Health Service Research

Chronic renal disease is not chronic kidney disease: implications for use of the QRISK and Joint British Societies risk scores

Sarah L Stevens*, Richard J Stevens, FD Richard Hobbs and Daniel S Lasserson

Nuffield Department of Primary Care Health Sciences, University of Oxford, Level 2, New Radcliffe House, Radcliffe Observatory Quarter, Woodstock Road, Oxford OX2 6GG, UK

*Correspondence to Sarah L Stevens, Nuffield Department of Primary Care Health Sciences University of Oxford, Level 2, New Radcliffe House, Radcliffe Observatory Quarter, Woodstock Road, Oxford OX2 6GG, UK; E-mail: sarah.stevens@phc.ox.ac.uk

Abstract

Background. Chronic kidney disease (CKD) is a major risk factor for cardiovascular disease (CVD) and European guidelines advocate assessment of CVD risk. QRISK and JBS3 risk calculators do not use the consensus definition of CKD stages 3–5 but instead use a definition referring to renal pathologies and CKD stages 4 and 5. Consequently, there is potential for doctors to misclassify their patients when using these risk calculators.

Objectives. To quantify the number of people who may be affected by such misclassifications.

Methods. Database analysis using the Clinical Practice Research Datalink (CPRD). We identified 2512053 adults aged 25–84 without prior history of CVD on 1st January 2014. We identified those with ‘chronic renal disease’ and/or CKD by searching medical event history data.

Results. The study population was 48.7% male with mean age of 50.2 years. A total of 80718 had diagnostic READ codes for CKD stages 3, 4 or 5. Of these, 6585 individuals (8.2%) were classified as having ‘chronic renal disease’ according to the updated QRISK 2014, up from 3365 according to QRISK 2013. Whilst the updated QRISK definition of ‘chronic renal disease’ in total identified 62% more people than previously and had improved sensitivity for CKD stages 3 to 5, sensitivity remained poor (8.16%; 95% CI: 7.97–8.35%).

Conclusion. Misuse of risk scores by general practitioners could result in clinically important differences in risk estimates. Users of risk scores should recognize the potential for error and developers should aim to label risk factors more clearly.

Key words: Chronic kidney disease, cardiovascular diseases, chronic renal diseases, risk factors.

Introduction

Worsening kidney function is an established risk factor for cardiovascular disease (CVD) (1) and cardiovascular death (2). Internationally, the consensus definition of chronic kidney disease (CKD) is CKD stages 3–5 if based on (estimated) glomerular filtration rate (eGFR) alone or stages 1 and 2 with additional evidence of renal pathology (3). This definition has been adopted, with incentives for diagnosis and monitoring, in UK primary care (Quality and Outcomes Framework, QOF) (4).
the QRISK investigators to define ‘chronic renal disease’. Recently, QRISK updated their definition of ‘chronic renal disease’ to include diagnostic READ codes for CKD stages 4 and 5, but codes for CKD stage 3 remain outside the scope of ‘chronic renal disease’. Despite this, the term ‘CKD’ appears on the QRISK Lifetime website and the question ‘Do you have a CKD?’ is asked by the JBS3 risk calculator. There is potential for general practitioners (or patients) to misclassify their patients (or themselves) by mistaking ‘chronic renal disease’ for the consensus definition of CKD when using these calculators. It is unclear how many patients may be affected by such misclassification and how this may impact subsequent disease management.

We aimed to quantify the number of people who may be affected by discrepancies between these definitions of ‘chronic renal disease’ and CKD using individual patient data from UK primary care. We also sought to extrapolate our results to a national level and comment upon the effects of misclassification on risk estimation.

Methods

We carried out a database study using the Clinical Practice Research Datalink, a database of electronic health records from ~8.5% of UK general practices. We identified adults (aged 25–84 years on the 1st January 2014), without prior history of CVD who were registered continuously with their GP throughout 2013. History of CVD included history of myocardial infarction, angina, other ischaemic heart disease, stroke, transient ischaemic attack and other cerebrovascular disease (see Supplementary Table 1 for full list of READ codes). Included individuals would hence be a potential candidate for cardiovascular risk assessment during 2014, when the changes to the QRISK definition of chronic renal disease were made. From our sample, we identified those with ‘chronic renal disease’ and/or CKD by searching the medical event history data for a relevant READ code up, for each of the original QRISK definition (9), updated QRISK definition (10) and CKD stages 3–5 as defined by QOF Business Rules (4) (see Supplementary Tables 2 and 3 for full list of codes). Stage of CKD based on READ codes was determined according to the most recent READ code in the record up to end 2013 (with no restriction on earliest date).

In secondary analysis, we determined stage of CKD from eGFR measurements. Serum creatinine measurements up to end 2013 were obtained from test results and we calculated eGFR using the Modification of Diet in Renal Disease (MDRD) (11) equation. Stage of CKD was then determined using the two most recent eGFR measures prior to 2014, taken at least 3 months apart, in line with international guidelines (Table 1) (3).

Data were reported graphically along with proportions and 95% confidence intervals. We used measures of sensitivity and specificity to compare the QRISK definitions for chronic renal disease to diagnoses of CKD stage 3–5. We also assessed agreement between diagnoses of CKD based on READ codes to those based on eGFR measures using kappa statistics. We used the most recent (2011) Census finding of 42.4 million adults aged 25–84 in the UK to estimate approximate numbers of individuals at UK population level (12). Analysis was carried out using Stata 14.0.

Results

We identified 2,512,053 adults in our initial sample with mean age 50.2 years (SD = 15.2 years) and 48.7% were male. Included patients were registered at practices across all regions of the UK (Table 2) with records dating back as far as 1987 for some patients. A total of 80,718 had diagnostic READ codes for CKD stages 3, 4 or 5. Of these, 4,668 (5.8% of 80,718) had CKD stages 4 or 5 according to their most recent code; the remainder (94.2% of 80,718) had CKD stage 3.

A total of 117,690 patients had two measurements of eGFR, 3 months apart, on which to evaluate their CKD status. Using the latest eGFR measurements, 65,935 patients had CKD stages 3, 4 or 5 of which 92.5% had CKD stage 3.

Change of definition of chronic renal disease in QRISK

Under the previous definition used in QRISK scores (QRISK 2013), 5218 (0.21% of the population; 95% CI: 0.20–0.21%) had history of chronic renal disease. Under the new definition introduced in 2014 (based on READ codes for chronic renal disease and CKD stages 4 and 5, QRISK 2014), an additional 3220 had history of chronic renal disease, making a total of 8438 (0.34% of the population; 95% CI: 0.33–0.34%). Hence the new definition identifies 61.7% more individuals than previously.

Discrepancy between chronic renal disease and CKD

Figure 1 shows the degree of overlap between diagnosis of chronic renal disease as defined by QRISK scores, and diagnosis of CKD stages 3, 4 and 5 based on READ codes. Under the previous definition of chronic renal disease, 3365 individuals with history of chronic renal disease (64.5% of 5218) also had history of CKD stages 3, 4 or 5. These 3365 individuals with both chronic renal disease and CKD represent 4.2% of the total 80,718 with CKD. Hence although the QRISK 2013 definition of chronic renal disease has very high specificity for CKD stages 3–5 (99.9%; 95% CI: 99.9–99.9%), it has very low sensitivity (4.17%; 95% CI: 4.03–4.31%).

### Table 1. Definition of chronic kidney disease (CKD) based on eGFR

<table>
<thead>
<tr>
<th>CKD Stage</th>
<th>eGFR (ml/min/1.73m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>≥ 90 with kidney damage</td>
</tr>
<tr>
<td>2</td>
<td>60–89 with kidney damage</td>
</tr>
<tr>
<td>3a</td>
<td>45–59</td>
</tr>
<tr>
<td>3b</td>
<td>30–44</td>
</tr>
<tr>
<td>4</td>
<td>15–29</td>
</tr>
<tr>
<td>5</td>
<td>&lt;15</td>
</tr>
</tbody>
</table>

### Table 2. Study population characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean (N)</th>
<th>SD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>50.2</td>
<td>15.2</td>
</tr>
<tr>
<td>Region</td>
<td></td>
<td></td>
</tr>
<tr>
<td>North East and West</td>
<td>325,539</td>
<td>13.0%</td>
</tr>
<tr>
<td>Yorkshire and the Humber</td>
<td>23,245</td>
<td>0.9%</td>
</tr>
<tr>
<td>East and West Midlands</td>
<td>223,495</td>
<td>8.9%</td>
</tr>
<tr>
<td>East of England</td>
<td>168,189</td>
<td>6.7%</td>
</tr>
<tr>
<td>South West</td>
<td>198,992</td>
<td>7.9%</td>
</tr>
<tr>
<td>South Central</td>
<td>319,067</td>
<td>12.7%</td>
</tr>
<tr>
<td>London</td>
<td>274,544</td>
<td>10.9%</td>
</tr>
<tr>
<td>South East</td>
<td>663,643</td>
<td>26.4%</td>
</tr>
<tr>
<td>Northern Ireland, Scotland and Wales</td>
<td>37,238</td>
<td>1.5%</td>
</tr>
<tr>
<td>Recorded black ethnicity</td>
<td>87.1 (N = 167,2719)</td>
<td>20.0</td>
</tr>
</tbody>
</table>

The QRISK definition of chronic renal disease (eGFR ≥ 90 with kidney damage) is defined as stage 1, 61.7% more individuals than previously. The new definition identifies 61.7% more individuals than previously.
Chronic renal disease is not chronic kidney disease: implications for risk estimation

Under the new QRISK definition of chronic renal disease, 6585 individuals with history of chronic renal disease (78.0% of 8438) also had history of CKD stages 3, 4 or 5. These 6585 individuals are 8.2% of the 80718 with CKD. Thus 77333 individuals (3.08% of the population; 95% CI: 3.06–3.10%) had CKD but not chronic renal disease, and 1853 individuals (0.074% of the population; 95% CI: 0.070–0.077%) had chronic renal disease but not CKD. The new definition of chronic renal disease has improved sensitivity for CKD stages 3–5 compared to the previous definition but is still generally poor (8.16%; 95% CI: 7.97–8.35%).

Similar lack of overlap was observed when we restricted analyses to those aged 35 years and above (N = 2041873), who are more likely to be targeted for risk assessment (Supplementary Fig. 1). Of the 80380 people aged 35+ with CKD stage 3 to 5, only 3260 (4.1%) and 8080 (10.1%) were identified by the QRISK 2013 and QRISK 2014 definitions of chronic renal, respectively. In this subgroup, the QRISK 2014 definition had sensitivity of 9.12% (95% CI: 8.90–9.34%) for CKD stages 3–5 based on READ codes.

When the QRISK 2014 definition of chronic renal disease was compared with diagnosis of CKD stages 3–5 based on eGFR measures (Supplementary Fig. 2) in the full sample, only 9.3% (6112 of 65935) of those with CKD stages 3–5 were identified by the QRISK 2014 definition (Supplementary Fig. 2) with sensitivity of 9.27% (95% CI: 9.05–9.49%).

Implications for risk estimation with QRISK Lifetime

Overall, coding for chronic renal disease, as currently defined by QRISK scores, was discrepant with coding for CKD stages 3, 4 and 5 in 3.2% of the population (79206 of 2512053). This corresponds to approximately 1.3 million adults aged 25–84 in the UK. The hazard ratios for chronic renal disease in QRISK Lifetime are 1.67 for women and 1.59 for men, so that misclassification for chronic renal disease corresponds to over- or under-estimation of risk by ~59–67%. Since the majority of those with discrepant coding had CKD stage 3 but not chronic renal disease (74133, 93.6% of 79206), misclassification of individuals will predominantly result in the over-estimation of risk. For example, for a 45-year-old, moderately affluent, white male, who is a light-smoker, with BMI of 23, total/HDL cholesterol of 6 mmol/l and systolic BP of 138 mmHg, with diabetes and CKD Stage 3 has an estimated 7.5% risk of CVD in the next 10 years according to the JBS 3 calculator. However, if a GP mistakenly ticks the ‘Do you have a CKD?’ box for this patient when using the JBS software, the risk estimate returned is 12%, reclassifying the patient over the recommended 10% risk threshold for initiation of statin therapy.

Agreement between READ code and eGFR based diagnoses

Table 3 shows the agreement between the most recent READ code diagnosis for CKD stages 3–5 and CKD diagnoses based on the two most recent eGFR measures. Those with no eGFR measures were assumed not to have CKD stages 3–5. Overall percentage agreement was 97.5% but this was primarily driven by the large number of people who do not have CKD stages 3–5 in either case. The kappa statistic for agreement was therefore more modest (0.564), as was the equivalent linear weighted kappa (0.583).

Conclusions

This study highlights that ‘chronic renal disease’ in QRISK and related scores, including the new JBS3 calculator, is not synonymous with familiar definitions of ‘CKD’ namely CKD stages 3–5. In total 3.2% of the population were identified as having CKD stages 3–5, and there was limited overlap between these individuals and those with QRISK-type ‘chronic renal disease’. Hence whilst the new QRISK definition of ‘chronic renal disease’ identifies 61.7% more people than previously, it only captures a small fraction of those with CKD stages 3–5.

Discussion

Strengths and limitations

The prevalence estimates from this study based on the old and new QRISK READ code definitions were in line with those obtained in separate QRISK derivation studies, so we are confident in the accuracy of the these estimates. A limitation of our study is that for patients who had no record of black ethnicity, we assumed these individuals were white for the purposes of eGFR calculation. Due to the very poor recording of black ethnicity, this may have resulted in underestimation of eGFR in some cases. However, it is likely that any underestimation has only affected CKD classification in a few cases and would not affect our overall conclusions. We also did not exclude patients with acute kidney injury, which may have resulted in some erroneous recording of CKD based on eGFR alone.

We did not assess the frequency with which those whose risk calculation is affected would cross a guidelines-specified risk threshold because thresholds are subject to change. Such an analysis is also difficult to specify when most individuals will have multiple risk assessments across their adult lifetime. This study is theoretical in nature and further research is required to determine how often GPs make the error discussed in risk calculation. Arguably, the likelihood of patients being misclassified in risk calculators will depend on how long ago codes for CKD or chronic renal disease were recorded. In our analysis the average time between the most recent CKD and chronic renal disease code was 2.86 years and codes for CKD or chronic renal disease were recorded more recently than those for chronic renal disease on average. The extent to which this would affect the likelihood of risk score misuse remains to be determined.

Implications for research and practice

This study has implications for a large number of patients. Understandable misuse of risk scores could result in clinically important differences in risk estimates in individual cases.
Table 3. Agreement between most recent READ code diagnosis for CKD Stages 3–5 and diagnosis based on most recent two measurements of eGFR at least 3 months apart

<table>
<thead>
<tr>
<th>CKD stages 3–5 eGFR diagnosis</th>
<th>CKD Stages 3–5 code diagnosis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No CKD</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2409.278</td>
<td>36305</td>
</tr>
<tr>
<td></td>
<td>212.79</td>
<td>38317</td>
</tr>
<tr>
<td></td>
<td>569</td>
<td>1281</td>
</tr>
<tr>
<td></td>
<td>209</td>
<td>147</td>
</tr>
<tr>
<td>Total</td>
<td>2431.335</td>
<td>76050</td>
</tr>
</tbody>
</table>

Differences may affect patient management decisions including the initiation of lifelong treatment. Whilst recent guidance welcomes the initiation of statin therapy to those in lower risk groups, patient preferences may be altered when presented with artificially high (or low) risk estimates. GPs should be cautious in interpreting results from risk calculators and be aware of the potential for error. Developers of risk calculators should also ensure that online tools are appropriately and clearly labelled to reduce misunderstanding. Consideration should be given not only to the clinical accuracy of the labelling but also to the interpretation of labels by non-clinicians or patients, who may also misuse scores if they are not provided with information in an accessible manner. In the long term, risk calculators could also be updated to bring them in-line with the consensus definition of CKD or utilize measurements of serum creatinine/eGFR in place of categorical risk factors which are less prone to misunderstanding.

Our results also have implications for published validation studies of the QRSK scores (13). If these identified ‘chronic renal disease’ using the same definition as the derivation study, then they inform us about portability of a computer algorithm from one database to another, but not about use of the online (or smartphone) QRSK and JBS3 software in clinical practice. Validation studies reflecting real-world use are required to determine the accuracy of these risk calculators (in terms of calibration and discrimination) before they are recommended for implementation in clinical practice.

Our study also illustrates challenges of epidemiology using ‘big data’ such as routine health care records from primary care. Identifying and labelling individuals with even common conditions such as CKD can raise questions of definition of which the users of research, as well as the authors, should be aware. Although previous studies have considered the validity of READ code diagnoses for CKD compared to using eGFR measures (14), this study is, to the authors’ knowledge, the first to consider discrepancies between diagnosis definitions for the purpose of risk estimation.

In summary, the well-established diagnostic criteria for CKD in clinical practice are very different from those used in the derivation and validation of QRSK and related scores. This has particular implications for users of the JBS3 guidelines, risk calculator and smartphone apps, who should recognize the potential for error. We would recommend that the instructions on both the QRSK and JBS 3 websites should be amended to refer unambiguously to CKD stages 4 and 5 to avoid over-estimation of risk.

Declaration
Funding: This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Ethical approval: The analyses described above were approved by the Independent Scientific Advisory Committee (ISAC) to the MHRA (approved protocol number 14_118).
Conflict of interest: none.

Supplementary material
Supplementary material is available at Family Practice online.

References