Electronic Tools to Support Creatinine Clearance Calculation for Direct-Acting Oral Anticoagulants (DOAC)

Summary:

- **Always use creatinine clearance for direct-acting oral anticoagulants (DOAC) dose calculations and NOT eGFR** as recommended by the MHRA and SPCs for relevant DOAC. Use of eGFR for dosing of DOACs is known to increase risk of bleeding events as a consequence of overestimating renal function.
- **Use either the SystmOne renal disease calculator or MD+Calc for calculating creatinine clearance as per your current practice.**
- **For overweight/obese patients**, the result of SystmOne CrCl is modified for overweight and obese patients, using **adjusted body weight**. MD+Calc presents value in a range using adjusted body weight (AdBW) and ideal body weight (IBW) due to the controversy that exists over which form of weight is most appropriate to use.
- When interpreting creatine clearance, ensure the renal function is in a steady state and an up-to-date weight and serum creatinine are documented. **Take into account the trend of creatine clearance changes rather than point estimated value while making any relevant dosage adjustment**.
- **Caution of clinical judgement and extra interpretation may require when the range falls within a dose adjustment boundary.** Specialist Anticoagulant advice for these patients should be obtained from our local hospitals:
  - **GWH**: gwh.anticoag.clinic@nhs.net or sarah.bond6@nhs.net Tel: 01793 60434
  - **RUH**: ruh-tr.AnticoagulationTeam@nhs.net or nathan.hutchinson-jones@nhs.net or via Cinapsis
  - **SFT**: nicolamcquaid@nhs.net or sft.anticoagulation.service@nhs.net

Background

Estimated glomerular filtration rate (eGFR) and creatinine clearance (CrCl) are two estimates of renal function available to prescribers. Clinical laboratories routinely report renal function in adults based on eGFR normalised to a body surface area of 1.73 m2. For most drugs and most situations, eGFR is an acceptable estimate of renal function.

However, eGFR can overestimate renal function compared with CrCL in some patient groups or clinical situations. This overestimation can result in patients receiving higher than recommended doses of their medicine in relation to their renal function. CrCl should be considered for dosage adjustment of medicines that are substantially renally excreted and have a narrow therapeutic index. In particular, CrCl should always be used to guide dose adjustment for DOACs.

What is the difference between using SystmOne Renal Disease Calculator compared to MD+Calc?

The Cockcroft-Gault equation is used to calculate CrCL but may be less accurate depending on a patient's body weight and BMI; by including patient's height in the SystmOne Renal Disease Calculator and MD+Calc tools can calculate the patients BMI which means they can establish if it is necessary to provide a modified estimate for patients with extremes of body weight.

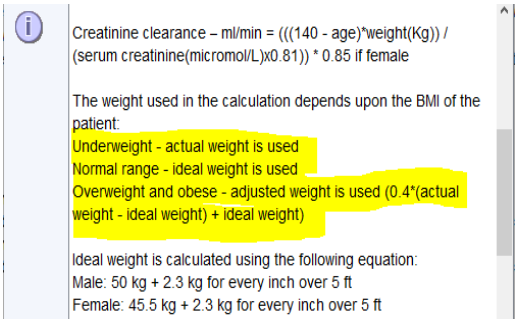
Both MD+Calc and the Renal Disease Calculator in SystmOne use the same algorithm to calculate CrCl in underweight, normal weight and overweight/obese patients as per the following screenshots:

MD+Calc:

Based on several papers and expert opinions, we provide adjustments to the Cockcroft-Gault equation based on body weight and BMI, as it appears to become less accurate in weight extremes (underweight and particularly overweight/obesity). As recommended by Brown et al and Winter et al, adjustments and estimates are made as follows:

Underweight	BMI <18.5	Calculation uses **actual**/total body weight (i.e., no adjustment)
Normal weight	BMI 18.5-24.9	Calculation uses **ideal** body weight, range uses actual body weight
Overweight / obese	BMI ≥25	Calculation uses **adjusted** body weight, range uses ideal body weight

SystmOne Renal Disease Calculator:

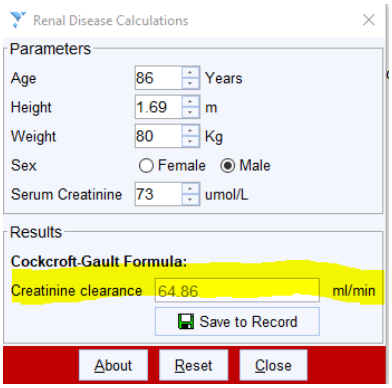


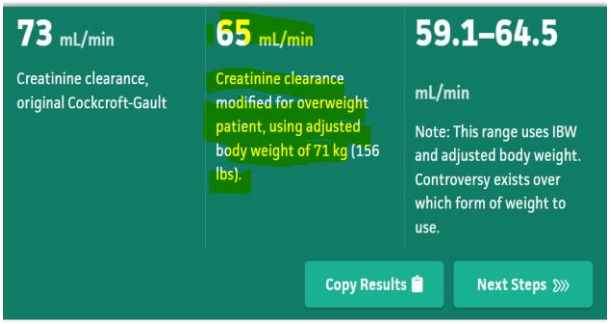
The BNF recommends using IBW to calculate the CrCl. Except in underweight patients where actual body weight (ABW) weight should be used.

The MHRA guideline recommends that we should be calculating CrCl to access renal function and potential dose adjustments in patients taking DOACs and not using the eGFR. It indicates MD+Calc as a suitable tool for calculating CrCl but it does so in a way not to exclude the use of other tools. It makes no suggestion to what weight should be used in the calculation other than to say that 'MD+Calc offers the ability to use adjusted body weight, ideal body weight or actual body weight as appropriate'. See MHRA guidance for more details.

The SystmOne and MD+Calc present the values in the following ways:

Example 1 **Patient with BMI 28 (overweight):**



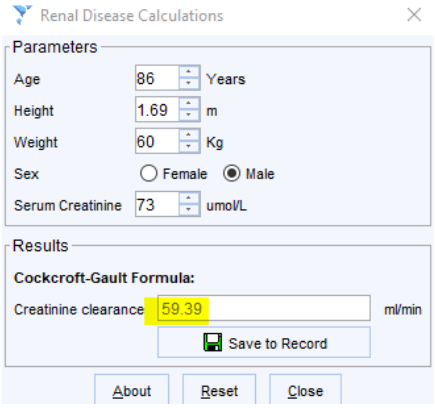


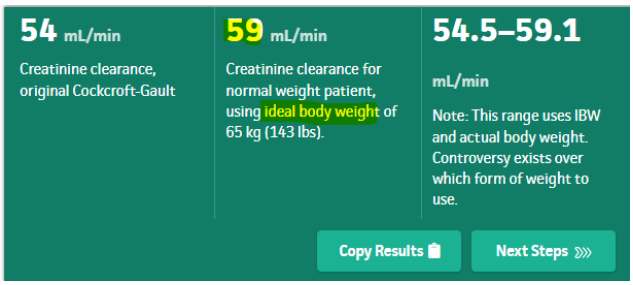
Result of SystmOne CrCl modified for overweight and obese patient, using **adjusted body weight**.

MD+Calc CrCl presented the result of CrCl modified for overweight patient using adjusted body weight AND presented a value range between AdBW and IBW.

MD+Calc presents you with a value range using **adjusted body weight (AdBW)** and **ideal body weight (IBW)** for overweight/obese patients, whereas the SystmOne renal disease calculator uses an AdBW only. Controversy still exists over which form of weight is most appropriate to use. Caution of clinical judgement and extra interpretation may require when the range falls within a dosage adjustment boundary.

Example 2: **Patient with BMI 21 kg/m2 (normal BMI):**

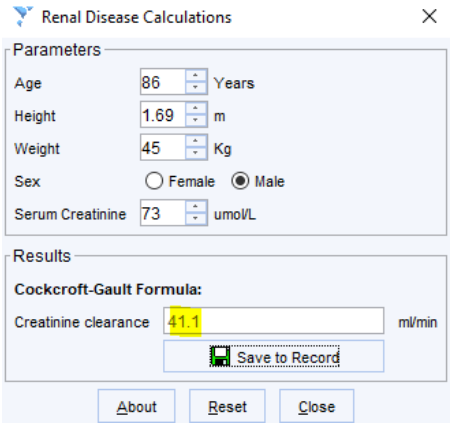


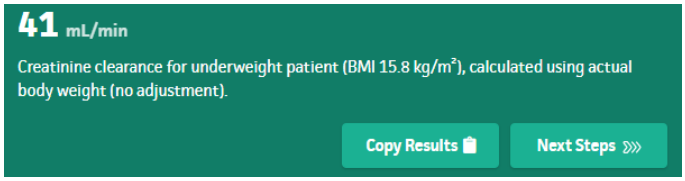


Result of SystmOne CrCl calculated for patient with normal range of BMI, using **ideal body weight**.

MD+Calc CrCl presented the result of CrCl for normal weight patient, using ideal body weight AND presented a value range between IBW and actual body weight.

Example 3: **Patient with BMI 12.4 kg/m2 (underweight BMI):**





Result of SystmOne CrCl calculated for patient with underweight BMI, using **actual body weight**.

MD+Calc CrCl presented the result of CrCl for underweight patient, calculated using actual body weight.

Reference Sources

British National Formulary (Online). *BNF is only available in the UK*. [online] NICE. Available at: https://bnf.nice.org.uk/medicines-guidance/prescribing-in-renal-impairment/#issues-encountered-in-renal-impairment.

MDCalc (Online). *Creatinine Clearance (Cockcroft-Gault Equation)*. [online] MDCalc. Available at: https://www.mdcalc.com/calc/43/creatinine-clearance-cockcroft-gault-equation.

Medicines and Healthcare products Regulatory Agency (2019). *Prescribing medicines in renal impairment: using the appropriate estimate of renal function to avoid the risk of adverse drug reactions*. [online] GOV.UK. Available at: https://www.gov.uk/drug-safety-update/prescribing-medicines-in-renal-impairment-using-the-appropriate-estimate-of-renal-function-to-avoid-the-risk-of-adverse-drug-reactions.