Reviewer's report

Title: Prognosis of patients with apparent treatment resistant hypertension - A feasibility study

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Reviewer: Marie Bradley

Reviewer's report:

This was a feasibility study conducted within three general practices to inform the development of a larger cohort study aimed at investigating prognosis of patients with resistant hypertension. Specifically it evaluated participation of practices and patients, availability of outcome measures and data collection duration time and presented some results for outcomes of interest in this smaller sample. This study appears to lack important details about the objective of the full cohort study and its data requirements which makes it difficult to understand if the data collection and other processes reported in the feasibility study are adequate. It is unclear as to why this more manual, labour intensive data collection and study approach and smaller sample size is advantageous over the numerous, more efficient, prior studies investigating this issue which utilized large electronic databases and had large cohort sizes.

I have outlined my main points below:

1. Background

Please add page numbers

Line 27-28 High level evidence? Please explain or rephrase. It could be argued that a retrospective cohort study from insurance claims data is not high level evidence given the limitations listed by the author but if the author believes this is high level evidence what is the justification for changing to the study design proposed.

Please explain what is meant by dosing? Do you mean they failed to account for the doses of medications used?

It needs to be made explicitly clear why previous studies examining prognosis of patients with TRH using electronic databases have been limited and exactly why a more labour intensive practice based prospective cohort is necessary with substantially fewer patients than previous studies.

Please give details of what the full cohort study will investigate in the introduction. What is the objective? This is necessary to set the scene.
2. Methods

Reviewing the records of every patient who uses an anti-hypertensive medication manually seems very labor intensive given the widespread use of these agents—please comment. Also, how was it determined if they were hypertensive? Although this is mentioned in the introduction, the definition used in this study needs to be explicit in the methods.

In the introduction, it was mentioned that dosing was not considered in previous studies. There was no mention in this study about assessing doses of medications from the patient medical records?

Cohort entry date? Will patients be followed up from the same defined point in the disease course to ensure a precise estimate of prognosis? There was no mention of follow-up time for the feasibility study in the methods or dates of follow-up?

Patient characteristics: this should be in the results. Please state the proportions that have true TRH vs apparent or pseudo TRH among the cohort of 646 patients. These groups are very different and considering these differences when designing the study is important.

More information is needed on outcome ascertainment in the practices. There is no mention of ensuring outcomes occurred after TRH was first diagnosed.

Cohort study design and analysis: based on the study by Daugherty et al (and your previous study on multi-morbidity and CV outcomes, which informed the current study) a comparator group, was used to compare outcomes in those with TRH versus non-TRH. It is not clear how informative this study will be without this. If a comparator group is to be used how will it be defined and data collected?

It would be useful to see some mention of a statistical analysis plan given that results are presented also consider reporting incidence rates in the cohort and also some consideration as to how to treat true and apparent TRH as different groups.

3. Discussion

Page 1 line 52-53 Please explain the sentence "it may reflect the phenotype of patients recruited within general practice….."
Last page of discussion line 2-3- in the methods it appears to be stated that it was possible to delineate true vs apparent TRH. How will this study be able to accomplish this and why were others unable to as this is an important issue?

Lines 7-8 please explain your concerns with power given that you are not comparing outcomes to another group.

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**Quality of written English**
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