Table 3.1.12 *Studies evaluating the accuracy of DTPA (radioactively labelled diethylenetriaminepentaacetate) for measuring GFR (glomerular filtration rate) using renal clearance of inulin as the reference method.*

Author Year Reference Country	**Aim**	**Study design Population Gender (M/F) Age GFR range**	**Index method (I)**	**Reference method (R)**	**Results**	**Study quality Comments**
Dai et al 2011 [2] China	To compare the clearance of ^{99m}Tc-DTPA and inulin simultaneously	Cross-sectional Adults with CKD (n=53) 35 M/18 F Age range not specified Mean GFR (SD): 42.4±27.6 mL/min/1.73 m^2	Plasma clearance of DTPA after iv injection. Blood samples after 120 and 240 min	Renal clearance of inulin	mL/min/1.73 m^2 I–R=10.5±8.6 (SD) I=1.055 R +8.167 r=0.96 Bias (GFR level): +9.8 (30) +11.5 (60) +13.1 (90)	High
Lewis et al 1989 [3] USA	To compare GFR determinations using a contrast agent, ^{99m}Tc-DTPA and inulin	Cross-sectional Renal and heart transplant recipients (n=21) and renal donor candidates (n=10) 20 M/11 F Age range: 22–72 years GFR range: 15–120 mL/min/1.73 m^2	Renal clearance of DTPA after iv injection. Three urine sampling periods	Renal clearance of inulin	mL/min/1.73 m^2 *I–R=–0.03±18 (SD) I=0.84 R +8.4 r=0.85 Bias (GFR level): +3.6 (30) –1.2 (60) –6 (90)	Moderate Small sample size
Perrone et al 1990 [4] USA	To compare simultaneously the renal clearance of three radioisotopic filtration markers commercially available in the USA (^{99m}Tc-DTPA, ^{168}Yb-DTPA, and ^{125}I-iothalamate) with clearance of inulin	Cross-sectional Volunteers (adults) with varying levels of renal function (n=20) (16 renal insufficiency, 4 healthy) Age range 18–75 years GFR range 5–130 mL/min/1.73 m^2 The protocol was repeated after 7–28 days	Renal clearance of ^{99m}Tc-DTPA after iv injection, four 20 min urine collections. Plasma samples at beginning and end of each period	Renal clearance of inulin	mL/min/1.73 m^2 Day 1: I–R=–0.50±2.82 (SD) Day 2: I–R=+1.68±3.07 (SD) ^{99m}Tc-DTPA clearance after single iv accurately measures GFR in subjects with renal insufficiency	Moderate Small sample size
Petri et al 1988 [5] USA	To determine the clearance of inulin, DTPA, iothalamate and creatinine repeatedly during three years in patients with lupus nephropathy	Cross-sectional Women with lupus nephropathy (n=25) Age range: 18–58 years GFR range: 23–123 mL/min	Renal clearance after iv DTPA injection. Six 30 minute urine collections. Blood samples at each period midpoint	Renal clearance of inulin	mL/min I=0.92 R +0.63, r=0.96 Bias (GFR level): –1.7 (30) –4.2 (60) –6.6 (90) Technetium-DTPA renal clearance correlated highly with clearance of inulin	Moderate Small sample size

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Table 3.1.12 *continued*

Author Year Reference Country	**Aim**	**Study design Population Gender (M/F) Age GFR range**	**Index method (I)**	**Reference method (R)**	**Results**	**Study quality Comments**
Shemesh et al 1985 [6] USA	To determine the reliability of creatinine clearance in comparison with three true GFR markers (inulin, ^{99m}Tc-DTPA, and dextran) in a large population of patients	Cross-sectional Patients with diverse glomerular diseases (n=171) GFR range 10–135 mL/min/1.73 m^2 45 patients were studied with both ^{99m}Tc-DTPA and inulin	Renal clearance with iv DTPA injection. Four timed urine collections. Blood samples at each period midpoint. Plasma clearance (2-compartment) was also calculated	Renal clearance of inulin	mL/min/1.73 m^2 Renal clearance I/R=1.02±0.14 (SEM) r=0.969 Plasma clearance of DTPA gave r=0.694 in comparison with inulin clearance. GFR calculated from the slope of elimination of DTPA from plasma does not correspond closely with the inulin clearance	Moderate Insufficient statistical analysis
Tomlanovich et al 1986 [41] USA	To elucidate whether the disparity between creatinine clearance and true GFR is enhanced also in the CsA-associated chronic nephropathy. ^{99m}Tc-DTPA clearance was studied in a subgroup	Cross-sectional Heart transplanted patients treated with CsA (n=100) Mean age: 36±1 years (SEM) GFR range: 20–129 mL/min/1.73 m^2 A subgroup (n=24) was examined with DTPA and inulin clearance	Renal clearance with iv DTPA injection. Four timed urine collections. Blood was sampled at beginning and end of each period	Renal clearance of inulin	mL/min/1.73 m^2 I/R=0.95±0.04 (SE) ^{99m}Tc-DTPA and inulin are unrestricted by the glomerular capillary wall and behave as true filtration markers in CsA-induced chronic nephropathy	Moderate Small sample size Insufficient statistical analysis
Wharton et al 1992 [7] USA	To assess ^{99m}Tc-DTPA urinary clearance in the clinical measurement of GFR in critically ill patients	Cross-sectional ICU patients with ARI (n=18) 10 M/8 F Age range: 49–92 years GFR range: 2–69 mL/min	Renal clearance with iv DTPA injection. Two one hour urine collections. Blood was sampled at beginning and end of each period	Renal clearance of inulin	mL/min I=1.12 R, r=0.85 *Bias: +3.6 (30) +7.2 (60) In patients in the intensive care unit, clearance of ^{99m}Tc-DTPA provides a rapid, accurate, and inexpensive clinical assessment of GFR, even at very low GFRs	Moderate Small sample size

* Calculations not reported by the author (s).

ARI = Acute renal injury; CKD = Chronic kidney disease; CsA = Cyclosporin A; DTPA = Diethylene triamine penta acetic acid; F = Female; GFR = Glomerular filtration rate; I = Index method; ICU = Intensive-care unit; M = Male; r = Pearson's correlation coefficient; R = Reference method; SD = Standard deviation; SE = Standard error; SEM = Standard error of mean

Table 3.1.13 *Studies evaluating the accuracy of ^{51}Cr-EDTA (radioactively labelled ethylenediaminotetraacetic acid) for measuring GFR (glomerular filtration rate) using renal clearance of inulin as the reference method.*

Author Year Reference Country	**Aim**	**Study design Population Gender M/F Age GFR range**	**Index method (I)**	**Reference method (R)**	**Results**	**Study quality Comments**
Bröchner-Mortensen et al 1969 [8] Denmark	To compare plasma clearance of ^{51}Cr-EDTA to renal inulin clearance	Cross-sectional 17 subjects 15 CKD, 2 healthy GFR range: 10–130 mL/min	Plasma clearance of ^{51}Cr-EDTA Administration by single injection, samples at 15 min–5 hrs (multi-exponential model using 11 plasma samples)	Renal clearance of inulin	mL/min I=1.017 R +1.6, r=0.97 *Bias (GFR level): +2.1 (30), +2.6 (60), +3.1 (90) Plasma clearance of ^{51}Cr-EDTA corresponds closely to renal inulin clearance	Moderate Small sample size
Chantler et al 1969 [9] United Kingdom	To compare the renal clearance of ^{51}Cr-EDTA to that of inulin, and to compare the renal- and plasma clearances of ^{51}Cr-EDTA	Cross-sectional 15 CKD, 6 nephrotic syndrome GFR range: 5–158 mL/min	Renal clearance of ^{51}Cr–EDTA Continuous infusion	Renal clearance of inulin	mL/min I/R=1.004±0.013 (SEM) (CKD) I/R=0.956±0.003 (SEM) (nephrotic syndrome) ^{51}Cr-EDTA may be used as a substitute for inulin in clinical studies	Moderate Small sample size
Ditzel et al 1972 [10] Denmark	To optimize the sampling scheme after single injection of ^{51}Cr-EDTA to measure GFR	Cross-sectional 20 patients GFR range: 6–166 mL/min	Plasma clearance of ^{51}Cr-EDTA Administration by single injection, samples at 5–240 min (bi-exponential model using 4, 6 or 12 plasma samples)	Renal clearance of inulin	mL/min *I–R=–1.45±11.7 (SD) *I/R=1.09±0.27 I=0.85 R +11,42, r=0.97 Bias (GFR level): +6.8 (30), +2.2 (60), –2.4 (90) Four plasma samples suffice to obtain accurate GFR determinations	Moderate Small sample size

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Table 3.1.13 *continued*

Author Year Reference Country	Aim	Study design Population Gender M/F Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Favre et al 1968 [11] United Kingdom	To compare clearances of ^{51}Cr-EDTA, inulin and creatinine in dogs and in patients with renal disease	Cross-sectional Patients with various renal disorders (n=20) Age range: 16–73 years GFR range: 2–147 mL/min	Renal clearance of ^{51}Cr-DTA Continuous infusion	Renal clearance of inulin	mL/min *I–R=+1.56±8.7 (SD) *I/R=1.03±0.09 (SD) I=1.024 R – 0.95, r=0.992 Bias (GFR level): –0.9 (30), –1.3 (60), –1.7 (90) ^{51}Cr-EDTA clearance is a reliable estimate of inulin clearance	Moderate Small sample size Insufficient method description
Favre 1978 [40] Schweiz	To establish valid criteria for investigation methods	Cross-sectional 40 patients	Plasma clearance of ^{51}Cr-EDTA 10–130 min (bi-exponential model)	Renal clearance of inulin	mL/min R/I=1.02±0.14 (SD?) Plasma clearance of ^{51}Cr-EDTA equals inulin clearance	Moderate Small sample size Insufficient statistical analysis
Gibb et al 1989 [12] United Kingdom	To compare the renal clearance of ^{51}Cr-EDTA to that of inulin and creatinine in diabetic children and healthy controls	Cross-sectional Diabetic children and healthy adolescents 11 diabetic children, 12 healthy adolescents Age range: 5.5–34 years GFR range: 80–200 mL/min/1.73 m^2 Drop-out 1 diabetic patient	Renal clearance of ^{51}Cr-EDTA Continuous infusion	Renal clearance of inulin	mL/min/1.73 m^2 All cases I–R=–7.4±2.5 (SEM) I/R=0.94 (CI 0.90; 0.98) Diabetics I–R=–7.9±5.1 (SEM) I/R=0.95 (CI 0.87; 1.02) r=0.93 Healthy young adults I–R=–6.9±1.9 (SEM) I/R=0.94 (CI 0.91; 0.97) r=0.40 ^{51}Cr-EDTA clearance under-estimates inulin clearance	Moderate Small sample size

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Table 3.1.13 *continued*

Author Year Reference Country	Aim	Study design Population Gender M/F Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Hagstam et al 1974 [13] Sweden	To compare clearances of ^{51}Cr-EDTA, inulin and creatinine in patients with chronic glomerular disease	Cross-sectional Patients with renal disorder 52 patients, 14–56 years (gross sample) 31 patients GFR range: 8–160 mL/min/1,73 m^2 (single injection sample) 16 patients GFR range: 30–120 mL/min/1,73 m^2 (infusion sample)	Plasma clearance of ^{51}Cr-EDTA. Administration by single injection, samples at 180–240 min (single compartment model with Bröchner-Mortensen correction) Renal clearance of ^{51}Cr-EDTA Continuous infusion	Renal clearance of inulin	mL/min/1.73 m^2 Renal clearance I=0.855 R +7.555, r=0.97 Bias (GFR level): +3.2 (30), –1.1 (60), –5.5 (90) I/R=0.96±0,07 Plasma clearance I=0.961 R +2.908, r=0.97 Bias (GFR level): +1.7 (30), +0.6 (60), –0.6 (90) I/R=1.01±0.15 Clearance of ^{51}Cr-EDTA after constant infusion or single injection both correspond well to inulin clearance	Moderate Small sample size
Heath et al 1968 [14] United Kingdom	To compare the renal clearances of ^{51}Cr-EDTA and inulin	Cross-sectional Healthy, CKD, disorders of calcium metabolism 39 individuals GFR range: 0–220 mL/min	Renal clearance of ^{51}Cr-EDTA Continuous infusion	Renal clearance of inulin	mL/min ^{51}Cr-EDTA 14–16% lower than inulin in the range 10–150 mL/min. *log (I)=1.016 *log (R) –0.1 *Bias (GFR level): –4.8 (30), –9.1 (60), –13.2 (90) ^{51}Cr-EDTA underestimates inulin clearance and cannot be considered suitable for accurate estimation of GFR	Moderate Small sample size Insufficient statistical analysis
Jagenburg et al 1978 [15] Sweden	To evaluate current methods for determining GFR in advanced renal disease	Cross-sectional Patients with uraemic symptoms 17 patients 11 M/6 F Age range: 19–64 years GFR range: 2–12 mL/min	Renal clearance of ^{51}Cr-EDTA. Administration by single injection	Renal clearance of inulin	mL/min Renal clearance I=1.05 R –0.3 r=0.97 Renal clearance of ^{51}Cr-EDTA can replace inulin as filtration marker	Moderate Small sample size Insufficient statistical analysis

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Table 3.1.13 continued

Author Year Reference Country	Aim	Study design Population Gender M/F Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Lavender et al 1969 [16] United Kingdom	To compare the renal clearances of inulin, ^{51}Cr-EDTA, creatinine and urea	Cross-sectional Patients with renal disease 28 adult patients GFR range: 1–157 mL/min	Renal clearance of ^{51}Cr-EDTA Continuous infusion	Renal clearance of inulin	mL/min I=0.96 R +0.26, r=0.994 I/R=0.96±0.0027 (SEM) *Bias (GFR level): –0.9 (30), –2.1 (60), –3.3 (90) ^{51}Cr-EDTA clearance agrees well with that of inulin throughout the whole range of GFR	Moderate Small sample size Insufficient statistical analysis
Manz et al 1977 [17] Germany	To compare different methods of measuring GFR in advanced chronic renal failure in children	Cross-sectional Children with advanced chronic renal failure 15 children Age range: 3–16 years GFR range: 0.9–18.1 mL/min/1.73 m^2	Plasma clearance of ^{51}Cr-EDTA. Administration by single injection, samples at 5–480 min/10 samples (1) alt 5–60 +1 440 min/ 6 samples (2), two compartment model	Renal clearance of inulin	mL/min/1.73 m^2 (1) I=0.635 R +6.21 *I–R=+2.8±4.5 (SD) I/R=2.2±4.1 (2) I=0.692 R +2.57 *I–R=+0.7±2.0 (SD) I/R=1.2±0.9 An acceptable correlation between single injection ^{51}Cr-EDTA and true GFR requires a late blood sample after 24 hours	Moderate Small sample size
Medeiros et al 2009 [18] Brazil	To investigate the concordance between ^{51}Cr-EDTA clearance and renal inulin clearance in renal transplant recipients and to determine the reproducibility of ^{51}Cr-EDTA clearance in kidney donors	Cross-sectional Renal transplant recipients 44 patients 32 M/12 F Age range: 42±11 (SD) years GFR range: 12–78 mL/min/1.73 m^2	Plasma clearance of ^{51}Cr-EDTA. Administration by single injection, samples at 2, 4, 6, 8 hrs (Bröchner-Mortensen correction), 4 samples evaluated in 15 different combinations. Table includes 2 + 4 + 8 hrs (1), 4 + 6 hrs (2), 4 + 8 hrs (3)	Renal clearance of inulin	mL/min/1.73 m^2 I–R= +2.2±5.8 (SD), r=0.95 (1) +2.7±5.9, r=0.95 (2) +2.8±5.8, r=0.95 (3) ^{51}Cr-EDTA clearance is a very precise method to measure GFR in renal transplant recipients	High

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Table 3.1.13 *continued*

Author Year Reference Country	**Aim**	**Study design Population Gender M/F Age GFR range**	**Index method (I)**	**Reference method (R)**	**Results**	**Study quality Comments**
Monteiro et al 1994 [19] Brazil	To investigate whether ^{51}Cr-EDTA clearance can be measured after subcutaneous administration	Cross-sectional Patients with glomerulopathy 20 patients Age range: 13–60 years 13 M/7 F GFR range: 35–166 mL/min/1.73 m^2	Renal clearance of ^{51}Cr-EDTA Subcutaneous injection + vasoconstrictor	Renal clearance of inulin	mL/min/1.73 m^2 *I–R=–5.0±10.7 (SD) *I/R=0.94±0.11 I=0.88 R +4.21, r=0.98 *Bias (GFR level): –3.0 (60), –6.6 (90) ^{51}Cr-EDTA clearance measured after subcutaneous administration is a convenient and clinically acceptable method to measure GFR	Moderate Small sample size
Stamp et al 1970 [20] United Kingdom	To evaluate the use of phosphate infusion as a measure of GFR in comparison with inulin and ^{51}Cr-EDTA clearances	Cross-sectional Patients with disorders of calcium and phosphorus metabolism, and healthy volunteers 15 subjects GFR range: 17–180 mL/min	Renal clearance of ^{51}Cr-EDTA Continuous infusion	Renal clearance of inulin	mL/min R=0.98 I +6.5 I/R=0.96±0.02 (SE) GFR is consistently underestimated by the use of ^{51}Cr-EDTA	Moderate Small sample size

* Calculations not reported by the author (s).

CI = Confidence interval; CKD = Chronic kidney disease; F = Female; GFR = Glomerular filtration rate; I = Index method; M = Male; r = Pearson's correlation coefficient; R = Reference method; SD = Standard deviation; SE = Standard error; SEM = Standard error of mean

Table 3.1.14 *Studies evaluating the accuracy of iohexol for measuring GFR (glomerular filtration rate) using renal clearance of inulin as the reference method.*

Author **Year** **Reference** **Country**	**Aim**	**Study design** **Population** **Gender (M/F)** **Age** **GFR range**	**Index method (I)**	**Reference method (R)**	**Results**	**Study quality** **Comments**
Berg et al 2011 [21] Sweden	To measure GFR simultaneously using renal clearance of inulin and plasma iohexol clearance	Cross-sectional 60 children with different renal disorders Age range: 11.6±4.5 (SD) years GFR range: 5–200 mL/min/1.73 m^2	Plasma clearance of iohexol, 1-compartment model with Bröchner-Mortensen correction 4 samples 3–4 hours if GFR >50, last sample after 7 hours if GFR 20–50 and last sample 24 hours if GFR <20 mL/min/1.73 m^2 (1) Single sample 4 hours, 7 hours and 24 hours respectively (2)	Renal clearance of inulin	mL/min/1.73 m^2 1. I=0.9 R +9.72, r=0.92 I–R=2.65±16.26 (SD) *I/R=1.09±0.23 Bias (GFR level): +6.7 (30), +3.7 (60), +0.7 (90) GFR >60 (n=34) I–R=1.8±20.8 GFR 30–60 (n=12) I–R=2.7±10.0 GFR <30 (n=14) I–R=4.8±3.7 2. I=0.9 R +8.76, r=0.92 I–R=2.0±16.05 (SD) *I/R=1.06±0.23 Bias (GFR level): +5.8 (30), +2.8 (60), –0.2 (90) GFR >60 I–R=1.5±20.3 GFR 30–60 I–R=3.6±10.8 GFR <30 I–R=1.8±4.7 Plasma clearance of iohexol shows good agreement with renal inulin clearance.	High

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Table 3.1.14 continued

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Brown et al 1991 [22] United Kingdom	To compare the clearance properties of iohexol and inulin and to study the accuracy of the single injection methods used with the x-ray fluorescence technique	Cross-sectional 30 subjects 27 M/3 F Age range: 21–89 years GFR range: 8–85 mL/min/1.73 m^2	Renal clearance of iohexol (1) Plasma clearance of iohexol (3+4 hours Bröchner-Mortensen correction) (2) Plasma clearance of iohexol (single sample 3 hours Jacobsson calculation) (3)	Renal clearance of inulin	mL/min/1.73 m^2 1. I=0.998 R –2.309, r=0.986 *Bias (GFR level): –2.4 (30), –2.4 (60), –2.5 (90) 2. I=0.947 R +4,92, r=0.983 I/R=1.10±0.29 (SD) *Bias (GFR level): +3.3 (30), +1.7 (60), +0.2 (90) I/R (<30)=1.55±0.62 (SD) I/R (30–60)=1.04±0.09 (SD) I/R (>60)=1.02±0.05 (SD) 3. I=0.875 R +12.63, r=0.962 I/R=1.25±0.59 (SD) *Bias (GFR level): +8.9 (30), +5.1 (60), +1.4 (90) I/R (<30)=2.18±1.30 (SD) I/R (30–60)=1.14±0.13 (SD) I/R (>60)=1.05±0.04 (SD) Iohexol clearance is an accurate alternative to inulin clearance for clinical and research purposes	Moderate Small sample size

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Table 3.1.14 continued

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Gaspari et al 1995 [23] Italy	To evaluate whether the plasma clearance of unlabeled iohexol is a reliable alternative in humans to renal inulin clearance	Cross-sectional 41 patients with renal disorders 30 M/11 F Age range: 20–62 years GFR range: 6–160 mL/min/1.73 m^2	Plasma clearance of iohexol 13 samples 5–600 min 2-compartment (1) One-compartment model with Bröchner-Mortensen correction (blood samples taken from 120 to 600 min) (2)	Renal clearance of inulin	mL/min/1.73 m^2 1. I=0.994 R +2.34, r=0.97 *Bias (GFR level): +2.2 (30), +2.0 (60), +1.8 (90) 2. I=0.994 R +1.81, r=0.98 *Bias (GFR level): +1.6 (30), +1.4 (60), +1.3 (90) I–R=–1.02±*6.25 LOA=(–15; 12) Subgroup of 20 patients with GFR <40 mL/min/1.73 m^2 I=0.85 R +4.79, r=0.91 *Bias (GFR level): +0.3 (30) The proposed method of measuring GFR by the plasma clearance of unlabeled iohexol is a good alternative to the inulin clearance	High

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Table 3.1.14 *continued*

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Lewis et al 1989 [3] USA	A systematic comparison of GFR determinations made utilizing x-ray fluorescence measurement of clearance of iohexol with simultaneously determined clearance rates of inulin as well as ^{99m}Tc-DTPA	Cross-sectional Population 31 subjects 29 subjects, 18 M/11 F 9 heart transplants, 10 renal transplants, 10 pre donation donors Age range: 22–72 years GFR range: 9–117 mL/min/1.73 m^2	Plasma clearance of iohexol Blood samples 3, 4 hours One-compartment model with Bröchner-Mortensen correction (1) Plasma clearance of iohexol (single sample 3 hrs Jacobsson calculation) (2)	Renal clearance of inulin	mL/min/1.73 m^2 1. I=0.85 R +8.79, r=0.86 I/R=1.09±0.06 (SEM) *I–R=0.68±17.7 *Bias (GFR level): +4.3 (30), –0.2 (60), –4.7 (90) GFR >40 (n=17) I/R=1.00±0.07 GFR 20–40 (n=6) I/R=1.06±0.05 GFR <20 (n=6) I/R=1.36±0.14 2. *I–R=–0.46±20.8 *I=0.81 R +10.87 *Bias (GFR level): + 5.2 (30), –0.5 (60), –6.2 (90) GFR >40 (n=17) I/R=1.03±0.06 GFR 20–40 (n=5) I/R=0.84±0.12 GFR <20 (n=6) I/R=1.95±1.0 (SEM) Contrast (iohexol) clearance determination utilizing the slope-intercept method is accurate and safe	Moderate Small sample size

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Table 3.1.14 *continued*

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Sterner et al 2008 [24] Sweden	To determine GFR in healthy young adults with clearance of inulin, iohexol and creatinine determined by renal and plasma clearance and to analyze the number of blood samples required	Cross-sectional 20 healthy subjects, 9 M/11 F Age range: 19–36 years *GFR range: 94–150 mL/min/1.73 m^2	Renal clearance of iohexol (2 x 1 hours) (1) Plasma clearance of iohexol, 16 samples from 2 to 240 min (2) Plasma clearance 5 last samples 150–240 min (3) Plasma clearance single sample 240 min (4)	Renal clearance of inulin (2 x 1 hour)	mL/min/1,73 m^2 Median I renal = 113 (IQR 105–125) Median I plasma (16 samples) = 115 (IQR 99–126) Median R = 118 (IQR 108–126) Original data were obtained 1. *I=0.97 R +2.64, r=0.686 *Bias (GFR level): –1.03 (90) *I–R=–0.98±14.41 *I/R=0.99±0.12 2. *I=0.963 R +2.30, r=0.706 *Bias (GFR level): –0.10 (90) *I–R=–1.99±11.89 *I/R=0.996±0.12 3. *I=0.623 R +36.3, r=0.49 *Bias (GFR level): 2.4 (90) *I–R=–7.9±14.3 *I/R=0.94±0.11 4. *I=1.326 R –38.23, r=0.777 *Bias (GFR level): –8.9 (90) *I–R=–0.04±13.79 *I/R=0.996±0.12 Iohexol gave similar values of GFR to inulin in healthy adults when tested with either a classical renal clearance or a plasma clearance using multiple blood samples. Underestimation of GFR was noted when plasma clearance was based on 4 but not 5 or more blood samples	Moderate Small sample size

* Calculations not reported by the author (s).

GFR = Glomerular filtration rate; I = Index method; IQR = Interquartile range; LOA = Limits of agreement; r = Pearson's correlation coefficient; R = Reference method; SD = Standard deviation; SEM = Standard error of mean

Table 3.1.15 *Studies evaluating the accuracy of iothalamate for measuring GFR (glomerular filtration rate) using renal clearance of inulin as the reference method.*

Author Year Reference Country	**Aim**	**Study design Population Gender (M/F) Age GFR range**	**Index method (I)**	**Reference method (R)**	**Results**	**Study quality Comments**
Anderson et al 1968 [25] USA	To compare the simultaneous clearances of cyanocobalamin, iothalamate (I^{125}) to inulin and to each other	Cross-sectional 8 normal subjects + 11 patients with renal diseases GFR range: 3–139 mL/min	Renal clearance of iothalamate (I^{125}). Urine sampling 5 x 10–20 min	Renal clearance of inulin	mL/min *I=0.99 R –0.04, r=0.95 *Bias (GFR level): –0.3 (30), –0.6 (60), –0.9 (90) *I–R=–0.67±13.4 (SD) *I/R=1.01±0.21 (SD) Iothalamate (I^{125}) is an excellent material to substitute for inulin clearance when measuring GFR in man	Moderate Small sample size
Cangiano et al 1971 [26] USA	To compare plasma clearance of iothalamate (I^{125}) with renal creatinine clearance and in addition to compare simultaneous constant infusion clearances of iothalamate (I^{125}) and inulin	Cross-sectional 18 patients GFR range: 0–160 mL/min	Renal clearance of iothalamate (I^{125})	Renal clearance of inulin	mL/min I=1.06 R +1.17, r=0.94 I/R=1.07 (range 0.73–1.26) *Bias (GFR level): +3.0 (30), +4.8 (60), +6.6 (90) Excellent correlation between iothalamate (I^{125}) and inulin clearances	Moderate Small sample size
Elwood et al 1967 [27] USA	To compare the simultaneous clearances of iothalamate (I^{125}) and inulin	Cross-sectional 21 patients with various diseases GFR range: 16–136 mL/min	Renal clearance of iothalamate (I^{125}) Urine sampling 1–4 x 15 min	Renal clearance of inulin	mL/min *I=1.05 R –2.43, r=0.997 *Bias(GFR level): –0.93 (30), +0.57 (60), +2.07 (90) *I–R=+0.85±3.1 (SD) *I/R=1.00±0.04 (SD) The iothalamate (I^{125}) clearance is identical to the inulin method	Moderate Small sample size
Israelit et al 1973 [28] USA	To study the feasibility and reliability of a single subcutaneous injection of iothalamate (I^{125}) to measure GFR	Cross-sectional 20 patients with renal diseases + 2 normal subjects GFR range: 6–125 mL/min	Renal clearance of iothalamate (I^{125}) (subcutaneous injection with epinephrine) Urine sampling 3 x 25–35 min	Renal clearance of inulin	mL/min I=1.05 R –3.07, r=0.97 I/R=1.05±0.04 (?) *Bias (GFR level): –1.45 (30), +0.17 (60), +1.79 (90) A single subcutaneous injection, oral water load, one or more timed urine clearance periods starting 60–90 min after subcutaneous injection gives accurate index of GFR	Moderate Small sample size

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Table 3.1.15 *continued*

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Maher et al 1971 [29] USA	To compare simultaneous renal clearances of iothalamate (I^{125}) and inulin	Cross-sectional 198 patients healthy, CKD, disorders of calcium metabolism GFR range: 2–153 mL/min/1.73 m^2	Renal clearance of iothalamate (I^{125})	Renal clearance of inulin	mL/min/1.73 m^2 R=0.537 +1.02 I *Imean-Rmean = –2.09 We have found no differences of importance between the renal clearances of iothalamate (I^{125}) and inulin. We recommend iothalamate (I^{125}) as a convenient and dependable substitute for inulin in evaluation of GFR	Moderate Insufficient statistical analysis
Maher et al 1969 [30] USA	To try to improve clearance relationships by including plasma binding calculations when evaluating renal clearances of iothalamate (I^{125})	Cross-sectional Population: 51 hypertensive patients 15 patients investigated GFR range: 30–118 mL/min/1.73 m^2	Renal clearance of iothalamate (I^{125}) Urine sampling 1 x 1 hour	Renal clearance of inulin	mL/min/1.73 m^2 I/R=0.92 (range 0.81–1.04) R=1.08 I *I–R=–5.9 Correcting clearance of iothalamate (I^{125}) for plasma binding yields values exceeding those of inulin clearance. Uncorrected it is satisfactory substitute for inulin clearance	Moderate Small sample size Insufficient statistical analysis
Malamos et al 1967 [31] Greece	To compare the simultaneously determined renal clearances of inulin, endogenous creatinine and iothalamate (I^{125})	Cross-sectional Population: 36 subjects (18 M, 18 F), 29 with various renal disorders and 7 healthy students 19 investigated subjects Age range: 13–90 years	Renal clearance of iothalamate (I^{125}) Urine sampling 4–6 x 15 min	Renal clearance of inulin	I/R=1.01±0.16 (SD) Calculated U/P ratio of I and R respectively U/P I=1.09 × U/P R –0.65, r=0.979 The clearance of iothalamate (I^{125}) can be substituted for the clearance of inulin	Moderate Small sample size

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Table 3.1.15 continued

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Mogensen 1971 [32] Denmark	To compare the simultaneously determined renal clearances of iothalamate (I^{125}) and inulin	Cross-sectional Population: 31 healthy, 20–30 years, 47 diabetic patients, 18–43 years 57 investigated subjects, 16 normal and 41 diabetics with varying duration of disease GFR range: 64–187 mL/min/1.73 m^2	Renal clearance of iothalamate (I^{125}) Urine sampling 3 x 20 min	Renal clearance of inulin	mL/min/1.73 m^2 All (n = 57): r=0.95 *I–R=2 Normal subjects: r=0.92 *I–R=2 Diabetics *I–R=1 after insulin treatment *I–R=11 in newly diagnosed diabetics before start of insulin treatment The good correlation found between inulin and ^{125}I-iothalamate clearance indicates that both substances are reliable filtration markers	Moderate Insufficient statistical analysis
Ott 1975 [33] USA	To compare clearances of both radioactive and o-iothalamate during constant intravenous infusion or after subcutaneous injection with inulin clearance obtained simultaneously	Cross-sectional 84 (intravenous) patients with various renal disorders and prospective kidney donors 97 (subcutaneous) subjects GFR range: 5–155 mL/min	Renal clearance of iothalamate (I^{125}) given intravenously with continuous infusion (1) and/or after subcutaneous bolus injection (2) Urine sampling 3 x 30 min	Renal clearance of inulin	mL/min 1. *I=1.04 R +2.11, r=0.932 *Bias (GFR level): +3.3 (30), +4.5 (60), +5.7 (90) 2. I=1.02, R=–0.61, r=0.982 *Bias (GFR level): –0.01 (30), +0.6 (60), +1.2 (90) Close correlation over the whole range of GFR. Clearance after subcutaneous injection of iothalamate(I^{125}) is as accurate as standard inulin clearance	High

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Table 3.1.15 *continued*

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Perrone et al 1990 [4] USA	To compare simultaneously the renal clearances of ^{99m}Tc-DTPA, ^{169}Yb-DTPA, and iothalamate (I^{125}) to that of inulin and to quantify the within-day vs between-day variation	Cross-sectional Population: 16 patients with renal insufficiency + 4 healthy subjects 17 investigated subjects, 13 patients, 4 healthy GFR range: 5–50 and 80–130 mL/min/1.73 m^2	Renal clearance of iothalamate (I^{125}) (subcutaneous injection without epinephrine) and renal clearance of non-radioactive iothalamate Urine sampling 4 + 4 x 20 min The protocol was repeated after 7–28 days (Day 1 and 2)	Renal clearance of inulin	mL/min/1.73 m^2 Day 1: I–R=0.65±2.77 (SD) (n=13) Day 2: I–R=2.76±4.18 (SD) (n=13) Day 1 and 2: *I–R=2.76±1.54 *I/R=1.14±0.08 Renal clearance of iothalamate (I^{125}) administered as a single intravenous or subcutaneous injection can be used to accurately measure GFR in subjects with renal insufficiency but overestimate GFR in normal subjects	Moderate Small sample size Insufficient presentation of data
Petri et al 1988 [5] USA	To compare the simultaneously determined renal clearances of iothalamate and inulin	Cross-sectional 25 SLE female patients with various medications Age range: 18–58 years GFR range: 20–120 mL/min	Renal clearance of iothalamate Urine sampling 6 x 30 min Iothalamate fluorescense technique	Renal clearance of inulin	mL/min I=1.08 R +3.36, r=0.99 Bias (GFR level): +5.8 (30), +8.2 (60), +10.6 (90) Iothalamate renal clearance correlated highly and is an acceptable alternative to inulin clearance	Moderate Small sample size

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Table 3.1.15 *continued*

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Rosenbaum et al 1979 [34] USA	To evauate other markers of GFR than creatinine such as iothalamate (I^{125})	Cross-sectional 23 invest subjects normal subjects, transplant recipients, kidney donors after nephrectomy GFR range: 7–146 mL/min	Renal clearance of iothalamate (I^{125}) Urine sampling at least 3 x 20–60 min	Renal clearance of inulin	mL/min All *I–R=16.4±18.8 (SD) *I/R=1.22±0.19 Normal subjects (n=6) *I–R=1.1±12.4 *I/R=1.01±0.1 Transplant recipients (n=9) *I–R=18.4±10.4 *I/R=1.35±0.18 Kidney donors (n=8) *I–R=17.5±8.8 *I/R=1.23±0.12 Good agreement between renal iothalamate and inulin clearances in normal subjects but clear overestimation in renal transplant recipients and donors interpreted as reduced filtration of inulin	Moderate Small sample sizes (Single decimal error noted in data presentation)
Sigman et al 1966 [35] USA	To investigate the use of radioactive form of iothalamate for measurement of GFR in man	Cross-sectional 16 subjects with or without renal impairment, 24 investigations, 100 clearance period GFR range: 2–167 mL/min	Renal clearance of iothalamate (I^{131}) Urine sampling 1–8 x 15 min	Renal clearance of inulin	mL/min *I=1.00 R +0.79, r=0.994 *Bias (GFR level): 0.76 (30), 0.73 (60), 0.70 (90) *I–R=0.7±4.2 (SD) *I/R=1.01±0.05 (SD) Iothalamate (^{131}I) provides an accurate measurement of GFR in man	Moderate Small sample size

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Table 3.1.15 continued

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Silkalns et al 1973 [36] USA	To determine in children the degree of accuracy of the single injection method when compared with classic clearance technique	Cross-sectional 99 children with suspected or known renal diseases Age: 6 months–17 years 61 investigated subjects GFR range: 10–190 ml/min/1.73 m^2	Plasma clearance of iothalamate (I^{125}), blood sampling 5, 10, 15, 20, 30, 40, 50, 60 min	Renal clearance of inulin	mL/min/1.73 m^2 I= 0.93 R +14.5, r=0.89 *Bias (GFR level): +12.4 (30), +10.3 (60), +8.2 (90) I/R=1.12±0.035 (SE) *I–R=10.3±2.1 The single injection method provides a simple and reliable alternative to the standard clearance technique for measurement of GFR	Low Samples taken too early Study included in table as it was the only study on plasma clearance of iothalamate that could be identified

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Table 3.1.15 *continued*

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Skov 1970 [37] Denmark	To investigate simultaneous renal clearances of iothalamate (I^{125}) and inulin in a group of patients with GFR below 25 mL/min/1.73 m^2	Cross-sectional 43 patients (18 M, 25 F) Age range: 14–80 years GFR range: 1.6–25 mL/min/1.73 m^2 GFR 15–25: 8 pts (1 M/7 F) GFR 5–15: 13 pts (5 M/8 F) GFR <5: 22 pts (12 M/10 F)	Renal clearance of iothalamate(I^{125}) Urine sampling 3 x 24–170 min	Renal clearance of inulin	mL/min/1.73 m^2 All *I=0.93 R +0.24, r=0.99 *Bias (GFR level): –1.9 (30) *I–R=–0.32±1.02 (SD) *I/R=0.97±0.08 (SD) GFR 15–25 I=1.083 R –3.46, r=0.968 I/R=0.92±0.071 (SD) *I–R=–1.77±0.98 (SD) GFR 5–15 I/R=1.0±0.057 (SD) *I=1.21 R –2.06, r=0.92 *I–R=0.06±1.28 (SD) GFR <5 I=0.972 R +0.01, r=0.999 I/R=0.98±0.06 *I–R=–0.07±0.19 (SD) It appears that iothalamate provides a new standard reference substance for measuring GFR even in patients with GFR below 15 mL/min and the excretion of iothalamate is independent of proteinuria	High

* Calculations not reported by the author (s).

CKD = Chronic kidney disease; GFR = Glomerular filtration rate; I = Index method; r = Pearson's correlation coefficient; R = Reference method; SD = Standard deviation; U/P = Urine/plasma

Table 3.1.16 *Studies evaluating the accuracy of plasma clearance of inulin for measuring GFR (glomerular filtration rate) using renal plasma clearance of inulin as the reference method.*

Author Year Reference Country	**Aim**	**Study design Population Gender (M/F) Age GFR range**	**Index method (I)**	**Reference method (R)**	**Results**	**Study quality Comments**
Müller-Suur et al 1983 [38] Sweden	To investigate the accuracy of the inulin single injection technique and compare it to the standard constant infusion technique	Cross-sectional 119 children, 62 adults Age range: 1–80 years 20 subjects investigated, 13 children, 7 adults GFR range: 60–150 mL/min/1.73 m^2	Plasma clearance of inulin. Two compartment model with blood samples at 5, 15, 30, 60, 90, 120, 180 min	Renal clearance of inulin	mL/min/1.73 m^2 I=0.79 R +22, r=0.86 *Bias (GFR level): +9.4 (60), +3.1 (90) Inulin single injection clearance is a reliable alternative to other methods of GFR determination	Moderate Small sample size Insufficient statistical analysis
Sterner et al 2008 [24] Sweden	To determine GFR in healthy adults as renal clearance of inulin and compare with other markers and clearance techniques	Cross-sectional 19 healthy subjects, 9 M/11 F Age range: 19–36 years *GFR range: 94–150 mL/min/1.73 m^2	Plasma clearance of inulin, multi-exponential model, 16 samples from 2 to 240 min	Renal clearance of inulin	mL/min/1,73 m^2 Median I=110 (IQR 99–126) Median R=118 (IQR 108–126) *I=0.945 R +4.85, r=0.588 Bias (GFR level): –0.1 (90) Original data were obtained Iohexol gave similar values of GFR to inulin in healthy adults when tested with either a classical renal clearance or a plasma clearance using multiple blood samples. Underestimation of GFR was noted when plasma clearance was based on 4 but not 5 or more blood samples	Moderate Small sample size

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Table 3.1.16 continued

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Wilkins 1992 [39] United Kingdom	To reevaluate the single injection method of inulin and compare it with the continuous infusion method	Cross-sectional 39 infants mostly with respiratory distress Age range: 0.5–33 days, gestational age 25–33 weeks GFR range: 0.5–1.6 mL/min/kg body weight	Plasma clearance of inulin, 2-3-compartment model with blood samples taken after 10, 40, 80, 120, 240, 360, 480 min (in some cases later)	Renal clearance of inulin	(mL/min/kg) I–R=–0.0673±0.079 (SD) 95% CI 0.025; 0.109 The single injection and continuous infusion methods are different but both should give accurate and similar results. The continuous infusion method cannot be used in infants less than 3 days old or in oedematous infants because of very slow equilibration time	Moderate Insufficient statistical analysis

* Calculations not reported by the author (s).

CI = Confidence interval; GFR = Glomerular filtration rate; CsA = Cyclosporin A; I = Index method; IQR = Interquartile range; r = Pearson's correlation coefficient; R = Reference method, SD = Standard deviation

Table 3.1.17 *Studies evaluating the accuracy of endogenous creatinine clearance for measuring GFR (glomerular filtration rate) using renal plasma clearance of inulin as the reference method.*

Author Year Reference Country	**Aim**	**Study design Population Gender (M/F) Age GFR range**	**Index method (I)**	**Reference method (R)**	**Results**	**Study quality Comments**
Alinei et al 1987 [42] Switzerland	To report the observations in infants, comparing various estimates of GFR to the standard clearance of inulin	Cross-sectional Infants referred for the investigation of possible renal disease n=66 Gender distribution not available Age range: 9–364 days GFR range: 17–137 mL/min/1.73 m^2 Selected from 167 infants	Creatinine clearance Mean of 4–5 timed urine collections during 3 hours	Renal clearance of inulin	mL/min/1.73 m^2 *I–R=+7.3 r=0.77 I=0.75 R +25.12 Bias (GFR level): +18 (30) +10 (60) + 3 (90)	High
Apple et al 1989 [75] USA	To compare creatinine clearance determined by enzymatic and nonenzymatic methods with GFR measured by inulin clearance in patients with varying degrees of renal function	Cross-sectional Patients with various degrees of renal function n=24 GFR range: 6–210 mL/min	Creatinine clearance with three 30 min urine collections	Renal clearance of inulin	mL/min r^2=0.915 I=1 R +15.363 Bias (GFR level): +15 (30) +15 (60) +15 (90)	Moderate Small sample size

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Table 3.1.17 *continued*

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Bauer et al 1982 [43] USA	To describe an assessment of creatinine clearance in human subjects with a wide range of renal function	Cross-sectional Men with hypertension and/or renal disease and healthy men Hypertension and/or renal disease (n=104) 104 M/0 F Mean age: 47±12 (SD) years 7 with missing data 19 healthy persons 19 M/0 F Mean age: 28±7 (SD) years GFR range: 4–148 mL/min/1.73 m^2	Creatinine clearance with three 30–40 min urine collections	Renal clearance of inulin	mL/min/1.73 m^2 GFR <40: *I–R=+29 GFR 40–70: *I–R=+48 GFR>70: *I–R=+20 Healthy men: *I–R=+15 I=0.683 R +52.4, r=0.62 Bias (GFR level): +43 (30) +33 (60) +24 (90)	High
Bauer et al 1982 [76] USA	To test the accuracy of the average of the creatinine and urea clearances as an indicator of GFR	Cross-sectional Patients with kidney disease n=31 25 M/6 F Age range: 31–69 years GFR: <20 mL/min/1.73 m^2	Creatinine clearance with three 30–60 min urine collections	Renal clearance of inulin	mL/min/1.73 m^2 I/R=1.54±0.48 (SD) I=1.29 R +1.85 r=0.83	Moderate Small sample size
Berg 1991 [77] Sweden	To analyse the accuracy of estimating GFR by means of formula clearance and the clearance of creatinine with short-term urine sampling	Cross-sectional Children with kidney transplants n=29 14 M/15 F Age range: 0.4–15.4 years GFR range: 12–88 mL/min/1.73 m^2 20 patients studied	Creatinine clearance with 4 hour urine collection	Renal clearance of inulin	mL/min/1.73 m^2 r=0.635 There is significant correlation, but generally creatinine clearance overestimates the GFR	Moderate Insufficient statistical analysis

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Table 3.1.17 *continued*

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Berg et al 2011 [21] Sweden	To measure GFR simultaneously using renal inulin clearance, plasma iohexol clearance, measured creatinine clearance and eGFR according to Schwartz et al [98]	Cross-sectional Children with kidney disease n=54 CKD stage 1–2 (n=29) CKD stage 3 (n=12) CKD stage 4–5 (n=13) Total sample 60 children Mean age: 11.6±4.5 years GFR range: 5–200 mL/min/1.73 m^2	Creatinine clearance with 3 hour urine collection	Renal clearance of inulin	mL/min/1.73 m^2 All: I–R=+18.8±30.1 (SD) CKD 4–5: I–R=+11.8±11.8 (SD) CKD 3: I–R=+24.9±25.1 (SD) CKD 1–2: I–R=+19.4±37 (SD) I=0.96 R +21.32, r=0.79 Bias (GFR level): +20 (30) +19 (60) +18 (90)	High
Bochud et al 2005 [44] USA	To estimate the heritability of three measures of GFR in hypertensive families of African descent in the Seychelles	Cross-sectional Adults in Seychelles n=348 195 M/153 F Mean age: 46.2±0.9 (SE) years 280 adults with complete urine collection judged from gender-specific creatininuria GFR range not specified	24 hour creatinine clearance	Renal clearance of inulin	mL/min All: *I–R=–3 r=0.49 Complete urine sampling: *I–R=+5 r=0.54 Incomplete urine sampling: *I–R=–35 Creatinine clearance overestimates GFR and may underestimate GFR if urine collection is incomplete	Moderate Insufficient statistical analysis

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Table 3.1.17 *continued*

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Caregaro et al 1994 [45] Italy	To evaluate the sensitivity of serum creatinine level and creatinine clearance in detecting renal failure and the magnitude and mechanisms of overestimation of GFR by creatinine clearance	Cross-sectional Cirrhotic patients n=56 38 M/18 F Age range: 36–70 years GFR range: 8.5–214 mL/min/1.73 m^2	24 hour creatinine clearance	Renal clearance of inulin	mL/min/1.73 m^2 All patients: *I–R=+14.6 GFR <80: I/R=1.51±0.55 (SD) GFR >80: I/R=1.10±0.24 (SD)	High
DeSanto et al 1991 [46] Italy	To explore the age-related changes in tubular function and in the renal reserve	Cross-sectional Healthy subjects n=98 Age range: 5–89 years GFR range: 60–140 mL/min/1.73 m^2 Group A (n=40) Age range: 5–18 years 20 M/20 F Group B (n=34) Age range: 19–60 years 17 M/17 F Group C (n=24) Age range: 61–89 years 12 M/12 F	24 hour creatinine clearance	Renal clearance of inulin	mL/min/1.73 m^2 All: I=0.23 R +107.06 r=0.26 Group A: *I–R=+24 I/R=1.23±0.03 (SE) Group B: *I–R =+17 I/R=1.17±0.04 (SE) Group C: *I–R=+32 I/R=1.4±0.06 (SE) Creatinine clearance was age-related and overestimated GFR at all ages and especially in the group C	Moderate Error in data presentation

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Table 3.1.17 continued

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
DeSanto et al 1991 [47] Italy	To assess the suitability of both predicted and measured creatinine clearance to evaluate GFR in patients with chronic renal disease of glomerular and non-glomerular origin by utilizing the clearance of inulin as gold standard	Cross-sectional Patients with chronic kidney disease (CKD) and healthy adults Patients CKD: n=62 30 M/32 F Mean age: 49±2.4 (SE) years Healthy adults: n=62 28 M/34 F Mean age: 54±3.5 (SE) years GFR range: 5–135 mL/min/1.73 m^2	24 hour creatinine clearance	Renal clearance of inulin	mL/min/1.73 m^2 All: I=1.06 R +11.78 r=0.91 Bias (GFR level): +14 (30) +15 (60) +17 (90) CKD: *I–R=+9.8 I/R=1.48±0.08 (SE) Healthy: *I–R=+21.8 I/R=1.24±0.03 (SE)	High

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Table 3.1.17 continued

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Englund et al 1997 [78] Sweden	Renal functional reserve determined by inulin and creatinine clearance was compared	Cross-sectional Children with kidney transplants, adult kidney donors, children with single kidneys Kidney transplant recipients: n=36 Age range: 3.7–20.9 years 20 M/16 F Adult donors: n=15 Age range: 27.9–55.6 years 6 M/9 F Children with single kidneys: n=15 Age range: 5.2–20.4 years 8 M/7 F 20 patients studied (12 kidney transplant recipients, 4 donors, 4 with single kidney) GFR range: 40–110 mL/min/1.73 m^2	2.5 hour urine collection	Renal clearance of inulin	mL/min/1.73 m^2 r=0.45 At baseline, creatinine clearance mostly overestimated the GFR, median 33% (range –66%–199%)	Moderate Small sample size in sub-groups Insufficient statistical analysis

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Table 3.1.17 *continued*

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Erley 2001 [79] Germany	To evaluate the accuracy and feasibility of clearances using iohexol/iopromide as a filtration marker in comparison with inulin clearance, with creatinine clearance and with Cockcroft and Gault's formula clearance in ICU patients	Cross-sectional ICU patients n=27 From 31 patients (17 with cardiac dysfunction, 3 with pneumonia, 1 with pulmonary embolism, 4 with cerebral ischaemia, 2 with sepsis, 4 miscellaneous) 20 M/11 F Age range: 21–83 years GFR range: 5–150 mL/min/1.73 m^2	24 hour creatinine clearance	Renal clearance of inulin	mL/min/1.73 m^2 I=1.03 R r=0.94 Bias (GFR level): +1 (30) +1.8 (60) +2.7 (90) Average percentage difference 37% I/R=1.03 (95% CI 0.54; 1.92)	Moderate Small sample size
Favre et al 1968 [11] United Kingdom	Simultaneous ^{51}Cr-EDTA, inulin and endogenous creatinine clearances were studied	Cross-sectional Patients with CKD n=20 Age range: 16–73 years GFR range: 2–146 mL/min	Creatinine clearance. Mean of 2–3 urinary samples each of 30 min	Renal clearance of inulin	mL/min *I–R=+23±22 (SD) I/R=1.36±0.2 (SD) r=0.908 I=1.282 R –2.49 Bias (GFR level): +6 (30) +14 (60) +23 (90)	Moderate Small sample size

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Table 3.1.17 continued

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Gibb et al 1989 [12] United Kingdom	To compare the renal clearance of ^{51}Cr-EDTA with that of inulin and endogenous creatinine in diabetic children, and to investigate whether the relationships between the different clearance methods are the same in diabetic children as in healthy controls	Cross-sectional Diabetic children (n=11) and healthy adolescents (n=12) Age range: 5.5–34 years GFR range: 50–160 mL/min/1.73 m^2 Drop-out 2 diabetic children	Creatinine clearance, 3–4 urine collection periods of 20–30 min	Renal clearance of inulin	mL/min/1.73 m^2 All: I–R=+37.6±3.3 (SEM) r=0.95 I/R=1.32 (95% CI 1.27; 1.37) Diabetic children: I–R=+44.2±4.6 (SEM) r=0.98 I/R=1.36 (95% CI 1.31; 1.41) Healthy adolescents: I–R=+32.6±4.2 (SEM) r=0.78 I/R=1.30 (95% CI 1.22; 1.38)	Moderate Small sample size
Hagstam et al 1974 [13] Sweden	In patients suffering from renal disease, simultaneous measurements of inulin, creatinine, ^{51}Cr-EDTA, and PAH were made	Cross-sectional Patients with CKD, mainly glomerulonephritis n=52 22 M/30 F Age range: 14–56 years GFR range: 20–160 mL/min/1.73 m^2 42 patients studied	Creatinine clearance. Mean of 4 urine collections, each of 15 min	Renal clearance of inulin	mL/min/1.73 m^2 I/R=1.30±0.20 (SD) I=0.917 R +27.5 r=0.94 Bias (GFR level): +25 (30) +23 (60) +20 (90)	High

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Table 3.1.17 continued

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Hellerstein et al 1992 [48] USA	To evaluate the plasma creatinine concentration and creatinine clearance for estimation of GFR	Cross-sectional Children with renal damage n=31 15 M/16 F Age range: 5.3–20.8 years GFR range: 2.8–135.8 mL/min/1.73 m^2	Creatinine clearance. Two 1 hour clearance periods	Renal clearance of inulin	mL/min/1.73 m^2 r=0.96 I–R=+16.7±10.3(SD) There is good correlation between creatinine clearance and inulin clearance, but the creatinine clearance consistently overestimates the inulin clearance and the range of likely (95% CI) values for inulin clearance based on an observed creatinine clearance is large	Moderate Small sample size
Kakuta et al 2010 [49] Japan	To compare the accuracy of eGFR and creatinine clearance values with that of inulin	Cross-sectional Potential living kidney donors n=87 31 M/54 F Age range: 28–78 years GFR range: 68–127 mL/min/1.73 m^2 2 drop-outs	24 h creatinine clearance	Renal clearance of inulin	mL/min/1.73 m^2 I–R=+21.1±19.8 (SD) P30=65.5% r=0.5	High
Lemann et al 1990 [50] USA	100/serum creatinine, creatinine clearance, and estimated creatinine clearance were compared with measurements of GFR using iothalamate in patients with established diabetic nephropathy and inulin in a group of mainly healthy men	Cross-sectional Healthy persons and hypercalciuric stone formers n = 110 (88 healthy persons, 14 stone formers, 7 relatives of stone formers and 1 with chronic glomerulonephritis) 109 M/1 F Mean age: 30±7.7 (SD) GFR range: 51–172 mL/min	Creatinine clearance with four 20 min urine collections	Renal clearance of inulin	mL/min I–R=+13±10 (SD) I=0.912 R +23.1, r=0.86 Bias (GFR level): +18 (60) +15 (90)	High

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Table 3.1.17 continued

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Luke et al 1990 [51] USA	To compare creatinine clearance as estimated by five mathematical equations with both measured creatinine clearance and inulin clearance in subjects with varying degrees of renal function	Cross-sectional Patients with CKD and healthy subjects n=109 86 M/23 F Mean age: 47±14 (SD) years GFR range: 6–209 mL/min	4 hour creatinine clearance (supine) and 24 hour ambulatory creatinine clearance	Renal clearance of inulin	mL/min All: 4 hour clearance: *I–R=+13 r=0.924 24 hour clearance: *I–R=+3 r=0.84 GFR 6–30: 4 hour clearance: *I–R=+8 24 hour clearance *I–R=+5 GFR 31–100: 4 hour clearance: *I–R=+14 24 hour clearance: *I–R=+7 GFR 101–209: 4 hour clearance: *I–R=+15 24 hour clearance *I–R=–1	Moderate Insufficient statistical analysis
Mariat et al 2004 [52] France	To compare the performance of six GFR tests with inulin clearance	Cross-sectional Renal transplant recipients n=294 200 M/94 F Mean age: 45±13 (SD) years 95% cadaveric donor kidneys, all patients on CsA-based immunosuppression. GFR range: 8–122 mL/min/1.73 m^2	24 hour creatinine clearance	Renal clearance of inulin	mL/min/1.73 m^2 *I–R=+7 r=0.71 LOA=–39 to +26 *Absolute difference* >10 mL/min/1.73 m^2 in 44% of patients >15 mL/min/1.73 m^2 in 34% of patients >20 mL/min/1.73 m^2 in 21% of patients	High

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Table 3.1.17 *continued*

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Martini et al 2003 [80] Switzerland	To evaluate the reliability of plasma cystatin C as a marker of GFR in comparison with that of plasma creatinine, creatinine clearance and the Haycock-Schwartz formula, using inulin clearance as the gold standard	Cross-sectional Children with kidney disease n=99 51 M/48 F Mean age: 8.3 years GFR range: 19–179 mL/min/1.73 m^2	Creatinine clearance with two 45 min urine collections	Renal clearance of inulin	mL/min/1.73 m^2 r=0.85 GFR >100: *I–R=–6 Median GFR <100: *I–R=+2 Median Creatinine clearance was the best parameter to discriminate between impaired and normal GFR	Moderate Insufficient statistical analysis
Motwani et al 1992 [53] United Kingdom	To compare in a group of stable CHF patients GFR as estimated by ^{51}Cr-EDTA elimination, creatinine clearance and inulin clearance	Cross-sectional Patients with chronic heart failure (CHF) and patients after myocardial infarction (MI) 20 patients post MI 16 M/4 F Mean age: 60±9.5 (SD) years 10 CHF patients 8 M/2 F Mean age: 66±10 years (SD) GFR range: 10–100 mL/min	Creatinine clearance. 2 x 120 min urine collections	Renal clearance of inulin	mL/min MI: I–R=+17.6±18.9 (SD) r=0.78 CHF: I–R=+26.8±17 (SD) r=0.9	Moderate Small sample size

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Table 3.1.17 *continued*

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Mpio et al 2003 [54] France	To compare creatinine clearance and Cockcroft-Gault formula to GFR in black Caribbean and Caucasian subjects	Cross-sectional Black Caribbeans and Caucasians Caribbeans: n=38 13 M/25 F Mean age: 45±8 (SD) years GFR range: 5–140 mL/min/1.73 m^2 Caucasians n=38 13 M/25 F Mean age: 46±7 (SD) years GFR range: 20–150 mL/min/1.73 m^2	Creatinine clearance with three 30 min urine collections	Renal clearance of inulin	mL/min/1.73 m^2 Caribbeans: r=0.89 I–R=+8.7±16.8 (SD) Caucasians: r=0.89 I–R=+7.2±15.7 (SD) Huge dispersion of GFR on Bland-Altman. Confidence for individual subjects low	Moderate Small sample size in sub-groups
Petri et al 1988 [5] USA	To determine whether the discrepancy between creatinine clearance and inulin clearance remains constant over time in each individual patient, and therefore whether serial measurements of creatinine clearance reliably reflect the direction and magnitude of change in inulin clearance	Cross-sectional Patients with SLE nephritis 0 M/29 F Age range: 18–58 years GFR range: 23–123 mL/min 4 drop-outs Measurement were performed repeatedly over three years	Creatinine clearance. Mean of six 30 min clearance periods	Renal clearance of inulin	mL/min *I–R=+23, +16, +18 at three different study occasions I/R=1.30±0.16 (SD) mean of several measurements The discrepancy between creatinine clearance and inulin clearance can vary greatly over time and does not accurately measure the direction or magnitude of change in GFR	Moderate Small sample size

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Table 3.1.17 continued

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Proulx et al 2005 [85] Canada	To review the accuracy of measured creatinine clearance from timed urine collections for estimating true GFR	Systematic review Patients with liver cirrhosis Seven articles n=193 79% male Age range: 29–89 years GFR range: 5–150 mL/min/1.73 m^2 Selected from 55 potentially relevant articles	Creatinine claerance with 12–24 hour urine collections	Renal clearance of inulin	mL/min/1.73 m^2 r=0.78 I=0.93 R +18.83 Bias (GFR level): +17 (30) +15 (60) +13 (90)	High One reviewed study (Caregaro, 1994 [45]) is in the current table even separately
Rapoport et al 1968 [55] Canada	To compare 24 hour clearances utilizing three creatinine analysis procedures and to compare the results with inulin clearances	Cross-sectional Patients with kidney disease, hypertension and kidney stones n=89 49 M/40 F Age range: 14-50 years GFR range: 3–150 mL/min	Creatinine clearance based on both 24 hour urine sample and on the same urine samples as for inulin clearance	Renal clearance of inulin	mL/min GFR <90: I–R=+5.2 to +11.8 I/R=1.25 to 1.34 (low proteinuria <2.5 g/24 hour) I/R = 1.5 to 1.6 (high proteinuria, >2.5 g/24 hour) GFR >90: I–R=+1.0 to+18 I/R=1.0 to 1.1 (low proteinuria) I/R=1.2 to 1.4 (high proteinuria) The results include different urine collection periods and three different methods of analyzing creatinine. Standard deviations are given	High

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Table 3.1.17 *continued*

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Robert et al 1993 [56] Canada	To evaluate the predictive ability of different creatinine clearance methods as compared with the criterion standard, inulin clearance	Cross-sectional ICU patients n=20 13 M/7 F Age range: 26–82 years GFR range: 2–107 mL/min/1.73 m^2	Creatinine clearance based on three 30 min urine collections and 24 hour urine collection	Renal clearance of inulin	mL/min/1.73 m^2 30 min collections: *I–R=+7.3±41.24 (SD) *I/R=1.19±0.83 (SD) 24 hour collections: *I–R=+4.4±32 (SD) *I/R=1.05±0.6 (SD) The 24 hour and 30 min creatinine clearances had significant biases and similar poor performance	Moderate Small sample size
Rosenbaum et al 1979 [34] USA	To investigate the discrepancy between the clearances of creatinine and inulin	Cross-sectional Healthy, renal transplant recipients and living donors following nephrectomy n=41 Age range and gender not specified GFR range: 7.3–146 mL/min	Creatinine clearance based on the mean of three up to 60 min urine collections	Renal clearance of inulin	mL/min Renal transplant recipients (n=20) I–R=+25.8 I/R=1.47±0.15 (SEM) Healthy subjects (n=11) I–R=+2.5 I/R=1.02±0.02 (SEM) Kidney donors (n=10) I–R=+23 I/R=1.34±0.06 (SEM) The mechanisms responsible for the decrease in inulin clearance relative to other markers of GFR cannot be established, but can be interpreted as tubular reabsorption of inulin	High (Single decimal error noted in data presentation)

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Table 3.1.17 *continued*

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Schück et al 2003 [57] Czech Republic	To evaluate whether serum cystatin in patients with GFR ≤40 mL/min/1.73 m^2 provides a more accurate estimate of GFR than serum creatinine does	Cross-sectional Chronic renal insufficiency n=67 38 M/29 F Age range: 18–64 years GFR range: 4–40 mL/min/1.73 m^2	Creatinine clearance. 60-90 min urine collections	Renal clearance of inulin	mL/min/1.73 m^2 All patients *I–R=+11.4 I=1.27 R +6.50 r=0.921 Bias (GFR level): +14.6 (30) GFR <10: I/R=2.11±0.29 (SD) GFR 10–20: I/R=1.72±0.3 (SD) GFR 21–40: I/R=1.53±0.25 (SD)	High
Shemesh et al 1985 [6] USA	To elucidate the disparity between creatinine clearance and the true GFR	Cross-sectional Patients with CKD 171 (173?) patients (66 with diabetes mellitus type 1 with nephropathy, 44 with lupus nephritis and 63 with glomerulo-nephritis) Age range and gender not specified GFR range: 1–170 mL/min/1.73 m^2	Creatinine clearance with 4 consecutive timed urine collections, collection time not specified	Renal clearance of inulin	mL/min/1.73 m^2 All patients (n=171) r=0.831 I/R=1.64±0.1 (SEM) GFR <40 (n=81): I–R=+20±2 (SEM) I/R=1.92±0.08 GFR 40–80 (n=50): I–R=+34±4 (SEM) I/R=1.57±0.06 GFR >80 (n=42): I–R=+21±7 (SEM) I/R=1.19±0.06	High

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Table 3.1.17 *continued*

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Shimokata et al 2010 [81] Japan	To evaluate the validity of the Calvert formula for Japanese patients with cancer and modify it for this population	Cross-sectional Patients with cancer scheduled for carboplatin treatment n=28 18 M/10 F Age range: 54–78 years GFR range: 17–105 mL/min	24 hour creatinine clearance	Renal clearance of inulin. Three 30 min clearance periods	mL/min MPE=+24±54 (SE)% r=0.845 RMSE=37.2%	High
Skov 1970 [37] Denmark	To investigate a group of patients using simultaneous inulin, creatinine and ^{125}iothalamate clearance	Cross-sectional Patients with markedly reduced GFR (n=43) 18 M/25 F Age range: 14–80 years GFR range: 1.6–25 mL/min/1.73 m^2 GFR <5: n=22, 12 M/10 F GFR 5–15: n=13, 5 M/8 F GFR 15–25: n=8, 1 M/7 F	Creatinine clearance. 3 x 24–170 min urine collections, at least 100 mL	Renal clearance of inulin	mL/min/1.73 m^2 GFR <5: *I–R=+0.74±0.82 (SD) I/R=1.27±0.14 I=1.287 R +0.04 r=0.981 GFR 5–15: *I–R=+5.5±4.2 (SD) I/R=1.52±0.14 I=2.17 R +6.25 r=0.843 GFR 15–25: *I–R=+10.9±12.2 (SD) I/R=1.53±0.18 I=2.52 R +19.92 r=0.598	High
Takahira et al 2001 [82] Japan	To determine whether serum concentrations of 2-(α-mannopyranosyl)-L-tryptophan (MPT) glyco-conjugate can be used as a marker of renal function	Cross-sectional Patients with CKD n=25 13 M/12 F Mean age: 49±12.7 (SD) years GFR range: 2–85 mL/min/1.73 m^2	Creatinine clearance calculated from three 20 min urine collections	Renal clearance of inulin	mL/min/1.73 m^2 I=1.84 R +16.6 r=0.81 Bias (GFR level): +42 (30) +63 (60)	Moderate Small sample size

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Table 3.1.17 *continued*

Author Year Reference Country	Aim	Study design Population Gender (M/F) Age GFR range	Index method (I)	Reference method (R)	Results	Study quality Comments
Tomlanovich et al 1986 [41] USA	To elucidate whether the disparity between creatinine clearance and the true GFR is enhanced also in the CsA-associated chronic nephropathy of heart transplantation recipients, the clearance of creatinine to that of two true filtration markers was compared	Cross-sectional Heart transplant recipients 58 consecutive patients (24 treated with azathioprine, 34 with cyclosporine) GFR range: 15–130 mL/min/1.73 m^2 From 100 patients receiving heart transplant before and 100 after Dec 1980 (after introduction of cyclosporine) Mean age: 36–38 years	Creatinine clearance with 4 consecutive timed urine collections, collection time not specified	Renal clearance of inulin	mL/min/1.73 m^2 Azathioprine group (n=24): I/R=1.19±0.05 (SEM) Cyclosporine group (n=34): I/R=1.51±0.05 (SEM)	Moderate Small sample sizes
Wilkins 1992 [39] United Kingdom	To re-evaluate the single-injection method and compare it with the continuous-infusion method using PF-S (Inutest), and also to investigate whether creatinine clearance is an accurate measure of GFR in pre-term infants	Cross-sectional Pre-term infants n=39 Age range: 0.5–33 days (gestational age at birth 25–33 weeks, birth weight 720–2 000 g) 16 with severe respiratory distress syndrome. 98 continuous infusion inulin tests GFR range: 0.35–1.52 mL/kg per minute	Creatinine clearance with urine samples obtained from spontaneous voiding into cotton wool	Renal clearance of inulin	mL/min/kg birth weight I/R=0.91 Creatinine clearance is usually less than inulin clearance, suggesting that there is some creatinine reabsorption in the renal tubule in sick very low birth weight infants	Moderate Insufficient statistical analysis. Small sample size

* Calculations not reported by the author(s).

CHF = Chronic heart failure; CKD = Chronic kidney disease; CsA = Cyclosporine A; GFR = Glomerular filtration rate; I = Index method; ICU = Intensive-care unit; LOA = Limits of agreement; MI = Myocardial infarction; MPE = Mean prediction error; r = Pearson's correlation coefficient; R = Reference method; RMSE = Root mean square error; SD = Standard deviation; SE = Standard error; SEM = Standard error of mean

Table 3.2.12 *Creatinine based equations in adults. Studies evaluating GFR prediction equations with creatinine assay calibration traceable to the original MDRD laboratory or to isotope dilution mass spectrometry (IDMS) in both the development and validation set. An exception was made for the commonly used Cockcroft-Gault equation. Ethnicity is given in percentage if ≥10 % of the total population, mean/median age and mean/median GFR in mL/min/1.73 m²*

(default) or mL/min. Results are given as percentage of GFR estimates within 30 % (P30) of measured GFR. Measures of variability are given as range (default), percentiles (eg 95 % = 2.5; 97.5), interquartile range (IQR) or standard deviation (SD). Confidence intervals (CI) for P30 were calculated by us when not available.

Author Year Reference Country	**Aim**	**Study design Population characteristics**	**Index method Equations (numbering corresponds to numbering in result column)**	**Reference method Measured GFR**	**Results P30 (%, 95% CI)**	**Study quality** Comments**
Bevc et al 2011 [48] Slovenia	To compare two creatinine-based formulas (MDRD formula and CKD-EPI creatinine formula), the CKD-EPI creatinine and cystatin formula, and the simple cystatin C formula (100/serum cystatin C) against ^{51}Cr-EDTA clearance in the elderly (>65 years)	Part of Hojs et al [28] Cross-sectional Retrospective External validation Consecutive Single centre GFR referrals (n=317) CKD Females: 54% Age: 73 (65–90) years GFR: 35 (±23)	1. CKD-EPI MDRD-original excluded since IDMS-traceable assay was used Equations including cystatin C excluded due to non-traceable assay	Plasma Cr-EDTA, multiple samples	1. 61 (56; 66*)	Moderate 100–499 examinations and 6 quality criteria fulfilled
Björk et al 2007 [36] Sweden	To evaluate newly developed equations to predict GFR in adult Swedish-Caucasians and to compare with the MDRD and Mayo Clinic equations in patients referred for GFR measurements	Cross-sectional Retrospective External validation (Eq 1,2), Development validation (Eq 3,4) Consecutive Multicentre (n=2) GFR referrals (n=850) Transplants: 5% Females: 44% Age: 60: (95% 28; 85) years GFR: 55 (95% 9; 121)	1. CG relative# 2. MDRD-IDMS 3. LM original 4. LM-LBM Mayo Clinic equation excluded since it is based on non-traceable creatinine assay	Plasma iohexol, single sample	1. 70 (67; 73) 2. 80 (77; 83) 3. 84 (82; 87) 4. 86 (83; 88)	Moderate Non-external validation of Eq 3,4
Björk et al 2012 [5] Sweden	To validate externally the Swedish Lund-Malmö creatinine based GFR equations (LM original and revised) in a Swedish cohort in comparison with the North American MDRD and CKD-EPI equations	Cross-sectional Retrospective External validation Consecutive Single centre GFR referrals (n=1 397) Females: 44% Age: 61 (95% 19–83) years GFR 44 (95% 12–116)	1. CG relative# 2. LM original 3. LM revised 4. MDRD-IDMS 5. CKD-EPI	Plasma iohexol, single sample	1. 67 (65; 69) 2. 82 (80; 84) 3. 84 (82; 86) 4. 80 (77; 82) 5. 79 (77; 81)	High

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Table 3.2.12 continued

Author Year Reference Country	Aim	Study design Population characteristics	Index method Equations (numbering corresponds to numbering in result column)	Reference method Measured GFR	Results P30 (%, 95% CI)	Study quality/ Comments
Brown et al 20111 [24] Australia	To determine, in an Australian population, which of the CG, MDRD or CKD-EPI formula aligned most closely with a gold standard measurement of GFR in patients with estimated GFR <60 mL/min/1.73 m^2	Cross-sectional Prospective External validation Consecutive Single centre eGFR <60 mL/min/1.73 m^2 (n=139) Caucasian: 65% European: 15% Diabetes: 26% Females: 45% Age: 64 (±15) years GFR: 47 (±28)	1. CG relative 2. MDRD 3. CKD-EPI *Bias* 1. –10 mL/min 2. –15 mL/min 3. –14 mL/min	Plasma Cr-EDTA, multiple samples	NR	Low Inclusion criteria eGFR <60 mL/min/ 1.73 m^2 implies large risk for biased estimates of formula performance
Eriksen et al 2010 [42] Norway	To compare published cystatin C equations with the most commonly used creatinine equation and to validate both against iohexol clearance in a representative sample of middle-aged persons from the general population	Cross-sectional Prospective External validation Random population Single centre Health survey (n=1 621) Female: 51% Age: 57 (50–62) GFR: 92 (SD 14)	1. CG relative 2. MDRD-IDMS 3. CKD-EPI External cystatin C equations excluded due to non-traceable assays	Plasma iohexol, single sample	1. 91 (90; 92) 2. 93 (92; 94) 3. 95 (94; 96)	High
Fehrman-Ekholm et al 2009 [25] Sweden	To evaluate creatinine and cystatin C GFR equations in very old people	Cross-sectional Prospective External validation Non-consecutive Single centre Healthy elderly (n=50) Female: 38% Age: 83 (71–110) years GFR: 68 (38–113)	1. CG relative MDRD-original excluded since IDMS-traceable creatinine assay was used Cystatin C equations reported in separate table	Plasma iohexol, multiple samples	1. 46 (32; 60)	Moderate <100 examinations

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Table 3.2.12 *continued*

Author Year Reference Country	Aim	Study design Population characteristics	Index method Equations (numbering corresponds to numbering in result column)	Reference method Measured GFR	Results P30 (%, 95% CI)	Study quality/ Comments
Froissart et al 2005 [1] France	To evaluate the performance of the 4-variable MDRD and CG equations in a cohort of 2 095 Europeans	Cross-sectional Retrospective External validation Consecutive Single centre CKD/healthy kidney donors (n=1 933/162) Non-black Females: 41% Age: 53 (IQR 40–67) years GFR: 61 (IQR 34–87)	1. CG relative 2. MDRD-original	Plasma Cr-EDTA, multiple samples	1. 78 (76; 80) 2. 87 (86; 88)	High
Hojs et al 2011 [28] Slovenia	To compare three serum creatinine based equations (CG, MDRD and CKD-EPI) and two serum cystatin C-based equations (local cystatin C formula and simple cystatin C formula) against ^{51}Cr-EDTA clearance in a population of patients with different stages of CKD	Cross-sectional Retrospective External validation Consecutive Single centre GFR referrals (n=764) Caucasian CKD Diabetes: 20% Females: 42% Age: 58 (18–90) years GFR: 48 (2–130)	1. CG relative 2. CKD-EPI MDRD-original excluded since IDMS-traceable creatinine assay was used Cystatin C equations excluded due to due to non-traceable assay/ development validation	Plasma Cr-EDTA, multiple samples	1. 59 (56; 62*) 2. 54 (50; 58*)	Moderate 6 quality criteria fulfilled
Ibrahim et al 2006 [39] USA	To evaluate the performance of the MDRD, CG and Mayo Clinic equations in predicting GFR in former renal donors	Cross-sectional Retrospective External validation Consecutive Single centre Former renal donors (n=112) White: 98% Females: 59% Age: 40 (SD 10) GFR: 72 (SD 12)	1. CG relative 2. MDRD-original	Plasma iohexol, multiple samples	1. 87 (81; 93) 2. 96 (92; 100)	Moderate 100–499 examinations and 5 quality criteria fulfilled

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Table 3.2.12 *continued*

Author Year Reference Country	Aim	Study design Population characteristics	Index method Equations (numbering corresponds to numbering in result column)	Reference method Measured GFR	Results P30 (%, 95% CI)	Study quality/ Comments
Issa et al 2008 [30] USA	To evaluate the performance of the MDRD and CG equations in living kidney donors and to evaluate whether these GFR estimations correlate equally with post-transplant graft function	Cross-sectional Retrospective External validation Consecutive Single centre Kidney donors (n=423) White: 83% Females: 59% Age: 41 (19–64) years GFR: 106 (73–166)	1. CG relative 2. MDRD-IDMS MDRD-original excluded since IDMS-traceable creatinine assay was used	Urinary iothalamate, multiple samples	1. 88 (85; 91) 2. 86 (83; 89)	Moderate 100–499 examinations and 4 quality criteria fulfilled
Lamb et al 2003 [26] United Kingdom	To evaluate the accuracy of the MDRD and CG equations in an ambulatory outpatient population of older people with CKD	Cross-sectional Retrospective External validation Consecutive Single centre Elderly individuals (n=52) Caucasians Females: 48% Age: 79 (69–92) years GFR: 53 (16–100)	1. CG relative 2. MDRD-original	Plasma Cr-EDTA, multiple samples	NR	Moderate <100 examinations
Lane et al 2010 [40] USA	To evaluate which GFR equation provides the most accurate renal function assessment in patients before and after nephrectomy	Cross-sectional Retrospective External validation Consecutive Single centre Nephrectomy patients (n=425) White: 91% Females: 33% Age: 58 (IQR 49–66) years GFR: 50 (4–142)	1. CG relative 2. MDRD-original 3. MDRD-IDMS 4. CKD-EPI	Urinary iothalamate, multiple samples	1. 68 (64; 72*) 2. 75 (71; 79*) 3. 75 (71; 79*) 4. 80 (76; 84*)	Moderate 100–499 examinations and 5 quality criteria fulfilled

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Table 3.2.12 *continued*

Author Year Reference Country	Aim	Study design Population characteristics	Index method Equations (numbering corresponds to numbering in result column)	Reference method Measured GFR	Results P30 (%, 95% CI)	Study quality/ Comments
Levey et al 2006 [29] USA	To describe the performance of the reexpressed 4-variable MDRD (IDMS) study equation and compare it with the 6-variable MDRD equation and the CG equation, with particular attention to the level of GFR in the MDRD. Study cohort of CKD patients	Cross-sectional Retrospective Development validation (Eq 1,3) External validation (Eq 2) Consecutive Multicentre (n=15) MDRD study cohort (n=1 628) White or other: 81% Black: 12% Females: 40% Age: 51 (SD 13) years GFR: 40 (SD 21)	1. MDRD-IDMS 2. CG relative 3. CG relative bias-corrected (factor 0.8)	Urinary iothalamate, multiple samples	1. 90 (89; 91) 2. 60 (58; 62) 3. 83 (81; 85)	Moderate Non-external validation of MDRD-IDMS
Levey et al 2009 [33] USA	To develop and validate a new estimating equation for GFR, the CKD-EPI equation, that would be as accurate as the MDRD Study equation at GFR <60 and more accurate at a higher GFR	Cross-sectional Retrospective Internal validation Pooled data Multicentre (n=10) CKD-EPI internal validation cohort (n=2 750, appendix 5, Table 6 to this reference) White or other: 64% Black: 31% Diabetes: 30% Transplants: 4% Renal donors: 12% Females: 44% Age: 47 (SD 15) years GFR: 67 (SD 40)	1. CKD-EPI 2. MDRD-IDMS Validation of MDRD regarded as internal since about 20% of the cohort originated from the MDRD study cohort	Urinary iothalamate, multiple samples	1. 84 (82; 85) 2. 82 (81; 84)	High Very large number of examinations despite non-external validation

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Table 3.2.12 *continued*

Author Year Reference Country	Aim	Study design Population characteristics	Index method Equations (numbering corresponds to numbering in result column)	Reference method Measured GFR	Results P30 (%, 95% CI)	Study quality/ Comments
Levey et al 2009 [33] USA	To develop and validate a new estimating equation for GFR, the CKD-EPI equation, that would be as accurate as the MDRD Study equation at GFR <60 and more accurate at a higher GFR	Internal validation (Eq 1) External validation (Eq 2) Pooled data Multicentre (n=16) CKD-EPI external validation cohort (n=3 896) White or other: 87% Black: 10% Diabetes: 28% Transplants: 29% Renal donors: 16% Females: 45% Age: 50 (SD 15) years GFR: 68 (SD 36)	1. CKD-EPI 2 MDRD-IDMS Validation of CKD-EPI regarded as internal since the results of this validation influenced which of the primary models that were finally selected as the CKD-EPI equation	Urinary iothalamate, multiple samples. Iohexol, NS EDTA, NS	1. 84 (83; 85) 2. 81 (80; 82)	High Very large number of examinations despite non-external validation
Murata et al 2011 [6] USA	To compare the accuracy of the MDRD and CKD-EPI equations for estimating GFR in a large group of patients having GFR measurements for diverse clinical indications	Cross-sectional Retrospective External validation Consecutive Single centre GFR referrals (n=5 238) Caucasians: 89% Kidney donors (n=583) Postnephrectomy kidney donors (n=97) Native CKD (n=2 324) Kidney recipients (n=1 375) Other organ recipients (n=859) Females: 45% Age: 56 (±15) years GFR: 56 (±30)	1. MDRD-IDMS 2. CKD-EPI	Urinary iothalamate, multiple samples	78 (76; 79*) 78 (77; 80*)	High
Nyman et al 2006 [2] Sweden	To evaluate the CG equation with various body weight expressions and the Sawyer equation with LBM in predicting absolute GFR (mL/min) and to derive a new equation using various body weight expressions in adult Swedish-Caucasians referred for GFR measurements	Same as reference [36] Lund-Malmö cohort (n=850)	1. LM absolute 2. CG absolute 3. CG absolute with adjusted body weight	Plasma iohexol, single sample	1. 86 (84; 89) 2. 70 (67; 73) 3. 79 (76; 81)	Moderate Non-external validation of absolute LM

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Table 3.2.12 *continued*

Author Year Reference Country	Aim	Study design Population characteristics	Index method Equations (numbering corresponds to numbering in result column)	Reference method Measured GFR	Results P30 (%, 95% CI)	Study quality/ Comments
Nyman et al 2011 [3] Sweden	To compare the CKD-EPI equation to estimate GFR in an adult Swedish-Caucasians with the MDRD equation in patients referred for GFR measurements	Same as reference [36] Lund-Malmö cohort (n=850)	1. MDRD-IDMS 2. CKD-EPI	Plasma iohexol, single sample	1. 80 (77; 83) 2. 80 (77; 82)	High
Sebasky et al 2009 [41] USA	To evaluate the performance of the MDRD-IDMS equation in comparison with Mayo Clinic equation and bias-corrected CG in kidney donors	Cross-sectional Retrospective External validation Random selection Single centre Post kidney donation (n=255) White: 99% Females: 62% Age: 53 (SD 10) years GFR: 72 (SD 12)	1. CG relative bias-corrected (factor 0.8) 2. MDRD-IDMS	Plasma iohexol, multiple samples	1. 89 (85; 93) 2. 94 (91; 97)	Moderate 100–499 examinations
Segarra et al 2011 [34] Spain	To evaluate the CKD-EPI equation and four cystatin C-based equations to estimate GFR in hospitalized patients	Cross-sectional Prospective External validation Random selection Single centre Hospitalized (n=3 114) Amputation or malnutrition 46% Females: 45% Age: 63 (SD 19) years GFR: 88 (SD 33)	1. CKD-EPI Equations containing cystatin C excluded due to non-traceable assay	Plasma iohexol, sampling NS	1. 82 (81; 83*)	High
Stevens et al 2007 [37] USA	To evaluate the performance of the MDRD-IDMS in a large diverse population and with particular attention to the level of GFR and participants characteristics in the CKD-EPI cohort	Cross-sectional Retrospective Internal validation Pooled data Multicentre (n=10) CKD-EPI development validation cohort (n=5 504) White and other: 63% Black: 32% Diabetes: 29% Females: 44% Age: 47 (SD 15) years GFR: 68 (SD 39)	1. MDRD-IDMS Validation of MDRD regarded as internal since about 20% of the cohort originated from the MDRD study cohort	Urinary iothalamate, multiple samples	1. 83 (83; 84)	High Very large number of examinations despite non-external validation

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Table 3.2.12 *continued*

Author Year Reference Country	Aim	Study design Population characteristics	Index method Equations (numbering corresponds to numbering in result column)	Reference method Measured GFR	Results P30 (%, 95% CI)	Study quality/ Comments
Stevens et al 2007 [27] USA	To assess the impact of creatinine calibration on performance of the MDRD and CG equations in the CKD-EPI cohort	Same as reference [37]	1. MDRD original (non-calibrated creatinine) 2. MDRD-IDMS (IDMS-calibrated creatinine 3. CG relative (non-calibrated creatinine) 4. CG relative (IDMS-calibrated creatinine)	Urinary iothalamate, multiple samples	1. 80 (80; 81) 2. 83 (83; 84) 3. 74 (74; 75) 4. 69 (69; 70) Same result of Eq 2 as in reference [37]	High Very large number of examinations despite non-external validation
Stevens et al 2010 [31] USA, Europe	The purpose was to describe bias of the CKD-EPI and MDRD equations according to clinical characteristics and discuss clinical implications of reporting estimated GFR >60	Same as reference [33] CKD-EPI external validation cohort (n=3 896)	1. CKD-EPI 2. MDRD-IDMS	Urinary iothalamate, multiple samples	1. 84 (83; 85) 2. 81 (80; 82) Same results of Eq 1,2 as in reference [33]	High Very large number of examinations despite non-external validation
Tent et al 2010 [32] The Netherlands	To compare the pre- and post donation performance of estimated GFR in high and lower ranges of GFR in the same individual within a limited time frame	Cross-sectional Retrospective External validation Consecutive Single centre Kidney donors (n=253) Females: 57% Age: 50 (IQR 43–56) years GFR: 102 (IQR 92–113)	1. CG relative 2. MDRD-IDMS 3. CKD-EPI	Urinary iothalamate, single sample	1. 90 (86; 94) 2. 73 (68; 79) 3. 89 (85; 93)	Moderate 100–499 examinations
Tent et al 2010 [32] The Netherlands	Same as above	Post-kidney donation (n=253) Caucasians Females: 57% Age: 51 (IQR 44–57) years GFR: 66 (IQR 59–72)	1. CG relative 2. MDRD-IDMS 3. CKD-EPI	Same as above	1. 93 (90; 96) 2. 71 (65; 76) 3. 89 (85; 93)	Same as above

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Table 3.2.12 *continued*

Author Year Reference Country	Aim	Study design Population characteristics	Index method Equations (numbering corresponds to numbering in result column)	Reference method Measured GFR	Results P30 (%, 95% CI)	Study quality/ Comments
Tidman et al 2008 [4] Sweden	To validate currently used formulas to estimate GFR upon creatinine and cystatin C and to compare two different methods for determination of cystatin C in patients referred for GFR measurement	Cross-sectional Retrospective External validation Consecutive Single centre GFR referrals (n=322) Females: 41% Age: 57 (SD 15) years GFR: 50 (SD 28)	1. CG relative 2. MDRD-IDMS Cystatin C equations reported in separate table	Plasma iohexol, single sample	1. 69 (64; 74) 2. 80 (76; 84)	Moderate 100–499 examinations
Tsinalis et al 2009 [86] Switzerland	To assess the accuracy of the MDRD-IDMS, the quadratic equation by Rule, CG and bias-corrected CG equations to predict GFR before and after kidney donation	Cross-sectional Retrospective External validation Consecutive Single centre Pre- and post-kidney donation (n=281) Females: 64% Age: 50 (22–73) years GFR: 69 (37–148)	1. MDRD-IDMS absolute Only external validation with IDMS-calibrated creatinine assay considered	Urinary inulin, multiple samples	1. NR	Moderate 100–499 examinations and 4 quality criteria fulfilled

* Results calculated by us based on published data.

** High study quality requires ≥500 examinations resulting in 95% CI ≤±3.5% at 80% P30 in an external validation and ≥7 of 11 modified QUADAS criteria fulfilled, moderate study quality requires 100–499 examinations resulting in 95% CI ≤±8% at 80% P30 and ≥4 of 11 of modified QUADAS criteria fulfilled. All other studies were classified as low quality.

Result calculated by us based on unpublished original data.

CG = Cockcroft-Gault equation; CKD = Chronic kidney disease; CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration equation; Eq = Equation; ^{51}CR-EDTA = Chromium Ethylenediaminettetracetate acid; GFR = Glomerular filtration rate; IQR = Interquartile range; LM = Lund-Malmö Study equation without body weight measure; LM-LBM = Lund-Malmö Study equation with lean body mass; MDRD = Modification of diet in renal disease study; MDRD-original = 4-variable equation based on creatinine assays traceable to the original MDRD laboratory; MDRD-IDMS = 4-variable equation based on creatinine assays traceable to IDMS; NR = Not reported; NS = Not specified; P30 = Percentage of GFR estimates within 30% of measured GFR; SD = Standard deviation

External validation: Validation in a different cohort and laboratory than where the equation was developed. Validation results must not influence the final equation presented.

Internal validation: Validation other than developmental but which could not fulfill the criteria for external.

Development validation: Results for the same cohort in which the equation was developed with the prerequisite that the cohort was initially divided into a development and validation set during equation modelling. Results where the entire cohort without subdivision was used for equation modelling are excluded.

Table 3.2.13 *Creatinine and cystatin C equations in various adult ethnic groups. Studies evaluating GFR prediction equations with creatinine assay calibration traceable to the original MDRD laboratory or to isotope dilution mass spectrometry (IDMS) in both the development and validation set and cystatin C assay calibration traceable to the laboratory where the equation was developed. An exception was made for the commonly used Cockcroft-Gault equation. Ethnicity is given in percentage if ≥10 % of the total population, mean/median age and mean/median GFR in mL/min/1.73 m². Results are given as percentage of GFR estimates within 30 % (P30) of measured GFR. Measures of variability are given as range (default), percentiles (eg 95 % = 2.5 to 97.5), interquartile range (IQR) or standard deviation (SD). Confidence intervals (CI) for P30 were calculated by us when not available.*

Author Year Reference Country	Aim	Study design Population characteristics	Index method Equations (numbering corresponds to numbering in result column)	Reference method Measured GFR	Results P30 (%, 95% CI)	Study quality** Comments
Emara et al 2008 [53] Egypt	To compare the performance of old and recent creatinine and cystatin C GFR equations (n=14 & 11, respectively) and to estimate the sensitivity and specificity of the current equations to correctly identify GFR ≤60 mL/min/1.73 m²	Cross-sectional External validation Consecutive Single centre Prospective CKD (n=101) Female: 45% Age: 52 (SD 12) years GFR: 54 (5–134)	1. MDRD-IDMS 2. CG relative External cystatin C equations excluded due to non-traceable assays	Urinary inulin, multiple samples	1. 53 (44; 63) 2. 54 (45; 64)	Moderate 100–499 examinations
Kwong et al 2010 [52] USA	To quantify the effect of measured GFR on the accuracy of creatinine and cystatin C GFR prediction equations	Cross-sectional External validation (Eq 1) Development validation (Eq 2,3) Consecutive Multicentre (NS) African American Study of Kidney Disease and Hypertension (AASK, n=949) African Americans Females: 39% Age: 55 (SD 11) years GFR 46 (90% 24; 64)	1. MDRD-IDMS 2. CKD-EPI cystatin C 3. CKD-EPI cystatin C-creatinine	Urinary iothalamate, multiple samples	1. 84 (82; 87) 2. 83 (80; 85) 3. 90 (88; 92)	Moderate Non-external validation
Lee 2010 [56] Republic of Korea	To derive the ethnic coefficients of the MDRD equations for Korean and to obtain novel proper estimating equations	Cross-sectional External validation Non-consecutive Single centre Prospective CKD and healthy volunteers (n=147) Koreans Females: 49% Age: 48 (19–80) years GFR: 56 (5–121)	MDRD-IDMS with Korean coefficient 0.99 (Eq 7) Remaining equations excluded since they do not fulfill our selection criteria or data difficult to interpret	Plasma inulin, multiple samples	1. 61 (53; 69*)	Moderate <50% quality criteria fulfilled, non-external validation and 100–499 examinations

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Table 3.2.13 *continued*

Author Year Reference Country	Aim	Study design Population characteristics	Index method Equations (numbering corresponds to numbering in result column)	Reference method Measured GFR	Results P30 (%, 95% CI)	Study quality** Comments
Matsuo et al 2009 [55] Japan	To evaluate MDRD-IDMS with Japanese coefficients and establish new 3- and 5-variable Japanese equations using standardized creatinine assays	Cross-sectional External validation (Eq 1) Internal validation (Eq 2,3) Consecutive Multicentre (n=80) Prospective Mostly nephrology in patients with CKD (n=350) Glomerulonephritis 55% Diabetes: 13% Females: 42% Mean age: 54 (19–91) years Mean GFR: 57 (3–229)	1. MDRD-IDMS 2. MDRD-IDMS with new Japanese coefficient (0.808, Eq 3 in the study) 3. New 3-variable Japanese equation (Eq 4 in the study) Eq 1, 2, 5, 6 in authors' Table 3 in the article did not fulfill inclusion criteria	Urinary inulin, multiple samples	1. 59 (54; 64) 2. 73 (59; 78) 3. 75 (70; 79)	Moderate Non-external validation, 100–499 examinations and 6 quality criteria fulfilled
Stevens et al 2007 [37] USA	To evaluate the performance of the MDRD-IDMS in a large diverse population and with particular attention to the level of GFR and participants characteristics in the CKD-EPI cohort	Cross-sectional Retrospective Internal validation Pooled data Multicentre (n=10) CKD-EPI development validation cohort (n=5 504) a) White and other (n=3 462) b) Black (n=1 737) c) Asian Americans (n=62) d) Native Americans/Pacific Islanders/Hispanic (n=243) Diabetes: 29% Females: 44% Age: 47 (SD 15) years GFR: 68 (SD 39)	1. MDRD-IDMS Validation of MDRD regarded as internal since about 20% of the cohort originated from the MDRD study cohort	Urinary iothalamate, multiple samples	1a. 83 (82; 84) 1b. 84 (82; 86) 1c. 87 (79; 95) 1d. 85 (81; 89)	High Very large number of examinations despite non-external validation

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Table 3.2.13 *continued*

Author Year Reference Country	Aim	Study design Population characteristics	Index method Equations (numbering corresponds to numbering in result column)	Reference method Measured GFR	Results P30 (%, 95% CI)	Study quality** Comments
Stevens et al 2011 [51] USA, Europe, China, Japan, South Africa	To report on the development of a GFR-estimating equation that includes a four-level race variable from the United States and Europe, and its evaluation compared with the CKD-EPI (two-level race) equation in separate populations from the United States and Europe as well as in populations from other countries	Cross-sectional Internal validation (cohorts a–d) External validation (cohorts e–g) Pooled data Multicentre (n=19) CKD-EPI external validation cohort (n=4 014, USA and Europe) a) White and other (n=3 378) Females: 45% Age: 49 (SD 15) years GFR 69 (SD 36) b) Black (n=384) Females: 48% Age: 50 (SD 15) years GFR: 62 (SD 34) c) Asian Americans (n=67) Females: 48% Age: 61 (SD 15) years GFR: 53 (SD 31) d) Native Americans & Hispanic (n=185) Females: 70% Age: 45 (SD 12) years GFR: 105 (SD 47) Non-USA and non-Europe e) Chinese (n=675) Females: 49% Age: 50 (SD 15) years GFR: 55 (SD 35) f) Japanese (n=248) Females: 45% Age: 50 (SD 18) years GFR: 53 (SD 31) g) Black South Africans (n=99) Females: 49% Age: 47 (SD 17) years GFR: 61 (SD 32)	1. CKD-EPI with two ethnic factors 2. CKD-EPI with four ethnic factors	Urinary iothalamate, multiple samples Iohexol, NS EDTA, NS DTPA, NS (used in Chinese, n=675) Inulin, NS	1a. 84 (83; 86) 2a. 84 (83; 85) 1b. 82 (78; 85) 2b. 82 (80; 85) 1c. 85 (76; 93) 2c. 85 (76; 93) 1d. 80 (74; 85) 2d. 81 (76; 87) 1e. 73 (70; 77) 2e. 72 (69; 76) 1f. 29 (24; 35) 2f. 36 (31; 42) 1g. 56 (47; 65) 2g. 56 (47; 65)	High Very large number of examinations despite non-external validation

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Table 3.2.13 *continued*

Author Year Reference Country	Aim	Study design Population characteristics	Index method Equations (numbering corresponds to numbering in result column)	Reference method Measured GFR	Results P30 (%, 95% CI)	Study quality** Comments
Van Deventer et al [54] 2008 South Africa	To examine the applicability of the 4-variable MDRD and CG equations for estimating GFR in black South Africans and to evaluate whether the ethnicity factor established for Africans Americans is appropriate for black South Africans	Included in reference [51] Cross-sectional External validation (Eq 1,2,3) Development validation (Eq 4) Consecutive Single centre Prospective CKD/risk factors for CKD (n=100) Black Hypertension: 36% Diabetes: 25% HIV: 20% Females: 49% Age: 47 (18–86) years GFR: 62 (3–132)	1. MDRD-IDMS with ethnic factor for African Americans 2. MDRD-IDMS without ethnic factor for African Americans 3. CG relative Bias-corrected CG excluded since adjustment was based on the present cohort	Plasma Cr-EDTA, multiple samples	1. 52 (42; 62) 2. 74 (65; 83) 3. 58 (48; 68)	Moderate 100–499 examinations

* Results calculated by us based on published data.

** High study quality requires ≥500 examinations resulting in 95% CI ≤±3.5% at 80% P30 in an external validation and ≥7 of 11 modified QUADAS criteria fulfilled, moderate study quality requires 100–499 examinations resulting in 95% CI ≤±8% at 80% P30 and ≥4 of 11 of modified QUADAS criteria fulfilled. All other studies were classified as low quality.

CG = Cockcroft-Gault equation; CKD = Chronic kidney disease; CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration equation; ^{51}CR-EDTA = Chromium Ethylenediaminettetracetate acid; DTPA = Diethylene triamine penta acetic acid; EDTA = Ethylenediaminettetracetate acid; Eq = equation; GFR = Glomerular filtration rate; HIV = Human immunodeficiency virus; MDRD = Modification of diet in renal disease study; MDRD-IDMS = 4-variable equation based on creatinine assays traceable to IDMS; NS = Not specified; P30 = Percentage of GFR estimates within 30% of measured GFR; SD = Standard deviation

External validation: Validation in a different cohort and laboratory than where the equation was developed. Validation results must not influence the final equation presented.
Internal validation: Validation other than developmental but which could not fulfill the criteria for external.

Development validation: Results for the same cohort in which the equation was developed with the prerequisite that the cohort was initially divided into a development and validation set during equation modelling. Results where the entire cohort without subdivision was used for equation modelling are excluded.

Table 3.2.14 *Creatinine, cystatin C and combined creatinine/cystatin C equations in adults. Studies evaluating GFR prediction equations with creatinine assay calibration traceable to the original MDRD laboratory or to isotope dilution mass spectrometry (IDMS) in both the development and validation set and cystatin C assay calibration traceable to the laboratory where the equation was developed. An exception was made for the commonly used Cockcroft-Gault equation. Ethnicity is given in percentage if ≥10 % of the total population, mean/median age and mean/median GFR in mL/min/1.73 m² (default) or mL/min. Results are given as percentage of GFR estimates within 30 % (P30) of measured GFR (in some instances P10 is also given). Measures of variability are given as range (default), percentiles (eg 95 % = 2.5 to 97.5), interquartile range (IQR) or standard deviation (SD). Confidence intervals (CI) for P30 were calculated by us when not available.*

Author Year Reference Country	**Aim**	**Study design Population characteristics**	**Index method Equations (numbering corresponds to numbering in result column)**	**Reference method Measured GFR**	**Results P30 (%, 95% CI)**	**Study quality** Comments**
Eriksen et al 2011 [57] Norway	To investigate whether regression models using cystatin C level alone or in combination with creatinine level in principle would improve GFR estimation in the general population compared with using creatinine level alone	Same population as reference [42] Cross-sectional Prospective Internal validation Random sample Single centre Healthy (n=1 621) Female: 51% Age: 58 (50–62) years GFR: 92 (22–139)	1. Local creatinine (age, sex) 2. Local cystatin C (age, sex) 3. Local creatinine + cystatin C (age, sex) 4. Local creatinine + cystatin C (age, sex, height, weight)	Plasma iohexol, single sample	97 (96; 98) 97 (97; 98) 98 (97; 99) 98 (97; 98) *P10* 62 (59; 64) 61 (58; 63) 66 (64; 68) 68 (65; 70)	Moderate Non-external validation
Fehrman-Ekholm et al 2009 [25] Sweden	To compare the performance of 7 different GFR estimates using cystatin C, creatinine and urea in 50 healthy individuals with plasma clearance of iohexol	Cross-sectional Prospective External validation Consecutive Single centre Healthy elderly (n=50) Female: 38% Age: 83 (71–110) years GFR: 68 (38–113)	1. CG relative 2. CKD-EPI cystatin C I 3. CKD-EPI cystatin C II For Eq 2,3 see reference [12] MDRD-original excluded since IDMS-traceable creatinine assay was used Grubb and Hoek external cystatin C equations excluded due to non-traceable assays	Plasma iohexol, multiple samples	1. 46 (32; 60) 2. 94 (87; 100) 3. 86 (76; 96)	Moderate <100 examinations

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Table 3.2.14 *continued*

Author Year Reference Country	Aim	Study design Population characteristics	Index method Equations (numbering corresponds to numbering in result column)	Reference method Measured GFR	Results P30 (%, 95% CI)	Study quality** Comments
Grubb et al 2005 [87] Sweden	To investigate the possibility of introducing cystatin C formulas without anthropometric variables to predict GFR and to compare the diagnostic efficiency with Cockcroft-Gault	Cross-sectional Retrospective External validation (Eq 1) Internal validation (Eq 2) Consecutive Single centre GFR referrals (n=149) Female: 50% Age: 58 (95% 24; 83) years GFR; 67 (95% 11; 142) mL/min Included in reference [59] and [11]	1. CG absolute (creatinine) 2. Grubb absolute (cystatin C, sex)	Plasma iohexol, single sample	1. 64 (60; 68) 2. 75 (71; 79)	Moderate Non-external validation, 100–499 examinations and 6 quality criteria fulfilled
Grubb et al 2005 [59] Sweden	To analyze if creatinine based GFR prediction equations for adults and children can be replaced by a simple equation based on cystatin C	Cross-sectional Retrospective Internal validation (Eq 2) Development validation (Eq 1) Consecutive Single centre GFR referrals (n=451) Transplants: 10% Female: 50% Age: 58 (95%, 24; 83) years GFR: 63 (95%, 11; 124) Included in reference [11]	1. MDRD bias-corrected 2. Grubb (cystatin C, sex, without juvenile factor) 3. Arithmetic mean Eq 1 & Eq 2	Plasma iohexol, single sample	1. 79 (75; 83) 2. 82 (79; 86) 3. 89 (86; 92)#	Moderate Non-external validation and 100–499 examinations
Nyman et al 2009 [11] Sweden	To test various ways of combining creatinine and cystatin C in equations to predict GFR	Cross-sectional Retrospective Development validation Consecutive Multicentre (n=2) GFR referrals (n=857) Transplants: 5% Females: 44% Age: 59 (95%, 26; 85) GFR: 55 (95%, 9; 121)	1. LM (creatinine) 2. Grubb (cystatin C, sex) 3. Arithmetic mean Eq 1 & Eq 2 4. Geometric mean Eq 1 & Eq 2 5. Linear regression on Eq 1 & Eq 2 6. Linear regression on Eq 1 and cystatin C 7. Linear regression on creatinine, cystatin C, age and gender	Plasma iohexol, single sample	1. 83 (81; 86) 2. 80 (77; 82) 3. 90 (87; 92) 4. 89 (87; 91) 5. 90 (88; 92) 6. 90 (88; 92) 7. 89 (87; 91)	Moderate Non-external validation

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Table 3.2.14 continued

Author Year Reference Country	Aim	Study design Population characteristics	Index method Equations (numbering corresponds to numbering in result column)	Reference method Measured GFR	Results P30 (%, 95% CI)	Study quality** Comments
Sterner et al 2009 [58] Sweden	To validate a cystatin C based GFR prediction equation in a different population from the derivation set but using the cystatin C assay of a single laboratory, and to compare the results with that of the creatinine based MDRD equation	Cross-sectional Prospective External validation (Eq 1) Internal validation (Eq 2,3) Consecutive Single centre GFR referrals (n=406) Females: 37%	1. MDRD-IDMS (creatinine) 2. Grubb (cystatin C, sex) 3. Arithmetic mean Eq 1 & Eq 2	Plasma iohexol, single sample	1. 80 (76; 84) 2. 79 (75; 83) 3. 85 (81; 89)#	Moderate Non-external validation and 100–499 examinations
Stevens et al 2008 [12] USA and Europe	To develop and evaluate GFR-estimating equations using cystatin C alone and cystatin C, creatinine, or both with demographic variables	Cross-sectional Retrospective Extern validation (MDRD) Internal validation (Eq 2–6) Pooled data Multicentre (n=4) Part of CKD-EPI cohort (n=438) White: 79% Black: 8% Other: 13% Females: 29% Age: 59 (SD 15) years GFR: 34 (90%, 11; 66)	1. MDRD-IDMS (creatinine) 2. Model 1 (cystatin C) 3. Model 2 (cystatin C, age, sex, race) 4. Model 3 (cystatin C, creatinine, age, sex, race) 5. Model 6 Arithmetic mean Eq 1 & Eq 2 in this list See Table 2 for Eq 2–4 in the original paper [12]	Urinary iothalamate, multiple samples	1. 85 (82; 88*) 2. 73 (69; 77*) 3. 79 (75; 83*) 4. 90 (87; 83*) 5. 90 (87; 93*)	Moderate Non-external validation, 100–499 examinations and 6 quality criteria fulfilled
Stevens et al 2008 [12] USA and Europe	Same as above	Development validation Pooled data Multicentre (n=4) Part of CKD-EPI cohort (n=3 418) White: 43% Black: 43% Females: 37% Age: 52 (SD 13) years GFR: 48 (90%, 15–95)	1. Local MDRD 2. CKD-EPI Cys 1 (cystatin C) 3. CKD-EPI Cys 2 (cystatin C, age, sex, race) 4. CKD-EPI Cys 3 (cystatin C, creatinine, age, sex, race) See Table 4 for Eq 2–4 in the original paper [12]	Same as above	1. 85 (84; 86) 2. 81 (80; 82) 3. 83 (82; 84) 4. 89 (88; 90)	

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Table 3.2.14 *continued*

Author Year Reference Country	Aim	Study design Population characteristics	Index method Equations (numbering corresponds to numbering in result column)	Reference method Measured GFR	Results P30 (%, 95% CI)	Study quality** Comments
Tidman et al 2008 [4] Sweden	To validate currently used formulas to estimate GFR based upon creatinine and cystatin C with two different methods for determination of cystatin C	Cross-sectional Retrospective External validation (Eq 1–3) Internal validation (Eq 4–7) Consecutive Single centre GFR referrals (n=322) Females: 41% Age: 57 (SD 15) GFR: 50 (SD 28)	1. CG relative (creatinine) 2. MDRD-IDMS (creatinine) 3. Local cystatin C (Dako) 4. Local cystatin C (Gentian) 5. Arithmetic mean Eq 3 and Eq 4 6. Arithmetic mean Eq 3 and Eq 5	Plasma iohexol, single sample	1. 69 (64; 74) 2. 80 (76; 85) 3. 66 (61; 72) 4. 82 (78; 86) 5. 81 (77; 85) 6. 87 (83; 91)	Moderate Non-external validation and 100–499 examinations

* Corrected results calculated by us based on published data.

** High study quality requires ≥500 examinations resulting in 95% CI ≤±3.5% at 80% P30 in an external validation and ≥7 of 11 modified QUADAS criteria fulfilled, moderate study quality requires 100–499 examinations resulting in 95% CI ≤±8% at 80% P30 and ≥4 of 11 of modified QUADAS criteria fulfilled. All other studies were classified as low quality.

Results calculated by us based on unpublished original data.

CG = Cockcroft-Gault equation; GFR = Glomerular filtration rate; CKD = Chronic kidney disease; CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration equation; Eq = Equation; LM = Lund-Malmö Study equation without body weight measure; MDRD = Modification of diet in renal disease study; MDRD-original = 4-variable equation based on non-IDMS-traceable creatinine assays, MDRD-IDMS = 4-variable equation based on creatinine assays traceable to IDMS-traceable creatinine; SD = Standard deviation

External validation: Validation in a different cohort and laboratory than where the equation was developed. Validation results must not influence the final equation presented.

Internal validation: Validation other than developmental but which could not fulfill the criteria for external. Development validation: Results for the same cohort in which the equation was developed with the prerequisite that the cohort was initially divided into a development and validation set during equation modelling. Results where the entire cohort without subdivision was used for equation modelling are excluded.

Table 3.2.15 *Creatinine, cystatin C and combined creatinine/cystatin C equations in children. Studies evaluating GFR prediction equations with creatinine assay calibration traceable to the original MDRD laboratory or to isotope dilution mass spectrometry (IDMS) in both the development and validation set, or traceable to the laboratory where the equation was developed, and cystatin C assay calibration traceable to the laboratory where the equation was developed. Ethnicity is given in percentage if ≥10 % of the total population, mean/median age and mean/median GFR in mL/min/1.73 m². Results are given as percentage of GFR estimates within 30 % (P30) of measured GFR (in some instances P10 is also given). Measures of variability are given as range (default), percentiles (eg 95 % = 2.5 to 97.5), interquartile range (IQR) or standard deviation (SD). Confidence intervals (CI) for P30 were calculated by us when not available.*

Author Year Reference Country	**Aim**	**Study design Population characteristics**	**Index method Equations (numbering corresponds to numbering in result column)**	**Reference method Measured GFR**	**Results P30 (%. 95% CI)**	**Study quality** Comments**
Andersen et al 2011 [13] Denmark	To develop a more accurate cystatin C-based model to estimate GFR in children by inclusion body cell mass (not including in the present analysis as it requires bio-impedance measurements – exclusion criteria)	Cross-sectional Retrospective Internal validation (n=60) Multicentre (n=2) Nephrologic disorders (n=119) Female: 41% Mean age: 9 (2–15) years Mean GFR; 98 (14–147)	1. Schwartz (creatinine)[a] 2. Bökenkamp (cystatin C)[a] 3. Filler (cystatin C)[a] 4. Bouvet (creatinine + cystatin C)[a] 5. Zapitelli (creatinine + cystatin C)[a] 6. Local model (creatinine + cystatin C)	Plasma Cr-EDTA, mutiple samples	1. 95 (n=60) 2. 88 (n=60) 3. 90 (n=60) 4. 96 (n=60) 5. 97 (n=60) 6. 98 (n=60) *P10* 1. 50 (n=60) 2. 42 (n=60) 3. 40 (n=60) 4. 56 (n=60) 5. 60 (n=60) 7. 62 (n=60)	Moderate 100–499 examinations and 5 quality criteria fulfilled
Bacchetta et al 2011 [7] France	To evaluate the new creatinine based Schwartz formula, some cystatin C formulas and combined formula using both cystatin C and creatinine	Cross-sectional Retrospective External validation (Eq 1,3) Internal validation (Eq 2) Pooled data Multicentre (n=2) Moderate CKD & normal GFR (n=252) Renal transplants: 17% Non-renal transplants: 10% Female: 48% Mean age: 11 (4–20) years GFR: 101 (SD 32)	1. Schwartz-IDMS (creatinine, *k*=36.5) 2. Schwartz local (creatinine, *k*=29, boys >13 years *k*=33) 3. Schwartz-original (creatinine, *k*=49, boys >13 years *k*=62) External cystatin C equations excluded due to non-traceable assay	Urinary inulin, multiple samples	1. 84 (79; 89) 2. 91 (87; 95) 3. 23 (18; 28)	Moderate Non-external validation and 100–499 individuals

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Table 3.2.15 *continued*

Author Year Reference Country	Aim	Study design Population characteristics	Index method Equations (numbering corresponds to numbering in result column)	Reference method Measured GFR	Results P30 (%. 95% CI)	Study quality/ Comments
Berg et al 2011 [8] Sweden	To measure GFR simultaneously using renal inulin, plasma iohexol and creatinine clearance, and to estimate GFR according to the new Schwartz formula in children with different kidney disorders	Cross-sectional Prospective External validation Pooled data Single centre GFR referrals of children with kidney disorders (n=60) CKD Transplants: 27% Age: 12 (SD 5) years GFR: 71 (SD 41)	Schwartz-IDMS (Crea, *k* = 36.5)	Urinary inulin, multiple samples	1. 78 (68; 88)	Moderate <100 individuals
Blufpand et al 2011 The Netherlands [61]	To compare the diagnostic performance of a creatinine equation and a cystatin C equation in pediatric patients with malignancy compared with controls	Cross-sectional Retrospective External validation Single centre Controls; GFR referrals kidney disorders (n=97) and long-term follow-up after treatment of cancers (n=24) Females: 40% Age: 13 (8–16) years GFR: 79 (SD 31)	Schwartz-IDMS Cystatin C-equation excluded due to non-traceable assay	Plasma inulin, multiple samples	1. 84 (77; 91*)	High
Nyman et al 2008 [9] Sweden	To evaluate the performance of the Lund-Malmö equations in a pediatric population compared with that of MDRD and the Counahan-Barratt equations as well as to that of the Grubb cystatin C equation	Cross-sectional Retrospective External validation (Eq 1,2,3,6) Development validation (Eq 4,5,7) Consecutive Multicentre (n=2) GFR referrals (n=85) Females: 44% Age: 12 (95%, 1; 17) years GFR: 108 (95%, 23; 221)	2. MDRD-IDMS (creatinine) 3. LM original (creatinine) 4. LM-LBM (creatinine) 5. LM-revised 6. Grubb (cystatin C, juvenile, sex) 7. Schwartz-IDMS (creatinine, *k*=36.5) 8. Arithmetic mean Eq 2+5 Bias-corrected Counahan-Barratt formula don't meet inclusion criteria	Plasma iohexol, single sample	1. 14 (7; 22) 2. 76 (67; 85) 3. 73 (64; 82) 4. 71 (61; 80)# 5. 82 (74; 90) 6. 68 (58; 78)# 7. 86 (78; 93)#	Moderate <100 individuals

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Table 3.2.15 *continued*

Author Year Reference Country	Aim	Study design Population characteristics	Index method Equations (numbering corresponds to numbering in result column)	Reference method Measured GFR	Results P30 (%. 95% CI)	Study quality/ Comments
Pottel et al 2010 [10] Belgium	To evaluate the validity of the updated Schwartz, other published and a new equation for healthy children (BCCH1)	Cross-sectional Retrospective External validation Random selection Single centre CKD (n=182) Females: 42% Mean age: 5 (2–9) years Mean GFR: 88 (11–144)	Schwartz-IDMS (creatinine, *k*= 36.5) Flanders (creatinine) LM original (creatinine) BCCH1 (creatinine) Leger (creatinine)	Plasma Cr-EDTA, multiple samples	1. 54 (47; 61) 2. 62 (55; 69) 3. 65 (58; 72) 4. 60 (53; 76) 5. 58 (51; 65)	Moderate 100–499 individuals and 6 quality criteria fullfilled
Schwartz et al 2009 [14] USA, Canada	To develop a formula that could be applied to the clinical treatment of children with CKD and to generate in clinical laboratories an estimated GFR (eGFR) from endogenous serum markers	Cross-sectional Retrospective Internal validation (all but Eq 5) Development validation (Eq 5) Multicentre (NS) CKiD Study cohort (n=168) White: 69% Black: 15% Hispanic: 15% Females: 39% Mean age: 11 (1–16) years GFR: 41 (IQR 32–52)	Schwartz-IDMS (creatinine, *k*=36.5) Leger (creatinine)[a] Filler (cystatin C)[a] Grubb (cystatin C)[a] creatinine + cystatin C (Eq IA in authors' Table 3) Bouvet (creatinine + cystatin C)[a] Zapitelli (creatinine + cystatin C)	Plasma iohexol, multiple samples	1. 73 (66; 80) 2. 71 (64; 78) 3. 72 (65; 79) 4. 72 (65; 79) 5. 82 (76; 88)[#] 6. 80 (74; 86) 7. 82 (76; 88)	Moderate Non-external validation, 100–499 individuals and 5 quality criteria fulfilled

* Results calculated by us based on published data.

** High study quality requires ≥500 examinations resulting in 95% CI ≤±3.5% at 80% P30 in an external validation and ≥7 of 11 modified QUADAS criteria fulfilled, moderate study quality requires 100–499 examinations resulting in 95% CI ≤±8% at 80% P30 and ≥4 of 11 of modified QUADAS criteria fulfilled. All other studies were classified as low quality.

Results calculated by us or by the authors on our request based on unpublished original data.

[a] Constants and/or coefficients recalculated to fit present study data.

BCCH = British Columbia Children's Hospital; CKD = Chronic kidney disease; CKiD = Chronic kidney disease in children; ^{51}CR-EDTA = Chromium Ethylenediaminettetracetate acid; Eq = Equation; GFR = Glomerular filtration rate; IDMS = Isotope dilution mass spectromety; IQR = Interquartile range; *k* = The factor in GFR equation *k* x height/Crea with creatinine expressed in mmol/L; LM = Lund-Malmö Study equation without body weight measure; LM-LBM = Lund-Malmö Study equation with lean body mass; MDRD = Modification of diet in renal disease study; MDRD-IDMS = 4-variable equation based on creatinine assays traceable to IDMS; NS = Not specified; SD = Standard deviation

External validation: Validation in a different cohort and laboratory than where the equation was developed. Validation results must not influence the final equation presented.

Internal validation: Validation other than developmental but which could not fulfill the criteria for external.

Development validation: Results for the same cohort in which the equation was developed with the prerequisite that the cohort was initially divided into a development and validation set during equation modelling. Results where the entire cohort without subdivision was used for equation modelling are excluded.

Table 3.3.3 *Solid organ transplant patients.*

Author Year Country Reference	Aim(s)	Study design Population-characteristics (number of subjects/patients, male/female, age, GFR) Setting	Index test eGFR (creatinine) equations eGFR (cystatin C) equations	Reference test	Results P30 (%, 95% CI)/ Mean bias mL/min/ 1.73 m^2	Study quality Comments
Berding et al 2010 [10] Germany	To assess creatinine and cystatin C-based estimation of GFR in children after liver transplantation	Cross-sectional Liver-transplanted children (n=48, 32 M/16 F) Mean age att follow-up: 12 (5–18) Mean age at liver transplantation: 6 (5–16) years GFR: 62±20 (11–114) mL/ min/1.73 m^2 All patients were on immuno-suppressive treatment including corticosteroids. 62% were on corticosteroids (type and doses not given)	p-creatinine (Crea Plus®, not specified if IDMS-traceable) *eGFR (creatinine) equation* Schwartz (modified according to Filler) s-cystatin C (PENIA, nephelometer BN2) *eGFR (cystatin C) equation* Filler	^{51}Cr-EDTA plasma clearance	P30 not given Individual bias (%, 95% CI) Schwartz 31 (–323; 103) Filler 6 (–31; 45) eGFR (cystatin C) Filler appears better than eGFR (creatinine) Schwartz	Low p-creatinine method not specified if IDMS-traceable. No formal statistical testing between methods reported
Boudville et al 2009 [4] Australia	To compare creatinine and cystatin C-based estimation of GFR in liver transplant patients	Cross-sectional Liver transplant patients (n=41, 22 M/19 F) Age: 56±13 years GFR: 58±20 mL/min/1.73 m^2 s-cystatin C only analysed in 30 patients. GFR: <60 mL/min/1.73 m^2 (n=23) All patients were on immuno-suppressive treatment including corticosteroids (proportion of patients on corticosteroids, type and doses not given)	*s-creatinine (kinetic colorimetric, IDMS-traceable), eGFR (creatinine) equations* CG MDRD s-cystatin C (immuno-nephelometry Dade Behring BNII) *eGFR (cystatin C) equations* Hoek Larsson Filler Le Bricon	^{51}Cr-EDTA plasma clearance	CG 63 (48; 78)/–7.3 MDRD 80 (68; 92)/–7.6 Hoek 73 (59; 87)/10.2 Larsson 60 (45; 75)/12.8 Filler 23 (10; 36)/23.5 Le Bricon 86 (75;97)/3.4 GFR <60 mL/min/1.73 m^2 CG 55 (35; 75)/–10.1 MDRD 86 (72; 100)/–1.7 Hoek 93 (83; 100)/0.98 Larsson 71 (52; 90)/4.0 Filler 21 (4; 38)/19.5 Le Bricon 79 (62; 96)/–6.0	Moderate s-cystatin C only analysed in 30 patients. Small subgroup <60 mL/min/ 1.73 m^2, n=23. No formal statistical testing between different methods or formulas

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Table 3.3.3 *continued*

Author Year Country Reference	Aim(s)	Study design Population-characteristics (number of subjects/patients, male/female, age, GFR) Setting	Index test eGFR (creatinine) equations eGFR (cystatin C) equations	Reference test	Results P30 (%, 95% CI)/ Mean bias mL/min/ 1.73 m^2	Study quality Comments
Daniel et al 2004 [15] France	To compare cystatin C and creatinine clearance for detection of renal failure in renal transplant patients	Cross-sectional Renal transplant patients (n=60, 39 M/21 F) 103 blood samples Age: 40±12 years GFR: 25–130 mL/min/1.73m^2 All patients were on immuno-suppressive treatment, including corticosteroids (proportion of patients on corticosteroids, type and doses not given)	s-creatinine (kinetic colorimetric technique using picric acid, not specified if IDMS-traceable) *eGFR (creatinine) equation* CG s-cystatin C (immuno-nephelometry Dade Behring BNII Automat) Crude 1/cystatin C	Renal inulin clearance	Specific numerical data not given No significant differences in sensitivity and specificity using ROC curves at GFR 60 and 90 mL/min/1.73 m^2 between different methods and formulas reported	Low s-creatinine method not specified if IDMS-traceable. Only eGFR (creatinine). CG and crude 1/cystatin C No numerical data. No formal statistical testing presented
Delanaye et al 2007 [17] Belgium	To compare eGFR estimates using creatinine and cystatin C-based formulas in heart transplant patients	Cross-sectional Heart transplant patients (n=27, 22 M/5 F) Age not given GFR: 8–75 mL/min/1.73 m^2 All patients were on immuno-suppressive treatment including corticosteroids. 73% were on corticosteroids (type and doses not given)	s-creatinine (kinetic rate compensated Jaffe method, not specified if IDMS-traceable) *eGFR (creatinine) equation* MDRD s-cystatin C (particle-enhanced nephelometric method) *eGFR (cystatin C) equation* Rule	^{51}Cr-EDTA plasma clearance	MDRD 43 (24; 62)/2.2 Rule 67 (49; 85)/6.9 No statistical difference between methods Overall poor predictive performance of both eGFR (creatinine) and eGFR (cystatin C) vs measured GFR	Low s-creatinine method not specified if IDMS-traceable Small sample, n=27. Patient characteristics poorly described

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Table 3.3.3 *continued*

Author Year Country Reference	Aim(s)	Study design Population-characteristics (number of subjects/patients, male/female, age, GFR) Setting	Index test eGFR (creatinine) equations eGFR (cystatin C) equations	Reference test	Results P30 (%, 95% CI)/ Mean bias mL/min/ 1.73 m^2	Study quality Comments
Maillard et al 2008 [1] France	To compare eGFR estimates using cystatin C- and creatinine-based formulas in renal transplant patients	Cross-sectional Renal transplant patients (n=120, 82 M/38 F) Mean age: 53 (22–77) years GFR: 13–119 mL/min/1.73 m^2 All patients were on immuno-suppressive treatment, including corticosteroids. 63% of patients on corti-costeroids (type not given), mean dose 4.4 mg/day	s-creatinine (enzymatic, IDMS-traceable) *eGFR (creatinine) equation* MDRD s-cystatin C (immuno-nephelometry Dade Behring BNII) *eGFR (cystatin C) equations* Hoek Larsson Filler Le Bricon Rule	Renal inulin plasma clearance	MDRD 58 (49; 67)/8.7 Hoek 82 (75; 89)/–4.0 Larsson 68 (60; 76)/–5.9 Filler, 71 (63; 79)/5.1 Le Bricon 78 (71; 86)/2.8 Rule 81 (74; 88)/–5.0 eGFR (cystatin C) equations Hoek, Filler, Le Bricon and Rule were significantly more accurate than eGFR (creatinine) MDRD, p<0.01	Moderate Creatinine analysis cali-brated by the authors which might contribute to uncertainty
Yeo et al 2010 [3] Republic of Korea	To compare creatinine and cystatin C-based eGFR renal transplant patients	Cross-sectional Renal transplant patients (n=102, 58 M/44 F, early post-operative (2–29 days), stable patients) Age: 42±10 years GFR: 41–124 mL/min/1.73 m^2 GFR <60 mL/min/1.73 m^2 (n=16) All patients were on immuno-suppressive treatment. 92% were on corticosteroids (prednisone), average dose 24 mg/day	s-creatinine (compen-sated kinetic Jaffe method, IDMS-traceable) *eGFR (creatinine) equations* CG MDRD s-cystatin C (particle-enhanced turbidometric immunoassay) *eGFR (cystatin C) equations* Hoek Larsson Filler Le Bricon Rule MacIsaac Orebro-cys	^{51}Cr-EDTA plasma clearance	All patients CG 89 (83; 95)/4.2 MDRD 94 (89; 99)/0.3 Hoek 76 (68; 84)/–12.7 Larsson 65 (56; 74)/–8.2 Filler 78 (70; 86)/0.03 Le Bricon 85 (78; 92)/–6.4 Rule 75 (67; 83)/–12.8 MacIsaac 82 (74; 90)/–8.0 Orebro-cys 76 (68; 84)/0.9 GFR <60 mL/min/1.73 m^2 CG 62 (38; 86)/10.7 MDRD 94 (82; 100)/3.7 Hoek 81 (62; 100)/–2.1 Larsson 69 (46; 92)/–1.0 Filler 69 (46; 92)/6.5 Le Bricon 75 (67; 83)/4.7 Rule 81 (62; 100)/–3.4 MacIsaac 69 (46; 92)/1.7 Orebro-cys 69 (46; 92)/0.9	Moderate No formal statistical testing between methods and formulas. High corti-costeroids doses may have influenced s-cystatin C levels

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Table 3.3.3 continued

Author Year Country Reference	Aim(s)	Study design Population-characteristics (number of subjects/patients, male/female, age, GFR) Setting	Index test eGFR (creatinine) equations eGFR (cystatin C) equations	Reference test	Results P30 (%, 95% CI)/ Mean bias mL/min/ 1.73 m^2	Study quality Comments
Zahran et al 2007 [2] Canada	To compare creatinine- and cystatin C-based eGFR in renal transplant patients	Cross-sectional Renal transplant patients (n=103, 63 M/40 F) Age: 47±14 years GFR: 12–122 mL/min/1.73 m^2 GFR <60 mL/min/1.73 m^2 (n=80) All patients were on immuno-suppressive treatment. 100% of patients on corticoste-roids (type and doses not given)	s-creatinine (enzymatic, IDMS-traceable) *eGFR (creatinine) equations* CG MDRD s-cystatin C (enzyme linked immunosorbent) *eGFR (cystatin C) equations* Hoek Larsson Filler Le Bricon Rule MacIsaac	Renal silustrin (an inulin analogue) clearance	GFR >60 mL/min/1.73 m^2 CG 61 (41; 81)/–0.04 MDRD 61 (41; 81)/–19.9 Hoek 45 (25; 65)/–23.5 Larsson 36 (16; 56)/–23.9 Filler 45 (25; 65)/–25.5 Le Bricon 50 (30; 70)/–16.9 Rule 41 (21; 61)/–18.2 MacIsaac 36 (16; 56)/24.8 GFR <60 mL/min/1.73 m^2 CG 44 (33; 55)/15.5 MDRD 69 (59; 79)/3.4 Hoek 58 (47; 69)/3.3 Larsson 54 (43; 65)/–2.3 Filler 57 (46; 68)/6.9 Le Bricon 53 (42; 64)/10.3 Rule 54 (43; 65)/–0.9 Most eGFR (creatinine) equations were more accurate than eGFR (cystatin C)	Moderate No formal statistical testing between methods or formulas was reported

CG = Cockcroft-Gault; CI = Confidence interval; ^{51}CR-EDTA = Chromium Ethylenedia-minettetracetate acid; eGFR = Estimated glomerular filtration rate; F = Female; GFR = Glomerular filtration rate; IDMS = Isotope dilution mass spectrometry; M = Male; MDRD = Modification of diet in renal disease; p-creatinine = Plasma-creatinine; ROC = Receiver operating curve; s-creatinine = Serum-creatinine; s-cystatin C = Serum-cystatin C

Table 3.3.4 *Patients with diabetes.*

Author Year Reference Country	Aim(s)	Study design, Population-characteristics (number of subjects/patients, male/female, age, GFR) Setting	Index test, eGFR (creatinine) equations eGFR (cystatin C) equations	Reference test	Results P30 (%, 95% CI) Mean bias mL/min/ 1.73 m^2	Study quality Comments
Beauvieux et al 2007 [6] France	To compare creatinine and cystatin C-based equations to predict GFR in patients with diabetes	Cross-sectional Patients with diabetes (n=124, 78 M/46 F, 36 T1D/88 T2D) Age: 62±13 (19–83) years GFR: 56.1±35.3 (8–164) mL/ min/1.73 m^2 (same patients as in [19])	s-creatinine (Jaffe, bichromatic, not specified if IDMS-traceable) *eGFR (creatinine) equations* CG MDRD rMDRD MC s-cystatin C (particle- enhancing immunone- phelometry, N latex CysC, Dade Behring) *eGFR (cystatin C) equations* Arnal-Dade Rule MacIsaac Tan	^{51}Cr-EDTA plasma clearance	CG 50 (41; 59) MDRD 68 (60; 76) rMDRD 64 (56; 72) MC 62 (54; 70) Arnal-Dade 64 (56; 72) Rule 67 (59; 75) MacIsaac 55 (46; 64) Tan 59 (50; 68) Mean bias not given	Moderate s-creatinine method not specified if IDMS-traceable No formal statistical testing between methods

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Table 3.3.4 *continued*

Author Year Reference Country	Aim(s)	Study design, Population-characteristics (number of subjects/patients, male/female, age, GFR) Setting	Index test, eGFR (creatinine) equations eGFR (cystatin C) equations	Reference test	Results P30 (%, 95% CI) Mean bias mL/min/1.73 m^2	Study quality Comments
Chudleigh et al 2009 [5] United Kingdom	To compare the performance of the MDRD equation with a selection of cystatin C-based formulas for estimation of GFR in normoalbuminuric patients with type 2 diabetes	Cross-sectional Normoalbuminuric T2D (n=106, 83 M/23 F) Age: 60.9±8.7 years GFR: 104.5±20.1 (~50–160) mL/min/1.73 m^2	s-creatinine (Johnson & Johnson dry-slide system, not specified if IDMS-traceable) *eGFR (creatinine) equation* MDRD s-cystatin C (colorimetric immunoassay) *eGFR (cystatin C) equations* Perkins Arnal Rule MacIsaac Tan Stevens (age) *eGFR (combined creatinine and cystatin C)* Stevens (combined)	^{51}Cr-EDTA plasma clearance	MDRD 65 (56; 74)/–27.1 Perkins 64 (55; 73)/20.0 Arnal 75 (66; 83)/–2.8 Rule 68 (59; 77)/–14.5 MacIsaac 85 (78; 92)/–2.4 Tan 84 (77; 91)/–2.9 Stevens (age) 75 (66; 83)/–8.5 Stevens (combined) 78 (70; 86)/–18.9 MacIsaac and Tan performed better than MDRD, p<0.05	Moderate s-creatinine method not specified if IDMS-traceable

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Table 3.3.4 continued

Author Year Reference Country	Aim(s)	Study design, Population-characteristics (number of subjects/patients, male/female, age, GFR) Setting	Index test, eGFR (creatinine) equations eGFR (cystatin C) equations	Reference test	Results P30 (%, 95% CI) Mean bias mL/min/1.73 m^2	Study quality Comments
Iliadis et al 2011 [7] Greece	To compare eGFR values with measured GFR in patients with type 2 diabetes and a broad range of renal function	Cross-sectional Type 2 diabetes patients (n=460, 216 M/244 F) Age: 65±10 years GFR: 73±23 mL/min/1.73 m^2 GFR 30–59 mL/min/1.73 m^2 (n=145)	p-creatinine (Roche, Jaffe Gen.2, IDMS-traceable) *eGFR (creatinine) equations* MDRD CKD-EPI S-Cystatin C (Tina-quant, particle-enhanced immunoturbimetric) *eGFR (cystatin C) equations* Perkins Arnal Rule MacIsaac Stevens Stevens (age) Tan Grubb Tidman Flodin	^{51}Cr-EDTA plasma clearance	All patients MDRD 79 (75; 83)/7.5 CKD-EPI 81 (77; 85)/7.1 Perkins 35 (31; 39)/24.6 Arnal 72 (68; 76)/1.1 Rule 74 (70; 78)/–6.9 MacIsaac 71 (67; 75)/6.3 Stevens 78 (74; 82)/–3.3 Stevens (age) 87 (84; 90)/5.1 Tan 71 (67; 75)/5.1 Grubb 47 (42; 52)/12.5 Tidman 62 (58; 66)/10.6 Flodin 60 (56; 64)/6.7 GFR 30–59 mL/min/1.73 m^2 MDRD 69 (65; 73)/7.5 CKD-EPI 63 (59; 67)/9.1 Perkins 24 (20; 28)/23.9 Arnal 68 (64; 72)/1.0 Rule 70 (66; 74)/–3.3 MacIsaac 64 (60; 68)/9.6 Stevens 77 (73; 81)/–0.3 Stevens (age) 84 (81; 87)/4.2 Tan 64 (60; 68)/7.7 Grubb 54 (49; 59)/2.0 Tidman 57 (52; 62)/9.9 Flodin 61 (54; 70)/2.9	Moderate No formal statistical testing between methods or formulas. An attempt to calibrate cystatin C measurements using a regression equation did not improve the accuracy of cystatin C-based formulas consistently

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Table 3.3.4 *continued*

Author Year Reference Country	Aim(s)	Study design, Population-characteristics (number of subjects/patients, male/female, age, GFR) Setting	Index test, eGFR (creatinine) equations eGFR (cystatin C) equations	Reference test	Results P30 (%, 95% CI) Mean bias mL/min/1.73 m^2	Study quality Comments
Perkins et al 2005 [19] USA	To assess how well serum cystatin C detect trends in renal function over time when GFR is normal or elevated in patients with type 2 diabetes	Cross-sectional Patients with T2D (Pima Indians/native American, n=30, 18 M/12 F) with GFR >120 mL/min/1.73 m^2 Age: 40±9 years BMI: 33±7 kg/m^2 GFR: 153±27 mL/min/1.73 m^2 (all measurements, n=144)	s-creatinine (modified picrate method of Jaffe calibrated to Cleveland clinic) *eGFR (creatinine) equations* CG MDRD s-cystatin C (Dade Behring) 100/s-cystatin C	Renal iothalamate clearance	P30 and mean bias not given 95% CI of difference between index and reference method (Bland-Altman) CG –42; 73 MDRD –43; 39 100/cystatin C –30; 32	Low Only crude 100/cystatin C Small population, n=30. No formal statistical testing between methods
Rigalleau et al 2008 [20] France	To assess if analysis of cystatin C improves the estimation of glomerular filtration rate (GFR) in patients with diabetes	Cross-sectional Patients with diabetes (n=124, 78 M/46 F, 36 T1D/88 T2D) with a wide range of GFR Age: 62±13 (19–83) years GFR: 56±35.3 (8–164) mL/min/1.73 m^2 GFR <60 mL/min/1.73 m^2 (n=76) (same patients as in [6])	s-creatinine (Jaffe method, not specified if IDMS-traceable) *eGFR (creatinine) equations* CG MDRD MC s-cystatin C (N Latex) Crude cystatin C eGFR (combined creatinine and cystatin C) Rule (composite)	Renal ^{51}Cr-EDTA clearance	All patients P30 and mean bias not given AUC (%, 95% CI) GFR <60 mL/min/1.73 m^2 CG 87 (81; 93) MDRD 94 (90; 98) MC 94 (90; 98) Cystatin C 96 (93; 99) Both s-cystatin C and eGFR (creatinine) MDRD perform better than eGFR (creatinine) CG, p<0.05 eGFR (combined creatinine and cystatin C). Rule (composite) has high precision (difference from measured GFR p=NS, but underestimate high GFR Bland-Altman p<0.001)	Low s-creatinine method not specified if IDMS-traceable. Only crude cystatin C

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Table 3.3.4 continued

Author Year Reference Country	Aim(s)	Study design, Population-characteristics (number of subjects/patients, male/female, age, GFR) Setting	Index test, eGFR (creatinine) equations eGFR (cystatin C) equations	Reference test	Results P30 (%, 95% CI)/ Mean bias mL/min/ 1.73 m^2	Study quality Comments
Willems et al 2009 [24] Belgium	To assess the predictive value of serum cystatin C in patients with diabetes with normal serum creatinine	Cross-sectional Patients with diabetes (n=67, 29 M/38 F, 21 T1D/46 T2D) with normal creatinine (men 0.72–1.17, women 0.55–0.96 mg/dL) Mean age: 52 (21–74) years GFR: 118±40 (44–328) mL/min/1.73 m^2	s-creatinine (Jaffe rate, IDMS-traceable) *eGFR (creatinine) equations* CG MDRD s-cystatin C (BNII) Crude cystatin C	^{51}Cr-EDTA plasma clearance	P30 and mean bias not given AUC (%, 95% CI) GFR <80 mL/min/1.73 m^2 CG 63 (51; 75) MDRD 83 (74; 92) s-cystatin C 75 (65; 85) s-cystatin C equal to MDRD and better than but no p-value reported	Low Only crude s-cystatin C. No formal statistical testing between methods reported

AUC = Area under the curve; BMI = Body mass index; CG = Cockcroft-Gault; CI = Confidence interval; CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; ^{51}CR-EDTA = Chromium Ethylenediaminettetracetate acid; eGFR = Estimated glomerular filtration rate; F = Female; GFR = Glomerular filtration rate; IDMS = Isotope dilution mass spectrometry; M = Male; MC = Mayo clinic equation; MDRD = Modification of diet in renal disease; p-creatinine = Plasma-creatinine; RMDRD = Revised modification of diet in renal disease; s-creatinine = Serum-creatinine; s-cystatin C = Serum-cystatin C; T1D = Type 1 diabetes; T2D = Type 2 diabetes

Table 3.3.5 *Patients with various diseases.*

Author Year Reference Country	Aim(s)	Study design Population-characteristics (number of subjects/patients, male/female, age, GFR) Setting	Index test eGFR (creatinine) equations eGFR (cystatin C) equations	Reference test	Results P30 (%, 95%CI) Mean bias mL/min/1.73 m^2	Study quality Comments
Beringer et al 2010 [11] USA	To compare the predictive performance of four equations for estimating GFR relative to measured GFR in patients with HIV	Cross-sectional HIV infected patients on treatment (n=22, 16 M/6 F) Mean age: 51 (42–60) years BMI: 27 (22–30) kg/m^2 GFR: 50–145 mL/min/1.73 m^2	s-creatinine (enzymatic, not specified if IDMS-traceable) *eGFR (creatinine) equations* CG MDRD s-cystatin C (Dade Behring) *eGFR (cystatin C) equation* Rule eGFR (combined creatinine and cystatin C) equation Stevens (combined)	^{125}Iothalamate plasma clearance	CG 50 (29; 71)/–9.2 MDRD 64 (44; 84)/–13.2 Rule 68 (48; 88)/–23.4 Stevens (combined) 77 (59; 95)/–16.8 No statistical differences between methods	Low s-creatinine method not specified if IDMS-traceable Small study, n=22. 2 patients with low BMI
Bölke et al 2011 [13] Germany	To determine the best method for GFR estimation in head neck cancer (HNC) patients in order to discriminate for the cut-off of 60 mL/min/1.73 m^2	Cross-sectional Patients with head and neck cancer (HNC) (n=52, 22 M/30 F) No age given GFR: 37–105 mL/min/1.73 m^2 Patients with high-dose steroids (type and dose not defined or given) were excluded from the study	p-creatinine (Crea Plus®, enzymatic, IDMS-traceable) *eGFR (creatinine) equations* CG MDRD Wright s-cystatin C (particle-enhancing immunonephelometry, N latex CysC, Siemens) eGFR (cystatin C) equations Hoek Larsson Dade-Behring	^{51}Cr-EDTA plasma clearance	CG 50 (36; 64) MDRD 63 (50; 76) Wright 79 (68; 90) Hoek 81 (70; 92) Larsson 48 (34; 64) Dade-Behring 40 (27; 53) Mean bias not given	Moderate Some uncertainty regarding s-creatinine method

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Table 3.3.5 *continued*

Author Year Reference Country	Aim(s)	Study design Population-characteristics (number of subjects/patients, male/female, age, GFR) Setting	Index test eGFR (creatinine) equations eGFR (cystatin C) equations	Reference test	Results P30 (%, 95%CI) Mean bias mL/min/ 1.73 m^2	Study quality Comments
Blufpand et al 2011 [12] The Netherlands	To assess the relationship of cystatin C and creatinine-based equations with renal function in children receiving treatment for malignancy	Cross-sectional Children during, or up to 3 months after, treatment for malignancy (n=68, 50 M/18 F) Mean age: 3.2 (1.4–7.8) years *GFR 114±25.5 mL/min/1.73 m^2* >90 mL/min/1.73 m^2 (n=53) 60–90 mL/min/1.73 m^2 (n=13) <60 mL/min/1.73 m^2 (n=2) *Aetiology of malignancy* Leukemia/lymphoma (n=9) Brain tumour (n=18) Neuroblastoma (n=3) Osteosarcoma (n=2) Hepatoblastoma (n=5) Rhabdomyosarcoma (n=4) Wilms tumour (n=1) Retinoblastoma (n=26) Patients were excluded if they had received gluco-corticosteroids within 10 days prior to clearance	p-creatinine (kinetic Jaffe method converted to IDMS standard) *eGFR (creatinine) equation* "new" Schwartz (2009) s-cystatin C (particle-enhancing immu-nonephelometry assay PENIA; Siemens on a Behring Nephelometer II) *eGFR (cystatin C) equation* Filler	Plasma Inulin clearance	Schwartz 72 (61; 83)/–14.3 Filler 82 (73; 91)/–7.3	Moderate Some uncertainty regarding p-creatinine method No formal statistical testing between methods reported

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Table 3.3.5 *continued*

Author Year Reference Country	**Aim(s)**	**Study design Population-characteristics (number of subjects/patients, male/female, age, GFR) Setting**	**Index test eGFR (creatinine) equations eGFR (cystatin C) equations**	**Reference test**	**Results P30 (%, 95%CI) Mean bias mL/min/ 1.73 m²**	**Study quality Comments**
Damman et al 2012 [14] The Netherlands	To assess the relationship of cystatin C and creatinine-based equations with renal function in patients with chronic heart failure	Cross-sectional Clinically stable systolic CHF patients with a left ventricular ejection fraction (LVEF) <45% (n=102) GFR: 75±27 mL/min/1.73 m² GFR ≥60 mL/min/1.73 m² (n=not given) GFR ≥30 mL/min/1.73 m² (n=not given)	p-creatinine (automated enzymatic method, Eastman Kodak) *eGFR (creatinine) equations* MDRD MDRD (simplified) s-cystatin C (immune-nephelometry, Dade Behring BNII) 1/cystatin C	^{125}Iothala-mate renal clearance during constant infusion	P30 and mean bias not given AUC (%) (95%CI) GFR ≥60 mL/min/1.73 m² MDRD 98 (96; 100) MDRDs 98 (96; 100) 1/cystatin C 95 (90–100) GFR ≥30 mL/min/1.73 m² MDRD 98 (95; 100) MDRDs 98 (95; 100) 1/cystatin C 99 (98; 100) No significant differences between AUCs at any level of GFR	Low p-creatinine method not specified if IDMS-traceable
Delanaye et al 2009 [16] Belgium	To study precision of cystatin C-based equations in patients with anorexia nervosa	Cross-sectional Patients with anorexia nervosa (n=27, 2 M/25 F) Age: 30±13 years BMI: 15±2 kg/m² GFR: 68±23 (13–134) ml/min	s-creatinine (compensated Jaffe, IDMS-traceable) *eGFR (creatinine) equations* CG MDRD s-cystatin C (immuno-nephelometric, Dade Behring) *eGFR (cystatin C) equations* Rule Larsson Levey1 Levey2 Levey3	^{51}Cr-EDTA plasma clearance	CG 63 (45; 81) MDRD 30 (13; 47) Rule 56 (37; 75) Larsson 30 (13; 47) Levey1 30 (13; 47) Levey2 26 (10; 42) Levey3 15 (2; 28) Both eGFR (creatinine) and eGFR (cystatin C) overestimate GFR in anorexia especially when GFR ≤60 ml/min (mean bias 18–51 ml/min)	Low Small study. No formal statistical testing between groups. P30 not given in subgroup ≤60 ml/min

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Table 3.3.5 *continued*

Author Year Reference Country	Aim(s)	Study design Population-characteristics (number of subjects/patients, male/female, age, GFR) Setting	Index test eGFR (creatinine) equations eGFR (cystatin C) equations	Reference test	Results P30 (%, 95%CI) Mean bias mL/min/1.73 m^2	Study quality Comments
Olsson et al 2010 [18] Sweden	To decide whether cystatin C or creatinine eGFR is preferred in monitoring lithium treated patients	Cross-sectional All patients on lithium treatment in a psychiatric clinic (n=201, 84 M/117 F) Age: 53±14 (23–90) years Duration of lithium treatment Age: 12±9 (0.3–42) years GFR: 82±19 (25–138) mL/min/1.73 m^2 111 patients performed iohexol plasma clearance	s-creatinine (enzymatic, not specified if IDMS-traceable) *eGFR (creatinine) equation* MDRD s-cystatin C (Dako) *eGFR (cystatin C) equation* Grubb 2005	Iohexol plasma clearance	P30 not given AUC (%, 95% CI) MDRD Sensitivity 72 (66; 78) Specificity 85 (80; 90) Mean bias –3.3 (–33; 27) Grubb 2005 Sensitivity 61 (54; 68) Specificity 94 (91; 97) Mean bias 14.6 (–26; 55) eGFR (cystatin C) not superior to eGFR (creatinine) MDRD in monitoring lithium treated patients	Low s-creatinine, but not s-cystatin C blood sampling timed with iohexol clearance. No formal statistical testing between methods and formulas presented
Rombach et al 2010 [21] The Netherlands	To determine the value of creatinine and cystatin C-based formulas for the estimation of GFR in Fabry patients	Cross-sectional Patients with Fabrys disease treated with algasidase α or β (n=36, 20 M/16 F) Mean age: 46.5 (17.1–72.5) years GFR: 15.5–148.6 mL/min/1.73 m^2	S- creatinine (enzymatic, IDMS-traceable) *eGFR (creatinine) equations* CG MDRD aMDRD CKD-EPI s-cystatin C (N latex kit) *eGFR (cystatin C) equations* Larsson Hoek Rule *eGFR (combined creatinine and cystatin C) equation* Stevens (combined)	^{125}Iothalamate plasma clearance	Mean bias not given CG 69 (54; 84) MDRD 74 (60; 88) aMDRD 78 (64; 92) CKD-EPI 74 (60; 88) Larsson 78 (64; 92) Hoek 80 (67; 93) Rule 88 (77; 99) Stevens (combined) 82 (69; 95)	Low Small study. Plasma samples not drawn at the same time as reference test was performed. No formal statistical testing between methods and formulas presented

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Table 3.3.5 *continued*

Author Year Reference Country	**Aim(s)**	**Study design Population-characteristics (number of subjects/patients, male/female, age, GFR) Setting**	**Index test eGFR (creatinine) equations eGFR (cystatin C) equations**	**Reference test**	**Results P30 (%, 95%CI) Mean bias mL/min/ 1.73 m²**	**Study quality Comments**
Segarra et al 2011 [22] Spain	To evaluate the performance of the CKD-EPI equation and four cystatin C-based equations compared with measured GFR in hospitalized patients with stable renal function including malnourished patients and patients with liver cirrhosis	Cross-sectional Random sample of hospitalized patients (n=3114) Malnourished patients (biochemical definition*) (n=1 555) GFR: 76±26 mL/min/1.73 m² Liver cirrhosis or Child's Class C** (n=63) GFR: 89±41 mL/min/1.73 m² * Elmore's equation (total lymphocyte count, serum albumin level) ** Child-Pugh classification	p-creatinine (Roche Lab "compensated" IDMS-traceable) *eGFR (creatinine) equation* CKD-EPI s-cystatin C (immune-nephelometry, Dade Behring BNII) *eGFR (cystatin C) equations* Stevens Stevens (age) Grubb *eGFR (combined creatinine and cystatin C) equation* Stevens (combined)	Iohexol plasma clearance	Malnourished patients CKD-EPI 70 (66; 74)/5.9 Stevens 78 (74; 82)/0.6 Stevens (age) 85 (82; 88)/1.0 Grubb 86 (83; 89)/1.3 Stevens (combined) 58 (54; 62)/7.8 Liver cirrhosis or Child's Class C CKD-EPI 77 (73; 81)/4.2 Stevens 80 (76; 84)/0.1 Stevens (age) 79 (75; 83)/−0.7 Grubb 79 (75; 83)/−0.3 Stevens (combined) 76 (72; 80)/8.7	Low No population characteristics in subgroups. Definition of malnutrition questionable. Plasma clearance may be inappropriate in patients with severe ascites. No formal statistical testing between different methods or formulas
Wang et al 2009 [23] China	To assess cystatin C as an early marker of renal dysfunction (GFR) after CABG operation	Cross-sectional Early postoperative CABG-patients (n=61, 35 M/26 F) Age: 65.1±11.7 years GFR: 104±25 mL/min/1.73 m² GFR <60 mL/min/1.73 m² (n not given)	s-creatinine (kinetic Jaffe, IDMS-traceable) *eGFR (creatinine) equations* CG MDRD s-cystatin C (particle-enhanced immuno-nephelometric method Dade Behring) 1/s-cystatin C	^{51}Cr-EDTA plasma clearance	P30 and mean bias not given GFR <60 mL/min/1.73 m² AUC (%, 95% CI) CG 85 (76; 94) MDRD 84 (75; 93) 1/s-Cystatin C 96 (91; 100) 1/s-Cystatin C performed better than CG and MDRD, p=0.033	Low Only crude 1/s-cystatin C

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Table 3.3.5 *continued*

Author Year Reference Country	Aim(s)	Study design Population-characteristics (number of subjects/patients, male/female, age, GFR) Setting	Index test eGFR (creatinine) equations eGFR (cystatin C) equations	Reference test	Results P30 (%, 95%CI) Mean bias mL/min/ 1.73 m^2	Study quality Comments
Xirouchakis et al 2011 [25] United Kingdom	To compare cystatin C and creatinine GFR formulas with measured GFR by ^{51}Cr-EDTA in cirrhotic patients of different aetiology	Cross-sectional Pooled patients with liver cirrhosis (n=74, 46 M/28 F) Age: 49±9.2 years GFR: 15–156 mL/min/1.73 m^2 26 patients with GFR ≤70 mL/min/1.73 m^2 *Aetiology of liver cirrhosis* Alcohol (n=12) Viral (n=28) Cryptogenic (n=13) PBC (n=14) Autoimmune (n=3) HCC (n=15) Other (n=4)	s-creatinine (compensated kinetic Jaffe, enzymatic Jaffe, not specified if IDMS-traceable) *eGFR (creatinine) equation* MDRD s-cystatin C (immunonephelometry, Dade Behring) *eGFR (cystatin C) equation* Hoek	^{51}Cr-EDTA plasma clearance	Mean bias not given MDRD 64 (53; 75) Hoek 68 (57; 79) p<0.05 GFR ≤70 mL/min/1.73 m^2 P30 (%, 95% CI) CG 61 (42; 80) MDRD 46 (27; 65) Hoek 42 (23; 61) eGFR (cystatin C) Hoek no additional benefit over eGFR (creatinine) MDRD Both eGFR (cystatin C) and eGFR (creatinine) overestimate measured GFR especially in patients with GFR ≤70 mL/min/1.73 m^2 (no data given)	Low Different creatinine methods, not specified if IDMS-traceable. No statistics given. No formal statistical testing between methods and formulas presented. Plasma clearance may be inappropriate in patients with severe ascites. Heterogeneous population. Small subgroup

aMDRD = Abbreviated modification of diet in renal disease; AUC = Area under the curve; BMI = Body mass index; CABG = Coronary artery bypass graft; CG = Cockcroft-Gault; CHF = Chronic heart failure; CI = Confidence interval; CKD-EPI = Chronic Kidney Disease Epidemiology Collaboration; ^{51}CR-EDTA = Chromium Ethylenediaminetetracetate acid; eGFR = Estimated glomerular filtration rate; F = Female; GFR = Glomerular filtration rate; HIV = Human immunodeficiency virus; IDMS = Isotope dilution mass spectrometry; M = Male; MDRD = Modification of diet in renal disease; p-creatinine = Plasma-creatinine; s-creatinine = Serum-creatinine; s-cystatin C = Serum-cystatin C