

# The case for changing from using MDRD to CKD-EPI for estimating glomerular filtration rate (eGFR)

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## Introduction

Identifying people with impaired renal function is important, since, with appropriate management, many people with early impaired function can recover function or avoid further decline in renal function. Since 2006, we have been reporting renal function in terms of estimated glomerular function (eGFR), using the MDRD (Modification of Diet in Renal Disease study) equation. We propose to change to the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation for calculating and reporting eGFR, because this equation better reflects renal function, especially in younger people without clinical renal disease, and therefore reports fewer false positive results. We already have agreement from the renal physicians, and are seeking agreement from the Oxfordshire CCG.

## Glomerular filtration rate

The glomerular filtration rate (GFR) measures how much plasma the kidneys filter in one minute. In principle, this can be calculated by measuring the amount of a substance that appears in the urine over a given amount of time and the concentration in the blood (for substances with a constant concentration) or the rate of disappearance from the blood (for exogenous substances). The ideal substance for this measurement should be freely filtered at the glomerulus, and not reabsorbed or excreted by the rest of the nephron. Several exogenous substances that fulfil these criteria have been identified, including inulin, EDTA (ethylene diamine tetra-acetic acid), and iohexol. However, they have to be administered, sometimes linked to a radioactive tracer, to the patient, and the rate of disappearance of the substance from the blood has to be calculated either by measuring the substance in blood specimens taken at timed intervals, or by collecting timed urine specimens.

Creatinine is an endogenously produced substance that has been used to assess renal function for many years. It is produced by conversion of creatine, which is found mainly in muscle. Under normal circumstances, its concentration is more or less constant, although the daily standard deviation of concentration is up to 10%, mostly in response to diet, especially meat, which contains creatine. In the past, the GFR was calculated by measuring the output of creatinine in a 24-hour urine collection and measuring the concentration in blood at some point in the collection.

A problem with creatinine measurements in the past was the method, originally developed in the 1880s, is subject to positive interference from other substances, and to negative interference in the presence of ketones. Some of these interferences can be avoided by changes to the method, and a major realignment in the method was introduced in 2009. However, most of these interferences can be avoided altogether by using an enzymatic method, and our laboratory has used this since 2015.

Another endogenous substance, cystatin C, has been proposed for calculating GFR. This is produced by many cells in the body, and is freely filtered at the glomerulus. It is broken down in the tubular system, and little reaches the urine, so its concentration in plasma reflects glomerular filtration. This is a better reflection overall of GFR, and has been suggested by NICE [1], but, at the moment, it is not offered by many laboratories.

## Equations for estimating GFR

In the 1970s, Cockcroft and Gault proposed that GFR could be estimated from the plasma creatinine, using the age, sex and weight of the patient, though only 4% of their study population were women.[2]

The MDRD equation is based upon measurements in patients with established renal disease. It uses creatinine, sex, age, and the ethnicity of the patient to calculate the glomerular filtration rate (GFR). Since it does not require the laboratory to know the weight of the patient, it is much more convenient than the Cockcroft-Gault equation. It also reflects GFR much more closely.[3]

The realignment of creatinine in 2009 led to a slight change in MDRD equation. [4]

The group that developed the MDRD equation subsequently developed the CKD-EPI equations, using data from patients who had normal and impaired renal function. These equations are thought to reflect renal function better than the MDRD equation. There is also a version that incorporates the measurement of cystatin C .[5]

## Classifying impaired renal function

Because kidney size is related to body size, reporting GFR may not give a true reflection of renal function, since, all other things being equal, a smaller person will have smaller kidneys and thus a lower GFR than a larger person. The Cockcroft-Gault formula incorporates weight, and uses an assumption that females have a 15% lower GFR than males, although they had few females in their study. Subsequent equations have relate GFR to a standard body surface area of  $1.73 \text{ m}^2$ . This allows someone's renal function to be placed in bands: CKD1 (above 90), CKD2 (60–90), CKD3 (30–60), CKD4 (15–30) and CKD5 (<15) [all 60 ml per minute per  $1.67 \text{ m}^2$ ].

## Present situation in Oxford

NHS England mandated that laboratories should report estimated GFR in 2006. At that time, the only viable equation was the MDRD equation, and we have reported eGFR since then using this equation.

Many laboratories in the UK are using the CDK-EPI equation, and we feel that the laboratories in Oxford should do so as well. This has the agreement of the renal physicians, and, in principle, of the Oxfordshire Clinical Commissioning Group. We are now asking for the Oxfordshire CCG to agree this change.

We seek the agreement of the CCG to change the equation.

## Effect of the change

We examined the difference in reported eGFR using these two equations, and found that the change would classify fewer young people and more older people with chronic kidney disease (See Figure). [6] This has also been found by authors. [7] As pointed out by Earley and colleagues [8], “neither the CKD-EPI nor the MDRD Study equation is optimal across all populations and GFR ranges. Using a single equation for reporting estimated GFR requires a tradeoff to optimize performance at either higher or lower GFR ranges. A general practice and public health perspective favors adopting the CKD-EPI equation in North America, Europe, and Australia”.

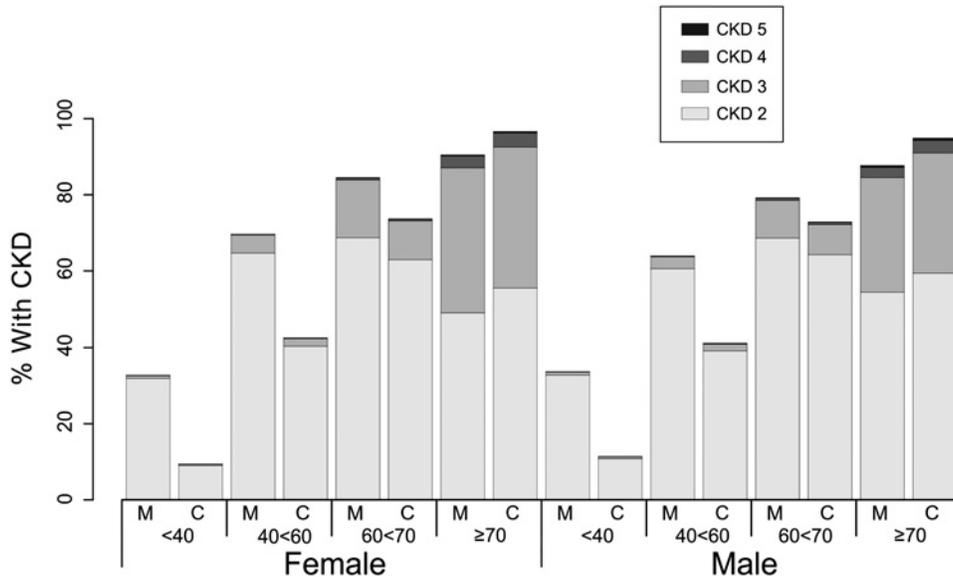


Figure 1: CKD classification by gender, age group and eGFR calculation equation [M = MDRD, C = CKD-EPI]

## Conclusion

While none of the available equations is universally optimal, opinion favours the CKD-EPI equation as being better for most purposes than the MDRD equation. We would therefore like to change to using this equation for reporting eGFR. This has support from renal physicians in Oxford, and, informally, from the Oxfordshire CCG, and we therefore wish to implement it. We would propose a 3-month consultation, with a view to implementing the change in June, 2017.

## References

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