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Comparison of combined urea and creatinine clearance and prediction equations as measures of residual renal function when GFR is low

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Summary

Background: UK, US and European guidelines recommend the decision to initiate dialysis should be based on a combination of measurements of kidney function, nutritional status and clinical symptoms. Such recommendations assume an accurate and reproducible measure of glomerular filtration rate (GFR).

Methods: Prospective study of 97 patients with chronic kidney disease (CKD) and serum creatinine $>200 \mu\text{mol/l}$ (2.26 mg/dl) who between them contributed 388 24 h urine collections. Our main outcome measure was the number of patients with low residual renal function identified by different tests, using widely accepted thresholds. We calculated sensitivity, specificity, positive and negative predictive values and receiver operating characteristic curves for each comparison using a combined urea and creatinine clearance of $<15 \text{ ml/min}$ to indicate the likely presence of end stage renal disease (CKD stage 5).

Results: Seventy five patients had a combined urea and creatinine clearance $<15 \text{ ml/min}$ during the study. Using the highest measurement of serum creatinine for each patient, the best of the prediction equations was the 4-variable modification of diet in renal disease (MDRD) equation (area under ROC curve 0.93). This was followed by Kt/V (AUC 0.91) and Cockcroft Gault with and without correction for ideal body weight (AUC 0.89). Further analyses showed that the 4-variable MDRD equation had higher NPV (64%) but lower PPV (89%) than the other tests (NPV 40–49%, PPV 92–100%), for identifying patients whose combined clearance was $<15 \text{ ml/min}$.

Conclusion: The 4-variable MDRD formula is currently the best available prediction equation for GFR, but will nevertheless over estimate residual renal function when this is significantly impaired in up to 36% cases. Collection of 24 h urine samples may still have a role in the assessment of patients with stages 4 and 5 CKD.

Introduction

It is increasingly accepted that morbidity and mortality within the renal population can be reduced by early referral to a nephrologist, timely creation of permanent vascular or peritoneal access and

initiation of dialysis before the onset of symptomatic uraemia.^{1–5} Because symptoms of renal failure are non-specific, some measure of residual renal function is required to prompt such interventions.

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A simple classification of chronic kidney disease (CKD) based on the severity of renal failure rather than the cause, suggests that patients with glomerular filtration rate (GFR) 15–29 ml/min/1.73 m² (CKD stage 4) begin preparation for renal replacement therapy and that dialysis be considered when GFR is <15 ml/min/1.73 m² (CKD stage 5).⁶ Such recommendations assume an accurate and reproducible measure of GFR.

Serum creatinine is not ideal for this purpose, partly because it is not linearly related to GFR and partly because it is influenced by other factors such as age, gender, race, muscle mass, diet, certain drugs, also by tubular secretion of creatinine as GFR falls.^{7,8} The most accurate ways to measure GFR are by clearance of inulin, radio-active markers or radio-contrast agents,⁹ but these are impractical for everyday use and not widely available. Surrogate markers of GFR are used instead. These include estimated GFR using the MDRD formula,^{10,11} estimated creatinine clearance using the Cockcroft and Gault formula with or without adjustment for ideal body weight,¹² and urea clearance (Kt/V).

Because tubular secretion of creatinine causes on average a 15% over estimate of creatinine clearance as renal function fails and tubular reabsorption of urea causes on average a 15% underestimate of urea clearance, the mean of these two measurements is believed to represent the most accurate non-invasive test of GFR in patients whose GFR is low.^{9,10,13–17} The purpose of our study was to examine the extent to which the different tests of residual renal function predicted a GFR <15 ml/min using combined urea and creatinine clearance as a surrogate for GFR.

Methods

The study took place in the Renal Unit of Dumfries Infirmary, a district general hospital serving the population of south west Scotland. We obtained the following parameters from all patients with serum creatinine >200 µmol/l (2.26 mg/dl) attending our pre-dialysis clinic—height and weight, serum creatinine, blood urea and 24 h urine collections for the measurement of urine volume, urine urea and urine creatinine concentrations. Each patient was given written instructions to improve the accuracy of the 24 h collections.

We used the 4-variable MDRD equation with 175 as the constant in keeping with current recommendations,¹¹ and the Cockcroft and Gault equation as published,¹² with and without adjustment for ideal body weight using a body mass index (BMI) of 22.5. Weekly urea clearance corrected for total body

water (Kt/V) was derived using widely available software.¹⁸ Combined urea and creatinine clearance was the arithmetic mean of the 24 h urea and creatinine clearances, corrected for body surface area. We used this measurement as a surrogate for GFR and a value of <15 ml/min/1.73 m² as the theoretic threshold for starting dialysis. All other measures of residual renal function were then compared to this using the following thresholds. These were estimated GFR from the 4-variable MDRD formula <15 ml/min; calculated creatinine clearance using Cockcroft and Gault formula with and without adjustment for ideal body weight <15 ml/min; weekly Kt/V <2.0.

We calculated receiver operator characteristic (ROC) curves using standard methodology implemented in SAS PROC LOGISTIC and plotted the curves of the four tests given in Table 1 against the 'gold standard' of combined clearance <15 ml/min. We also calculated sensitivity, specificity, negative and positive predictive values, to investigate whether disagreements between test and combined urea and creatinine clearance were more likely to be falsely positive or falsely negative. Three analyses were undertaken for each comparison of tests of residual renal function: the first measurement of residual renal function for each patient, the measurement of residual renal function that corresponded to the highest serum creatinine for each patient, and all readings for all patients.

Results

A total of 440 24 h urine collections on 115 consecutive stable pre-dialysis patients were considered for analysis. One patient consistently provided 48 h worth of urine in his collection and was excluded from the study as were 52 urine collections from 37 other patients that were judged to be incomplete: 12 samples <1000 ml volume, 18 samples with urine creatinine <7.7 mmol (87 mg)/24 h in a man, 11 samples <5.6 mmol (63 mg)/24 h in a woman and a further 11 samples with serum creatinine <200 µmol/l (2.26 mg/dl).¹⁹ This resulted in the omission of all the data from 18 subjects. All other 97 subjects and 388 urine collections were included in the analysis which comprised 71 Caucasian men average age 64 years (range 19–87 years) with average (SD) urine creatinine 12.1 (3.2) mmol [137 (3.6) mg]/24 h and 26 Caucasian women average age 60 years (range 34–84) with average (SD) urine creatinine 8.3 (1.9) mmol [94 (2.2) mg]/24 h.

The relation between serum creatinine and combined urea and creatinine clearance was inverse

Table 1 Relation between different tests of residual renal function

Measure	True (Positive)	True (Negative)	False (Positive)	False (Negative)	Sensitivity ^c (%)	Specificity ^d (%)	NPV ^e (%)	PPV ^f (%)	Area under ROC curve
<i>First measurement (n = 97)</i>									
Combined clearance <15 ml/min	57	40	0	0					
4-Variable MDRD <15 ml/min	42	32	8	12	79	80	73	85	0.89
Cockcroft Gault <15 ml/min	23	40	0	34	40	100	54	100	0.88
Ideal Cockcroft <15 ml/min ^a	34	36	4	23	60	90	61	89	0.86
Urea clearance (Kt/V) <2 ^b	28	38	2	29	49	95	57	93	0.87
<i>Highest measurement (n = 97)</i>									
Combined clearance <15 ml/min	75	22	0	0					
4-Variable MDRD <15 ml/min	67	14	8	8	89	64	64	89	0.93
Cockcroft Gault <15 ml/min	42	22	0	33	56	100	40	100	0.89
Ideal Cockcroft <15 ml/min	57	17	5	18	76	77	49	92	0.89
Urea clearance (Kt/V) <2	51	20	2	24	68	91	45	96	0.91
<i>All measurements (n = 388)</i>									
Combined clearance <15 ml/min	261	127	0	0					
4-Variable MDRD <15 ml/min	219	104	23	42	84	82	71	90	0.91
Cockcroft Gault <15 ml/min	100	124	3	161	38	98	44	97	0.84
Ideal Cockcroft <15 ml/min	171	113	14	90	66	89	56	92	0.86
Urea clearance (Kt/V) <2	144	120	7	117	55	94	51	95	0.90

Keys: ^aIdeal Cockcroft <15 ml/min=estimated creatinine clearance adjusted for ideal body weight <15 ml/min; ^burea clearance (Kt/V) <2=urea clearance corrected for estimated total body water <2; ^csensitivity=proportion of true positives detected; ^dspecificity=proportion of true negatives detected; ^eNPV(negative predictive value)=proportion of negatives that are true negatives; ^fPPV (positive predictive value)=proportion of positives that are true positives.

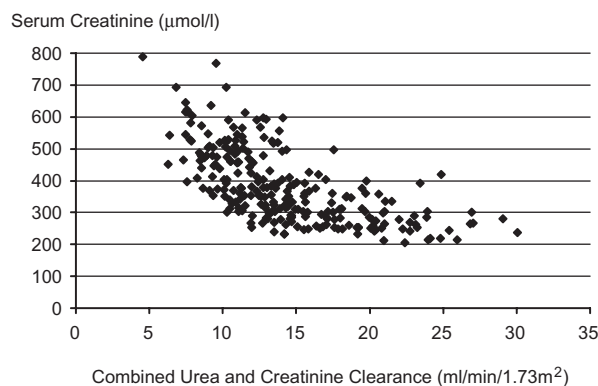


Figure 1. Relation between serum creatinine and combined urea and creatinine clearance corrected for body surface area, showing that some patients with serum creatinine below 300 μmol/l (3.39 mg/dl) have already reached end stage renal failure.

and curvilinear as shown in Figure 1, which gives all values for the 97 patients. Serum creatinine in patients with combined clearance <15 ml/min ranged from 230 to 1023 μmol/l (2.6–11.6 mg/dl) confirming that serum creatinine itself is an unreliable indicator of the severity of renal failure, and indicating that some patients with creatinine <300 μmol/l (3.39 mg/dl) had already reached end stage renal failure. The average (unweighted across all measurements) combined urea and creatinine

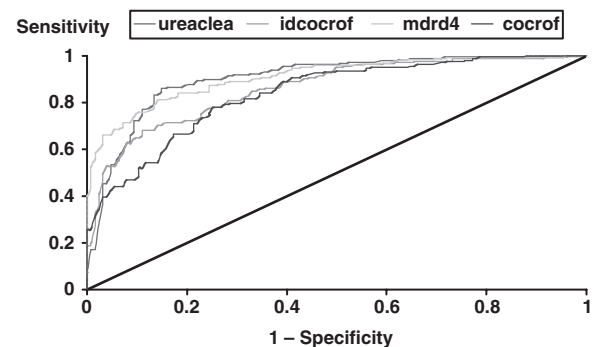


Figure 2. The ROC for 4-variable MDRD formula (pale blue), Cockcroft Gault formula (dark blue), Cockcroft Gault formula adjusted for ideal body weight (green) and weekly Kt/V (red) against non-invasive gold standard of combined urea and creatinine clearance less than 15 ml/min.

clearance in those with combined clearance <15 ml/min was 11.2 (range 4.5–15.0) ml/min. The corresponding average serum creatinine in this group was 441 μmol/l (4.99 mg/dl).

The ROC curves are shown in Figure 2. Using the highest measurement of serum creatinine for each patient, the best of the prediction equations was the 4-variable MDRD equation with an area under ROC curve of 0.93. This was followed by Kt/V (AUC 0.91) and Cockcroft Gault with and without correction for

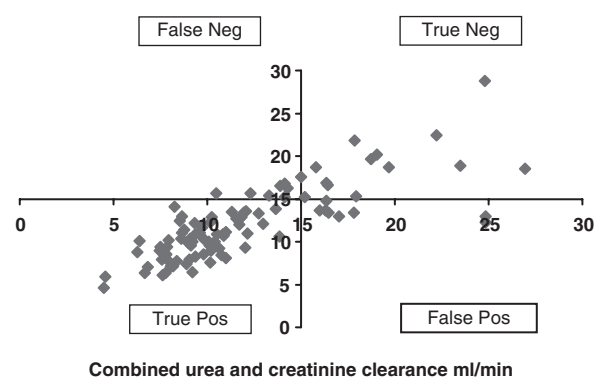


Figure 3. Scatter plot showing relation between 4-variable MDRD GFR (vertical axis) and combined urea and creatinine clearance for the highest measurement of serum creatinine in 97 consecutive patients whose serum creatinine was $>200 \mu\text{mol/l}$.

ideal body weight (AUC 0.89). Further analyses showed that the 4-variable MDRD equation had higher negative predictive value (64%) but lower positive predictive value (89%) than Cockcroft Gault with (NPV 49%, PPV 92%) and without (NPV 40%, PPV 100%) correction for ideal body weight, and than Kt/V (NPV 45%, PPV 96%) for identifying patients whose combined clearance was $<15 \text{ ml/min}$. (Table 1).

The implication of these findings is that all prediction equations tend to overestimate GFR when this is low. The 4-variable MDRD formula may be less likely than Cockcroft Gault and Kt/V to do so, but will nevertheless overestimate residual renal function in up to 36% of cases (negative predictive value of 64%). (Table 1, Figure 3). There was little difference between the positive and negative predictive values for the 71 men and 26 women (NPV 74% and 67%, PPV 79% and 95%, respectively). There was no suggestion that the MDRD formula performed any differently in the 40 subjects with BMI >30 (NPV 75%, PPV 80%) than in the 57 subjects with BMI ≤ 30 (NPV 71%, PPV 88%). Similar results were obtained for the MDRD formula when we used the measurement of residual renal function that corresponded to the first serum creatinine for each patient (NPV 73%, PPV 85%), or all measurements for all patients (NPV 71%, PPV 90%).

Discussion

The decision on precisely when to start dialysis is unresolved. The belief that patients should 'earn their dialysis' by becoming ill before they start treatment has been replaced by the view that it is unwise to allow patients to develop severe

malnutrition, acidosis or uraemia prior to renal replacement therapy. Against this background, the main findings of our study are that the non-invasive assessment of residual renal function is associated with more pitfalls than might be supposed. Serum creatinine, the most readily available of the non-invasive tests, does not predict end stage renal failure reliably enough to be used for this purpose. Serum creatinine in patients with combined urea and creatinine clearance $<15 \text{ ml/min}$ varied from 230 to $1023 \mu\text{mol/l}$ (2.6–11.6 mg/dl) indicating that some patients with serum creatinine $<300 \mu\text{mol/l}$ had already developed end stage renal failure (Figure 1). Similar findings have been reported by others.^{7,8}

The current recommendations of best practice groups in Europe, the United States and United Kingdom regarding initiation of dialysis are as follows. In Europe 'dialysis should be instituted whenever the GFR is $<15 \text{ ml/min}$ and there is one or more of the following: symptoms or signs of uraemia, inability to control hydration status or blood pressure, or a progressive deterioration in nutritional status. In any case dialysis should be started before the GFR has fallen to $6 \text{ ml/min}/1.73 \text{ m}^2$ even if optimal pre-dialysis care has been provided and there are no symptoms'.¹⁵ To ensure that dialysis is started before GFR is $<6 \text{ ml/min}$, clinics should aim to start at $8\text{--}10 \text{ ml/min}$.¹⁵ In the United States, the dialysis outcomes quality initiative (DOQI) guidelines suggest dialysis should begin when the weekly Kt/V is <2.0 , equivalent to a renal creatinine clearance of $\sim 14 \text{ ml/min}/1.73 \text{ m}^2$, unless the patient has a stable or increased oedema free body weight, a dietary protein intake of $>0.8 \text{ g/kg/day}$ and no evidence of clinical uraemia.²⁰ Current UK guidelines also recommend that the decision to initiate dialysis be based on a combination of measurements of kidney function, nutritional status and clinical symptoms: 'Dialysis should be considered when the weekly urea clearance falls below the equivalent of a Kt/V of 2.0, equivalent to a GFR of approx 14 ml/min . Dialysis will be indicated in such patients if there is evidence of malnutrition or if symptoms interfere with quality of life'.²¹

These recommendations come at a time of increasing interest in prediction equations for estimating creatinine clearance and GFR, of which the two most widely used are the MDRD equations proposed by Levy and colleagues^{10,11} and the formula of Cockcroft and Gault.¹² The MDRD equations were validated against an iothalamate clearance estimate of GFR normalized to a body surface area of 1.73 m^2 and the Cockcroft and Gault formula against creatinine clearance. These prediction equations require either that body weight

(Cockcroft and Gault), racial origin (4-variable MDRD), or racial origin, serum urea and albumin (6-variable MDRD) be measured or recorded in addition to serum creatinine for an estimate of GFR to be made. Much has been written of the advantages and limitations of estimating kidney function in adults using these equations, with the balance of evidence²² and current opinion^{23–25} supporting the use of the 4-variable MDRD equation over both the 6-variable MDRD equation and the Cockcroft and Gault formula when estimating residual renal function.

The MDRD formula is, however, not without limitation. It was validated in a population of 1628 predominantly middle aged adults with known kidney disease whose average GFR was 40 ml/min/1.73 m². It performs best in the population in which it was derived, underestimates GFR when this is normal or only mildly reduced, and overestimates GFR when this is severely impaired. Although attention has been drawn to the poor performance of MDRD at higher levels of GFR^{22,26} there has been less discussion of its limitations in advanced CKD.¹⁹ Our results, which clearly show that the MDRD formula overestimates GFR in end stage renal disease, are closely similar to those of Froissart and colleagues.²⁷ In a study of 2065 adult Europeans, 128 of whom had measured GFR <15 ml/min, the MDRD formula had a false negative rate of 35.2%.²⁷

Most others, but not all, have drawn similar conclusions. Kuan *et al.*,²⁸ in a study of 26 non-diabetic subjects whose baseline creatinine was >400 µmol/l (4.52 mg/dl), found that the MDRD formula underestimated GFR when inulin clearance was >8 ml/min/1.73 m² and overestimated GFR when inulin clearance was <8 ml/min/1.73 m².²⁸ Rule studied 320 patients with CKD, 22 of whom had measured GFR <15 ml/min by iothalamate clearance. The MDRD GFR overestimated residual renal function in this group.²⁹ Hallan and colleagues showed that the MDRD formula underestimated GFR at near normal levels but overestimated GFR when this was low in 107 subjects with 'various grades of kidney failure' and concluded that while eGFR using the MDRD formula might be useful for better timing of such important pre-dialytic preparations as construction of an AV fistula, placement of a PD catheter or transplant work up, GFR should probably be measured using a plasma clearance technique before deciding when to start renal replacement therapy.³⁰

In contrast, Barroso and colleagues found that the 6-variable MDRD equation underestimated GFR when measured by Tc^{99m} DTPA in 99 patients whose average DTPA-GFR was 16.2 ml/min/1.73 m².³¹ The reasons for this different result are

not clear but may reflect the use of the 6-variable and not 4-variable MDRD formula. Notwithstanding, the consensus view is that the MDRD formula overestimates GFR when this is low.^{27–30} One possible explanation for this is the relatively lower serum creatinine concentration for a given level of GFR in these patients as a result of reduced muscle mass and/or under nutrition when compared with the middle aged population in which the MDRD formula was derived.

Our study has strengths and weaknesses. Strengths were that we deliberately chose to study consecutive patients for whom an accurate measurement of residual renal function is necessary in order to initiate dialysis. The 4-variable MDRD formula has not been tested very often in this patient population. Our main limitation is that we did not use an exogenous marker such as inulin or iodine labelled iothalamate to estimate GFR. Inulin has long been regarded as the most accurate estimate of GFR, but even inulin has some extra-renal clearance, equivalent to 6 ml/min for a 70 kg man.²² Also it would have been impractical to infuse an exogenous marker given the need to assess GFR on a regular basis in the run up to dialysis in our patients. Against this background we chose to assess residual renal function using combined urea and creatinine clearance as this is widely believed to be the most accurate of the non-invasive tests for GFR when GFR is low.^{9,10,13–17} Recognizing that timed urine collections are cumbersome and susceptible to error we limited our analyses to those collections judged likely to be accurate by excluding those with low urine creatinine. The fact that the MDRD formula overestimated GFR when GFR was low to the same extent as in the paper by Froissart and colleagues,²⁷ who used chromium labelled EDTA as a gold standard, supports our belief that the combined urea and creatinine clearance may be an acceptable alternative.

Although our study is not primarily concerned with the timing of dialysis, discussion of the initiation of dialysis is relevant if the decision to start treatment is to be based not just on symptoms but on some measurement of residual renal function.¹³ We believe, therefore, that our observations have implications for the referral and subsequent management of patients with chronic renal failure. The first is that some patients with serum creatinine as low as 300 µmol/l (3.39 mg/dl) will already have developed end stage renal failure, and the second that a combined urea and creatinine clearance corrected for body surface may give a better estimate of residual renal function than measures based purely on creatinine or urea which tend to overestimate GFR when this is significantly impaired.

In light of these findings we believe that collection of 24 h urine samples may still have a role in the assessment of patients with stages 4 and 5 CKD.

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References

- Ismail N, Neyra R, Hakim R. The medical and economical advantages of early referral of chronic renal failure patients to renal specialists. *Nephrol Dial Transplant* 1998; **13**:246–50.
- Roderick P, Jones C, Thomson C, Mason J. Late referral for dialysis: improving the management of chronic renal disease. *QJM* 2002; **95**:363–70.
- Wavamunno MD, Harris DC. The need for early nephrology referral. *Kidney Int* 2005; **95**(Suppl.):S128–32.
- Wauters JP, Lameire N, Davison A, Ritz E. Why patients with progressive kidney disease are referred late to the nephrologist: on causes and proposals for improvement. *Nephrol Dial Transplant* 2005; **20**:490–6.
- Vanholder R. Chronic kidney disease in adults – UK guidelines for identification, management and referral. *Nephrol Dial Transplant* 2006; **21**:1776–7.
- Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, et al. National Kidney Foundation Practice Guidelines for chronic kidney disease: evaluation, classification and stratification. *Ann Intern Med* 2003; **139**:137–47.
- Shemesh O, Golbetz H, Kriss JP, Myers BD. Limitation of creatinine as a filtration marker in glomerulopathic patients. *Kidney Int* 1985; **28**:830–8.
- Levey AS, Perrone RD, Madias NE. Serum creatinine and renal function. *Ann Rev Med* 1988; **39**:465–90.
- Traynor J, Mactier R, Geddes CC, Fox JG. How to measure renal function in clinical practice. *Br Med J* 2006; **333**:733–7.
- Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. For the modification of diet in renal dialysis study group. A more accurate method to estimate GFR from serum creatinine: a new prediction equation. *Ann Intern Med* 1999; **130**:461–70.
- Levey AS, Coresh J, Greene J, et al. Expressing the MDRD study equation for estimating GFR with IDMS traceable (gold standard) serum creatinine values. *J Am Soc Nephrol* 2006; **16**:69A.
- Cockcroft DW, Gault MW. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976; **16**:31–41.
- Jacobs C. At which stage of renal failure should dialysis be started? *Nephrol Dial Transplant* 2000; **15**:305–7.
- Ledebo I, Kessler M, Van Biesen W, Wanner C, Wiecek A, Prichard S, et al. Initiation of dialysis – opinions from an international survey: report on the Dialysis Opinion Symposium at the ERA-EDTA Congress, 18 September 2000, Nice. *Nephrol Dial Transplant* 2001; **16**:1132–8.
- European Best Practice Guidelines. Measurement of renal function, when to refer and when to start dialysis. *Nephrol Dial Transplant* 2002; **17**(Suppl. 7):7–15.
- Douma CE, Smit W. When to start dialysis? *Nephrol Dial Transplant* 2006; **21**(Suppl. 2):ii20–4.
- Herget-Rosenthal S, Bokenkamp A, Hofmann W. How to estimate GFR – serum creatinine, serum cystatin C or equations. *Clin Biochem* 2007; **40**:153–6.
- PD Adequest 2.0 for Windows. Baxter healthcare corporation. Deerfield, Illinois, 1994.
- Whelton A, Watson AJ, Rock RC. Nitrogen metabolites and renal function, in Burtis CA, Ashwood ER, eds. *Tietz Textbook of Clinical Chemistry*. 2nd edn. Oxford, WB Saunders, 1994; 1535.
- National Kidney Foundation Dialysis Outcomes Quality Initiative. Clinical practice guidelines for peritoneal dialysis adequacy: update 2000. *Am J Kidney Dis* 2001; **37**(Suppl. 1):S68–71.
- Renal Association. Treatment of adults and children with renal failure. *Standards and Audit Measures*. 3rd edn. 2002. [www.renal.org (accessed October 2006)].
- Lamb EJ, Thomson CR, Roderick PJ. Estimating kidney function in adults using formulae. *Ann Clin Biochem* 2005; **42**:321–45.
- Joint Specialty Committee for Renal Disease, Royal College of Physicians of London and the Renal Association. Chronic kidney disease in adults: UK guidelines for identification, management and referral. London. UK, Royal College of Physicians of London, 2005.
- National Kidney Disease Education Programme (NKDEP) of the North American National Institutes of Health. Guidelines for identification of patients with chronic kidney disease. [www.nkdep.nih.gov/healthprofessionals/nkdep_labrationale-factsheet.pdf (accessed December 1 2007)].
- MacGregor MS. How common is early chronic kidney disease? A background paper prepared for the UK Consensus Conference on Early Chronic Kidney Disease. *Nephrol Dial Transplant* 2007; **22**(Suppl. 9):ix8–18.
- Stevens LA, Coresh J, Greene T, Levey AS. Medical progress: assessing kidney function – measured and estimated glomerular filtration rate. *N Engl J Med* 2006; **354**:2473–83.
- Froissart M, Rossert J, Jacquot C, Paillard M, Houillier P. Predictive performance of the modification of diet in renal disease and Cockcroft-Gault equations for estimating renal function. *J Am Soc Nephrol* 2005; **16**:763–73.
- Kuan Y, Hossain M, Surman J, El Nahas AM, Haylor J. GFR prediction using the MDRD and Cockcroft and Gault equations in patients with end stage renal disease. *Nephrol Dial Transplant* 2005; **20**:2394–401.
- Rule AD, Larson TS, Bergstralh EJ, Slezak JM, Jacobsen SJ, Cosio FG. Using serum creatinine to estimate glomerular filtration rate: accuracy in good health and in chronic kidney disease. *An Intern Med* 2004; **141**:929–37.
- Hallan S, Asberg A, Lindberg M, Johnsen H. Validation of the modification of diet in renal disease formula for estimating GFR with special emphasis on calibration of the serum creatinine assay. *Am J Kidney Dis* 2004; **44**:84–93.
- Barroso S, Martinez JM, Martin MV, Rayo I, Caravaca F. Accuracy of indirect determinations of glomerular filtration in advanced renal failure. *Nefrologia* 2006; **26**:344–50.