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**SCALING HEMODIALYSIS TARGET DOSE TO  
REFLECT BODY SURFACE AREA, METABOLIC  
ACTIVITY AND PROTEIN CATABOLIC RATE  
- A Prospective Cross-sectional Study**

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## **ABSTRACT**

### **Background:**

Women and small men treated by haemodialysis (HD) have reduced survival. This may be due to the practice of using total body water (V) as the normalising factor for dialysis dosing. Our aim in this study was to explore the equivalent dialysis dose that would be delivered using alternative scaling parameters corresponding to the current recommended minimum Kt/V target of 1.2.

### **Study Design:**

Prospective, cross-sectional study

### **Setting and Participants:**

1500 HD patients on thrice weekly schedule were recruited across five different centres.

### **Predictors:**

Age, sex, weight, ethnicity, comorbidity level and employment status

### **Outcomes:**

Kt was estimated by multiplying V by 1.2. Kt/BSA, Kt/REE, Kt/TEE and Kt/nPCR equivalent to a target Kt/V of 1.2 were then estimated by dividing Kt by the respective parameters.

### **Measurements:**

Anthropometric and HD adequacy details were obtained from direct measurements and medical records of patients. Body surface area (BSA) was estimated using Haycock formula. Resting energy expenditure (REE) was estimated using a novel validated equation. Total energy expenditure (TEE) was calculated from physical activity data obtained using Recent Physical Activity Questionnaire. Normalised Protein Catabolic Rate (nPCR) was estimated using standard formula.

### **Results:**

Mean BSA was 1.87 m<sup>2</sup>, mean REE 1545 kcal/day, mean TEE 1841 kcal/day and mean nPCR 1.03 g/kg/day. For Kt/V of 1.2, there was a wide range of equivalent doses expressed as Kt/BSA, Kt/REE, Kt/TEE and Kt/nPCR. The mean equivalent dose was lower in women for all 4 parameters (p<0.001). Small men would also receive lower doses compared to larger men. Younger patients, those with low comorbidity, those employed and those of South Asian ethnicity would receive significantly lower dialysis doses with current practice.

### **Limitations:**

Cross-sectional study and the physical activity data has been collected by an activity questionnaire

### **Conclusion:**

Our data suggest that current dosing practices risk under-dialysis in women and men of lower body size and in specific subgroups of patients. Using BSA, REE or TEE based dialysis prescription would result in higher dose delivery in these patients.

**Keywords:**

Metabolism, energy expenditure, dialysis adequacy, body size, physical activity

## **INTRODUCTION**

One of the major objectives of dialysis is to remove metabolic waste products derived from nitrogen protein metabolism that accumulate in patients with chronic kidney failure. Hence, it has been suggested that minimum dialysis requirement should relate to the rate of metabolic waste production and could be based on factors which reflect the metabolic activity. However haemodialysis (HD) adequacy is currently measured by a dimensionless parameter  $Kt/V$ , where  $K$  is dialyser urea clearance,  $t$  is the dialysis time and  $V$  is the urea distribution volume (or Watson Volume) equating to total body water<sup>1</sup>.  $V$  is linearly related to body weight such that smaller individuals will require relatively less dialysis dose compared to their larger counterparts to achieve the same  $Kt/V$  target. However, the relative concentration of metabolic wastes per unit of body weight may be higher in small individuals<sup>2</sup> as the ratio of lean muscle mass and visceral organs is relatively higher compared to body fat<sup>3</sup> and hence, they risk being under-dialysed in relation to their metabolic needs.

A subgroup analysis of HEMO study suggested that women had a survival benefit when given higher dialysis doses<sup>4</sup>. Others have also demonstrated an inverse relationship with mortality and body size in HD patients<sup>5-8</sup>. There are a number of possible explanations for this phenomenon one of which may be the prescription of haemodialysis based on  $V$  rather than on the patient's metabolic need. A number of alternate parameters for scaling dialysis dose, which better reflect the metabolic activity, have been suggested<sup>9-11</sup>.

Body surface area (BSA) has been proposed as an alternative for scaling dialysis dose as normalising the dose based on BSA will provide more dialysis for women than when using Kt/V <sup>12</sup>.

Resting energy expenditure (REE) is the sum total of all metabolic activities at rest and as such may reflect the rate of metabolic waste production. Physical activity increases the urea generation rate in haemodialysis patients <sup>13</sup> and as such, may increase dialysis requirements. Total Energy Expenditure (TEE) encompasses both REE and energy expenditure from physical activity and hence, may reflect total metabolic waste production. Our aim in this study was to explore the equivalent dialysis dose that would be delivered using the above parameters for scaling corresponding to the current recommended minimum Kt/V target of 1.2. We also aimed to identify patient characteristics that would be associated with risk of sub-optimal delivered dialysis doses with current dosing practice.

## **SUBJECTS AND METHODS**

### ***Ethical Review***

The study was approved by the North Wales Regional Ethics Committee. All subjects gave informed written consent to take part.

### ***Subjects***

Chronic adult HD patients older than 18 years and with dialysis vintage greater than 3 months were recruited from the participating renal units. Exclusion criteria included patients dialysing for other than thrice weekly frequency, those with amputated limbs and those with no capacity to consent. Study information sheet, consent forms and

questionnaires were translated into Bengali and Urdu to facilitate data collection from non-English speaking patients in the participating units.

### ***Study Protocol***

#### *Data collection*

The following data were collected from each patient.

1. Demographic data including age, sex, dialysis vintage, employment status
2. Anthropometric data including height and weight were collected by direct measurement pre- and post-dialysis. Pre-dialysis weight was used to estimate Watson Volume (V).
3. Comorbidity data was collected by using a self-report questionnaire<sup>14</sup>. This scale is based on self-reporting of the presence and severity (grade 1-3) of 7 potential comorbidities - arthritis, cancer, diabetes, heart disease, lung disease, liver disease, and stroke. The maximum score is 21. High comorbidity is designated as a composite self-report comorbidity score (CSCS) > 3.
4. Routine pre- and post-dialysis biochemistry and haematology results were obtained from the local pathology system. Single-pool Kt/V (spKt/V) was calculated using Daugirdas formula<sup>15</sup>.
5. Physical activity data was obtained through Recent Physical Activity Questionnaire (RPAQ). RPAQ enquires about activities performed at home, work and leisure time and also the time spent on each activity in the preceding 4 weeks. It has been validated against doubly labelled water technique in general population<sup>16</sup> and has been shown to be a reliable tool for estimation of energy expenditure in CKD patients<sup>17</sup>.

### ***Estimation of Alternative Scaling Parameters***

*Body surface area (BSA)* using the Haycock formula<sup>18</sup> and *Watson Volume (V)*<sup>1</sup> were derived from these measurements.

*Normalised protein catabolic rate (nPCR)* was estimated using the below formula.

$$nPCR = 5.42 * G/V + 0.17$$

where G is the urea generation rate and V is the total body water.

*Resting Energy Expenditure (REE)* was estimated from a newer predictive equation which was derived and validated in a cohort of HD patients<sup>19</sup>. This disease-specific equation was found to be at least, if not more, accurate as previous equations derived from non-dialysis populations but associated with less bias. The newer equation is given below.

$$REE = -2.497 * Age(years) * Factor_{age} + 0.011 * Height^{2.023}(cm) + 83.573 * Weight^{0.6291}(kg) + 68.171 * Factor_{sex}$$

where  $Factor_{age}$  is 0 if age <65 and 1 if  $\geq 65$  and  $Factor_{sex}$  is 0 if female and 1 if male

*Physical activity data* - Each reported activity was assigned a Metabolic Equivalent of Task (MET) value as per the Compendium of Physical Activities<sup>20</sup>. Sleep time per day was assumed to be 8 hours and any unreported time during the day was assumed as the time performing light activities at home as per the published literature<sup>17</sup>. The total daily MET was calculated by summation of each individual MET values from

the activities. A Mean daily MET value was then calculated by dividing the total daily MET by 24 hours<sup>17</sup>.

*Total Energy Expenditure (TEE)* was estimated from the following equation.

$$TEE = REE * Mean Daily MET$$

### *Scaling of Dialysis dose*

KDOQI guidelines recommend a minimum spKt/V of 1.2 per dialysis session for thrice-weekly schedule. Hence, in order to compare minimum dialysis targets using alternative scaling parameters, Kt was calculated as below.

$$Kt = 1.2 * V$$

Hypothetical target values of Kt/nPCR, Kt/BSA, Kt/REE and Kt/TEE for each patient were calculated by dividing Kt by the observed value for each parameter.

### *Statistics*

Statistical analysis was carried out using SPSS<sup>®</sup> version 19 (SPSS Software, IBM Corporation, New York, USA). Normally distributed data are presented as mean  $\pm$  SD.

The significance of differences between means was determined by Student's t-test.

The significance of differences between multiple group means was assessed by ANOVA with differences between individual groups being assessed using the post-hoc Bonferroni correction for multiple analyses, with p-value of <0.05 being assumed to indicate statistical significance. Multivariable regression models to examine predictors of Kt/TEE were developed using forward stepwise linear regression. The variables used in the model were age, sex, employment status, ethnicity, body weight and comorbidity score. Ethnicity was deployed as a categorical variable as belonging

to South Asian ethnic origin or not and Black ethnic origin or not. A p-value of 0.05 was set as threshold for entry to and 0.10 for exit from the model. Collinearity testing was carried out after every step change in the variable list in the regression model and variables with only low variance inflation factor (<10) were included. Concurrent models were implemented in SPSS using unstandardized and standardized variables. Standardization of the variables was carried out by subtracting the mean from the each individual value and dividing by the standard deviation of the variable. A p-value of <0.05 was assumed to indicate statistical significance.

## **RESULTS**

A total of 1500 patients (910 men and 590 women) were recruited. Their main demographic, biochemical and dialysis characteristics are set out in Table 1. Women were slightly younger, a higher proportion of them classified themselves as black, and fewer classified themselves as employed. All body size parameters were significantly greater in men than women. Men had slightly higher serum urea and haemoglobin levels compared to women. Watson Volume, BSA, REE, mean daily METs, PAEE and TEE were all significantly lower in women than men.

Table 2 reports the metabolically normalised dialysis doses mean (Kt/BSA, Kt/REE, Kt/TEE and Kt/nPCR) values equivalent to a Kt/V of 1.2. There were large gender differences. The equivalent dose expressed as Kt was markedly less in females than males ( $38,700 \pm 5,900$  vs.  $49,300 \pm 7,900$  ml;  $p < 0.001$ ). There were also marked gender differences in the metabolically normalised parameters. Kt/BSA was  $21,900 \pm 200$  ml/m<sup>2</sup> for women and  $25,400 \pm 1,200$  ml/m<sup>2</sup> for men ( $p < 0.001$ ). For Kt/REE

these were  $27.18 \pm 1.87$  ml/kcal for women and  $30.34 \pm 1.25$  ml/kcal for men ( $p < 0.001$ ) and for Kt/TEE,  $23.36 \pm 2.60$  ml/kcal for women and  $25.60 \pm 2.73$  ml/kcal for men ( $p < 0.001$ ).

There were also marked differences in these parameters with respect to body size. Table 2 shows the influence of the body weight (expressed in quartiles). For each parameter there was a significant difference between the means across the quartiles as judged by one-way ANOVA. Smaller patients received a much lower overall dose expressed in terms of Kt. The effects of body size on target dose expressed in terms of the metabolically normalised parameters studied were similar though of lesser magnitude.

Patient age also influenced these parameters (Table 2). For Kt there was a significant reduction across age quartiles by ANOVA. The magnitude of the reduction was smaller for Kt/BSA but still significant. However both Kt/REE and Kt/TEE increased with increasing age, suggesting a need for higher dialysis doses, by these criteria, in the younger age groups.

Table 2 also shows the differences between these parameters with respect to ethnicity. In general the equivalent dose for South Asians was lower than that for Blacks which was lower than that for Whites. For Kt, Kt/REE, Kt/TEE there was a significant difference in means between ethnic groups by one-way ANOVA. For Kt/BSA the differences were not significantly different. These findings suggest ethnic differences in dialysis requirement, with relatively higher doses being required in the South Asian group, though it should be emphasized that this is based on differences in body size

characteristics and estimated physical activity, rather than any possible ethnic differences in energy metabolism.

Patients with high comorbidity (CSCS >3) had slightly higher Kt/REE and Kt/TEE levels than their counterparts with lower comorbidity, though values of Kt/BSA were slightly lower (Table 2). Values of Kt/REE and Kt/TEE were consistently higher in those with arthritis, cancer, diabetes and heart disease than in those without these conditions. This implies that patients without comorbidities need higher dialysis doses according to these criteria, though again, these findings, based mainly on body size and physical activity, do not take into account potential differences in energy metabolism which may be associated with the specific comorbidities.

Patients in employment had lower levels of Kt/TEE than those not employed, though levels of both Kt and Kt/BSA were higher (Table 2). This reflects the significantly greater weight ( $79.4 \pm 18.4$  vs.  $74.7 \pm 18.2$  kg;  $p < 0.001$ ) and physical activity energy expenditure ( $707 \pm 339$  vs.  $242 \pm 124$  kcal/day;  $p < 0.001$ ) of employed individuals.

We also estimated Kt/nPCR and examined the relationships amongst different variables as shown in Table 2. Kt/nPCR was found to be significantly lower in women ( $40200 \pm 12900$  vs.  $51100 \pm 15700$  ml/g/kg/day,  $p < 0.001$ ) and in those with lower comorbidity ( $46100 \pm 15100$  vs.  $48500 \pm 16400$  ml/g/kg/day,  $p = 0.008$ ). Kt/nPCR was also the lowest in those in the first weight quartile compared to the rest of the quartile groups with significant difference noted between the means across the quartiles using One-way ANOVA ( $p < 0.001$ ). There was no significant difference noted in the dose that would be delivered using Kt/nPCR in employed people

compared to unemployed ( $47400 \pm 14500$  vs.  $46700 \pm 15700$  ml/g/kg/day,  $p = 0.604$ ), in patients of different ethnicity or across age quartiles using One-way ANOVA.

Given the major influence of gender on these parameters we examined the within gender differences in relation to body weight, age, ethnicity, comorbidity and employment status. Figure 1 depicts the effect of weight on these parameters. It can be seen that gender has a major effect on these parameters with females having much lower levels of all four parameters i.e. Kt, Kt/BSA, Kt/REE and Kt/TEE. Smaller males have significantly lower levels for all parameters than larger males whilst for women there is little additional effect of weight on parameter value. This implies that females have a requirement for a greater dialysis dose – and that this overrides any effect of weight, whilst smaller males require a greater relative dose than larger males. The effect of age, ethnicity, comorbidity, and employment status on Kt/TEE is shown in Figure 2 – chosen since the findings were most consistent for this parameter. In both males and females Kt/TEE was lower for younger patients, for those with low comorbidity, and for those in employment. In males, there seemed little influence of ethnic group on Kt/TEE, whereas in South Asian females Kt/TEE was slightly but significantly lower than in other females ( $24.17 \pm 2.70$  vs.  $24.93 \pm 2.94$  ml/kcal;  $p < 0.001$ ). In linear regression models (Table 3), age, sex, weight and South Asian ethnicity were found to be independent predictors of Kt/BSA and Kt/REE. In addition to these variables, employment status was also found to be an independent predictor in the model with Kt/TEE as the dependant variable. In the model with Kt/nPCR as the dependent variable, sex, weight and South Asian ethnicity were found to be independent predictors.

## **DISCUSSION**

This study aimed to explore the minimum dialysis dose corresponding to current recommended Kt/V target that would be delivered using some of the alternative scaling parameters and also to identify the characteristics of patients who are at risk of under-dialysis with current dosing practice. We found that the predicted minimum delivered dialysis dose would be significantly lower in women compared to men if any of the three parameters – BSA, REE or TEE – are used though they all would have had identical Kt/V sessional values. Small women would have received lower doses compared to larger women if Kt/BSA was used. However, small men would have received significantly lower doses compared to their larger male counterparts irrespective of whatever the scaling parameter was used. Besides gender, younger age, employment, South Asian ethnicity and comorbidity status also have an impact on dosing based on these metabolic factors.

There has been an ongoing debate as to how best adjust haemodialysis sessional dosing for individual patients. Some authors have argued that Kt/V is the best parameter to make adjustments, while others have refuted it <sup>21,22</sup>. Daugirdas et al have shown that BSA-based dialysis dosing will result in higher delivered dialysis doses to women and small men <sup>23</sup>. A recent study has also shown a better relationship with survival for the BSA-based dosing compared to current practice <sup>24</sup>. On the other hand, Morton and Singer have argued that the dialysis dose should be based on metabolic rate because of the non-linear correlation between body mass and metabolic rate <sup>25</sup>. We have previously reported that women have relatively higher urea generation rate

and TEE is an independent predictor of urea generation rate <sup>13</sup>. This would mean that TEE could also be considered a potential scaling parameter for dialysis dosing. The pros and cons of some of these proposed parameters for scaling dialysis dose have been discussed previously <sup>9</sup>.

Our study demonstrates that with V-based dosing, women of all body sizes are at risk of under-dialysis compared to similar-sized men if equivalent doses are estimated using alternate metabolic parameters. This shows that V-based dosing targets need to be gender-specific unlike current recommendations. We also found that smaller individuals, both women and men, would receive significantly lower dialysis dose with BSA-based dosing compared to their larger counterparts as per the current minimum dialysis dose target. This implies that V-based dosing targets also need to be body-size specific. Alternately, using parameters such as BSA, REE or TEE may inherently adjust for these gender and body size differences thus negating the difficulty of having multiple dose target thresholds.

We also explored the use of nPCR as a scaling parameter, and found that for an identical target  $Kt/V$ ,  $Kt/nPCR$  was lower in women, in those in the lowest weight quartile and in those with low comorbidity. This is not dissimilar to the other three parameters we have investigated. Use of  $Kt/nPCR$  though has the disadvantage of only being available post-hoc following peri-dialytic blood sampling, so though it may have utility in assessing delivered dose, it may be of limited value in dialysis prescription.

We also identified other possible patient characteristics that may be associated with risk of under-dialysis. Younger patients, those with low comorbidity and those who were employed would receive lower doses compared to their counterparts irrespective of whatever metabolic parameter was used for comparison. Patients of South Asian ethnicity are also found to be at risk of under-dialysis if REE or TEE were considered as scaling parameters. Bioimpedance studies have suggested differences in body composition, particularly muscle mass, in South Asians compared to Whites and Blacks <sup>26</sup>. However, these subgroup differences are likely to be secondary to the differences in body weight, and physical activity levels rather than a direct effect of these characteristics on metabolic needs. Given this relationship between age, sex, weight, ethnicity and employment and energy metabolism, these factors were shown to be significant in predicting Kt/TEE in a linear regression model.

There is dearth of comparative clinical studies using these 3 parameters and hence, it is difficult to ascertain if one of these parameters is superior to others in providing dialysis dose based on metabolic needs of the individual. Daugirdas et al have argued that theoretically using REE, unlike BSA, will not result in substantial increase in dialysis dose to women <sup>9</sup>. However, there is evidence to suggest that metabolic rate drives the glomerular filtration rate (GFR) <sup>27</sup>. Also, GFR and metabolic rate scale to body mass with virtually the same exponent <sup>28</sup>. Hence, metabolic rate i.e., REE could be a potential scaling parameter. Physical activity contributes to increased metabolism and thereby, higher metabolic waste production. It could be argued that TEE, incorporating both REE and physical activity, could be a better parameter more accurately reflecting total metabolic activity. As in the resting state, muscle metabolism is low but muscle mass is associated with physical activity. However,

these are theoretical arguments and there is need for comparative outcome-based studies employing standardised forms of these parameters to examine the effects of dialysis based on these different scaling factors.

Our study has some limitations. This was a cross-sectional study with estimations of metabolic parameters carried out from a single anthropometric reading. However, we recruited 1500 patients and directly measured anthropometric values from each subject and not derived from historic medical records. We also recruited an ethnically diverse population and also did not restrict patient size, and as such, included patients with very different body composition. TEE was calculated from physical activity data collected through a recall questionnaire, which enquires about various activities in the preceding 4 weeks. As with any questionnaire methods, recall bias is a potential confounder in the accuracy of the data. Nevertheless, the physical activity level in our study cohort is in line with many previously published studies in haemodialysis patients. Although doubly labelled water is the gold standard method to measure TEE, the cost and cumbersome nature of studies using this method precludes it from being employed in large-scale epidemiological studies such as ours. We also used these anthropomorphic measurements to calculate total body water using the Watson equation, and subsequently used this value to estimate target Kt. Use of bioimpedance may have provided a more precise estimate of total body water as well as data on body composition. However in this multicenter study of 1500 patients, bioimpedance equipment was not available in all centres as is often the case in many centres in routine clinical practice. Hence all current clinical guidelines recommend using the Watson equation to calculate V. As such our methodology followed currently published clinical guideline recommendations.

In conclusion, we have demonstrated that some of the metabolic parameters may be used to scale delivered dialysis dose and that V-based dialysis dosing used in current clinical practice risks under-dialysing women and small men. Our study findings additionally suggest a gender-, body size- and physical activity-specific V-based dosing or dosing based on these alternate metabolic parameters. Further outcome-based studies will be useful in assessing the applicability of these alternate scaling parameters in routine clinical practice.

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Contributions: Research idea and study design: SS, EV, JR, KF; Data acquisition: SS, AD, NA, MA, AB; Data analysis/interpretation: SS, EV, AD, KF; Supervision: JR, KF. Each author contributed important intellectual content during manuscript drafting or revision and accepts accountability for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved. SS takes responsibility that this study has been reported honestly, accurately, and transparently; that no important aspects of the study have been omitted, and that any discrepancies from the study as planned have been explained.

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**TABLE 1**

**Demographic, anthropometric, dialysis and energy metabolism characteristics of 1500 study patients.**

	<b>All Patients (n = 1500)</b>	<b>Males (n = 910)</b>	<b>Females (n = 590)</b>	<b>p-value</b>
<b>Age (years)</b>	62.9 ± 15.5	63.8 ± 15.6	61.6 ± 15.1	0.007
<b>Weight (kg)</b>	75.2 ± 18.3	78.4 ± 17.3	70.4 ± 18.6	<0.001
<b>Height (cm)</b>	165.9 ± 10.0	170.6 ± 8.2	158.7 ± 8.2	<0.001
<b>Ethnicity (South Asian: Black: White)</b>	418: 400: 682	249: 218: 443	169: 182: 239	0.003
<b>Body Mass Index (kg/m<sup>2</sup>)</b>	27.3 ± 6.0	26.9 ± 5.3	27.9 ± 7	0.002
<b>High Comorbidity (%)</b>	442 (29.5)	261 (28.7)	181 (30.7)	0.417
<b>Employed (%)</b>	173 (11.5)	119 (13.1)	54 (9.2)	0.021
<b>Blood urea (mmol/L)</b>	19.3 ± 5.7	19.6 ± 5.6	18.7 ± 5.8	0.004
<b>Dialysis Time (minutes)</b>	225 ± 29	229 ± 29	219 ± 27	<0.001
<b>Blood flow rate (ml/min)</b>	316 ± 41	322 ± 40	306 ± 40	<0.001
<b>Dialysate flow rate (ml/min)</b>	592 ± 123	596 ± 126	587 ± 118	0.157
<b>Haemoglobin (g/dl)</b>	10.9 ± 1.2	11.0 ± 1.2	10.8 ± 1.2	0.002
<b>Watson Volume (L)</b>	37.5 ± 7.4	41.0 ± 6.6	32.2 ± 4.9	<0.001
<b>nPCR (g/kg/day)</b>	1.03 ± 0.26	1.02 ± 0.26	1.03 ± 0.27	0.591
<b>Body Surface Area (m<sup>2</sup>)</b>	1.87 ± 0.26	1.93 ± 0.24	1.77 ± 0.26	<0.001
<b>REE (kcal/day)</b>	1545 ± 250	1621 ± 230	1429 ± 236	<0.001
<b>Mean daily MET</b>	1.19 ± 0.13	1.20 ± 0.14	1.17 ± 0.10	<0.001
<b>Physical Activity EE (kcal/day)</b>	295 ± 221	327 ± 251	247 ± 154	<0.001
<b>TEE (kcal/day)</b>	1841 ± 388	1948 ± 390	1676 ± 322	<0.001

Values are expressed as mean ± SD. Proportions of categorical variables are expressed as percentages. REE: resting energy expenditure, EE: energy expenditure, TEE: total energy expenditure, MET: metabolic equivalent of task, BSA: body surface area, nPCR: normalised protein catabolic rate

**TABLE 2**

**Dialysis dose equivalent to a Kt/V of 1.2 expressed in terms of Kt, Kt/BSA, Kt/REE, Kt/TEE and Kt/nPCR.**

	NUMBER	Kt (ml)	Kt/BSA (ml/m <sup>2</sup> )	Kt/REE (ml/kcal)	Kt/TEE (ml/kcal)	Kt/nPCR (ml/g/kg/day)
<b>All patients</b>	1500	45,100 ± 8,900	24,000 ± 2,000	29.10 ± 2.17	24.72 ± 2.89	46,800 ± 15,600
<b>GENDER</b>						
<b>Male</b>	910	49,300 ± 7,900	25,400 ± 1,200	30.34 ± 1.25	25.60 ± 2.73	51,100 ± 15,700
<b>Female</b>	590	38,700 ± 5,900	21,900 ± 200	27.18 ± 1.87	23.36 ± 2.60	40,200 ± 12,900
<b>p-value (t-test)</b>		<0.001	<0.001	<0.001	<0.001	<0.001
<b>WEIGHT Quartiles (kg)</b>						
<b>≤ 62.3</b>	375	35,600 ± 3,900	22,800 ± 1,500	28.08 ± 2.11	24.08 ± 2.65	36,800 ± 10,300
<b>62.4 to 73</b>	375	42,200 ± 3,900	23,800 ± 1,800	28.90 ± 1.86	24.50 ± 2.65	44,000 ± 13,000
<b>73.1 to 85.2</b>	375	46,900 ± 4,400	24,300 ± 1,800	29.31 ± 1.96	24.80 ± 2.91	48,500 ± 12,800
<b>&gt; 85.2</b>	375	55,600 ± 7,400	25,100 ± 2,100	30.11 ± 2.24	25.48 ± 3.17	57,900 ± 17,200
<b>p-value (ANOVA)</b>		<0.001	<0.001	<0.001	<0.001	<0.001
<b>AGE Quartiles (years)</b>						
<b>≤ 52</b>	375	46,900 ± 10,200	24,700 ± 2,500	28.15 ± 2.45	22.98 ± 3.13	46,700 ± 15,900
<b>52 to 65.3</b>	375	46,000 ± 9,200	24,100 ± 2,000	27.60 ± 1.99	23.28 ± 2.60	47,800 ± 16,200
<b>65.4 to 75.5</b>	375	45,200 ± 8,500	23,800 ± 1,700	30.36 ± 1.43	26.22 ± 2.06	47,100 ± 16,000
<b>&gt; 75.5</b>	375	42,200 ± 6,600	23,400 ± 1,200	30.29 ± 0.86	26.38 ± 1.62	45,600 ± 13,900
<b>p-value (ANOVA)</b>		<0.001	<0.001	<0.001	<0.001	0.244
<b>ETHNICITY</b>						
<b>South Asian</b>	418	42,700 ± 8,100	23,900 ± 2,000	28.60 ± 2.26	24.16 ± 2.70	45,500 ± 13,900
<b>Black</b>	400	46,500 ± 8,600	24,000 ± 2.100	28.87 ± 2.18	24.57 ± 2.93	47,900 ± 14,800
<b>White</b>	682	45,800 ± 9,200	24,100 ± 1,900	29.54 ± 2.02	25.14 ± 2.92	47,000 ± 16,900
<b>p-value (ANOVA)</b>		<0.001	0.244	<0.001	<0.001	0.074
<b>COMORBIDITY</b>						
<b>Low</b>	1058	44,900 ± 8,900	24,100 ± 2,000	28.98 ± 2.19	24.40 ± 3.00	46,100 ± 15,100
<b>High</b>	442	45,400 ± 8,800	23,800 ± 1,800	29.38 ± 2.11	25.47 ± 2.46	48,500 ± 16,400
<b>p-value (t-test)</b>		0.412	<0.01	<0.001	<0.001	0.008
<b>EMPLOYMENT</b>						
<b>Working</b>	173	48,600 ± 9100	24,900 ± 2,200	28.83 ± 2.18	20.61 ± 2.68	47,400 ± 14,500
<b>Not working</b>	1327	44,600 ± 8700	23,900 ± 1,900	29.13 ± 2.17	25.25 ± 2.46	46,700 ± 15,700
<b>p-value (t-test)</b>		<0.001	<0.001	0.086	<0.001	0.604

K is urea clearance, t is session length, BSA is body surface area, REE is resting energy expenditure, TEE is total energy expenditure, nPCR is normalised Protein Catabolic Rate.

**TABLE 3**

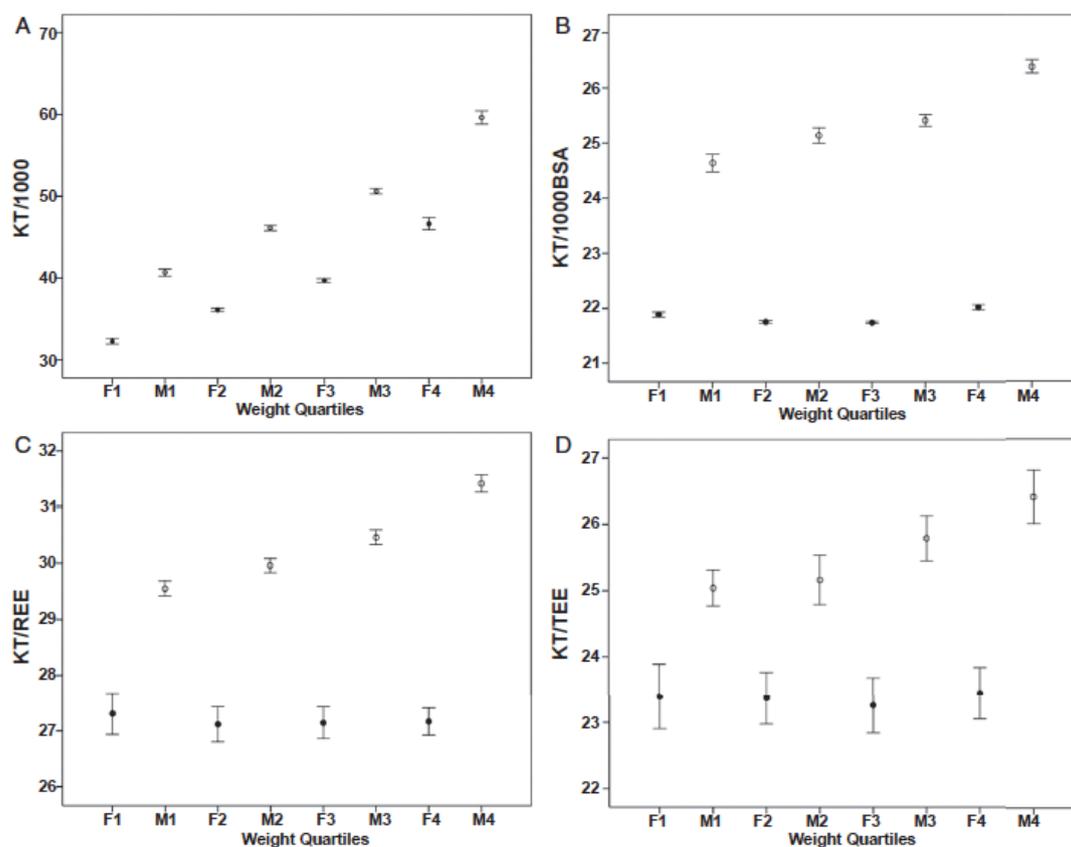
**Linear regression model of factors predicting Kt/BSA, Kt/REE, Kt/TEE and Kt/nPCR.** The variables entered in the model were age, sex, weight, employment status, South Asian ethnicity (vs other ethnic groups) and Black ethnicity (vs other ethnic groups).

Model	Unstandardised Coefficients		Standardised Coefficients (Beta)	p-value
	B	SE		
<b>Kt/BSA (r<sup>2</sup> = 0.917)</b>				
Constant	22899.90	122.86		< 0.001
Age (years)	-39.37	1.03	-0.308	< 0.001
Sex (Female vs. Male)	3438.73	31.17	0.851	< 0.001
Weight (kg)	22.65	0.85	0.21	< 0.001
South Asian Ethnicity	-119.72	36.59	-0.027	0.001
Black Ethnicity	-18.16	36.97	-0.004	0.623
<b>Kt/REE (r<sup>2</sup> = 0.705)</b>				
Constant	21.94	0.25		< 0.001
Age (years)	0.055	0.002	0.390	< 0.001
Sex (Female vs. Male)	2.812	0.064	0.633	< 0.001
Weight (kg)	0.028	0.002	0.237	< 0.001
South Asian Ethnicity	-0.235	0.076	-0.049	0.002
Black Ethnicity	0.003	0.076	0.001	0.966
<b>Kt/TEE (r<sup>2</sup> = 0.573)</b>				
Constant	9.490	0.407		< 0.001
Age (years)	0.064	0.003	0.344	< 0.001
Sex (Female vs. Male)	2.021	0.103	0.341	< 0.001
Weight (kg)	0.029	0.003	0.186	< 0.001
South Asian Ethnicity	-0.321	0.121	-0.050	0.008
Black Ethnicity	0.111	0.123	0.017	0.367
Unemployed	4.140	0.160	0.457	< 0.001
<b>Kt/nPCR (r<sup>2</sup> = 0.355)</b>				
Constant	4843.18	2692.87		0.072
Sex (Female vs. Male)	7640.76	683.20	0.240	< 0.001
Weight (kg)	431.87	18.56	0.507	< 0.001
South Asian Ethnicity	1803.69	802.00	0.052	0.025
Black Ethnicity	812.10	810.31	0.023	0.316

## TITLES AND LEGENDS

### FIGURE 1

Predicted delivered dialysis dose in relation to gender-specific mean body weight using (A) Kt (B) Kt/BSA (C) Kt/REE and (D) Kt/TEE.



Error bars represent mean and 95% confidence interval.

Males (open circles) and females (filled circles). BSA – Body surface area, REE –

Resting Energy Expenditure, TEE – Total Energy Expenditure

**FIGURE 2**

Effect of age, ethnic group, comorbidity and employment status on Kt/TEE in males (open circles) and females (filled circles)

Error bars represent mean and 95% confidence interval.

