Electronic Tools for Creatinine Clearance Calculation to Support Dosing of Direct-Acting Oral Anticoagulants (DOACs)

Summary:

- This is an updated to the previous version of this BSW document to cover the NEW renal disease calculator included within SystmOne in October 2023. The old SystmOne renal disease calculator will be removed from SystmOne clinical tools in subsequent SystmOne maintenance updates.
- **Always use creatinine clearance for direct-acting oral anticoagulants (DOAC) dose calculations and NOT eGFR** as recommended by the MHRA and SPCs for relevant DOACs. 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.**
- **Based on several papers (Winter et al 2012 and Brown et al 2013) and local expert opinions, BSW ICB support an adjustment to the Cockcroft-Gault equation based on patient's BMI, as it appears to become less accurate in weight extremes (underweight and particularly overweight/obesity). Based on local experts' consensus, adjustments and estimates should be considered as follow:**

	Body Mass Index (kg/m²)	Adjustments and Estimates
Underweight or Normal weight or Overweight	BMI < 30	Calculate CrCl by using **actual** body weight
Obese	BMI ≥30	Calculate CrCl by using **adjusted** body weight

- When interpreting creatine clearance, ensure the renal function is in a steady state and an up-to-date serum creatinine are documented. **Take into account the trend of creatine clearance changes rather than point estimated value while making any relevant dosage adjustment**.
- **When interpreting BMI, ensure an up-to-date weight (in last 12 months) and height (in last 5 years) are documented**. Take into account any other unintentional rapid weight changes, sign of acute stress or a serious illness that may require most accurate available measurements.
- **Caution in clinical judgement and extra interpretation may be 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.

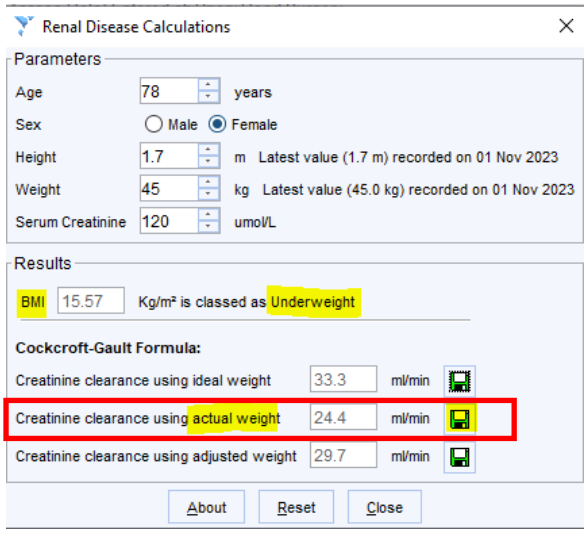
However, eGFR can overestimate renal function compared with CrCl in some patient groups or clinical situations. This overestimation can result in patients receiving higher than recommended doses of their medicine in relation to their renal function. CrCl should be considered for dosage adjustment of 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.

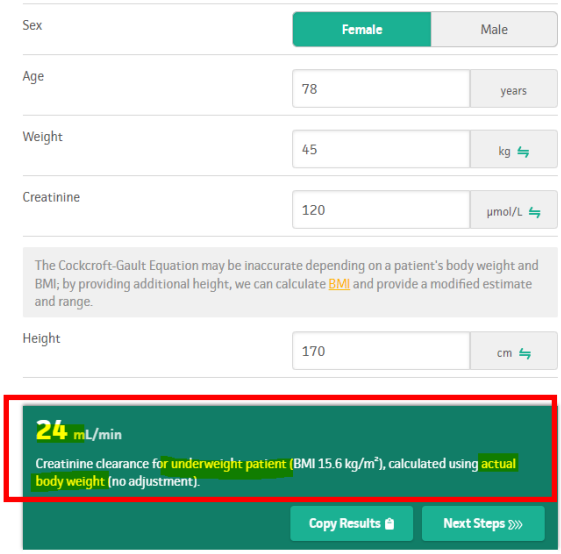
Practical consideration when utilising the NEW SystmOne Renal Disease Calculator and MD+Calc

There are currently NO national consensus on how to adjust the Cockcroft-Gault equation based on a patient's weight. The BNF recommends using ideal body weight to calculate the CrCl. Except in underweight patients where actual body weight should be used. The MHRA guideline recommends that we should be calculating CrCl to assess 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.

Based on several papers (Winter et al 2012 and Brown et al 2013) and local expert opinions, BSW ICB support an adjustment to the Cockcroft-Gault equation based on a patient's BMI, as it appears to become less accurate in weight extremes (underweight and particularly overweight/obesity). Based on local experts' consensus, adjustments and estimates should be considered as follow:

Underweight, BMI < 18.5 kg/m²

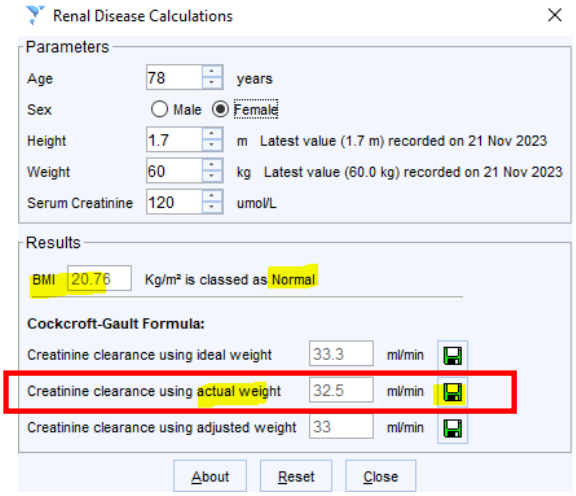




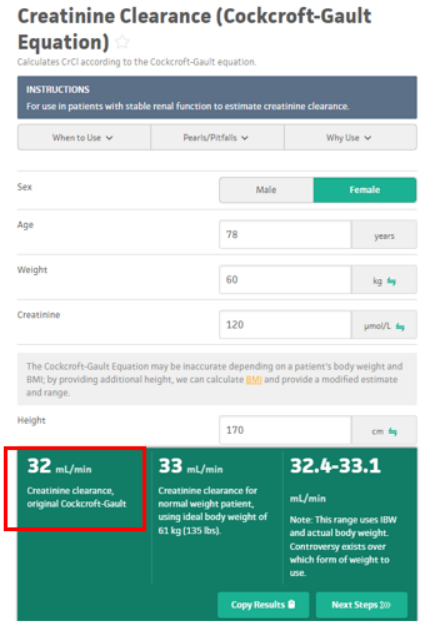
Based on local experts' consensus, for underweight patient (BMI <18.5 kg/m²) consider calculating CrCl by using **actual body weight.**

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

Normal weight or overweight 30 kg/m² > BMI > 18.5 kg/m²

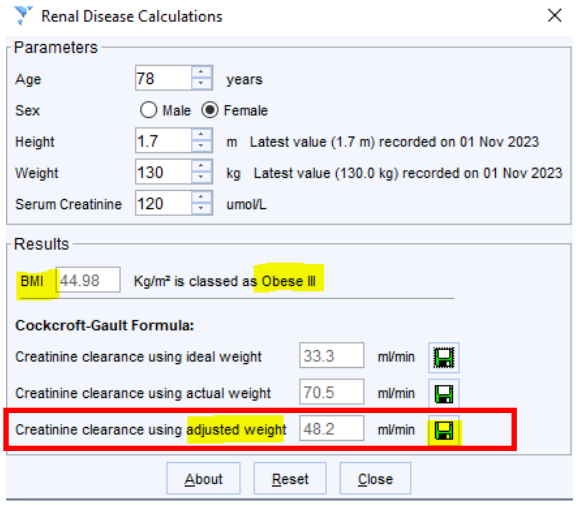


Based on local experts' consensus, for normal weight or overweight patient (BMI 18.5- 29.9 kg/m²) consider calculating CrCl by using **actual body weight**

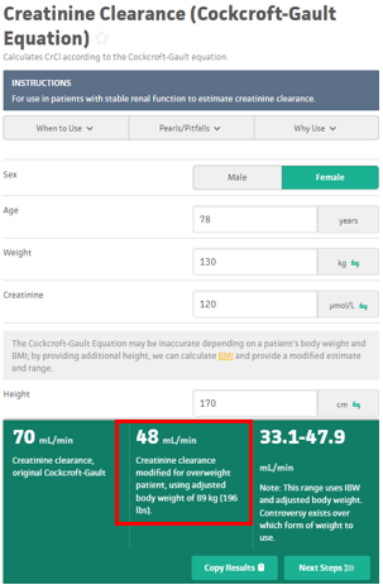


MD+Calc presents the result of CrCl for a normal weight patient, using **actual** and ideal body weight as a 'value range' due to lack of consensus over which form of weight to use.

Overweight/Obese, BMI ≥30 kg/m²



Based on local experts' consensus, for overweight/obese patients (BMI ≥30 kg/m²) consider calculating CrCl by using **adjusted body weight.**



MD+Calc presents the result of CrCl for obese patient, calculated using **adjusted body weight**, and also presents a value range due to lack of consensus over which form of weight to use.

Exercise caution in clinical judgement and interpretation when the range falls within a dosage adjustment boundary. For instance, in the obese scenario, we observed that the CrCl; results by actual weight and adjusted weight falls into a different Edoxaban BNF dosage boundary for prophylaxis of stroke. Based on local experts' consensus, use the result generated by use of the adjusted weight or seek advice from your local Anticoagulant Specialist in the event of any uncertainty regarding which dose is best to use.

Specialist Anticoagulant advice for these patients can also 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

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.

Brown, D.L., Masselink, A.J. and Lalla, C.D. (2013). Functional Range of Creatinine Clearance for Renal Drug Dosing: A Practical Solution to the Controversy of Which Weight to Use in the Cockcroft-Gault Equation. *Annals of Pharmacotherapy*, 47(7-8), pp.1039–1044. doi:https://doi.org/10.1345/aph.1s176.

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.

Winter, M.A., Guhr, K.N. and Berg, G.M. (2012). Impact of Various Body Weights and Serum Creatinine Concentrations on the Bias and Accuracy of the Cockcroft-Gault Equation. *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, 32(7), pp.604–612. doi:https://doi.org/10.1002/j.1875-9114.2012.01098.x.