Having residual kidney function should lessen the requirement for hemodialysis. If the kidney still removes waste solutes to some extent, less dialysis is necessary to limit their accumulation in the body. A well-reasoned case has been made for reducing the intensity of dialysis in patients with residual function, particularly in those initiating dialysis. However, major barriers hinder reducing hemodialysis time, frequency, or both for patients with residual kidney function.

Current Guidelines for Incorporating Residual Function in the Dialysis Prescription

The first barrier to reducing dialysis time for patients with residual kidney function is encountered in determining an appropriate dialysis prescription. The 2015 Update of the Kidney Disease Outcomes Quality Initiative (KDOQI) Clinical Practice Guideline for Hemodialysis Adequacy adopted weekly standard Kt/V urea (stdKt/V) as an index of adequacy and provided formulas for stdKt/V that incorporate residual urea clearance (Kru). For hemodialysis schedules other than thrice weekly, it suggests targeting a stdKt/V of 2.3 to achieve a minimum delivered stdKt/V of 2.1. It also suggests the dialysis prescription can be reduced for patients with significant residual function.

The 2015 guideline update not only adopted stdKt/V as a measure of adequacy, but changed the definition of this parameter. As originally defined by Gotch, stdKt/V depended on the average peak urea concentration during the weekly dialysis cycle. If urea production and body size were held constant, different dialysis prescriptions provided the same stdKt/V if the weekly average peak urea concentration was the same. However, when the 2015 update adopted stdKt/V as an adequacy measure, it increased the weight given to residual kidney function and abandoned Gotch’s original definition of stdKt/V. Different prescriptions that provide the same stdKt/V according to the 2015 update will no longer yield the same weekly peak urea concentrations.

The increased weight given to Kru appears in the formulas the 2015 update provides for calculating stdKt/V. Dargvadas et al. had developed formulas that allowed approximation of Gotch’s stdKt/V from the single pool Kt/V (spKt/V) for an individual treatment, the treatment frequency (n), the weekly ultrafiltration volume, and Kru. The update employs these formulas, but changes the factor by which Kru is multiplied. A value for equilibrated Kt/V (eKt/V) is first obtained from spKt/V using the following formula:

\[ eKt/V = spKt/V \times \frac{t}{t+30} \]

A value very close to the value for stdKt/V the patient would have in the absence of residual function can then be calculated as follows:

\[ stdKt/V_{\text{without residual function}} = \frac{10,080}{1 - \frac{0.974}{V} \times \frac{Uf}{V}} \]

In this formula, V is the volume of distribution of urea and F is the number of treatments per week (also referred to as N). The contribution of residual function to stdKt/V is then reflected by the addition of one more term. A value very close to stdKt/V as defined by Gotch is given by the following:

\[ stdKt/V = stdKt/V_{\text{without residual function}} + Kru \times \frac{0.974}{spKt/V + 1.62} + 0.4 \times \frac{10,080}{V} \]

However, the 2015 update specifies that stdKt/V should be calculated as follows:

\[ stdKt/V = stdKt/V_{\text{without residual function}} + Kru \times \frac{10,080}{V} \]

The removal of the multiplier (0.974/ (spKt/V + 1.62) + 0.4) increases the weight given to Kru. This change, which went largely unheralded, appears minor on examination of the formulas. It has, however, a large effect on the treatment time required to achieve a target stdKt/V for patients with significant Kru, as illustrated in Figure 1. Although the 2015 update adopted stdKt/V as an adequacy measure, it maintained the previous guidelines’ recommendations to reduce the intensity

Correspondence: Dr. Timothy W. Meyer, Nephrology, 111R, VA Palo Alto Health Care System, 3801 Miranda Avenue, Palo Alto, CA 94304. Email: twmeyer@stanford.edu

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of thrice-weekly dialysis only for Kru > 2 ml/min and reduce dialysis frequency only for Kru > 2 or 3 ml/min.

A Mobile Phone Application to Facilitate Calculation of stdKt/V

The increased weight given to Kru in the 2015 update has not stimulated much effort to reduce treatment time for hemodialysis patients with residual function. One barrier to reducing time is the difficulty of the required calculations. Monthly reports generated by dialysis providers generally do not include stdKt/V calculated as described in the 2015 update, and prescribing physicians who attempt to calculate stdKt/V for themselves face a daunting task. The web-based program Solute Solver What If simplifies this task, but requires entering multiple time values to estimate stdKt/V as a function of time.6

We created a mobile phone application (app) to simplify estimating the treatment time required to reach a target stdKt/V (Figure 2). The app first requires an estimate of the urea distribution volume. A physician can either enter a urea volume obtained from the provider’s monthly report or enter the patient’s age, sex, weight, and height to obtain the body water volume calculated by the Watson formula. The physician then enters the treatment time, spKt/V, Kru, estimated weekly fluid gain, and a target stdKt/V. The default target stdKt/V is 2.3, as recommended in the 2015 update, but different values can be entered. From these values, the app calculates the treatment times required to reach the target stdKt/V if thrice-weekly treatment frequency is maintained, and if treatment is reduced to twice weekly. The app provides an alert if suggested treatment times would result in fluid removal rates in excess of a commonly cited maximum of 13 ml/kg per hr. The Supplemental Materials describe the calculations used by the app (Supplement 1) and offer documentation that results obtained with the app are close to those obtained with a urea kinetic program over a wide range of modeled dialysis prescriptions (Supplement 2). The app is available as stdKtV Calculator for iOS through the App Store and as stdKt/V Calculator for Android in the Play Store.

Administrative Barriers to Incorporating Residual Function in the Dialysis Prescription

In the United States, there are also administrative impediments to reducing treatment time and/or frequency for patients with residual kidney function. The End Stage Renal Disease Quality Incentive Program (QIP) and related policies of the Centers for Medicare & Medicaid Services pose a barrier to reducing treatment time.7

The QIP requires each dialysis facility to report the fraction of adult patients on hemodialysis achieving a threshold spKt/V $\geq$ 1.2. However, it specifically prohibits including residual function in this measure, despite its inclusion being recommended in reporting adequacy for patients on peritoneal dialysis. Excluding residual function from adequacy assessment likely lengthens treatment times. Most patients have Kru $\geq$ 2 ml/min when they begin dialysis, and some maintain this for a considerable period. Dialysis prescriptions for these patients may be adequate by KDOQI standards and yet not meet the QIP threshold, as shown in Table 1. Because dialysis facilities must report the portion of their patients meeting the threshold, they are thus encouraged to maintain longer thrice-weekly treatment times than would be required to provide adequate dialysis by KDOQI standards in patients with residual function.

Figure 1. Treatment times required for a twice-weekly regimen to provide an stdKt/V_{area} of 2.3 using the KDOQI 2015 update and Gotch’s original formulation of stdKt/V_{area}. The treatment times required per session for twice-weekly hemodialysis to provide a stdKt/V_{area} of 2.3 are plotted as a function of residual kidney urea clearance Kru. The blue line depicts times required with stdKt/V_{area} calculated as described in the 2015 update and the red line depicts the treatment times required to provide the same stdKt/V_{area} calculated as originally described by Gotch. The arrows mark the times required with Kru 2.5 ml/min using the 2015 update stdKt/V_{area} (3.6 hours) and the original stdKt/V_{area} (4.8 hours). Modeled for a patient with the characteristics described in Supp 3.
The QIP does not pose a barrier to reducing treatment frequency, because adequacy reporting is not required for patients dialyzed twice weekly. However, twice-weekly treatment may prove costly for facilities. It could leave gaps in standard Monday-Wednesday-Friday and Tuesday-Thursday-Saturday dialysis schedules. Decreasing the treatment frequency could also reduce revenue from commercial insurers, which pay as much as four times the Medicare rate for each hemodialysis treatment.8 The small share of patients with commercial insurance provides a disproportionate

Table 1. Thrice weekly treatment times required to reach std\text{Kt/V} = 2.3

<table>
<thead>
<tr>
<th>Kru (ml/min)</th>
<th>Larger Body Size (V_{d\text{urea}} = 42 L)</th>
<th>Smaller Body Size (V_{d\text{urea}} = 32 L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Required Time (Min)</td>
<td>spKt/V</td>
</tr>
<tr>
<td>0</td>
<td>225</td>
<td>1.35</td>
</tr>
<tr>
<td>1</td>
<td>189</td>
<td>1.17</td>
</tr>
<tr>
<td>2</td>
<td>158</td>
<td>0.98</td>
</tr>
<tr>
<td>3</td>
<td>131</td>
<td>0.86</td>
</tr>
</tbody>
</table>

Treatment times required per session for a thrice-weekly hemodialysis regimen to provide a std\text{Kt/V} of 2.3 calculated as specified in the 2015 update. In patients with residual function treatments that provide adequate std\text{Kt/V} will often result in spKt/V values below the target value of 1.2 imposed by the End Stage Renal Disease QIP. Times were calculated using Solute Solver What If8 for patients with the specified two pool urea distribution volumes (V_{d\text{urea}}), and assuming a dialytic clearance for urea of 250 ml/min. Kru values were multiplied by 0.93 to convert values, which are usually calculated in terms of ml of plasma per minute to ml of water per minute for entry into the urea kinetic modeling program.

Figure 2. App to facilitate calculation of treatment times required to achieve a target std\text{Kt/V}. Screenshots of a mobile phone app that estimates treatment time to achieve a desired std\text{Kt/V} calculated as prescribed in the 2015 update of the KDOQI Guideline for Hemodialysis Adequacy. The user first declares whether a urea volume of distribution is available (left panel) and then enters values describing the patient’s status and a desired std\text{Kt/V} value (middle panel). The app then provides estimates of treatment time required to achieve this std\text{Kt/V} for both twice- and thrice-weekly treatment (right panel). Hitting “More Info” provides additional information about twice- and thrice-weekly treatment schedules on additional panels (not shown).
share of facilities’ revenue. To the extent that commercial insurance coverage is, as with residual function, more commonly maintained early in the course of dialysis, placing patients with residual function on twice-weekly dialysis would reduce revenues. Together, governmental policies and financial constraints thus encourage at least thrice-weekly treatments, providing spKt/V ≥1.2 for all patients on in-center hemodialysis, regardless of residual function.

Other Barriers to Reducing Dialysis Time and Frequency
Reducing treatment requires more rapid ultrafiltration. In patients with residual function, however, urine output reduces the need for ultrafiltration, and can be increased by diuretics. Further studies are needed to ensure that diuretics do not impair residual clearance of uremic solutes or have other undesirable consequences. Limiting salt intake also reduces the need for ultrafiltration, and although difficult, might be achieved more often if patients were offered reduced treatment time in return.

Elevated plasma potassium and phosphate concentrations sometimes preclude reducing dialysis time and frequency. Residual function, however, helps remove both potassium and phosphate, and diuretics can increase residual excretion of potassium. In general, patients with residual function have been reported to have lower-than-average potassium and phosphate levels, and neither high potassium nor high phosphate has posed a notable barrier to initiating incremental hemodialysis.9,10

Finally, maintaining dialysis times in patients with residual function might be presumed necessary to remove some unmeasured uremic toxin(s). However, our reliance on urea to assess solute removal by both dialysis and residual kidney function can be misleading. Urea has the highest dialytic clearance of any known solute, but the kidney, by contrast, clears many solutes more rapidly than urea, which is in part reabsorbed in the proximal tubule. Low molecular weight proteins such as β2 microglobulin are cleared at rates close to the GFR. Tubular secretion raises the clearances of many other solutes above the GFR, and their high clearances relative to urea are preserved at least to some extent in residual functioning kidneys of patients on dialysis. The increased weighting of residual function in the 2015 update can thus be scientifically defended. This is most apparent by comparing predicted levels of different solutes in patients with and without residual function who receive treatments that provide the same stdKt/V, as shown in Figure 3. As previously noted, although patients with residual function will have slightly higher average peak urea levels, levels of other solutes will tend to be lower. Thus, without a clinical study demonstrating benefit, extending treatment of patients with residual function beyond the 2015 update’s target stdKt/V seems hard to justify.

Future Directions
Reliance on urea kinetics prevents confident assessments of the relative values of different dialysis prescriptions.11 Some modification of the urea-based KDOQI Guidelines and of Centers for Medicare & Medicaid Services’ policies thus seem warranted.

One possible approach is the strategy advocated by the International Society of Peritoneal Dialysis,12 which still recommends routine assessment of toxin removal using urea and/or creatinine as surrogates, but does not oblige a patient on peritoneal dialysis who feels well to increase volume or frequency of exchanges to meet a numeric target. An analogous approach to hemodialysis would require continued measurement of stdKt/V. Low values would suggest that symptoms such as fatigue and poor appetite were due to inadequate toxin removal and alert physicians to poor vascular access function. In many patients,

Figure 3. The effect of residual function on the plasma levels of different uremic solutes. Predicted plasma solute levels in a patient with no residual function (red lines) and with a Kru of 2 ml/min (blue lines) dialyzed thrice weekly to provide a stdKt/V of 2.3 calculated using the KDOQI 2015 update. The treatment time is 210 minutes in the patient without residual function and 130 minutes in the patient with residual function. Peak (solid line) and time averaged (dashed line) concentrations of urea are slightly higher in the patient with residual function (left panel). At the same stdKt/V, however, the patient with residual function has lower plasma concentrations of β2 microglobulin (middle panel) and even more markedly lower concentrations of hippurate (right panel). Reviewing the figure, it is tempting to increase the weighting of residual function above the level assigned in the 2015 update as described by Casino and Basile.2 Modeled for a patient with characteristics described in Supplement 3.
time on dialysis, bene
more intense treatment is additional
fi
long-term bene
sary to improve symptoms provides
solute removal beyond the level neces-
dialysis to achieve a target stdKt/V.

However, individual
patients who feel well and have adequate volume and inorganic ion control would not be obliged to spend more time on dialysis to achieve a target stdKt/V.

Trials have largely failed to show that solute removal beyond the level necessary to improve symptoms provides long-term benefit. When the burden of more intense treatment is additional time on dialysis, benefit should be better established. To proceed beyond treatment on the basis of symptom control, we will need better knowledge of uremic solutes and clinical trials assessing the benefit of controlling their levels.

DISCLOSURES

The results presented in this paper have not been published previously in whole or part, except in abstract form. T.L. Sirich and T. Meyer have served as consultants for Baxter. T. Meyer has a patent application pending for improved removal of protein-bound solutes by dialysis; reports receiving research funding from Outset Medical; and reports being a scientific advisor or member of the JASN Editorial Board, and Kidney Internation al on the Editorial Board. J.K. Leyoldt reports serving as a consultant for Baxter International, Diality, Novaflux, and NxStage (Fresenius). All remaining authors have nothing to disclose.

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SUPPLEMENTAL MATERIAL

This article contains the following supplemental material online at http://jasn.asnjournals.org/lookup/suppl/doi:10.1681/ASN.2021030361/-/DC Supplemental.

Supplement 1. How the stdKt/V calculator program works.
Supplement 2. Testing of the stdKt/V calculator app.
Supplement 3. Parameters used in modeling dialysis treatment times and plasma solute levels in patients with residual function.

REFERENCES

7. Centers for Medicare & Medicaid Services (CMS), HHS: Medicare Program; End-Stage Renal Disease Prospective Payment System, Payment for Renal Dialysis Services Furnished to Individuals with Acute Kidney Injury, End-Stage Renal Disease Quality Incentive Program, Durable Medical Equipment, Prosthetics, Orthotics and Supplies (DMEPOS) Competitive Bidding Program (CBP) and fee schedule amounts, and technical amendments to correct existing regulations related to the CBP for Certain DMEPOS, Final rule. Fed Regist 83: 56922–57073, 2018
Supplemental Table of Contents

Supplement S1: How the stdKt/V Calculator Program Works

Supplement S2: Testing of the stdKt/V Calculator App

Supplement S3: Parameters Used in Modeling Dialysis Treatment Times and Plasma Solute Levels in Patients with Residual Function
Supplement S1: How the stdKt/V Calculator Program Works

The required inputs are:

- Urea Volume of Distribution or Anthropometric Data from which the App can estimate a Urea Volume of Distribution
- Weight (kg)
- Current Dialysis Time (min)
- Weekly Ultrafiltration (L/wk)
- Kru mL/min
- Current spKt/V
- Target stdKt/V (the default is the target stdKt/V value of 2.3 specified in the 2015 update of the KDOQI Clinical Practice Guideline for Hemodialysis Adequacy)

After obtaining the necessary inputs, the program proceeds to arrange the variables to determine dialysis treatment times necessary to achieve the target stdKt/V. The program first obtains a value for urea’s volume of distribution. The program’s developers found that some dialysis units provide estimates of urea’s volume of distribution in their monthly patient reports while others do not provide such values. If the user has a value for urea’s volume of distribution, the user enters that value and the program uses it in calculating stdKt/V. If the user does not have a value for urea’s volume of distribution, the program requires inputs of gender, age, weight, and height and then calculates estimated body water volume according to the formulas of Watson et al.2 shown below:

\[
\begin{align*}
(1) \text{ Male Volume: } & \quad 2.447 - (0.09156 \times \text{ age}) + (0.1074 \times \text{ height}) + (0.3362 \times \text{ weight}) \\
(2) \text{ Female Volume: } & \quad -2.097 + (0.1069 \times \text{ height}) + (0.2466 \times \text{ weight})
\end{align*}
\]

The Watson body water volume is then multiplied by 0.9 to obtain an estimate of the effective urea volume of distribution.

Once the urea volume of distribution is obtained, the program employs an iterative method to estimate the time on dialysis required to achieve the specified target stdKt/V. The program assumes that other dialysis prescription parameters including the blood flow, dialysate flow, dialyzer type, and end treatment weight will not change and that the prescriber will change only the treatment time in an effort to reach the target stdKt/V. The iterative method works by repeatedly estimating new time values and calculating a new value for stdKt/V denoted ‘stdKt/V trial’ for each time value. It stops iterating and specifies a required time when the absolute value of the difference between the ‘stdKt/V trial’ for that time and the target stdKt/V is less than 0.1% of the target stdKt/V. The program goes through this iterative method first to calculate the time required to achieve the target stdKt/V if dialysis is performed twice a week and then again to calculate the time required to achieve the target stdKt/V if dialysis is performed three times a week. After the iterative processes are completed, the program calculates the maximum ultrafiltration rates which
would be observed if dialysis treatments were performed for the specified times. This is
done assuming the longest interval between treatment will be four days for twice a week
treatment and three days for three times a week treatment. The program then checks if these
maximal ultrafiltration rates exceed 13 mL/kg/hr. If the maximum ultrafiltrate rates exceed
13 mL/kg/hr, the program calculates the time(s) that would be required to reduce the
ultrafiltration rate(s) to 13 mL/kg/hr and provides these value(s) to the user.

The main output page of the program (pictured) thus provides the following values for twice
a week dialysis and for three times a week dialysis:

stdKt/V target (the user’s input value is repeated)
Time required: (the time required to reach the stdKt/V target, in minutes)
Ultrafiltration Rate: (the ultrafiltration rate expected after the longest interdialytic interval
at the specified time. If this value is greater than 13 mL/kg/hr, the program specifies a longer
treatment time which would reduce the rate to 13 mL/kg/hr.)

The program’s iterative method requires that it calculate ‘stdKt/V trial’ values for a
candidate dialysis times t’ assuming a three times per week and a two times per week
schedule. This is done by calculating values for eKt/V, the equilibrated Kt/V. Two
assumptions are made. First, the program assumes that an accurate value for eKt/V can be
obtained from spKt/V using the equation provided in the 2015 update of the KDOQI
Clinical Practice Guideline for Hemodialysis Adequacy.1 Second the program assumes that
a change in dialysis time results in a proportional change in eKt/V if the end treatment
volume remains constant and if the dialysis blood flow, dialysate flow, and dialyzer are
unchanged. Neither of these assumptions is precisely correct however the errors in eKt/V
are small over the ranges of spKt/V, dialysis time, and urea volume of distribution we deal
with in clinical practice. This was confirmed by our finding that results obtained with our
mobile phone program are close to those obtained with a urea kinetic program over a wide
range of modeled dialysis prescriptions (Supplementary Materials Item S2).

The program determines a ‘stdKt/V trial’ for a given dialysis time as follows:

a. eKt/V is calculated using the input values for the current spKt/V and the
current dialysis prescription using the equation:

\[ eKt/V = \frac{spKt/V \times time}{time + 30} \]

b. A value for the "effective urea clearance" (K_eff) is then calculated from eKt/V
and the values for the urea distribution volume V and the current dialysis
time:

\[ (4) K_{eff} = \frac{V \times 1000 \times eKt/V}{time} \]
With values for $K_{eff}$ and $V$ the program can calculate a value of ‘stdKt/V trial’ for any assumed time $t'$. The program begins the process of iteration using the current dialysis time as the initial value. To calculate a stdKt/V value for each treatment time the program first calculates an spKt/V for each treatment time by reversing equation (3) and then follows the steps for calculating stdKt/V from spKt/V described in the 2015 update of the KDOQI Clinical Practice Guideline for Hemodialysis Adequacy.1

(1) Equation (3) is used in reverse to calculate a new spKt/V' for a given time $t'$, $K_{eff}$ and Volume, with the equation below:

$$spKt/V' = \frac{K_{eff} \cdot t'}{V + 1000 \cdot \frac{t'}{t' + 30}}$$

(2) eKt/V: Equation (3) is then used again to calculate a new eKt/V' for the new spKt/V' that was produced in step (1)

(3) stdKt/V_Leypoldt: The program then calculates the stdKt/V predicted for the given value eKt/V if that value of eKt/V' were obtained with dialysis from a single compartment of fixed-volume as described by Leypoldt.3 This calculation is based on the currently assumed dialysis time $t'$, the number of dialysis per week ($N$) and the eKt/V' calculated in step (2) as shown in the equation below:

$$stdKt/V_{Leypoldt} = \frac{10,080 \cdot a/t'}{eKt/V} - \frac{10,080}{N \cdot t'} + \frac{1}{a/eKt/V}, \text{where } a = 1 - e^{-eKt/V'}$$

(4) UF Factor: The program then multiplies the stdKt/V_Leypoldt by an ultrafiltration factor (UFF) to take into account the effect on stdKt/V of the reduction of the urea distribution volume which occurs during dialysis treatment. This factor is:

$$UFFactor = \frac{1}{1 - 0.74 \cdot \text{weekly UF}}$$

where $N$ is the number of treatments per week, and weekly UF is the input value for the weekly ultrafiltration.

(5) KruAdd: The program then adds a factor to account for the contribution of the residual urea clearance $Kru$ to stdKt/V as defined in the 2015 update of the KDOQI Clinical Practice Guideline for Hemodialysis Adequacy.1 This added factor is:
\[
KruAdd = \frac{10,080 \times Kru}{V \times 1000}
\]

(6) stdKt/V_{trial}: The program has thus obtained a value stdKt/V_{trial} for time t'.

\[
(9) stdKt/V_{trial} = UF Factor \times stdKt/V_{Leypoldt} + KruAdd
\]

The program then determines whether the value of the difference between the ‘stdKt/V trial’ and the stdKt/V_target is higher or lower than 0.1% of stdKt/V_target. If the absolute value of the difference is smaller than 0.1% the program specifies t' as the time required to meet the user specified stdKt/V_target. If it does not, the program needs to perform a further iteration. To do so, it first determines whether the stdKt/V_{trial} is higher or lower than the target value. If it is lower, the program needs to try a longer time. If it is higher, the program needs to try a shorter time. The program makes step changes of 0.1 minute but reports the treatment time required in units of 1 minute.

When the program has determined time values that will provide the target stdKt/V for twice a week and for three times a week dialysis, it proceeds to calculate the maximum ultrafiltration rates (called removal rates in the program) which would be encountered during a week of treatment with those dialysis times. This is done with the removal rate function, which has the form:

(1) weightGainPerDay: calculates the weight gained daily

\[
weightGainPerDay = \frac{weeklyUFInput}{daysOfTheWeek (ie: 7)}
\]

accumulationFactor: Selects the longest between dialysis treatments. For twice a week dialysis, this is four days and for three times a week dialysis this is three days.

(2) Weight Accumulation: Calculates the weight accumulated over the longest time between treatments (in mL):

\[
Weight\_accumulation = weightGainPerDay \times accumulationFactor \times 1000
\]

(3) Removal Rate Calculation: Calculates the removal rate in mL/(kg*hours) as the Weight Accumulation over the product of the dialysis treatment time in hours and the weight of the patient in kg.

\[
Removal\ Rate = \frac{weight\_accumulation}{(time/60) \times weight\ of\ Patient}
\]

The removal rates for dialysis performed twice a week and dialysis performed three times a week are then displayed as the Ultrafiltration Rates on the main output page. The program then checks whether these rates are less than 13.0 mL/(kg*hr). If the time required to reach
the target stdKt/V results in a removal rate higher than 13.0 mL/(kg*hr), the application uses a Removal Rate Adjustment function which calculates the longer time required to reduce the removal rate to 13.0 mL/(kg*hr). This time is calculated as:

\[
(14) \quad \text{time} = \frac{60 \ast \text{weight\_accumulation}}{\text{weight of Patient} \ast 13}
\]

The program offers the user more information ("More Info") for both twice a week dialysis and three times a week dialysis. First, it uses the Tattersall equation (equation (3) above) to calculate the spKt/V value the user may expect to see when if the dialysis time is changed to the time required to meet the specified target stdKt/V. It does further calculations if the times required to limit the removal rate to 13 ml/(kg*hr) are greater than the time required to achieve the target stdKt/V for either twice a week dialysis or three times a week dialysis. It calculates value for the spKt/V and stdKt/V using the equation (3) above and then stdKt/V using equations (6) to (9) for the longer time(s).

The program’s developers found that most nephrologists calculate the residual urea clearance Kru in terms of ml of plasma per minute. This is the result obtained when the amount of urea in a urine collection is divided by the time of the collection and by an average of pre and post treatment "BUN" values reported by the clinical laboratory. Most online calculators determine Kru in this manner. The program does not correct the entered value for Kru to ml/min of water per minute in calculating stdKt/V. The 2015 update of the KDOQI Clinical Practice Guideline for Hemodialysis Adequacy does not specify whether or not this should be done, and values obtained entering Kru in ml of plasma per minute are close to those obtained with a urea kinetic program over a wide range of modeled dialysis prescriptions (Supplemental Materials Item S2).
Supplement S2: Testing of the stdKt/V Calculator App

The mobile phone app *stdKt/V Calculator* estimates the treatment times required for a patient currently on 3X weekly dialysis with a known spKt/V to achieve a specified stdKt/V on 3X weekly dialysis and on 2X weekly dialysis if no changes are made in the blood flow, dialysate flow, or dialyzer. The accuracy of the program's estimates were tested by entering the program's time values into the established urea kinetic modeling program *Solute Solver What-if4* and comparing the stdKt/V value obtained by the kinetic modeling program with the target stdKt/V value entered into *stdKt/V Calculator*. This testing was done for a set of hypothetical patients on 3X weekly dialysis with arbitrarily chosen values for urea volume of distribution, dialysis time, weekly ultrafiltration rate, residual urea clearance, and dialytic urea clearance. *Solute Solver Lite5* was used to generate hypothetical patients with the range of values shown in the table below.

<table>
<thead>
<tr>
<th>Dialysis Parameter</th>
<th>Values Employed in Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea Volume of Distribution (liters)</td>
<td>20, 30, 40, 50</td>
</tr>
<tr>
<td>Dialysis Time (min)</td>
<td>180, 210, 240</td>
</tr>
<tr>
<td>Weekly UF (liters/week)</td>
<td>7, 18</td>
</tr>
<tr>
<td>Kru (ml/min)</td>
<td>0, 1, 2, 3, 4</td>
</tr>
<tr>
<td>Dialytic Urea Clearance (ml/min)</td>
<td>200, 250, 300</td>
</tr>
</tbody>
</table>

Using all possible combinations of the 4 values for urea volume of distribution, 3 values for dialysis time, 2 values for weekly UF, 5 values for Kru, and 3 values for dialytic urea clearance resulted in the generation of 360=4x3x2x5x3 hypothetical patients. The values for time, weekly UF, and Kru listed in the table above were entered into the *stdKt/V Calculator*. The values entered into the *stdKt/V Calculator* for urea volume of distribution and dialytic clearance were generated by
entering different combinations of hypothetical pre- and post-dialysis BUN values into Solute Solver Lite to obtain values close to those listed in the table.

We initially tested whether the stdKt/V Calculator estimated correct times to achieve the target stdKt/V of 2.3 specified in the 2015 Update of the KDOQI Guideline1 for both 3x weekly and 2x weekly dialysis. The values of spKt/V generated by Solute Solver Lite for each of the hypothetical patients along with the values for urea volume of distribution, dialysis time, weekly ultrafiltration rate, and residual urea clearance were entered into the stdKt/V Calculator with the target stdKt/V left at the default value of 2.3. This yielded 720 treatment times values (360 for 3x weekly dialysis and 360 for 2x weekly dialysis) that stdKt/V Calculator estimated would be required to achieve a stdKt/V of 2.3. These times were then entered along with the hypothetical patients' values for urea volume of distribution, dialysis time, weekly ultrafiltration rate, residual urea clearance, and dialytic urea clearance into Solute Solver What-If to obtain stdKt/V values by urea kinetic modeling. In this testing we initially included values for all of the 360 possible combinations of parameters listed in Table S1 including clinically unreasonable combinations such as 300 minute treatments with a dialytic urea clearance of 300 ml/min in small patients.

Solute Solver What-If declined to calculate stdKt/V for 69 of the 720 sets of entered values because the treatment time was outside the range of 30 to 720 minutes or because the resultant spKt/V values would have been extremely high. For the other 651 sets of values the stdKt/V value obtained by urea kinetic modeling averaged 2.32 ± 0.04 (mean ± sd) and the ratio of the value obtained by urea kinetic modeling to the target value of 2.3 was 1.01 ± 0.02. The stdKt/V values obtained by kinetic modeling were even closer to the stdKt/V Calculator target when an additional 64 treatment times of less than 60 minutes were excluded from analysis. When this was done the stdKt/V values obtained by urea kinetic modeling averaged 2.31 ± 0.03 (mean±sd) and the ratio of the value obtained by urea kinetic modeling to the target value of 2.3 was 1.01 ± 0.02. A histogram of the values obtained by urea kinetic modeling is presented in Figure S1 below.
Figure S1.

The figure shows the distribution of stdKt/V values obtained by urea kinetic modeling using Solute-Solver What-If for 587 hypothetical cases in which the stdKt/V Calculator program was used to estimate the time required to obtain a stdKt/V of 2.3 based on input values for spKt/V, urea volume of distribution, treatment time, weekly ultrafiltration rate, and residual urea clearance Kru. Cases in which a treatment time of less than 60 minutes was estimated as required to achieve the target stdKt/V were excluded.

We further tested whether the stdKt/V Calculator estimated correct times to achieve target stdKt/V values of 2.5 and or 2.1. The values of spKt/V generated by Solute Solver Lite for each of our 360 hypothetical patients along with their values for urea volume of distribution, dialysis time, weekly ultrafiltration rate, and residual urea clearance were entered into the stdKt/V Calculator with the target stdKt/V set to 2.5 and to 2.1.

For a target stdKt/V of 2.5 Solute Solver What-If declined to calculate stdKt/V for 81 of the 720 sets of entered values because the treatment time was outside the range of 30 to 720 minutes or because the resultant spKt/V values would have been extremely high. For the other 639 sets of values the stdKt/V values obtained by urea kinetic modeling averaged $2.52 \pm 0.04$ (mean $\pm$ sd) and the ratio of the value obtained by urea kinetic modeling to the target value of 2.5 was $1.01 \pm 0.02$. The stdKt/V values obtained by kinetic modeling were again even closer to the
stdKt/V Calculator target when an additional 50 treatment times of less than 60 minutes were excluded from analysis. When this was done the values the stdKt/V value obtained by urea kinetic modeling was averaged 2.51 ± 0.03 (mean ± sd) and the ratio of the value obtained by urea kinetic modeling to the target value of 2.5 was 1.01 ± 0.01. A histogram of the values obtained by urea kinetic modeling is presented in Figure S2 below.

Figure S2.
The figure shows the distribution of stdKt/V values obtained by urea kinetic modeling using Solute-Solver What-If for 589 hypothetical cases in which the stdKt/V Calculator program was used to estimate the time required to obtain a stdKt/V of 2.5 based on input values for spKt/V, urea volume of distribution, treatment time, weekly ultrafiltration rate, and residual urea clearance Kru. Cases in which a treatment time of less than 60 minutes was estimated as required to achieve the target stdKt/V were excluded.

For a target stdKt/V of 2.1 Solute Solver What-If declined to calculate stdKt/V for 66 of the 720 sets of entered values because the treatment time was outside the range of 30 to 720 minutes or because the resultant spKt/V values would have been extremely high. For the other 654 sets of values the stdKt/V values obtained by urea kinetic modeling averaged 2.16 ± 0.06 (mean ± sd) and the ratio of the value obtained by urea kinetic modeling to the target value of 2.1
was $1.03 \pm 0.03$. The stdKt/V values obtained by kinetic modeling were again even closer to the stdKt/V Calculator target when an additional 89 treatment times of less than 60 minutes were excluded from analysis. When this was done the values the stdKt/V value obtained by urea kinetic modeling was averaged $2.14 \pm 0.05$ (mean ± sd) and the ratio of the value obtained by urea kinetic modeling to the target value of 2.1 was $1.02 \pm 0.02$. A histogram of the values obtained by urea kinetic modeling is presented in Figure S3 below.

**Figure S3.**

The figure shows the distribution of stdKt/V values obtained by urea kinetic modeling using Solute-Solver What-If for 565 hypothetical cases in which the stdKt/V Calculator program was used to estimate the time required to obtain a stdKt/V of 2.1 based on input values for spKt/V, urea volume of distribution, treatment time, weekly ultrafiltration rate, and residual urea clearance Kru. Cases in which a treatment time of less than 60 minutes was estimated as required to achieve the target stdKt/V were excluded.
The testing described above was performed with the iOS version of the program. A subset of the hypothetical test patients was rerun on the Android version of the program to confirm that it yielded the same values.
References


Supplement S3: Parameters Used in Modeling Dialysis Treatment Times and Plasma Solute Levels in Patients with Residual Function

Figure 1 depicts treatment times required for a hypothetical patient with a two-compartment urea volume of distribution of 36 liters, an inter-compartmental urea clearance of 576 ml/min, a fluid gain of 1 liter/day removed by dialysis, and a dialytic urea clearance of 260 ml/min.

Figure 2 shows solute were modeled for a patient with a urea volume of 36 liters and a dialytic urea clearance of 260 ml/min using distribution volumes and dialytic and residual clearances for other solutes relative to those of urea and a non-renal clearance for \( \beta_2 \) microglobulin obtained from previous publications.\(^1\)\(^3\)

