Reviewer's report

Title: Rationale, design and baseline results of the Treatment Optimisation in Primary care of Heart failure in the Utrecht region (TOPHU) study: a cluster randomised controlled trial

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Reviewer: Romain Eschalier

Reviewer's report:

Valk et al. described a very interesting rationale, design and baseline results of a cluster randomised controlled trial. The aim of the TOPHU study is to assess whether treatment optimisation in primary care of HFREF patients may have a positive impact on QoL, hospitalization and mortality in such population.

Major Compulsory Revisions
1. Will the study design adequately test the hypothesis?

The design of the present study is clear. However, several points need to be more precisely described especially on the statistical point of view.

. Considering this study as a cluster randomized trial, we thank the authors to explain, why the statistical considerations (sample size and analyses) do not take into account between and within cluster variability? For sample size estimation, an intra-class correlation coefficient should be considered in order to avoid lack of statistical power. For statistical analyses, the use of random-effects models seems more relevant because usual statistical tests don’t consider the correlated data.

. Page 4 : it is not clear what is the period of 1 year : the screening period ?

. 2 hours for 2 years follow-up seems to be a very low period of formation to treat adequately HF patients. Some new formations during the follow-up period may be considered.

. The criteria of the HF guidelines for HF diagnosis may be presented in a dedicated table to help readers.

. It is not clear if QoL, drugs, CV outcomes will be evaluated at each time point or just at 6 months for drugs, 12 months for QoL and 24 months for CV outcomes. Indeed all these informations, in my opinion, must be obtained at each time point. It will be very interesting and relevant.

. Use of Ivabradine will not be evaluated ? It is now clearly described in the guidelines.

2. Are sufficient details provided to allow replication of the work or comparison with related analyses: if not, what is missing?

The protocol is quite well described. However, several informations are missing:
. A detailed description of the uptitration chart is required.
. A detailed description of the 2 hours training is required.
. How the primary care practices will be chosen and randomized?

Minor Essential Revisions

Moreover I have some others questions / comments about the results section:
. I think it will be more interesting and relevant to present the results of HFREF population since this population is the center of the study. Furthermore, as well explained by the authors, use of drugs in HFPEF is not clearly established.
. I don't understand why 100% of patients have not a TTE?

Level of interest: An article of importance in its field

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’