Reviewer’s report

Title: The QICKd study protocol: a cluster randomised trial to compare quality improvement interventions to lower systolic blood pressure in chronic kidney disease (CKD) in primary care [ISRCTN56023731]

Version: 1 Date: 23 March 2009

Reviewer: Tom Crocker

Reviewer’s report:

Summary
The protocol is for a cluster randomised trial examining approaches to improve the primary care management of patients with chronic kidney disease (CKD). Two interventions are to be tested over two years, ‘guidelines and prompts’ (information about appropriate CKD management with 6 monthly updates) and ‘audit-based education’ (group sessions comparing the adherence to guidelines of the attending practices based on anonymised electronic practice records) alongside a control group. Additionally, a subset of practices in each arm of the study will answer questionnaires to examine the impact of the interventions on GPs’ confidence in managing CKD. Finally, there will be a qualitative study of four practices to help understand the way in which the interventions work (or why they don’t). The study uses control of blood pressure as its primary indicator, but collects many other variables as well as performing economic and qualitative analyses.

The study described is important, with interest to those involved in chronic kidney disease or quality improvement in primary care. It is good to see multiple approaches and measures being used to attempt to gain an understanding of whether these interventions work, by how much and why. I understand that this study has already received ethics and funding approval and therefore any changes to the protocol will need to be minor. It is important that this protocol is publicly available and that this large study is as fruitful as possible. It is with this purpose that the following comments are made.

Acknowledgements
Dr Arnold Zermansky has kindly commented on and contributed to this review

Discretionary revisions

1. The plan is to conduct a two-year study but the authors state their experience is that ABE is more effective in its second and third years. Can they justify running a large study for two years that may show no significant effect because it didn’t run for a third year?

2. The themes given for the interventions are largely clinical measures and the appropriate clinical response. Process of delivering care is mentioned and it may be that this is a more fruitful area of education to explore. We would advocate
including advice on adherence, effective call/recall of patients and adverse drug effects and interactions if this is possible.

3. It is difficult for the reader to get a strong sense of the interventions that are being tested and this is vital for learning lessons at the end of the study (whether outcomes are positive or negative). For example, what sort of size of document will the guidelines and prompts guidance be and in what format? How long is an ABE workshop likely to last, how many participants are likely to be at one session and what training is the local GP to have received? If the authors could explicitly point readers to specific examples they aim to emulate or provide more detail this would be of great use.

4. Practices are to be recruited to the study and all of their population with CKD are to be the subjects. However, the primary research participants are to be general practitioners. Are the general practitioners to be consented individually or is the consent of the practice as a whole enough to include them. In other words, are all GPs in a practice to be participants or may they choose to abstain and if so how does that affect the sampling of all patients in a practice. It also appears that practice managers and nurses are to participate in the interventions, but they are not named as participants. Furthermore, I presume patients are not to be consented but if this was stated it would offer clarity.

5. The study will define CKD in the subjects by two or more measures of eGFR < 60 at least 3 months apart. There doesn’t seem to be a planned analysis of the impact of the interventions on the measuring and recording of eGFR or of the difference between practices at baseline. As this is likely to impact upon the proportion of subjects defined by the study as having CKD, serious consideration should be given to the effect on analyses. If however the subjects will only be included if both measures of eGFR occurred prior to baseline this should be stated.

6. In paragraph 3 in the ‘Epidemiology of Chronic Kidney Disease’ section, the authors state “Studies have demonstrated a need to improve both information and training available with the aim of closing the gap in the quality of care currently provided.7”, yet they cite only one study which appears to demonstrate that targets are frequently unmet and documented hypertension was often untreated, but not the reasons for this. The authors do not state to whom the information and training should be made available (patients or practitioners).

7. The protocol does not include a rationale for the use of a cluster randomised trial.

8. The four practices to be used for the in-depth process evaluation are to be purposively selected but the authors don’t state the type of purposive selection, the criteria to be considered, or how or why these practices will be selected.

9. Practices will be randomly allocated to the three arms in blocks of nine. This will leave three practices to be allocated in each group (75-72 and 30-27) to reach the sample sizes required. Will these be allocated via a block of three at the end or will the study accept uneven sample sizes. Additionally, the authors do not state in what order practices will be allocated to groups (e.g. upon agreement or alphabetically).
10. Both of the final points in the boxes describing the intervention themes seem to relate to the process evaluation (rather than the intervention). If not, how is the information (e.g. how the intervention can be improved) to be fed back to the researchers and analysed?

11. The precise primary outcome measure is unclear and the reason for choosing systolic blood pressure is not given. Hypertension is not defined nor when the measurement was taken: is it an SBP >=130mmHg or >=140mmHg at baseline for example? Is the desired outcome a change in mean SBP over the two years of -3mmHg in the ABE arm or a difference between arms in change over the two years of >3mmHg or a difference between arms in mean SBP >3mmHg at the 2 year point or something else?

12. The use of a mean value to measure impact has the potential to hide a multitude of possible scenarios. The authors should consider including a secondary measure of, for example, percentage of patients hypertensive at baseline whose SBP fell by (say) 5mmHg. If a significant difference is found this will provide stronger evidence of the impact of the intervention to patients’ health.

13. The authors have chosen to include patients with CKD stages 4 and 5 in their analysis when many of these patients will (or should) be substantially managed by a renal consultant. Can the authors justify this inclusion? It is quite possible this will reduce the apparent effectiveness of the intervention. The authors could state upfront an intention to perform secondary analyses of their primary outcome measure across these different patient groups, hypothesising that the intervention would have less effect in CKD 4 and 5 because of specialist management.

14. There is no age cut-off in the analysis, which I believe is justifiable as there will hopefully be an effect across the patient cohort. Again, secondary analyses could compare the intervention between young, typical and very old age groups.

15. There is no stated analysis of, or adjustment for, the impact of deaths on outcomes. Will dead patients be included or excluded? About 4000 patients (12%) will die in 2 years and those most likely to die are those with the highest BPs. This could reduce the power of the study because the high BP people in the control arm are likely to die and leave those with the lowest BP still in the project. This is really difficult.

16. The comparative analyses described include multiple regression analyses to examine the “relations between independent variables (e.g. known demographics and risk factors such as smoking status, level of cholesterol, obesity, anaemia, alcohol consumption etc) and dependent variables (e.g. CKD stage 3-5 and diabetes).” The ‘independent’ variables are likely to be highly correlated and this needs to be taken into consideration as part of the analysis. Including anaemia as an independent variable in a regression to explain CKD is problematic as causality is probably bi-directional.

17. On page 16 the focus groups and their analysis are described. Will any particular approach be taken in conducting the analysis? In addition, is it IC (rather than IS) who will conduct the qualitative analysis?
18. In the final paragraph of the discussion, before the conclusions the authors discuss external factors (QOF and NICE) that may impact upon their outcome measures. They say that these factors will equally influence all three arms of the study but that assumes a simple additive effect. It could be that these factors will have a greater impact on the control than the intervention groups because there are diminishing returns to investment for example. Alternatively, the external factors could have a positive interactive effect with the intervention by some reinforcement mechanism. Either way, we don’t know and cannot say. But the authors will be able to speculate on the impact when they have their results, if they are aware that it may not have an equal impact.

19. The study’s control relies on limited contact between general practices and renal units. In some parts of the country, renal units are engaging with general practices, both through education sessions and shared management of patients. Do the investigators know the extent of this in the areas they will be operating in or are they able to record this, for example through their questionnaire?

20. On page 8 the authors state “We will be able to compare questionnaire and non-questionnaire practices in each arm at the end of the study”. However, they don’t acknowledge the differing impacts the interventions (and control) could have on the results of the questionnaire itself. As well as genuinely increasing confidence, the interventions in the context of a study could lead to over-reporting of confidence or similarly under-reporting among the control group. The questionnaire may be useful and should be retained but this potential bias could be acknowledged.

Minor essential revisions - Clarity and readability

1. It may help the readers if the aims and objectives are moved up to the start of the methods section.

2. I found the protocol felt slightly disjointed at times and thought it could benefit from a stronger single narrative.

3. When talking about the QOF with reference to quality of GP data the authors suggest uncritically that the QOF has improved diagnosis recording, yet they appeared to suggest that data could be less reliable because of the QOF on the previous page. The authors should clarify this.

4. The protocol contains a large number of spelling mistakes and the punctuation could be improved. For example, “presence of absence of”, “enbale” and on page 6, “...their own practices’...” should be “...their own practice’s...”.

5. The use of abbreviations is inconsistent throughout the text and they are not always introduced. The list of abbreviations is also incomplete. For example in paragraph 2, in the ‘Epidemiology of Chronic Kidney Disease’ section, ‘rate’ is missing from the text ‘estimated glomerular filtration rate (eGFR)’. Later, GFR is used in place of eGFR and estimated glomerular filtration rate continues to be used.

6. In paragraph 3 in the ‘Epidemiology of Chronic Kidney Disease’ section, “a threshold for intervention of 140/90 is recommended”; the authors should indicate this refers to BP and the units, mmHg.
7. When introducing the parallel study (page 7) the authors label its parts a) and b), but when they describe it they reverse the order and label its parts (1) and (2). To add to the confusion, the participant groups in figure 2 are labelled (1), (2) and (3), where (2) and (3) in the figure refer to (2) and (1) respectively in the text. This should be clarified.

8. On page 7, the sentence “They will validate our questionnaire to assess confidence; during the study proper report on the intervention exposure (...) and programme fidelity (...)” could be made clearer to the reader by changing it to “They will validate our questionnaire to assess confidence and, during the study proper, report on the intervention exposure (...) and programme fidelity (...).”

9. On page 4, paragraph 1, sentence 3 it could be made clearer that the models under review are of practice improvement interventions.

10. In paragraph 3 in the ‘Epidemiology of Chronic Kidney Disease’ section, “with a target for optimal management of a systolic BP of between 130 and 139” could be rearranged as “with a target systolic BP of between 130 and 139 for optimal management”.

11. In paragraph 6 in the ‘Epidemiology of Chronic Kidney Disease’ section, the fourth sentence (on over-aggressive guidance) should be rewritten and can be supported by citation.

12. It isn’t always clear which parts of the study are being referred to, for example, in “The study will use a model developed by the Primary Care Data Quality project” study means ABE and in “The content and focus of the guidelines and prompts arms of the study will be the same.” this again means as the ABE.

13. There is a citation in the discussion to reference 57, but the reference list stops at 45. Similarly, there is a missing citation (Error! Bookmark not defined) in the discussion.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests