Author's response to reviews

Title: The efficacy of computer reminders on external quality assessment for point-of-care testing in Danish general practice: Rationale and methodology for two randomised trials

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Author's response to reviews: see over
Dear Implementation Science,

First of all thank you for the positive and constructive reviews. We have addressed all the points stated by the reviewer. Please refer to our comments marked with red. We upload a version where changes from the last submission are visible and a file without visible changes.

Yours sincerely
Frans Boch Waldorff

Reviewer: Bernard Croal
Reviewer’s report:
Major Compulsory Revisions - None
Minor essential Revisions - None
Discretionary Revisions - as discussed below.
1. Will the study design adequately test the hypothesis? - Yes
2. Are sufficient details provided to allow replication of the work or comparison with related analyses: if not, what is missing? Yes
3. Is the planned statistical analysis appropriate? Not qualified to fully comment.
4. Is the writing acceptable? Yes

Overall Protocol Review

Thank you for the opportunity to comment on this protocol. Point-of-Care Testing (PoCT) as a means of primary analysis is increasing dramatically across the world. Unfortunately, the necessary quality standards that should be in place to support PoCT are in a lot of instances not. These planned studies are therefore very much welcomed as they will try to assess the impact of intervention aimed at increasing the uptake and potentially performance of an external quality assurance scheme (EQA) for PoCT.

The first comment to make however would be that the actual mechanism for assessing “EQA” for PoCT employed in this area is one that could be regarded in many settings as inadequate. Split sample analysis while providing a basic comparison between a lab method and the PoCT method would not cover the same assessment as that provided by a more standard EQA scheme employing full external analysis and peer comparison with other labs using similar methodology. While this is a criticism of the nature of the EQA scheme employed, it is not necessarily relevant to the quality of these planned studies, and so there is no suggestion that this aspect should be changed. It may that in this region, or indeed in this country, that EQA of this nature is deemed to be satisfactory. It is the case that in many instances around the world, PoCT is carried out with no associated EQA. It may be therefore that the results of this study may in some way be generalisable to other more complex forms of EQA and the associated compliance.

Overall, I find these studies very well thought out, with much thought and planning going in to comparing standard practice with reminders sent by post and by electronic means. It is noted that the comparative effect will be difficult to tease out across different types of test – for example the effect of reminders may be more noted in PoCT involving INR due to the apparent more serious nature of the test/consequences for producing a wrong result. Thus, a direct comparison of electronic delivered reminders will not be made in this setting for INR with standard practice.
We fully agree with the comments in the two above paragraphs and have incorporated these in the discussion.

Not being a statistician, I can only assume the power calculations are correct. I remain unsure as to why only 4 months was chosen for the intervention period – perhaps 6 months could be considered as an alternative so as to allow more time for non-compliance to surface and for the effect of reminders to become apparent. This however is only a suggestion and will however increase the study period which may have other consequences, including the cost of the study.

The reasons why we decided on four-month periods were primarily because of Study A (INR analyses) as the authorities demanded an action to increase the adherence to EQA guidelines before the end of 2011. For pragmatic reasons a four-month period was also chosen for Study B.

I therefore find these planned studies adequate in their ability to address the research questions of whether such reminder intervention can improve compliance with their EQA scheme. The secondary outcomes of whether there is an associated change in analyser performance (i.e. comparative agreement) is interesting but I am not sure whether there is any hypothesis that could be suggested that may drive such a change. Analyser performance should be an independent function regardless of whether EQA schemes are in place. It may be however that there will be occasional “flyers” or even identification of rogue analysers as a result of EQA performance – whether there will be time for replacement/improvement to be realised within the 4 month study period remains to be seen. These studies are therefore important and should identify whether these different interventions for improving compliance and performance within an EQA scheme for PoCT do actually have an effect. The outcomes may direct other similar laboratories/community sites to interact in this way if found to be effective.

Reviewer: Ian Steen
Reviewer’s report:
I agree with the authors that we can regard these as two randomised controlled trials (rather than cluster randomised controlled trials). In general variables are measured at the level of the practice (although there are one or two variables measured at the level of the GP). The overall study design is adequately described.

I have two major concerns to be addressed:
1. Description of outcomes
2. Proposed method of analysis of a dependent variable that takes the form of a count.

In more detail:
1. The main issue for me was determining the nature of the primary outcome variable. We have the following statements:
   “Outcomes are measured by the number of split tests received by the laboratory” (p2)
   “The guidelines recommend a split test procedure each month for each POCT
instrument.” (p6)
“The split test procedure is illustrated in figure 1.” (p6)
Figure 1 as submitted shows the flow of practices through the study rather than
the split test procedure.

We have deleted this reference to Figure 1.

I am uncertain as to the relationship between a “split
test” and an “external quality assessment”. Are they the same thing?

We have addressed this in the second sentence in third paragraph. In order to reduce the confusion
regarding EQA vs. split tests we have decided to use the term split test procedures for the current
implementation and reserve EQA for the overall concept.

“Combined, this monitoring gives a series of up to four measures (defined by
several outcomes, see below) of EQA adherence” (p7)
For study A the primary outcome is defined as “Total number of EQA for INR
performed by the practice” (p9). The binary secondary outcomes are defined.
Corresponding outcomes are defined for study B (p11)
I would have found the paper much easier to read if all this information had been
drawn together preferably before the description of the statistical analysis. In
addition how many EQAs do we expect in each practice each month?

As suggested by the reviewer we have moved a generic description of the outcomes for both studies to a
paragraph before the description of statistics. Furthermore we have clarified the concepts of split test
procedures, e.g. how many split test procedures are possible in each period. In the description of study A
and B we have briefly stated the specific study-related outcomes.

2 Statistical analysis
“In order to investigate the development of EQA adherence over the up to four
periods relative to the (changing intervention), logistic (binary outcomes) and
linear (continuous outcomes) regression is used with GEE methods to account
for the repeated measurements.” (p8)
With respect to the secondary outcomes I am happy with this suggested analysis
— logistic regression with GEE.
With respect to the main outcome I do have some concerns. The number of
EQAs performed is a count variable. For many reasons I would prefer to see the
use of negative binomial regression rather than linear regression. I don’t know
many EQAs are expected in each period for each practice but if this is related to
list size or number of lab tests ordered I would expect this to be taken into
account by way of an exposure variable. (In stata I would use xtnbreg which
allows for the fitting of population averaged (GEE) models to count data. I don’t
know the name of the corresponding SAS procedure.)

We agree with the reviewer that Poisson regression is more adequate for the analysis of our primary
outcome than linear regression that were originally proposed. We considered the proposed negative
binomial regression, but decided to use a more general Poisson regression with GEE in order to account
both for repeated measures and for robustness to violations of the model assumptions. In order to
investigate the differences between the two statistical approaches, we conducted a preliminary analysis based on data collected up to now, and we did not find substantial differences in the results between the two methods. Since the number of split tests within a four-month period cannot exceed the number of months the POCT analysis was performed, this is accounted for in the analysis by means of an offset (the logarithm of the number of months the POCT analysis was performed in the given four-month period).