# Multiregression analysis on predictors determining the urinary potassium excretion and radiocaesium body burdens in two different ethnic groups

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**Abstract.** Within the field of environmental radiology, the levels of potassium and creatinine in urine are sometimes used to estimate the 24h excretion of radiocaesium from single urine samples. This is done in order to estimate the whole-body content of radiocaesium and the associated absorbed dose rate in man. Data on human urinary potassium excretion from various sources are available in the literature, but there are clear discrepancies between the ICRP 23 values for the reference man and these data which vary with the geographical location of the population. The relationship between urinary potassium and creatinine excretion and the correlation to parameters such as age, sex, body weight and ethnicity were investigated through multiple regression analysis. The groups of adults studied were a group from the city of Lund in southern of Sweden (1987-1994) and a group from rural areas outside the city of Bryansk, Russia (1994-1997). A significant difference was found in the relationship between the urinary potassium concentration and the creatinine concentration between the Swedish and Russian subjects. The elevated potassium concentrations found in the rural Russian subjects indicate a high dietary intake of potassium, which is in accordance with results from a Russian food habit questionnaire in the Bryansk area. No significant correlations were found between urinary potassium concentration and weight or age. The significant difference in the relationship between urinary potassium and creatinine between the two populations could explain the difference of a factor of two found in estimations of the whole-body content of $^{137}$Cs for the Russian group, depending on which of the two substances, creatinine or potassium, was used for estimation of the body burden of $^{137}$Cs from single urine samples.

## 1. INTRODUCTION

An alternative method of determining the whole-body content of caesium in man is by collecting partial day urine samples from a group of individuals and then using established ratios of whole-body to 24h excretion to obtain an estimate of the average body burden of caesium in the group [1-2]. The use of partial-day sampling may be justified when considering group averages rather than individual values [3]. Various methods for normalising the partial-day content of caesium in urine to a 24h level were suggested as early as the beginning of the 1960s [4], in order to improve the accuracy of whole-body estimates made from urinary assay.

Caesium and potassium are congeners in the periodic system and behave in a similar manner in the bio-kinetic processes in the human organism [5]. Therefore, it has been considered natural to normalise the caesium content in a fractional urine sample to its potassium content, assuming a constant 24h excretion of potassium [4, 6-7]. If standard values of the 24h potassium excretion and body content from the literature are applied to urine samples (e.g. [8]), it is then possible to obtain an estimate of the average whole-body content of caesium in the investigated subjects. An alternative to potassium-normalisation to obtain the 24h excretion of $^{137}$Cs in urine is creatinine-normalisation [9-10]. Creatinine is a metabolite produced in the muscle tissues during the transformation of chemical energy, in the form of *creatine*, into muscular work [10-11]. The production and excretion of creatinine are assumed to be relatively constant for each individual, and the 24h excretion level is therefore correlated to the body muscle mass (in analogy with the whole-body content of potassium), provided that the individual has a stable fraction of protein in his/her daily diet [11].

The aim of this work was to further investigate the results obtained in a previous study on urine samples from Swedish and Russian subjects containing radiocaesium in measurable quantities [2, 7, 12-14]. The prime goal was to test statistically whether it was any significant difference in the urinary concentrations of potassium and creatinine between the two ethnic groups, in order to study the effects on

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the estimates of whole-body contents of caesium from urine assays. Furthermore, by performing multiregression analysis on the combined data from both groups, it was possible to investigate whether parameters such as age, weight and sex had any significant influence on the relation between the contents of potassium and creatinine in urine.

## 2. METHODS

### 2.1 Urine sample collection in the Swedish and Russian group

The collection of the 24h urine samples in the Swedish group has been described by Rääf *et al.*, in 1999[7]. The data originate from a group of 16 subjects who participated in urinary sample collections and whole-body assays between 1987 and 1994. The details of the group and its formation have been described earlier [15-18].

The Russian study was carried out in co-operation with the University of Göteborg and the Russian Institute of Radiation Hygiene in St Petersburg [2, 8], and was supported by the national radiation protection institutes of Sweden and Norway. The study involved annual surveys of rural inhabitants living in the Bryansk area. These surveys included the collection of partial-day urine samples (in contrast to the Swedish 24h urine sampling). The handling of the Russian partial-day samples was described by Wallström in 1998[18]. Data from individuals over 18 years of age were selected from the Russian survey for multiregression analysis in order to include only adults in the study.

The $^{137}$Cs concentration in the urine samples was determined by high resolution gamma spectrometry [7]. The potassium concentration in the samples from the Swedish subjects was determined by gamma spectrometry as well, but for the regression analysis the values were converted into the corresponding concentrations of stable potassium expressed as mmol $l^{-1}$. The potassium concentrations in the Russian urine samples were determined by atomic absorption photospectrometry (AAS) at the Department of Clinical Chemistry, Malmö University Hospital. The compatibility of the two sets of potassium concentration data was confirmed by determining the potassium concentration with both methods (gamma spectrometry and AAS) in samples taken from a solution of 20 g KCl in 2 l distilled water.

### 2.2 Application of urinary concentrations of creatinine and potassium estimates of whole-body content of $^{137}$Cs

The body burden of $^{137}$Cs, $Q_{Cs}$ [Bq], can be estimated through urinary assays of the concentration of $^{137}$Cs using calibration factors between body burden and urinary excretion rates taken from the literature. Normalising the $^{137}$Cs content in partial-day samples to the corresponding 24h level through the determination of the amount of potassium or creatinine in the sample, is assumed to compensate for intra-day variation in the excretion rate, thereby possibly improving the accuracy of the body burden estimates. A standard value of the so-called potassium-normalised caesium excretion, $A$ [dimensionless] can be used in combination with an estimated average body potassium concentration, $q_K$ [Bq $^{40}$K/kg body weight] or [g stable K/g] to obtain an estimate of the body burden of radiocaesium, $Q_{Cs,i}$, in the subject $i$ from a partial-day urine sample (Eq. 1);

$$Q_{Cs,i} = Q_{K,st} \cdot \frac{e_{Cs,i}}{e_{K,i}} \cdot A_{st} = w_i \cdot q_{K,ICRP} \cdot \frac{e_{Cs}}{e_K} \cdot A_{st} \qquad \text{Eq. 1}$$

where:

$$A_{st} = \left(\frac{Q_{Cs}}{Q_K}\right) / \left(\frac{E_{u,Cs}}{E_{u,K}}\right) \qquad \text{Eq. 2}$$

and $e_{Cs,i}$ [Bq $^{137}$Cs $l^{-1}$] and $e_{K,i}$ [Bq $^{40}$K $l^{-1}$] are the $^{137}$Cs and potassium concentrations in the partial-day urine samples from subject $i$, respectively. $w_i$ is the body weight of the subject. $A_{st}$ is a standard value of the potassium-normalised caesium excretion and is the ratio between the body burden of $^{137}$Cs and $^{40}$K ($Q_{Cs}$ and $Q_K$, respectively) divided by the ratio between the 24h urinary excretion of $^{137}$Cs and $^{40}$K ($E_{u,Cs}$ and $E_{u,K}$, respectively). Standard values of $A$ can be obtained from the literature [6, 14]. Standard values of $q_K$ for males and females (62 Bq $^{40}$K $kg^{-1}$ and 50 Bq $^{40}$K $kg^{-1}$, respectively) can be found in ICRP [8].

Estimates of the body burden of radiocaesium of a subject, $Q_{Cs,i}$, can also be made by using a standard value of the 24h urinary creatinine excretion, $CRE_{24h,st}$, in combination with a standard value of the ratio of the body burden-to-24h excretion of $^{137}Cs$, $(Q/E_u)_{Cs,st}$, (Eq. 3);

$$Q_{Cs,,i} = (\frac{Q}{E_u})_{Cs,st} \cdot e_{Cs,i} \cdot (\frac{CRE_{24h,st}}{CRE_i}) \quad \text{Eq. 3}$$

Standard values of both $(Q/E_u)_{Cs}$ and $CRE_{24h}$ can be obtained from several sources (e.g. [8]). For more extended literature reviews on urinary creatinine and caesium excretion data the reader is referred to Rääf *et al.*, 1999 [7] and Rääf *et al.*, 2000[14].

### 2.3 Regression analysis of possible predictors for the urinary potassium concentration, *K*

Since both 24h creatinine and potassium excretion are proportional to the body cell mass, one would expect that the slope of the linear relationship between potassium and creatinine concentration in urine would be the same for different populations. Calculations based on relationships given by the ICRP [8] for a male adult of 70 kg give the following expression relating the diurnal urinary potassium excretion, $E_{u,K}$ [mmol K $d^{-1}$] to the creatinine excretion, $CRE_{24h}$ [mmol CRE $d^{-1}$] (Eq. 4);

$$E_{u,K} = (2.7/140) \cdot 113.2 \cdot 2.2\ CRE_{24h} = 4.80\ CRE_{24h} \quad \text{Eq. 4}$$

A molecular weight of 113.2 mg $mmol^{-1}$ was used for the substance creatinine. The ratio of the 24h excretion-to-body burden for potassium (2.7/140) was taken from the ICRP [8]. Thus the slope of the linear relationship between 24h potassium and creatinine in urine is estimated to be about 4.8 [mmol K/mmol CRE], with an intercept of zero. Assuming that the excretion rates of the two substances are constant throughout the day, Eq 4, can be rewritten as (Eq 5):

$$K=4.8 \cdot CRE \Rightarrow K=\beta_0+\beta_1 \cdot X_1(=CRE) \quad \text{Eq. 5}$$

where $K$ is the urinary potassium concentration [mmol $l^{-1}$] and $CRE$ is the creatinine concentration in the same sample [mmol $l^{-1}$]. The right-hand side of the equation is a simple regression equation, including an intercept, $\beta_0$, and a slope, $\beta_1$. These coefficients can be obtained through multiple regression analysis. To test the relationship in Eq. 5 by means of multiple regression analysis, the potassium concentration, $K$, was chosen as the dependent variable.

It is possible to extend the regression analysis of the urinary potassium concentration, $K$, to include variables such as age, sex and body weight of the Swedish and Russian subjects. In this study, a method called the all-possible-regression procedure was used in combination with partial F-analysis [19]. The regression procedure begins by defining a so-called maximum model, where all variables (predictors) available in the raw data are included (predictors $X_1$ to $X_n$; Eq. 6), including a selection of quadratic and first-order interaction terms between these variables ($X_j \cdot X_j = X_j^2$ and $X_i \cdot X_j$ in Eq. 6).

$$K=\beta_0+\beta_1 \cdot X_1+\beta_2 \cdot X_2+\ldots+\beta_i \cdot X_i+\ldots+\beta_p \cdot X_p+\beta_{11} \cdot X_1 \cdot X_1+\beta_{12} \cdot X_1 \cdot X_2+\ldots+\beta_{ij} \cdot X_i \cdot X_j+\ldots+\beta_{pp} \cdot X_p \cdot X_p \quad \text{Eq. 6}$$

Eq. 6 gives the first-order predictors, three continuous and two so-called categorical variables, which can assume one of two discrete values only. By including the categorical parameters geographical location and sex, systematic differences between the categories in the prediction of $K$ can be detected [19]. In Table 1 are the first order independent variables presented.

Table 1

*Predictors in the maximum model used for all-possible-regression of urinary potassium concentration, K [mmol $l^{-1}$].*

| Predictor | Unit |
|---|---|
| *AGE* (age) | year |
| *BWT* (body weight) | kg |
| *CRE* (urinary creatinine concentration) | mmol $l^{-1}$ |
| *SEX* (sex/gender) | Male subject=0; Female subject=1 |
| *GEO* (ethnicity - geographical origin) | Swedish subject=0; Russian subject=1 |

The next step is to define a starting model (Model A), including the three continuous predictors; age, *AGE*, creatinine concentration, *CRE*, and body weight, *BWT*, combined with the two categorical variables geographical origin, *GEO*, and gender, *SEX* (Table 2). Two additional expanded models can be defined,

containing interaction terms (Model B) and quadratic terms (Model C). By using partial F-analysis it is possible to detect if there is any interaction between the predictors of the potassium concentration in urine.

Table 2
*Overview of the predictors included in the starting model (Model A) and the two expanded models (Model B and Model C).*

| | **Predictors** |
|---|---|
| Model A | *(AGE, CRE, BWT, GEO, SEX)* |
| Model B | *(AGE, CRE, BWT, GEO, SEX + AGE·CRE, AGE·BWT, GEO·AGE, GEO·CRE, GEO·BWT, SEX·AGE, SEX·BWT, SEX·CRE, BWT·CRE)* |
| Model C | *(AGE, CRE, BWT, GEO, SEX + $AGE^2$, $CRE^2$, $BWT^2$)* |

After the partial F-test has been completed, a new starting model, containing the predictors of Model A and the identified interaction terms of Model B and Model C, is obtained. By applying different selection criteria to the starting model it is possible to select the reduced model that shows the best fit to experimental data with the minimum number of predictors [19].

The statistical software STATISTICA 6.0™ [20], was used to calculate the estimates as well as the asymptotical standard error on a 95% confidence level ($\alpha$=0.05) of the regression coefficients, $\beta_i$, in the regression equations. All predictors were transformed by centring the predictor values to the mean value and by normalisation to the standard deviation of the given predictor. This was done in order to avoid collinearities between the predictors which obscure the regression analysis [19]. After each regression procedure, a residual analysis was performed by plotting the residual vs. predicted values. In extreme cases, outliers were identified from these plots and the regression was rerun with the outliers omitted.

## 3. RESULTS

### 3.1 Multiregression analysis for the prediction of the potassium concentration in urine, *K*

The potassium concentration is shown as a function of the creatinine concentration in Fig. 1. For the Bryansk group the regression line was found to be (Errors=±1 SE): $K_{Bryansk}$=6.29(±1.66)·$CRE_{Bryansk}$ + 63.5(±14.2); $R^2_{adj}$=0.143. Higher significance was found in the Lund reference group, with a regression equation of: $K_{Lund}$=4.44(±0.42)·$CRE_{Lund}$ + 11.7(±3.68); $R^2_{adj}$=0.518. There was a significant difference ($p<0.01$) between the intercepts of the regression lines for the two groups, whereas no significant difference was found in the slopes of the regression lines.

From the all-possible-regression procedure, starting with model A (Table 2), seven of the 31 reduced models were selected for closer scrutiny (Table 3). Using the quality criteria described by Kleinbaum *et al.*, 1998[19], it was found that Model 7, including two predictors; *CRE* (urinary creatinine concentration) and *GEO* (geographical origin), scored best in three of the four quality tests. The difference in the adjusted correlation coefficient, $R^2_{adj}$, and the mean square residual, $MSE(p)$, was minor between the different models. None of the cross-terms in model B and the quadratic terms of Model C was found to be significant by the partial F-test.

Table 3
*Predictors of the urinary potassium concentration (K) of the selected reduced models.*

| Model | Predictors | $R^2_{adj}$ (=Adjusted Coefficient of Variation [20]) |
|---|---|---|
| Model 1 | *SEX, AGE, GEO, CRE* | *0.492* |
| Model 2 | *SEX, BWT, GEO, CRE* | *0.492* |
| Model 3 | *AGE, BWT, GEO, CRE* | *0.492* |
| Model 4 | *SEX, GEO, CRE* | *0.495* |
| Model 5 | *AGE, GEO, CRE* | *0.495* |
| Model 6 | *BWT, GEO, CRE* | *0.494* |
| Model 7 | *GEO, CRE* | *0.497* |

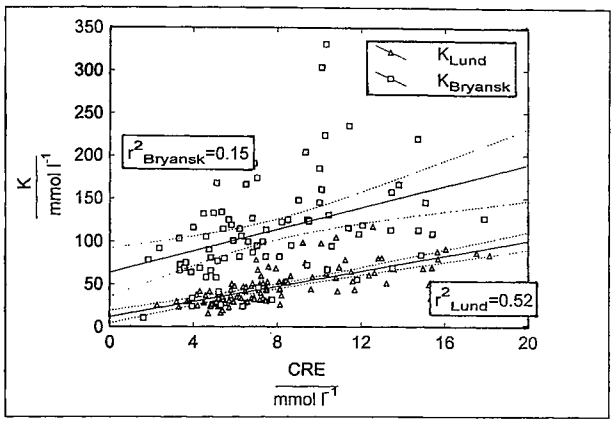


**Figure 1**: Potassium concentration (*K*) vs. the creatinine concentration (*CRE*) in urine for the Bryansk group and the Lund reference group. Dotted lines indicate the 95% confidence intervals of the regression lines.

## 4. CONCLUSIONS

The all-possible-regression analysis of the data from the Lund and Bryansk subjects shows that two main factors determine the potassium concentration in urine: creatinine concentration in urine, *CRE*, and geographical location, *GEO*, corresponding to Model 7 in Table 3. The intercept of the *K* vs. *CRE* regression line for the Bryansk group was significantly higher ($p<0.05$) than that of the corresponding regression line for the Swedish group (Figure 1). As has been mentioned in a previous study [7], it is suspected that this difference is due to the differences in diet, since potassium is found in most foodstuffs. The elevated potassium concentration in the Russian samples further confirms previous assumptions regarding the dietary habits of the Bryansk population [21]. This *systematic* difference in the dietary intake between different populations will therefore considerably influence the predictions of the whole-body content of $^{137}$Cs when using the potassium-normalisation method (Eqs 1-2).

The results confirm that potassium is less suitable than creatinine for the normalisation to 24h urinary excretion and estimation of whole-body content of radiocaesium, $Q_{Cs}$. If certain populations in their daily diet ingest an excess proportion of potassium that cannot be retained by the body cells, the excess fraction is directly excreted through urine leading to higher potassium concentration in urine than in other populations and consequently to *under*estimates of the body burden of $^{137}$Cs from urinary assays.

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