Reviewer's report

Title: A cluster randomized controlled trial to determine the effectiveness of a complex intervention in reducing potentially inappropriate prescribing in primary care: OPTI-SCRIPT study protocol

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Reviewer: Rolf Wahlstrom

Reviewer's report:

The authors have responded very well to the comments on the initially submitted manuscript. Several clarifications have made it possible to better understand how the study is designed and planned to be implemented.

However, before considerations on publication, there are a few matters that need further attention.

Major revisions

General

The authors do not agree that the intervention is not particularly complex and provide, in my mind, unnecessary strong arguments that they are correct. Fair enough, but there is no need to emphasize the complexity and not really any need to define academic detailing in the text. Obviously, as the authors state themselves ("a short educational presentation about PIP as a concept") is the qualification component to call it academic detailing, and I think it is quite obvious that this is not a very strong component of the intervention. However, that can be accepted. It is more difficult to accept what is presented as one of the other components of the 'intervention'. The authors claim that "Medicines Review" is one such component, but that is in fact an intermediate outcome of the intervention. The main aim of the "academic detailing" is to give the GPs motivation and tools to perform medicines reviews on a number of specified patients. We don't know whether the GPs will do this or not, and if they do it, whether they will follow the suggested protocol by using the web-based algorithm or do it in some other way. So, as I see it, the intervention comprises the following components: a) practice visit by pharmacist for education on PIP and on how to conduct a medicines review, plus demonstration of the web-based algorithm and how to use it; b) making the web-based algorithm available for the GPs for the selected patients, with detailed feedback on PIPs including treatment recommendations; c) individually developed information leaflet for the patients.

Title

The authors have not responded to my suggestion to declare the type of intervention in the title. This should be reconsidered. The term ‘a complex intervention’ does not give any information about the kind of intervention, regardless whether we agree on the complexity or not. The reader wants to know
the type of intervention under investigation, not that it is something anonymously complex. It is more informative to see words like “medicines review” or “treatment algorithm” or similar in the title than “potentially inappropriate prescribing”. Why not build on the initial title and, for example, write: Optimizing prescribing for older people in primary care through practice-based medicines reviews: a cluster randomised trial (OPTI-SCRIPT study protocol), or Effectiveness of medicines review with web-based treatment algorithms to reduce inappropriate prescribing (optional: for older people) in primary care: a cluster randomised trial (OPTI-SCRIPT study protocol), or something similar. Whatever the choice, the title should not start with the type of study.

Aims
In line with my reasoning above the need to revise the aims remains. First, the initial part about conducting a cluster RCT should be deleted. This refers to the method of study to respond to the aim, and is not an aim in itself. So the real aim starts with “… to determine the effectiveness and acceptability of a complex, multi-faceted intervention …”. In this part, ‘medicines review’ is mentioned, and this has to be modified as commented above.

Methods
It is now clearer, but still not totally clear how the GPs will be recruited. The authors write (Methods, Recruitment and allocation, 1st paragraph): “All eligible practices will be invited to participate …” and “When a GP agrees to participate, they (or the practice nurse/secretary) will be asked to identify a random sample of 50 patients …”. So practices are invited, but individual GPs agree? And then someone (?) selects a random sample of 50 patients. It is also stated in the first section of Methods (Trial design) that “… participation will be defined as attendance at the academic detailing visit and undertaking a medicines review.”

The following questions remain:

a. Is it correct that participation is exclusively decided by an individual GP or can participation be decided at group level by one person representing all GPs in a group practice?

b. How will the random selection of 50 patients take place? Will it take place for each of the GPs that have accepted participation, or will the patients for all accepting GPs be combined to one group before the random selection. In the first scenario: how will the 50 patients be distributed among, for example, three participating GPs? Dependent on number of listed patients? In the second scenario: what will happen if three GPs have accepted but the selected ten patients are listed on two of the GPs?

c. What will happen if a GP has accepted to participate, but does not show up for the visit by the pharmacist or does not perform any medicines review?

Sample size
The authors confirm that they have not assumed any change in the control practices. However, their arguments are not fully convincing for two reasons: a)
In this study the control GPs will receive feedback on PIP for only ten patients per practice. In my assessment this is a more specific intervention than what the authors refer to as “less intensive feedback”. Therefore, I still think it is more likely than not, that some of these GPs will be motivated to change their prescribing towards less PIP; b) The authors reference to Cochrane reviews on audit and feedback is relevant, but it should be remembered that this is not evidence that changes may not occur for other reasons. It is also not uncommon that one reason for no intervention effect is that the control arm has also changed in the intended direction. When conducting RCTs, it is mostly recommended to rather be on the safer side, which in this case would mean to assume a slight improvement in the control arm as well.

It is good that the study will include an evaluation of reasons for any detected impact on the performance of the control group, although “brief telephone interviews” may not be the most appropriate assessment method. Some more comments on this potential weakness of the study should be added.

It is not quite clear how the final sample size has been decided on the basis of the two separate calculations, which resulted in 22 practices and 106 patients per arm, and 14 practices and 66 patients per arm, respectively. It is stated (Sample size, last sentence) that “… at least 22 practices and 220 patients will be required for this study.” In the Abstract it is also stated that “This study” will involve “22 practices (clusters) and 220 patients”. Two questions must be answered:
a. Isn’t it correct that the total sample should be 22 practices in each arm?
b. How was the reasoning behind deciding on 220 patients (=10 patients per practice), when the first calculation indicated 106 patients and the second calculation indicated 66 patients?

Intervention
As mentioned above, the authors should modify the description of the components of the intervention.

Monitoring
The authors state in their response (and on page 13) that “The academic detailing will demonstrate the process of the medicines review with the intervention practices but the research team will not monitor how the GP implements the study protocol after this”. However, already on page 8 it has been stated that “… practices will be asked to complete 10 medicines reviews within a 6-8 week period, with a reminder if they are not completed within that time frame.” To me, these two statements are not fully compatible. It is further not clear what will happen if the reviews are not completed within the time frame. Will there be further reminders? Extended time frame?

Minor revisions
Editorial
There are still errors, like missing words, e.g., in Discussion, limitations (p. 17), fourth and sixth sentences; as well as in Table 1, third section, third line. There
are also errors in Table 2 like: no space between words or incorrect space; no capital letter at start of entry; truncated word.

Tables should start on a new page.

References:
The reference list is now almost free from editorial errors.
To become perfect the following should be corrected:
Ref #1: Full stop after title.
Ref #9 and 10: No space before and after hyphen.
Ref #14: Semicolon after publisher.
Ref #16: Add all authors up to 30.
Ref #26: Colon before page numbers; page numbers shown as II-2 – II-45, or II 2-45.
Ref #27: Citation is not complete (see the article for required style; cf. #29!).
Ref #48: Are page numbers available?