Reviewer's report

Title: Early identification of people with autosomal dominant polycystic kidney disease: a cross sectional study

Version: 1 Date: 23 July 2014

Reviewer: Daniel Gale

Reviewer's report:

Major Compulsory Revisions

McGovern et al have examined a large repository of primary care clinical data in order to determine whether it is possible to use routinely collected data in those under 60 in order to identify individuals at high risk of polycystic kidney disease, with a view to potential future demand for population screening for ADPKD. Major strengths of the study are the large sample size and the high quality of the statistical analysis used. In this real-world UK population the prevalence of a diagnosis of polycystic kidney disease in primary care records (1:2700) is well below the accepted prevalence of the disease (~1:800), implying that the diagnosis is not being made (or at least accurately recorded in GP records) in a significant number of people with the disease.

However, there are a number of issues which make it difficult for this paper to achieve its stated aim of showing that routine data could be used to stratify patients’ risk of having undiagnosed ADPKD.

1. The PKD group are identified by their coding in the primary care records. Since their primary care provider must therefore be aware of the diagnosis, it follows that they are more likely to undergo blood pressure and renal function measurements than the non-PKD population, and that more aggressive blood pressure control is likely to be employed, so statistical differences in these parameters may be caused by the diagnosis rather than the disease. This hypothesis is supported by their finding that undocumented renal function has an odds ratio for PKD of 0.28 (p<0.001). This ascertainment bias implies that extrapolation to the undiagnosed PKD population of the identified risk factors may not be completely justified.

2. The authors build a regression model using a number of parameters including CKD stages 3B (OR 42.35), 4 (OR 101.27) and 5 (OR 75.08) and haematuria (OR 1.85). According to the National Institute of Health and Clinical Excellence Guidelines for the Identification and Management of Chronic Kidney Disease, these are all indications for a renal ultrasound scan. This implies that individuals with these clinical features should all be either diagnosed with PKD or have a diagnosis of PKD excluded, so incorporating these factors in a risk score for undiagnosed PKD is unlikely to improve the clinical management of these patients. In addition, proteinuria and hypertension (particularly hypertension
requiring multiple agents) in a young (<60 year old) patient is likely to warrant clinical investigation that would include a renal ultrasound scan in many cases.

3. There is no mention of the role of family history in stratification of patients. Since ADPKD is a Mendelian condition with high penetrance, a majority (probably over 80%) of affected individuals have a family history of kidney disease. According to the National Institute of Health and Clinical Excellence Guidelines for the Identification and Management of Chronic Kidney Disease a family history is also an indication for offering screening for this condition.

I do not think the aim of this paper has been completely met. In order to address the question posed, the authors would need to re-analyse the data including only those patients in whom ultrasound scanning is not indicated by clinical data and family history under current national guidelines.

**Level of interest:** An article of limited interest

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests