

## Calculating Renal Function for Patients Prescribed DOACs\* in Primary Care

This paper has been issued as a supplement to the ‘Anticoagulation for Stroke Prevention in Non-Valvular Atrial Fibrillation: Joint primary and secondary care guidance (SPAF guidelines)’.

For further details re DOAC dosing and monitoring please refer to [SPAF guidelines](#).<sup>1</sup>

\*DOAC i.e. direct oral anticoagulants previously known as NOAC non-vitamin K oral anticoagulants.

### Creatinine Clearance Calculation

It is important to calculate the creatinine clearance (CrCl) for patients prescribed DOACs to determine the dose as these drugs are renally cleared and accumulation of the drug can have severe implications. Use of eGFR for dosing of DOACs is known to increase the risk of bleeding events as a consequence of overestimating renal function and should not be used.<sup>2</sup> ([MHRA 2019](#)).

The Cockcroft and Gault equation is used to calculate the CrCl:

A= 1.04 (female) or  
1.23 (male)

$$\text{Calculated CrCl (ml/min)} = \frac{(140 - \text{age}) \times \text{weight (kg)} \times \mathbf{A}}{\text{serum creatinine (micromol/L)}}$$

There is ongoing debate regarding the best way to adjust the Cockcroft and Gault (CG) equation to account for extremes of body weight that affect the production of creatinine. Using an adjusted body weight is considered to improve the accuracy of the CG equation; however, the suitability of these adjustments for DOACs has been questioned.<sup>3</sup>

- Using a lower dose when patients do not meet the criteria for dose reduction may increase the risk of embolic events and result in potentially preventable strokes.
- Using a higher dose where the renal function indicates that a dose reduction is necessary may increase the risk of bleeding.

Sheffield CCG recommends the use of the clinical systems renal function calculators, which use the CG equation to estimate CrCl but modify the body weight in different ways. This is discussed further under the individual clinical systems sections (see [appendix](#)). Either tool is appropriate provided clinical judgement is used to interpret the result.

It must be recognised that the calculated CrCl is an **estimate** and should not be considered in isolation. Decisions on dosing should always take into account the calculated renal function in conjunction with an estimate of stroke risk, bleeding risk and individual patient factors.

### Clinical system renal function calculators

See [appendix](#) to clarify where the calculators can be found in each system and guidance on their use. Users of EMIS Web are advised to note the changes to the calculator for DOACs since the previous version of this guidance.<sup>6</sup>

Links to:     [SystemOne](#)     [EMIS Web](#)

## Interface issues

As noted above, the Cockcroft and Gault equation provides an **estimate** of CrCl and clinical judgement is always required in determining the dose and suitability of a DOAC. The dose or choice of drug determined in secondary care may differ from that calculated in primary care in a small number of cases. This may occur if adjustment to the equation has not been made for patients with extremes of body weight, or if the eGFR rather than the calculated CrCl has been used in secondary care, or due to other individual patient factors. In these cases the primary care clinician is advised to review the dose or drug and make amendments when judged clinically appropriate.

## Further guidance on DOACs in renal impairment

- All DOACs are contraindicated in CrCl <15ml/min; warfarin is the anticoagulant of choice in these patients. (Note dabigatran is contraindicated in CrCl <30ml/min).
- For CrCl 15ml/min to 50ml/min: the level of CrCl where dosage adjustments are required varies for the individual DOACs and in some cases is dependent on other patient factors; details are given in the [SPAF guidelines](#), summarised from the SPC for the individual drugs, and reproduced in [Table 1](#) (page 3).

The SPCs are available at <https://www.medicines.org.uk/emc/> and should be consulted for indications other than SPAF.

## References

1. Anticoagulation for Stroke Prevention in Non-Valvular Atrial Fibrillation: Joint primary and secondary care guidance. Sheffield Teaching Hospitals NHS Foundation Trust and NHS Sheffield CCG August 2018  
[https://www.intranet.sheffieldccg.nhs.uk/Downloads/Medicines%20Management/prescribing%20guidelines/Anticoagulation\\_for\\_SPAF.pdf](https://www.intranet.sheffieldccg.nhs.uk/Downloads/Medicines%20Management/prescribing%20guidelines/Anticoagulation_for_SPAF.pdf)
2. MHRA: Prescribing medicines in renal impairment: using the appropriate estimate of renal function to avoid the risk of adverse drug reactions. 18 October 2019  
<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>
3. Specialist Pharmacy Service. Direct Acting Oral Anticoagulants (DOACs) in Renal Impairment: Practice Guide to Dosing Issues. 24th July 2019  
<https://www.sps.nhs.uk/wp-content/uploads/2019/07/DOAC-dosing-in-renal-impairment-vs2-July-2019-AW.pdf>
4. Electronic Medicines Compendium <https://www.medicines.org.uk/emc/>
5. British National Formulary- NICE <https://bnf.nice.org.uk/>
6. Cockcroft-Gault Creatinine Clearance Equation template (EMIS Web)  
[https://www.emisnow.com/csm?id=kb\\_article&sys\\_id=b9791ec61b55b7048ceaa64c2e4bc8](https://www.emisnow.com/csm?id=kb_article&sys_id=b9791ec61b55b7048ceaa64c2e4bc8)

[Appendix](#) – Calculators on clinical systems – see page 5-8

**Table 1 DOAC dose reductions for SPAF**

| <b>DOAC</b> | <b>Full dose</b> | <b>Dose reduction</b>   |
|-------------|------------------|---|
| Apixaban    | 5mg BD           | <p>Reduce dose to:<br/> <b>2.5mg BD</b> in CrCl 15-29ml/min, or if <b>two</b> or more of the following criteria apply:</p> <ul style="list-style-type: none"> <li>• Age ≥ 80 years</li> <li>• Body weight ≤ 60kg</li> <li>• Serum creatinine ≥133 micromole/L</li> </ul> <p><b>Do NOT use if CrCl &lt;15ml/min</b></p>  |
| Dabigatran  | 150mg BD         | <p>Reduce dose to:<br/> <b>110mg bd</b> if age ≥ 80 years or taking concomitant verapamil</p> <p>Consider reducing dose to 110mg BD if <b>one</b> or more of the following apply:</p> <ul style="list-style-type: none"> <li>• Age 75-80 yrs</li> <li>• CrCl 30-50ml/min</li> <li>• PMH: gastritis, esophagitis, gastroesophageal reflux</li> <li>• Increased risk of bleeding</li> </ul> <p><b>Do NOT use if CrCl &lt;30ml/min</b></p> |
| Edoxaban    | 60mg OD          | <p>Reduce dose to:<br/> <b>30mg od</b> if <b>one</b> or more of the following apply:</p> <ul style="list-style-type: none"> <li>• CrCl 15-50ml/min</li> <li>• Weight ≤ 60kg</li> <li>• Concomitant use of the following P-glycoprotein (P-gp) inhibitors: ciclosporin, dronedarone, erythromycin, or ketoconazole.</li> </ul> <p><b>Do NOT use if CrCl &lt;15ml/min</b></p>   |
| Rivaroxaban | 20mg OD          | <p>Reduce dose to:<br/> <b>15mg od</b> if CrCl &lt;50ml/min</p> <p><b>Do NOT use if CrCl &lt;15ml/min</b></p>   |

## **Version history**

Version 3: January 2020

Written by:

Shameila Afsar, Clinical Practice Pharmacist

Hilde Storkes, Formulary Pharmacist

Medicines Optimisation Team

Version 1 approved by APG: 20<sup>th</sup> April 2017

Version 2 approved by APG: 20<sup>th</sup> September 2018

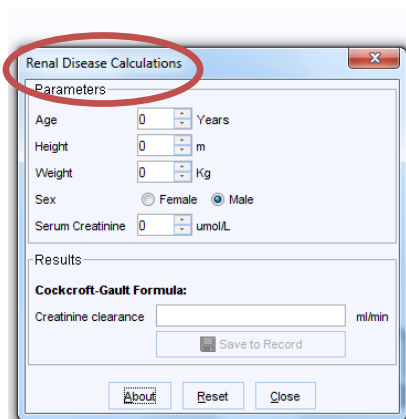
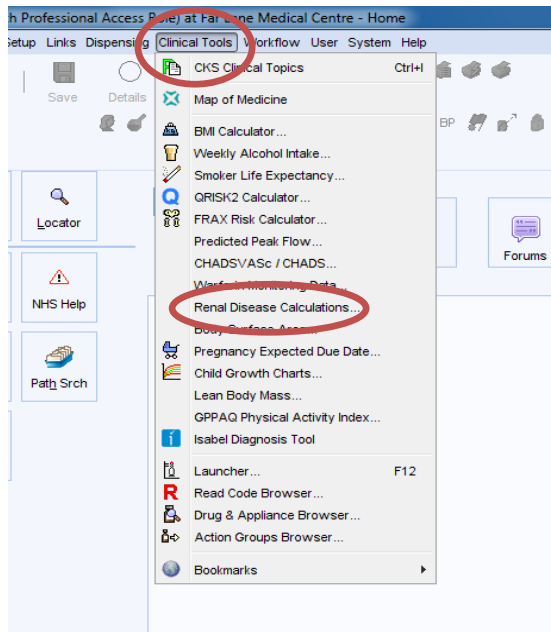
Version 3 approved by APG: 16<sup>th</sup> January 2020

Review date: January 2025

## Appendix: Calculators on clinical systems

### SystemOne

For SystemOne- the renal function calculator can be found in Clinical Tools, Renal disease calculations.



The patient's clinical parameters are pulled directly into the CG calculator from the clinical system. Please ensure the patient's height and weight are from the last 12 months (this will allow a more accurate result for the elderly patients, where a drop in height may be noted). Also ensure the serum creatinine is from the last 3, 6, or 12 months depending on the degree of renal impairment (see [SPAF guidelines](#) on-going monitoring page 8-9).

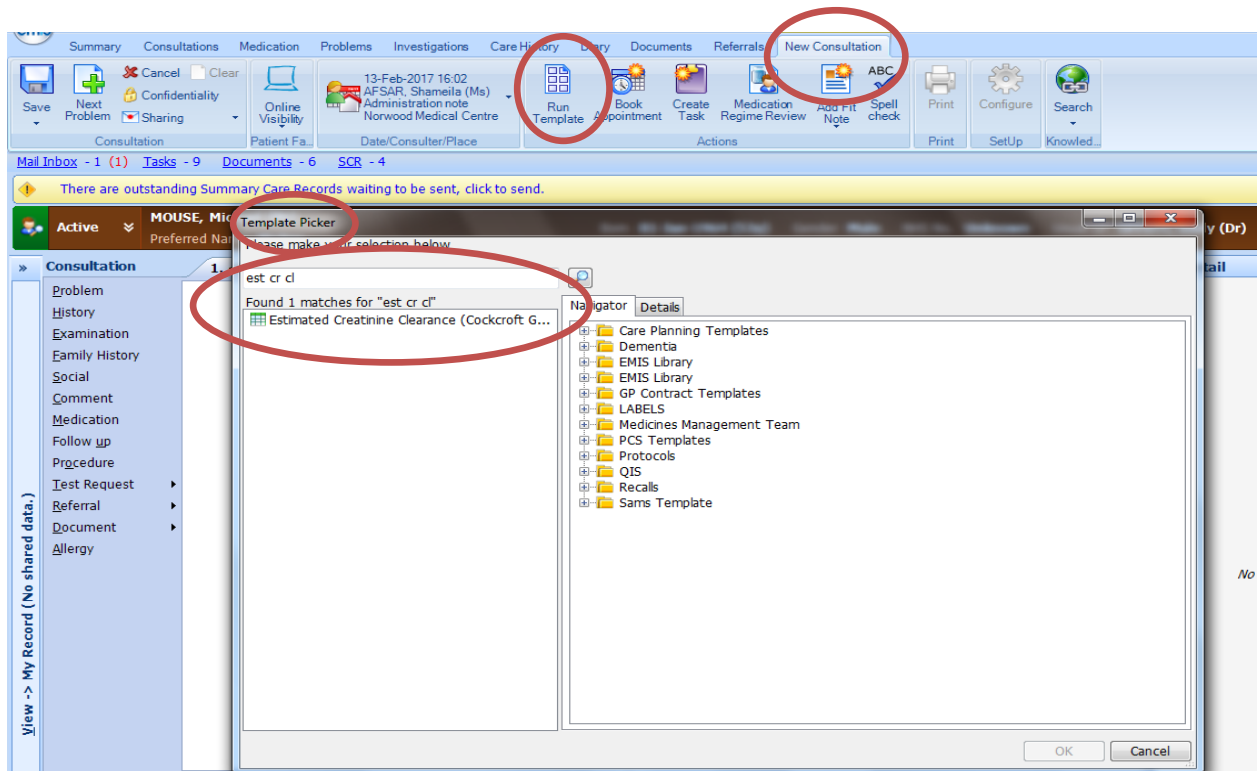
The calculator uses an adjustment to actual body weight, based on BMI, provided that a height is recorded. Click on the 'About' tab for details of the weight adjustment used. If a

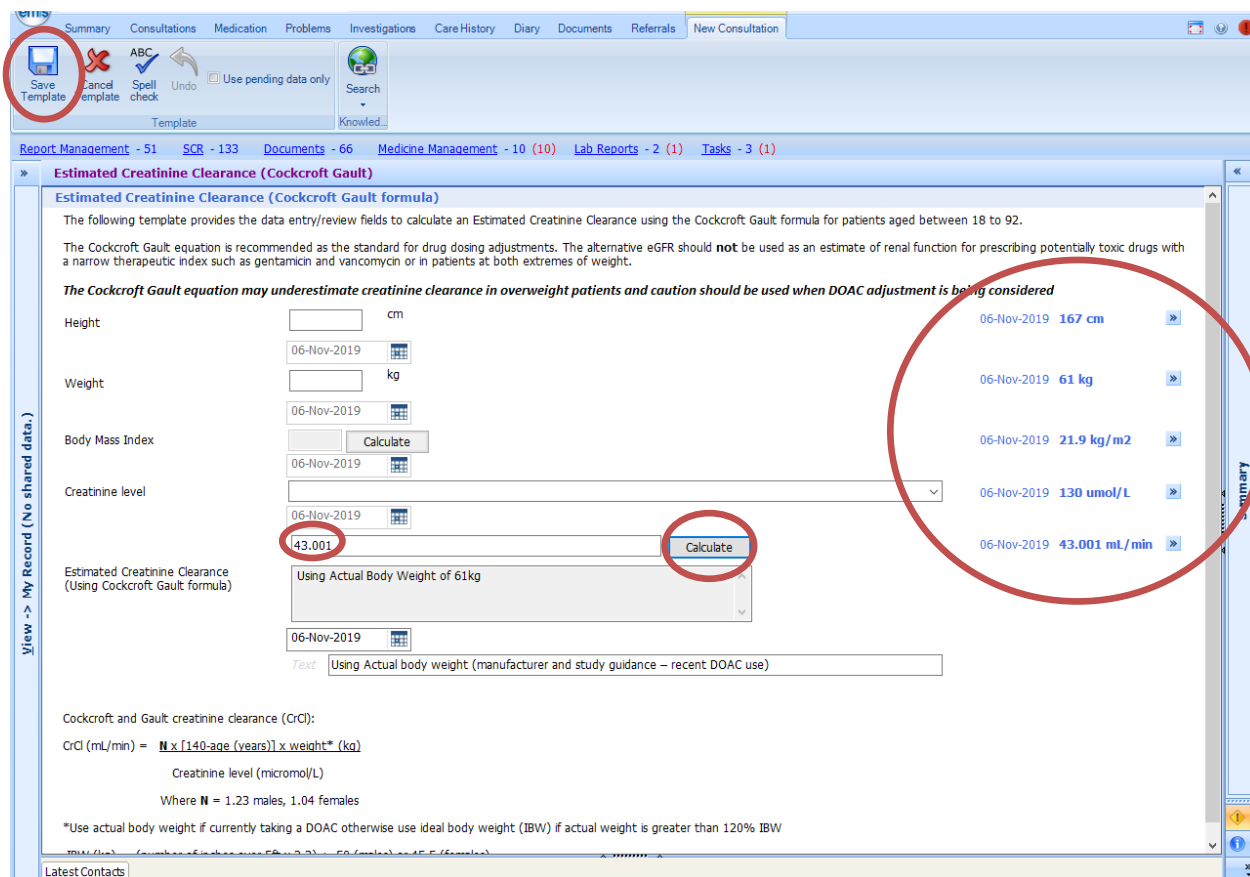
patient's height is not available, the tools will calculate CrCl based on the actual body weight. Consideration should be given to using the actual weight where a patient's increased weight is due to high muscle mass not excess body fat. Other patient factors affecting serum creatinine include amputation, muscle wasting disorders, vegans.

Where the results cross or are close to a CrCl level that may require a dose change or a DOAC to be contraindicated, removing the height from the tool will show the calculated CrCl based on actual weight. This allows comparison between the 2 values of CrCl (calculated using adjusted body weight and actual body weight) which may support the clinician making a dosing decision.

## EMIS Web

**For EMIS web-** the renal function calculator can be found under New Consultation, Run Template; using Template picker search for Estimated creatinine clearance (Cockcroft and Gault formula), click ok; click on Calculate next to Estimated Creatinine Clearance, then click Save template to save the result into the patient's record.





EMIS Web renal function calculator uses ideal body weight (IBW) if the actual weight is greater than 120% of the IBW. For overweight/obese patients using actual body weight in the Cockcroft and Gault equation overestimates the calculated CrCl whereas using IBW underestimates the calculated CrCl. However, the calculator has changed for DOACs since the previous versions of this guidance. There is no adjustment to the body weight in the calculator for patients who have an active repeat or an issue within the last 3 months of apixaban, rivaroxaban or edoxaban i.e. actual body weight is used for all patients. However, an IBW adjustment is made for those on dabigatran who are overweight or obese. See [link](#) for the background to this amendment.

Note: The EMIS Web calculator page has a rider that 'The Cockcroft Gault equation may underestimate creatinine clearance in overweight patients and caution should be used when DOAC adjustment is being considered'. This statement refers to where the calculator is used before a DOAC is initiated, as it will adjust for body weight as for any other non DOAC medication. EMIS Web assesses that underestimating the creatinine clearance is potentially more serious for DOACs than for other drugs; an unwarranted dose reduction may result in the patient being under dosed, increasing the risk of a thrombotic event.

When using the calculator, the patient's clinical parameters are shown on the right hand side of the template. Check that the weight is from the last 12 months and the serum creatinine is from the last 3, 6, or 12 months depending on the degree of renal impairment (see [SPAF guidelines](#) on-going monitoring page 8-9). For dabigatran ensure the patient's height is also from the last 12 months (this will allow a more accurate result for the elderly patients, where a drop in height may be noted).

If the clinician wishes to determine the CrCl using an adjusted body weight, then use of the web based application [MD+Calc calculator](#) may be considered. This allows for calculations based on actual body weight, adjusted body weight and ideal body weight, giving a range of possible values for CrCl. Where these results cross or are close to a CrCl level that may require a dose change this range can further support the clinician making a dosing decision.