters (see below), the amount of phosphorus removed during a week, and therefore the net phosphorus generation rate, can be readily calculated (assuming the patient is in steady state) as described in the Appendix.

If the net phosphorus generation rate and the phosphorus kinetic parameters are not altered by the change in the HD prescription, then the resulting predialysis serum phosphorus concentration can be readily calculated based on the new HD prescription parameters. The full mathematical details when using this approach have been previously described [26]. When the oral phosphorus binder prescription is altered simultaneously with the HD prescription, then those changes can be accounted for by altering the net phosphorus generation as described further below.

This study only considered changes from thrice weekly HD prescriptions as specified in kinetic modeling sessions during the HEMO Study to those during short daily and long nocturnal HD therapies. Predicted values of the resulting predialysis serum phosphorus concentration after altering the HD prescription were calculated individually for 774 patients for whom patient-specific phosphorus kinetic parameters had been estimated previously [25] (see below). It should be emphasized, however, that the approach described is general and can be used for any HD prescription and also for non-zero residual kidney function. The equations used for these calculations are outlined in the Appendix.

**Prescription parameters during thrice weekly HD**

HD prescription parameters from kinetic modeling sessions during the HEMO study were previously described in detail [25]. For these patients, the blood flow rate was 340 ± 63 (mean ± standard deviation) mL/min, the dialysate flow rate was 684 ± 128 mL/min and the treatment time was 207 ± 29 min. The calculated volume of blood processed (blood flow rate times the treatment time) was 71.0 ± 19.3 L. These treatments resulted in a midweek predialysis serum phosphorus concentration of 1.91 ± 0.60 mmol/L. (Note that all serum phosphorus concentrations were originally recorded in units of mg/dL but were converted to mmol/L by dividing by 3.097.)

**Estimated phosphorus kinetic parameters**

Assuming a pseudo one-compartment model, the phosphorus mobilization clearance (\(K_{M} \)) and the postdialysis phosphorus central distribution volume (\(V_{pos} \)) were previously determined from intradialysis and postdialysis serum phosphorus concentration measurements from kinetic modeling sessions during the HEMO study [25]. The distribution of those parameter estimates for 774 patients are shown in Figure 1. The characteristics of the patients enrolled in the HEMO study are comparable with patients treated in the USA during the 1990s, but females and patients of black race were
over-represented. Nonetheless, Figure 1 demonstrates that a wide range of kinetic parameters are necessary to describe phosphorus kinetics during HD. The median values (interquartile range or IQR: 25th–75th percentiles) for $K_M$ and $V_{\text{post}}$ were 87 (65–116) mL/min and 9.4 (7.2–12.0) L, respectively.

RESULTS

Figure 2 shows predicted changes in predialysis serum phosphorus concentration when changing from thrice weekly to long nocturnal (filled diamonds) or to short daily HD (open circles) using phosphorus kinetic parameters determined during the HEMO study ($n = 774$) as a function of the concentration during thrice weekly HD. The correlation between the decrease in concentration and the concentration during conventional thrice weekly hemodialysis was 0.947 ($P < 0.001$) for long nocturnal and 0.845 ($P < 0.001$) for short daily HD.

The latter parameter was chosen arbitrarily but reflects a common practice to use lower blood and dialysate flow rates and smaller surface-area dialyzers during long nocturnal HD treatments. Reductions in predialysis serum phosphorus concentration were observed for both frequent HD prescriptions, but the decreases in predialysis serum phosphorus concentration were substantially greater for long nocturnal than for short daily HD. For both frequent HD therapies, the decrease in predialysis serum concentration was strongly associated with the predialysis serum phosphorus concentration during thrice weekly HD. This finding suggests that the percent decrease in predialysis serum phosphorus concentration after altering the HD prescription is relatively constant among all patients when considering these frequent therapies as shown in Figure 3. The median (IQR) percent decreases in predialysis serum phosphorus concentration for these short daily and long nocturnal HD therapies were 13.8 (10.9–16.3)% and 53.7 (49.7–57.5)% respectively. Further, the median absolute differences in the predicted decrease in predialysis serum phosphorus concentration when an approximate constant percent decrease in concentration was assumed compared with the full model were 0.042 or 0.071 mmol/L during short daily and long nocturnal therapies, respectively. It should be noted, however, that the average percent decrease in the predialysis serum phosphorus concentration only approximates the decrease in concentration predicted by the full kinetic model, and the accuracy of the approximation may be patient-specific. Indeed, there were weak statistical associations between the percent decrease in serum phosphorus concentration and log (logarithm to

Table 1. Example frequent HD treatment prescriptions: short daily and long nocturnal HD

<table>
<thead>
<tr>
<th>HD modality</th>
<th>Treatments per week</th>
<th>Session treatment time (min)</th>
<th>Dialyzer phosphorus clearance (mL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short daily</td>
<td>6</td>
<td>$103 \pm 15$</td>
<td>$139 \pm 18$</td>
</tr>
<tr>
<td>Long nocturnal</td>
<td>5</td>
<td>$480^a$</td>
<td>$70 \pm 9$</td>
</tr>
</tbody>
</table>

$^a$Assumed for all patients.
the base 10) $K_M$ (regression coefficient or $R = −0.071$, $P = 0.049$) and log $V_{post}$ ($R = −0.412$, $P < 0.001$) during long nocturnal therapy; the associations were generally stronger between the percent decrease in serum phosphorus concentration and log $K_M$ ($R = −0.781$, $P < 0.001$) and log $V_{post}$ ($R = 0.171$, $P < 0.001$) during short daily therapy. These associations suggest that the largest potential bias would be patients treated with short daily therapy who had extreme values of $K_M$, where decreases in predialysis serum phosphorus concentrations for patients who had very large $K_M$ values would be overestimated and those who had very small $K_M$ values would be underestimated.

The effects of weekly treatment time and frequency were then explored by predicting changes in predialysis serum phosphorus concentration for various short daily HD prescriptions. Treatment times considered for four, five and six treatment sessions per week were calculated for a weekly treatment time equal to that during thrice weekly HD (620 min during the HEMO Study) and when each treatment was extended by 30, 60 and 90 min. For each patient, the blood flow rate and dialyzer phosphorus clearance was assumed equal to that during thrice weekly HD; thus, the increase in the volume of blood processed was more substantial for higher treatment frequencies when treatment time was extended as shown in Table 2. For all short daily HD prescriptions, the decrease in the predialysis serum phosphorus concentration was a strong function of the predialysis serum phosphorus concentration during thrice weekly HD when considering four, five or six treatments per week, similar to that shown in Figure 2; such relationships confirm that the percent decrease in predialysis serum phosphorus concentration will be relatively constant among all patients when the HD prescription is altered under these conditions. Figure 4 summarizes the predicted percent decreases in predialysis serum phosphorus concentration during these short daily therapies; note the relatively narrow interquartile ranges in the percent decrease in concentration under all conditions considered. When weekly treatment time and blood volume processed were held constant, predialysis serum phosphorus concentration decreased modestly as treatment frequency increased. For a fixed treatment frequency, adding treatment time per session resulted in substantial further reductions in predialysis serum phosphorus concentration. To further assess the importance of treatment time, independent of treatment frequency, the effect of doubling treatment time per session and halving the blood flow rate (same volume of blood processed) was next evaluated, an experimental approach used previously by others [18, 19]. After reducing the blood flow rate and lengthening the treatment, the dialyzer phosphorus clearance is decreased to 93 ± 15 mL/min (based on a phosphorus dialyzer mass transfer-area coefficient of 273 ± 45 mL/min) and the predicted percent reduction in predialysis serum phosphorus concentration is 27.7 (IQR: 24.7–30.0)%.

The effect of treatment frequency, dialyzer phosphorus clearance and the oral phosphorus binder prescription was then examined for HD prescriptions during long, 8-h nocturnal treatments. To quantify the oral phosphorus binder prescription, the concept of EPBD, as described recently, was used [21, 27]. This concept is general and can be used to quantify several different oral phosphorus binders when used in any combination. Based upon that previous work [27], 1 g of EPBD is able to inhibit 45 mg (1.45 mmol) of phosphorus absorption from the intestinal tract, and will therefore decrease the net generation of phosphorus accordingly. For example, if the net phosphorus generation rate was initially 2 g (64.6 mmol) per week and 2 g fewer of EPBD are prescribed per day, the net new phosphorus generation rate would be higher at 2.63 g (84.9 mmol) per week (in mmol: 64.6 + 7 × 2 × 1.45). Table 3 summarizes the long nocturnal HD prescriptions considered; dialyzer phosphorus clearance was arbitrarily assumed as equal to two-third, one-half or one-third the value during thrice weekly HD for a treatment frequency of three, Table 3. Example frequent HD treatment prescriptions: long nocturnal HD—effect of dialyzer phosphorus clearance and effective phosphorus binder dose

<table>
<thead>
<tr>
<th>Treatments per week</th>
<th>Session treatment time (min)</th>
<th>Dialyzer phosphorus clearance (mL/min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>480*</td>
<td>139 ± 18</td>
</tr>
<tr>
<td>4</td>
<td>480*</td>
<td>93 ± 12</td>
</tr>
<tr>
<td>5</td>
<td>480*</td>
<td>70 ± 9</td>
</tr>
<tr>
<td>6</td>
<td>480*</td>
<td>46 ± 6</td>
</tr>
</tbody>
</table>

*Assumed for all patients.

The baseline weekly treatment time was 620 ± 88 min, and the blood flow rate was assumed equal for all treatments.

Table 2. Example frequent HD treatment prescriptions: short daily HD—effect of treatment frequency and time

<table>
<thead>
<tr>
<th>Treatments per week</th>
<th>Volume of blood processed per week (L)</th>
<th>For equal weekly treatment time plus additional treatment time per session</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>+0 min</td>
</tr>
<tr>
<td>4</td>
<td></td>
<td>213 ± 58</td>
</tr>
<tr>
<td>5</td>
<td></td>
<td>213 ± 58</td>
</tr>
<tr>
<td>6</td>
<td></td>
<td>213 ± 58</td>
</tr>
</tbody>
</table>

*Assumed for all patients.

FIGURE 4: Predicted percent decrease in predialysis serum phosphorus when changing from thrice weekly to short daily therapies with prescriptions of equal weekly treatment time as during thrice weekly HD and the addition of treatment time as indicated. The dialyzer phosphorus clearance for all therapies was assumed as 139 ± 18 (mean ± standard deviation) mL/min. Median values are shown with error bars denoting the interquartile range for four treatments per week in blue, five treatments per week in pink and six treatments per week in green.
immediate postdialysis serum phosphorus concentrations \[28\], bilization clearance can be approximated from predialysis and hemodialysis treatment \[22, 25\]. Although the phosphorus mo-
several serum phosphorus concentrations during and after a patient, and the latter evaluations require the measurement of 
compartment model. In general, such an approach requires 
using phosphorus kinetic modeling based on a pseudo one-
phosphorus when changing from thrice weekly to long nocturnal HD treatments with prescriptions as shown in Table 3 for various reduc-
tions in the effective phosphorus binder dose or EPBD. The dialyzer phosphorus clearance for each therapy was reduced for more frequent therapies as defined in the text. Median values are shown with error bars denoting the interquartile range for three treatments per week in magenta, four treatments per week in blue, five treatments per week in pink and six treatments per week in green.

![FIGURE 5: Predicted percent decrease in predialysis serum phosphorus when changing from thrice weekly to long nocturnal HD treatments with prescriptions as shown in Table 3 for various reductions in the effective phosphorus binder dose or EPBD. The dialyzer phosphorus clearance for each therapy was reduced for more frequent therapies as defined in the text. Median values are shown with error bars denoting the interquartile range for three treatments per week in magenta, four treatments per week in blue, five treatments per week in pink and six treatments per week in green.](image)

four, five or six times per week, respectively. Figure 5 shows the predicted percent decreases in predialysis serum phosphorus concentration when altering the HD prescription from thrice weekly to long nocturnal HD. Also shown in this figure are comparable predictions when the EPBD is reduced in pa-
tients treated using these alternative HD prescriptions. In the absence of any change in EPBD, decreases in predialysis serum phosphorus concentration are large. With the reduction in EPBD by 2 g per day, the percent decrease in predialysis serum phosphorus concentration was \(~12\)% lower on average (range of 10–13\%); these findings were similar for all long nocturnal HD therapies considered.

**DISCUSSION**

This study describes an approach for predicting changes in predialysis serum phosphorus concentration when altering the HD prescription from thrice weekly to alternative HD prescriptions using phosphorus kinetic modeling based on a pseudo one-
compartment model. In general, such an approach requires prior determination of phosphorus kinetic parameters (mobil-
ization clearance and central distribution volume) for each patient, and the latter evaluations require the measurement of 
several serum phosphorus concentrations during and after a hemodialysis treatment \[22, 25\]. Although the phosphorus mo-
bilization clearance can be approximated from predialysis and immediate postdialysis serum phosphorus concentrations \[28\], the phosphorus central distribution volume would still require estimation, perhaps using anthropometric means. This com-
plete and systematic approach therefore requires substantial additional effort and cost.

Changes in predialysis serum phosphorus concentration after altering the HD prescription were predicted in this study using phosphorus kinetics parameters from a large cohort of patients treated by thrice weekly HD \[25\]. Those kinetic param-
eters likely span those of typical HD patients, at least those in the USA. Despite this wide range of phosphorus kinetic parameters, however, predicted changes in predialysis serum phosphorus concentration were strongly associated with the predialysis serum phosphorus concentration during thrice weekly HD and relatively independent of the patient-specific kinetic parameters. These predictions are consistent with the recent findings from the FHN Daily and Nocturnal Trials where the reduction in predialysis serum phosphorus concent-
tration resulting from the intervention of a more frequent HD prescription was more pronounced with higher serum phosphorus concentrations at baseline during thrice weekly HD \[21\]. The current findings suggest that the percent change in the predialysis serum phosphorus concentration is primarily dependent on the HD prescriptions and not on patient-specif-
ic phosphorus kinetic parameters. Thus, although phosphorus kinetics during HD treatments are patient-specific, percent changes in the predialysis serum phosphorus concentration when altering the HD prescription are relatively independent of such patient specificity. This latter simplified approach to phosphorus kinetic modeling could lead to simple nomograms or computer algorithms that could provide practical clinical guidance for prescribing alternative HD therapies to target the predialysis serum phosphorus concentration. It should be em-
phasized that the approach described in this study is general and can be made from any HD prescription to another, in-
cluding changes in treatment frequency, treatment time, dialy-
zzer phosphorus clearance, residual kidney phosphorus clearance and oral phosphorus binder prescription.

The effects of treatment time and frequency on the predialy-
sis serum phosphorus concentration predicted in this study are consistent with previous predictions by Eloot et al. \[29\] who evaluated the effect of alternative HD prescriptions on the removal and solute concentrations of urea and several guanidi-
no compounds. Those investigators showed that the effects of treatment time and frequency on serum concentrations of these uremic toxins were primarily dependent on their kinetically de-
determined distribution volume; namely, increases in treatment frequency were more effective in reducing solute concentrations for those solutes with small distribution volumes but increases in treatment time were more effective in reducing solute concent-
trations for those solutes with large distribution volumes. The pseudo one-compartment model of phosphorus kinetics assumes a very large peripheral compartment and therefore a large effective distribution volume; thus, the more substantial effect of treatment time in decreasing predialysis serum phosphorus concentration is expected based on extrapolations from this previous report by Eloot et al. \[29\].

The predictions from this study shown in Figure 4 are also consistent with previous work by Ayus et al. \[16\] who evalu-
ated phosphorus removal during short daily HD treatments. Those workers showed that longer 3-h, as opposed to 2-h, treatments 6 days per week were necessary to substantially in-
crease phosphorus removal and decrease predialysis serum phosphorus concentrations from that during 4-h thrice weekly HD treatments.

An example patient from the HEMO study data set will il-
lustrate how the current approach could be used clinically. Consider a patient who was dialyzed thrice weekly for 220 min
per treatment with a dialyzer phosphorus clearance of 155 mL/min and had a predialysis serum phosphorus concentration of 2.23 mmol/L. If that patient was treated with long nocturnal HD five times per week with a reduced dialyzer phosphorus clearance of 77 mL/min for 480 min per treatment, the simplified approach for phosphorus kinetic modeling based on the results in Figure 5 would predict a reduction in predialysis serum phosphorus concentration with no change in EPBD by 54% and achieve a concentration of 1.02 mmol/L (0.46 × 2.23 mmol/L). If the EPBD was also lowered by 4 g/day, then the predialysis serum phosphorus concentration would only be reduced by 32% and achieve a concentration of 1.52 mmol/L (0.68 × 2.23 mmol/L).

This study has several limitations. First, the predicted changes in predialysis serum phosphorus concentration are model dependent; thus, the predictions described here depend on the validity of a pseudo one-compartment model for describing phosphorus kinetics during various HD prescriptions. Although we have used this kinetic model for describing phosphorus kinetics during short daily and long nocturnal HD therapies [23], the predictions from the current study remain to be tested prospectively. Other kinetic models, such as that described by Spalding et al. [30] could also have been used to predict changes in serum phosphorus concentrations when altering the HD prescription; however, the latter kinetic model has also not been prospectively tested and it is more complex than the pseudo one-compartment model used here. It should also be noted that previous theoretical predictions using the model by Spalding et al. suggested that treatment frequency was more important than treatment time in decreasing serum phosphorus concentrations [31], a prediction that is inconsistent with many experimental observations [14–19]. Based on the previous work of Eloot et al. [29] noted above, the relative importance of treatment frequency predicted by the model of Spalding et al. is likely because the latter investigators assumed phosphorus was distributed in a relatively small distribution volume (compared with that assumed in the pseudo one-compartment model). Secondly, the previously determined phosphorus kinetic parameters and the predictions made in this study used dialyzer phosphorus clearances that were only estimated and not directly measured. Biases or errors in such estimations are likely to influence the magnitude of the predictions in this report; however, they are unlikely to alter the predicted percent decreases in predialysis serum phosphorus concentrations when altering the HD prescription, the main novel finding of this study. Thirdly, there are additional assumptions used in the model predictions, specifically that HD treatments are applied symmetrically during the week and that the oral phosphorus binder prescriptions are adhered to by the patient. Because HD treatments during a week are rarely applied symmetrically during a week, the current approach best applies for predicting midweek predialysis serum phosphorus concentrations as they represent average values. Fourthly, the current approach assumes a constant dietary intake of phosphorus. If altering the HD prescription substantially changes dietary protein intake, then the dietary phosphorus intake will also change. In the latter case, it may be possible to predict changes in dietary protein and phosphorus intake by simultaneously performing urea kinetic modeling in conjunction with phosphorus kinetic modeling as previously proposed by Gotch et al. [32]. Finally, the approach proposed here can only predict changes in predialysis serum phosphorus concentration for a patient who is currently being treated by HD, or other alternative extracorporeal therapies, and is at steady state.

This study demonstrates that phosphorus kinetic modeling based on a pseudo one-compartment model can be used to predict changes in predialysis serum phosphorus concentration when altering the HD prescription and that a simplified form of phosphorus kinetic modeling can provide practical clinical guidance to target specific changes in predialysis serum phosphorus concentration. Prospective validation of this approach in future studies is warranted.

CONFLICT OF INTEREST STATEMENT

All authors of this manuscript are employees of Baxter Healthcare Corporation with ownership interests. The results presented in this paper have not been published previously in whole or part, except in abstract form.

REFERENCES

phosphorus concentration (C_{\text{pre}}), phosphorus mobilization clearance (K_M), postdialysis phosphorus central distribution volume (V_{\text{post}}) and dialysis phosphorus clearance (K_d), assuming negligible residual kidney phosphorus clearance, the net generation rate of phosphorus (G) can be calculated by the following equations [26]:

$$\dot{C}_T = \frac{K_M}{K_M + K_d - Q_L} + \left[1 - \frac{K_M}{K_M + K_d - Q_L}\right] \left(\frac{V_{\text{pre}}}{T} + \frac{1}{K_M + K_d}\right) \left[1 - \frac{(V_{\text{post}} - V_{\text{pre}}) (K_d + Q_L)}{V_{\text{pre}}}ight],$$

(A2)

where has been assumed that the patient is in steady state and treatments are equally spaced during the week. Here, $T$ denotes the HD treatment time per session and $\theta$ denotes the average interdialytic interval during the week of interest. Equation (A1) can be applied during one combined intradialytic plus an adjacent interdialytic interval or over an entire week. If applied during one 4-h thrice weekly HD treatment and the adjacent interdialytic interval, for example, the variables in Equation (A1) would have units of mmol/min for $G$, mmol/L for $C_{\text{pre}}$, L/min for $K_d$, min for $T$ (240 min) and $\theta$ (3120 min).

Note that $C_T$ is dimensionless. The parameter $C_T$ denotes the time-average normalized serum phosphorus concentration and is calculated by [26]

$$V_{\text{pre}} = V_{\text{post}} + Q_L \times T.$$

(A3)

This equation assumes that all fluid is removed from the phosphorus central distribution volume during the treatment.

To calculate the predialysis serum phosphorus concentration under an alternative HD prescription, Equation (A1) is rearranged and solved for $C_{\text{pre}}$ using the previously calculated value of $G$ and the new HD prescription parameters ($T$, $\theta$, $K_d$, $Q_L$) while retaining the kinetic parameters constant. In all predictions reported here, the ultrafiltration rate was adjusted for changes in weekly treatment frequency by assuming the same amount of weekly dietary fluid intake.

When the number of oral phosphorus binders is also altered with the new HD prescription, the value of $G$ was modified by subtracting additional absorbed phosphorus at the rate of 45 mg (1.45 mmol) of phosphorus for every additional 1 g of EPBD per day or an equivalent amount per week.

For patients treated by thrice weekly HD (for example during the HEMO study) with measured predialysis serum phosphorus concentration (C_{\text{pre}}), phosphorus mobilization clearance (K_M), postdialysis phosphorus central distribution volume (V_{\text{post}}) and dialysis phosphorus clearance (K_d), assuming negligible residual kidney phosphorus clearance, the net generation rate of phosphorus (G) can be calculated by the following equations [26]:

$$G = \frac{C_{\text{pre}} \times K_d \times T \times \dot{C}_T}{T + \theta},$$

(A1)

where has been assumed that the patient is in steady state and treatments are equally spaced during the week. Here, $T$ denotes the HD treatment time per session and $\theta$ denotes the average interdialytic interval during the week of interest. Equation (A1) can be applied during one combined intradialytic plus an adjacent interdialytic interval or over an entire week. If applied during one 4-h thrice weekly HD treatment and the adjacent interdialytic interval, for example, the variables in Equation (A1) would have units of mmol/min for $G$, mmol/L for $C_{\text{pre}}$, L/min for $K_d$, min for $T$ (240 min) and $\theta$ (3120 min).

Note that $C_T$ is dimensionless. The parameter $C_T$ denotes the time-average normalized serum phosphorus concentration and is calculated by [26]