Author's response to reviews

Title: Cost-effectiveness analysis of guidelines for antihypertensive care in Finland

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Responses to reviewer’s comments

General comments

We extend our thanks for the reviewer’s strenuous efforts with regards to our manuscript, the reviewer’s suggested and proposed revisions are, broadly, welcomed and will undoubtedly increase the transparency of this cost-effectiveness analysis.

In response to the reviewer’s general comments we offer the following explanations concerning the timing and type of study presented in our manuscript. It should be noted that this research seeks to offer information on the cost-effectiveness of guidelines, i.e. a scenario of care, rather than on the cost-effectiveness of individual antihypertensive treatments. In Finland the Current Care organization has planned to update the guidelines every two to three years. Preliminary results from this study were made known to the workgroup undertaking the update of the ACCG in 2006 and the preliminary finding of cost saving in the target population overall has been presented to the Current Care organization. However, as four members of the workgroup which produced the manuscript have had extensive training in economics we could not, as professionals, unreservedly promote the use of the term ‘cost saving’ due to the outcomes in some of the subgroups.

Further, Finland is a fairly small nation, with finite human resources in terms of economic evaluation experts, which would be a hindrance to the simultaneous (or prior) drawing up of guideline cost-effectiveness analyses and guidelines. Nevertheless, researchers in Finland on a number of occasions have attempted to broach the (often rather complicated) question of the cost-effectiveness of guidelines.

As to the reviewer’s valid question concerning clarification as to why this study is important, we turn to the reviewer’s own comments for a succinct line of argumentation and offer thanks for their general reminder that many health care decision-makers seem to assume the intrinsic usefulness of developing clinical practice guidelines and, as this is the case, the analysis is clearly warranted in order to offer a relatively rare source of evidence on such assumptions.

We thank the reviewer for revealing the relative lack of clarity with which we described the aims and purpose of this study in the original draft. In the revised version we hope to have stated both the aims and results in a more reader-friendly manner.

Major Compulsory Revisions

1) Although high blood pressure is the biggest primary cause of cardiovascular-related morbidity and mortality in Finland, we are very aware that reducing blood pressure alone will not fully “normalise” the associated cardiovascular risk. Our research was primarily designed to provide cost-effectiveness information on the Antihypertensive Current Care Guidelines (ACCG) for the Finnish setting and we believe that the rich administrative databases and the ability to link individual level data serve this purpose adequately. Here, we would like to reiterate our statement in the original manuscript that the estimates of the effects of blood pressure group on cardiovascular-related mortality and morbidity should be treated only as indicative of the extent and direction of the likely associations between blood pressure group and health status. The effect of treatment (medication and lifestyle interventions) in this study is to lower blood pressure; we assume the average effects are those available from the literature, for medications Law, et al. (2003) and for the ACCG lifestyle intervention Kastarinen et al. (2002). The assumed effect size (in terms of blood pressure changes) of treatment is set out in Tables 7 and 8 in Additional file 1. This lowering of blood pressure resulting from treatment, in turn, results in changes in the distribution of individuals (i.e., movement) between blood pressure groups. Instead of calculating the usual relative risk reduction due to treatment/no treatment at the individual level, our individual level data is used to provide estimates of the effect of treatment on blood pressure group membership - in keeping with the framework of the ACCG. We have added text to this effect in our revised manuscript. The effect of blood pressure group membership (in terms of morbidity/mortality) is calculated using a series of Cox models. In an attempt to model the heterogeneity of the subgroups considered to be important in a cost-effectiveness analysis, calculations for groups, stratified by age, gender and blood pressure, were undertaken. The assumption of ‘full effect’, used by Weinstein and Stason (1976) in their seminal work, provides an upper bound for the maximum hypothetical changes which could be brought about by the implementation of the ACCG scenario as well as an upper bound for the
maximum hypothetical changes which could be brought about by the use of the PCP scenario. For brevity, calculations of relative risk reduction and the estimated baseline hazard functions are combined together (in Table 9 in Additional file 1) as quinquennial intensity rates for the four blood pressure groups.

2) We refer to the previous comment and to the lower part of the Tables 7, 8 and 9 in Additional file 1.

3) We were fully aware at the time we submitted our manuscript of the results from recent Cochrane reviews (e.g., Fahey et al. 2005 and 2006) and, in the absence of larger randomised controlled trials, we stand by our decision to use the small (but favourable) effects shown in Kastarinen et al. 2002. The following reasons are also offered for using a single study: Our research was primarily designed to provide cost-effectiveness information in the Finnish setting and thus the decision was taken to use a study highly relevant to the Finnish primary care setting. This decision also led to increased precision concerning the costing of the lifestyle intervention. We have added text to this effect in our revised manuscript and have incorporated a reference to the important work of the Cochrane collaboration.

4) At the time of undertaking this research, direct linkage of individual-level data on risk factors with exact concurrent usage of medication was not possible. Only simplified adjustment was undertaken (raising SBP by 10 mmHg and DBP by 6 mmHg). Therefore, as the reviewer suggested, we were only able to assess the volume of prescribing that would result from adherence to the ACCG scenario and compare this with the volume of prescribing observed in Finland in the autumn of 2001.

5) We agree that the assumption of full adherence is unrealistic; however, such assumptions are standard in cost-effectiveness analyses. This assumption provides an upper bound for the maximum hypothetical changes which could be brought about by implementation of the ACCG scenario as well as an upper bound for the maximum hypothetical changes which could be brought about by the use of the PCP scenario. During the course of this research, we have analysed the impact of a partial implementation of the ACCG scenario. When we compared a partial (20%) implementation of the ACCG scenario to full implementation of the PCP scenario the ‘base-case’ results (aggregated over all subgroups) suggest that the ACCG scenario implementation would be around €100m less expensive and would produce around 10,000 more life-years overall. We do not consider that the inclusion of such information in the manuscript would be entirely helpful, as it may well reduce the comparability of this study and increase its opacity.

6) In large part, the subgroup results differ according to blood pressure group (BPG). Generally, in blood pressure group 0 (BPG 0, where SBP is below 130 mmHg and DBP is below 85 mmHg) the effect of the application of the ACCG scenario was to reduce expected costs at the same time as reducing the expected number of life-years. This result reflects the fact that the PCP scenario, with at least some use of medication, is always treated by the model as being more effective than mere monitoring (i.e., in BPG 0 active surveillance is the only treatment option under the ACCG scenario). Largely, for BPG 1 and BPG 2 (where SBP is 130–139 mmHg and/or DBP 85–89 mmHg and SBP is 140–159 mmHg and/or DBP 90–99 mmHg, respectively), the ACCG scenario was shown to be cost saving (with decreased costs and increased life-years expected). Indeed, these two groups are those for which, a priori, we expected to see the most benefit from lifestyle interventions, either alone (in the case of BPG 1) or in combination with medication for individuals at increased risk of CHD (in the case of BPG 2). Generally, in BPG 3 (where SBP is over 160 mmHg or DBP over 100 mmHg), increased expected costs are associated with an increase in the expected number of life-years. This reflects the fact that the ACCG scenario applies drug treatment to all individuals in BPG 3, whereas the PCP scenario only treats a portion of individuals in this group. Other factors which are likely to have contributed to the probable cost-effectiveness of the ACCG scenario include: 1) the manner in which the ACCG scenario performs diagnosis and 2) treatment using inexpensive medications from within each pharmacological subgroup. We have amended the original manuscript to reflect the above. As the reviewer also seemed to have found difficulty in understanding the probable cost-effectiveness of the ACCG scenario, we have replaced Figure 3 and its accompanying text with what we consider to be a much more relevant supplementary description of the cost-effectiveness results in the 56 subgroups.

7) In our original manuscript we state the following: “This study did not consider the cost of ACCG development, nor the costs of ACCG implementation in clinical practice, either”. The main reasons for this approach were that 1) the costs of PCP development and implementation were unknown and 2) this cost-effectiveness study covers the hypothetical implementation of only part of the ACCG for a broad, but nevertheless restricted, target population - what we refer to as the ACCG scenario. This
ACCG scenario is not identically equivalent to the whole of the evidence-based ACCG; hence, we did not include estimates of development or implementation costs in our study.

“Was developing the evidence-based clinical practice guidelines worth the effort?” – the answer to this question is, as we point out in our conclusions, dependent on the values decision-makers hold when evaluating the relative merits of the alternative scenarios. However, the following information may help to reduce concerns surrounding the costs of guideline production relative to the resultant overall costs or changes in life years.

The Current Care organization produces around ten new guidelines and 10-20 updates per year and uses the equivalent of approximately 35 full time staff, of which two thirds of the work is on a voluntary basis. The average cost of a new Current Care guideline is around 100,000 euros and the cost of updating a guideline is around 50,000 euros. These figures are for the development of the guidelines and also for electronic dissemination and e-implementation (i.e., web courses and slide shows).

(Source: Eeva Ketola, Chief Editor of Current Care, personal information 15.05.2007).

We have amended the original manuscript to reflect the above.

Minor Essential Revisions

8) We have made changes in order to refer to the addition files in a more logical manner.

9) According to the ACCG the rational first-line treatment would be thiazides for 60% of the population (not complicated by other cardiovascular-related disease) for which drug treatment would be recommended. We would also like to point to some of the sensitivity analyses undertaken on this assumption, see Additional file 5. For example, page 27 of this additional file shows the impact of reducing the initial use of thiazides to 20%, which does not seem to dramatically change the overall (or subgroup-specific) results. We have amended the original text to reflect this.

10) We have made changes in order to refer to the tales in a more logical manner.