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 Adequacy1)

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 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:

(1) $Male\ Volume: 2.447 - (0.09156 * age) + (0.1074 * height) + (0.3362 * weight)$
(2) $Female\ Volume: -2.097 + (0.1069 * height) + (0.2466 * weight)$

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:

$$eKt/V = \frac{spKt/V \; * \; time}{time + 30}$$

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:

$$(4)\; K\_eff = \frac{V * 1000 * eKt/V}{time}$$

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:

$$(5)\ spKt/V' = \frac{\frac{K\_eff*t'}{V*1000}}{\frac{t'}{t'+30}}$$

(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:

$$(6)\ \ stdKt/V'_{Leypoldt} = \frac{10{,}080 * a/t'}{\frac{a}{eKt/V} + \frac{10{,}080}{N*t'} - 1}, where\ a = 1 - e^{-eKt/V'}$$

(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:

$$(7)\ UFFactor = \frac{1}{1 - \frac{0.74*weekly\ UF}{N*V}}$$

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:

$$(8)\ KruAdd = \frac{10{,}080 * Kru}{V * 1000}$$

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

$$(9)\ stdKt/V_{trial} = UF\ Factor * stdKt/V'_{Leypoldt} + KruAdd$$

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

$$(10)\ weightGainPerDay = \frac{weeklyUFInput}{daysOfTheWeek\ (ie{:}\ 7)}$$

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):

$$(12)\mathrm{Weight\_accumulation} = \mathrm{weightGainPerDay} * \mathrm{accumulationFactor} * 1000$$

(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.

$$(13)\ Removal\ Rate = \frac{weight\_accumulation}{({}^{time}/_{60}) * weight\ of\ Patient}$$

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:

$$(14)\ time = \frac{60 * weight\_accumulation}{weight\ of\ Patient\ * 13}$$

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).

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-If*4 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 S1. Dialysis Parameters of Hypothetical Patients Employed in Testing *stdKt/V Calculator*

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

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.

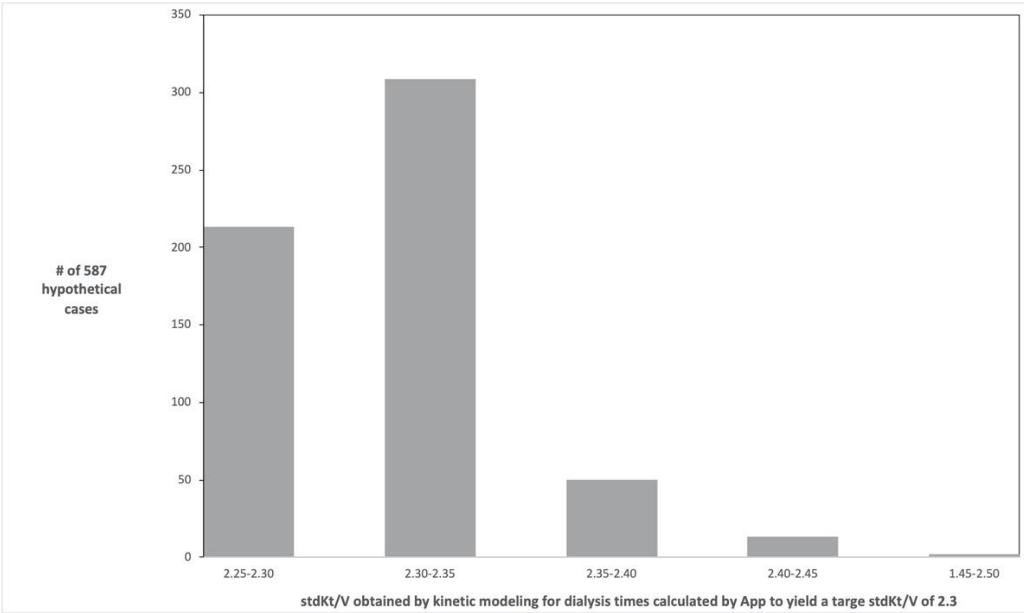

Figure S1.

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± 0.04 (mean ± sd) and the ratio of the value obtained by urea kinetic modeling to the target value of 2.5 was 1.01 ± 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.

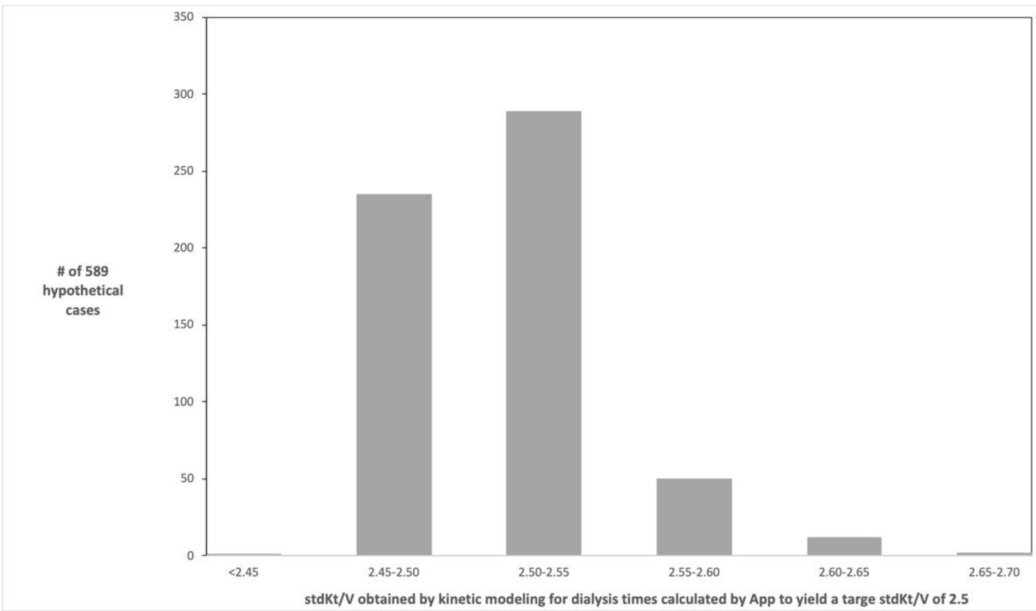

Figure S2.

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 ± 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 ± 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 ± 0.02. A histogram of the values obtained by urea kinetic modeling is presented in Figure S3 below.

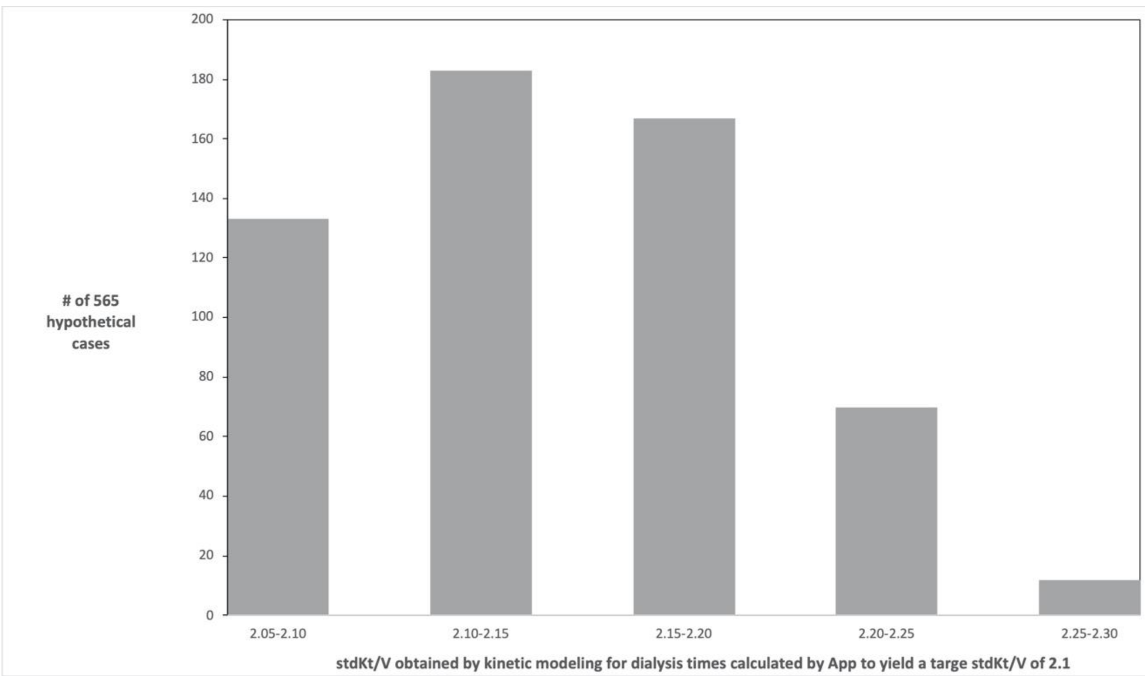

Figure S3.

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

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