Author’s response to reviews

Title: Comparative effectiveness of the different components of care provided in heart failure clinics - protocol for a systematic review and network meta-analysis

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Version: 1 Date: 04 Dec 2018

Author’s response to reviews:

Reviewer #1: The aim of the systematic review and network meta-analysis (NMA) is to determine which components of care provided in heart failure clinics are the most effective in a reduction in mortality, hospitalization and visits to emergency department and improvements to quality of life.

Abstract: It would be good to mention in the abstract that separate NMA would be conducted for RCT and observational studies.
Response: We have amended the Methods section of the abstract to clarify that separate analyses will be conducted.

Interventions: Some of the potential interventional components have been suggested. It is not clear that whether authors would consider different intensity of the components the same or not. For example, for education and counselling if one study had one session on education and another study had 5 sessions. Will these two be treated as the same components?

Response: Thank you for this important comment. Based on this feedback, we have included an additional post hoc analysis to explore the possible effects of the intensity of different components. Similar to a Cochrane systematic review and meta-analysis of the effectiveness of disease management interventions for patients with heart failure (HF) [1], we will define a subjective measure of the “intensity” of each intervention for each intervention, agreed upon by the study team. We will then perform subgroup analyses using stratified network meta-analysis to assess the impact of component intensity. As noted for all subgroup analyses, this will be conditional upon data availability. We have updated the Methods section to include this important subgroup analysis.

Comparator: Standard care was listed as the comparator. As there is no restriction in the country in the search. Authors did not discuss the possibility of the standard care being different in different countries. In addition, authors did not discuss whether the standard care could have improved since 1990. It is important to consider these issues in the evidence synthesis.

Response: We thank the reviewer for bringing up this important issue. We agree that standard of care may differ between countries and may have changed over time. There have been a few major changes to standard of care: most notably, the introduction of remote monitoring [2-3], and new medication and medication protocols introduced in 2016 [4]. As such, depending on data availability, we will conduct subgroup analyses to assess if there is a difference in effectiveness of interventions across time and in low- or middle-income countries where standard care may be quite different and modified the Methods section to incorporate these additional analyses.

Outcome: There is a cut off that the outcomes of interest need to be assessed after a follow-up of 30 days or more. But no range was given. It is important to have a reasonable range of follow-up specified to avoid misleading conclusions.

Response: We will report the range of length of follow-up for the included studies and have planned to do subgroup analyses looking at the effect of follow-up period. However, we do not
want to exclude any studies on the basis of length of follow-up period. Based on the follow-up periods of the included studies (the follow-up period of studies included in a previous Cochrane systematic review and meta-analysis of the effectiveness of disease management interventions for HF patients [1] ranged from the minimum of 6 months to 2 years), we will stratify the follow-up period into appropriate categories (e.g., 6-12 months, 12-24 months, 24+ months).

Health-related quality of life (HRQoL) using validated measure or a composite end-point of any of these is one of the outcome of interest. It is not clear how different measures of HRQoL could be synthesised.

Response: We agree that different measures of HRQoL will be unable to be synthesized. However, we did not want to specify a priori which HRQoL measures will be considered as this could potentially exclude studies that chose to use a different measure. If many different HRQoL measures are reported, we may be unable to provide a quantitative synthesis of the results. In this case, we would report a narrative synthesis of the effect of heart failure clinic care on HRQoL.

Setting: It was stated that there will be no restrictions on the type of setting. Authors need to consider whether inventions and standard care delivered in different settings would be different. This in terms should have an impact of the design and conduct of the analysis.

Response: As noted in a previous response, we agree with the reviewer that standard of care may differ between countries. As such, depending on data availability, we will conduct a subgroup analysis to assess if there is a difference in effectiveness of interventions in low- or middle-income countries where standard care may be quite different. This is now described in the Methods section.

Language: It was specified that non-English language articles will be considered. However, in the search it is not clear how non-English language articles will be identified.

Response: We have amended the description of the search strategy to clearly state that no language restrictions will be applied to the search in order to capture non-English language articles.

Synthesis of results: It was stated that hazard ratio will be estimated for each outcome. Hazard ratio is not the appropriate summary measure for HRQoL.
Response: Thank you for noting our error. We assume that most HRQoL measures will be continuous and thus will estimate the mean difference between the intervention and control groups. We have included this change in the Methods section.

Authors also proposed subgroup analyses for gender, follow-up period, HF severity, method of enrolment and referral. Follow-up period is continuous data. It is not clear how subgroup analyses would be performed as what the subgroups are in this case. It depends on the clinical judgement on whether the settings, country or year of the study would be the potential treatment effect modifiers. Authors could also consider these factors in the analysis of explaining heterogeneity.

Response: As noted in an earlier response, we will stratify the follow-up period into appropriate categories (e.g., 6-12 months, 12-24 months, 24+ months) based on the follow-up periods of the included studies (in a previous Cochrane systematic review and meta-analysis of the effectiveness of disease management interventions for HF patients [1], follow-up periods of included studies ranged from a minimum of 6 months to 2 years). We agree that other factors such as the setting, country and year of study may also be important factors to consider and have added this to our planned subgroup analyses.

Reviewer #2: A well-written protocol with a sensible approach to a complex question.

I have just minor comments:

Population: will studies that recruited a mixed population including some eligible participants be included or excluded? Will a % contamination be tolerated? Will studies reporting subgroups of eligible participants be included?

Response: Studies that recruited a mixed population including some eligible participants will be excluded unless the authors reported outcome data for the subgroup of eligible participants. To clarify this, we have added the following text to the Methods section:

Studies that included both eligible and ineligible participants will be excluded unless they report data for the subgroup of patients who are eligible for this study.

Comparators/study designs: for cohort studies, should these be parallel design, or will studies with a historic control be eligible? Will controlled clinical trials (ie experimental, but not randomised) be eligible?
Response: Any cohort study design will be eligible for inclusion. Any controlled clinical trial will also be eligible for inclusion; we have amended the text in the abstract and Methods sections as required.

Study selection: what remedial steps would be taken in case of a poor kappa statistic? What would be considered a poor kappa statistic?

Response: We would consider a kappa of less than 0.6 to be ‘poor’ (kappa values of 0.6 or greater are considered to have moderate or stronger agreement) [5]. We will report agreement for each stage of the review process. We anticipate the agreement to be lower during the title and abstract screening; at this stage both reviewers do not need to agree for a study to proceed to the next stage of review. However, at the full text screening phase, any disagreements will be resolved through discussion with the senior author.

References:


