Author’s response to reviews

Title: Prevention of cardiovascular diseases: a cost study in family practices

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Author's response to reviews: see over
Concerning – revision manuscript: 6795928205230707

Rotterdam, 22 May 2011

Dear Prof. Wilson,

Thank you for offering us the opportunity to submit a revised version of our manuscript entitled “Primary prevention of cardiovascular diseases: a cost study in family practices” (MS: 6795928205230707) subject to reviewers comments.

We thank the three reviewers and the associate editor for their generally positive and very valuable comments. We are pleased to enclose the revised version in which we addressed their feed-back point-by-point.

Reviewer #1 Vanessa Selak

“I think this article provides important information regarding the health service resource implications of the primary prevention of CVD, which is often not adequately considered when guidelines and recommendations are developed.”

“Major Compulsory Revisions”

1. “Provide basis on which ethical review not required for questionnaire or video recordings (this may be acceptable in the Netherlands but is unusual in other jurisdictions)”

Response: According to Dutch legislation, approval by a medical ethics committee was not required for this observational study, because the study did not interfere with a GPs usual work process and patients were not confronted with whatever project-related intervention. We added this sentence to the manuscript (see Methods / Video recordings, p.7).

2. “Specify whether the consent that was obtained from GPs & patients for video recording consultations allowed for use of the video recordings for the current study (as the recordings were obtained for an earlier study with a different purpose).”

Response: Patient’s consent included the use of the video recordings for communication research and was formulated in such a general way as to allow secondary analyses at a later state. The studies were carried out according to Dutch privacy legislation. The privacy regulation was approved by the Dutch Data Protection Authority. Our research did comply

We added more details to the manuscript; see Methods / Video recordings, p.7 or the following text: The study protocol adheres to the Dutch privacy legislation, approved by the Dutch Data Protection Authority. However, approval by a medical ethics committee was not required for this observational study, because the study did not interfere with a GPs usual work process and patients were not confronted with whatever project-related intervention. Our research complied with the Helsinki Declaration. All participating general practitioners and patients filled in an informed consent form before the recording of the consultation.

“Minor Essential Revisions”

1. “Provide references for the literature on which the questionnaire was based. Ideally this will include guidelines that are used locally, with a clear link between the guidelines and the activities selected for the questionnaire.”

Response: The two main references for the literature on which the questionnaire was based were the following: (i) Dutch Institute for Healthcare Improvement CBO. The Dutch multidisciplinary guideline for cardiovascular risk management. [http://www.cbo.nl/Downloads/217/rl_cvrm_2006.pdf]; and (ii) De Backer G, Ambrosioni E, Borch-Johnsen K, et al. European guidelines on cardiovascular disease prevention in clinical practice. Third Joint Task Force of European and Other Societies on Cardiovascular Disease Prevention in Clinical Practice. Eur Heart J 2003; 24: 1601-10. We added these references to the manuscript; see Methods / Questionnaire, page 6 and References, p.18.

2. “Provide a brief summary of local recommendations for CVD prevention, particularly for primary prevention, including how people without a history of CVD are risk assessed (as this should form the basis of primary prevention interventions such as medications).”

Response: The Dutch multidisciplinary guideline for cardiovascular risk management recommends that people without a history of CVD or endocrine disease complaints should receive primary prevention interventions such as lifestyle recommendations, blood pressure measurements or blood tests if there is a positive family history, clear overweight, or a
patient’s request. The European guideline does not give thresholds (age, blood pressure value, cholesterol value) for recommending cardiovascular risk profiling. However, it is clear that cardiovascular risk profiling is more cost-effective in patients with one or more risk factors. Based on considerations of feasibility, the Dutch multidisciplinary guideline for cardiovascular risk management recommends to use the following threshold values for blood pressure \( \text{SBD} \geq 140 \text{ mmHg} \) and cholesterol \( \text{TC} \geq 6.5 \text{ mmol/l} \), which are above the average Dutch population, for cardiovascular risk profiling. Moreover, this Dutch multidisciplinary guideline recommends cardiovascular risk profiling if the combination age (men \( \geq 50 \) year, women \( \geq 55 \) year) and smoking exists. This guideline reports that the decision to advise medications for people without a history of CVD or endocrine disease complaints depends especially on the value of the estimated risk of CVD and the value of the SBD and \( \text{TC/HDL} \)-ratio. However, it depends on patient’s preferences as well. We included a brief summary of these local recommendations for CVD primary prevention in the manuscript; see Background, pp. 4-5.

3. “Explain why only 80 of the 161 FPs in the Netherlands Information Network were sent the questionnaire, and how these 80 were selected.”

Response: Each year there are approximately 80 family practices participating in the Netherlands Information Network. So there was one questionnaire for each of these 80 practices in the network in 2009. In the period 2005 – 2009 there were 161 practices that participated in the network for at least one year.

4. “Explain the basis for the statement that that the ‘LINH is a representative network of Dutch FPs’.”

Response: The sample of practices originates from the mid 1990’s. Practices participate on a voluntary basis. In order to enable longitudinal analyses, changes in the set of participating practices are kept to a minimum. There is a waiting list for practices to participate in the network. When a practice quits participating in the network, a new practice is invited, taking into account the representativeness of the network regarding practice type, urbanicity and the software system that is used. Practices that are allowed to the network have successfully completed a three month test period in which their recording behaviour is monitored. We explained the basis for the statement that the ‘LINH is a representative network of Dutch FPs’ in the manuscript; see Methods / Questionnaire, p.6) or the text following text: Each year LINH contains 80 FPs and is a representative network of Dutch FPs as it takes into account

5. “What is the representativeness of the 40 GPs that participated in the video recordings.”
Response: Forty Dutch general practitioners participated in the study. These general practitioners are representative of Dutch general practitioners regarding age, practice form and number of days worked (Noordman, J., Verhaak, P., Beljouw, I. van, Dulmen, S. van. Consulting room computers and their effect on GP patient communication: comparing two periods of computer use. Family Practice 2010; 27: 644-651). We added this sentence and reference to the manuscript; see Methods / Video recordings, p.7.

6. “What is the representativeness of the 808 consultations video-recorded.”
Response: Eight hundred and eight consultations were video-recorded. These consultations were randomly recorded on week days, and are expected to represent Dutch general practice consultations. We added this sentence and reference to the manuscript; see Methods / Video recordings, p.7.

7. “Clarify whether patients with a history of CVD were also excluded from the LINH data extract (in addition to ‘patients who had consulted their general practitioner for cardiovascular problems in 2005-2007’).”
Response: Patients with a history of CVD that did not contact their general practitioner at least once for cardiovascular or endocrine diseases in 2005-2007 were regarded as primary preventive nature. Hence, these patients were included in the LINH data extract. We assumed that all patients with a history of CVD should have contacted their general practitioner at least once for cardiovascular reasons (e.g. to follow up blood pressure or blood values, or for obtaining a repeat prescription) in 2005-2007. This assumption may be a limitation of the study. However, as this latter group is small, we do not expect that the reported results are changed considerably. We added this assumption as a limitation to the manuscript; see Discussion, third limitation, p.14.
8. “Define what is meant by ‘endocrine diseases’. Is this limited to diabetes (types 1 & 2) or more extensive?”

Response: ‘Endocrine diseases’ consist of diabetes (types 1 and 2) and/or disorders of lipid metabolism (e.g. hypercholesterolemia). We added these details to the manuscript; see Methods / Data analyses, second paragraph, p.8.

9. “Results / prescription / 3rd sentence: specify what is meant by ‘lowest part’ and ‘highest part’ – do you mean the FP with the lowest and highest prescription rates, respectively? (clarification of same point required in Table 3).”

Response: Indeed, we meant the FP with the lowest and highest prescription rates, respectively. We changed the text accordingly in the manuscript; see Results / Prescription of cardiovascular medication in FPs / third sentence, p.11 and Table 3, or the following text:

On average 19.2% (30,275/157,137) of the patients of the FPs had a prescription for cardiovascular medication; the prescription rate for cardiovascular medication varied between 12.0% and 27.0% for the FP with the lowest and highest prescription rates, respectively.

10. “While it is good that patient characteristics are acknowledged as an important determinant of variability between FPs in prescription rates, the overriding issue is appropriateness of prescribing which should be based on absolute cardiovascular risk (which takes into account patient characteristics). This point should be acknowledged.”

Response: We agree with the reviewer that this point should be acknowledged; see Discussion / third paragraph, p.13 or the following text: The substantial differences in prescription of PPCM in FPs can partly be explained by the various combinations of patient characteristics per FP as the appropriateness of prescribing should be based on absolute cardiovascular risk.

11. “Change anamnesis to history (presuming that is what is meant) throughout document.”

Response: We changed anamnesis to history throughout the manuscript.

12. “Change counseling to counselling throughout document (presuming US spelling is not being used in the journal).”

Response: We changed counseling to counselling throughout the manuscript.
13. “Change behavior to behaviour throughout document (presuming US spelling is not being used in the journal).”
Response: We changed behavior to behaviour throughout the manuscript.

14. “Change life style to lifestyle throughout document.”
Response: We changed life style to lifestyle throughout the manuscript.

15. “Change risk profile drafting to cardiovascular risk profiling throughout document.”
Response: We changed risk profile drafting to cardiovascular risk profiling throughout the manuscript.

Response: We changed spending to spent (see Abstract / Methods / second sentence, p.2).

17. “Abstract / results / first sentence: change expenditures to expenditure.”
Response: We changed expenditures to expenditure (see Abstract / Results / first sentence, p.2).

18. “Abstract / conclusion / second sentence: delete ‘a’.”
Response: We removed ‘a’ (see Abstract / Conclusion / second sentence, p.2).

Response: We inserted ‘to determine’ after needed (see Abstract / Conclusion / third sentence, p.2).

20. “Background / third paragraph / first sentence: delete ‘size of the’ and change it to are.”
Response: We removed ‘size of the’ and changed it to are (see Background / third paragraph / first sentence, p.4).

21. “Background / third paragraph / second sentence: change an to a.”
Response: We changed an to a (see Background / third paragraph / second sentence, p.4).

22. “Background / third paragraph / fourth sentence: first part ‘Also information is lacking what part of prescription of cardiovascular medication is primary preventive’ needs to be
changed. How about ‘Also, information is lacking on the proportion of cardiovascular medication prescriptions that are for primary prevention’.”

Response: We changed the text as follows: Moreover, information is lacking on the proportion of cardiovascular medication prescriptions that are for primary prevention (i.e., cardiovascular medication aimed at a determinant of cardiovascular disease for people with neither cardiovascular nor endocrine diseases), and how much general practitioners differ in prescribing behaviour regarding primary preventive cardiovascular medication. (see Background / third paragraph / fourth sentence, p.4).

23. “Background / third paragraph / fifth sentence: move ‘be’ from between may and not to between always and strictly.”

Response: We moved ‘be’ from between may and not to between always and strictly (see Background / third paragraph / fifth sentence, p.4).

24. “Background / fourth paragraph / second sentence: change wording of iii) to the proportion of cardiovascular medication prescriptions that are for primary prevention.”

Response: We changed wording of iii) to the proportion of cardiovascular medication prescriptions that are for primary prevention (see Background / fourth paragraph / second sentence, p.5).

25. “Methods / questionnaire / third sentence: add ‘the’ between of and above.”

Response: We added ‘the’ between of and above (see Methods / Questionnaire / third sentence, p.6).

26. “Methods / video recordings / second sentence: change what to of and delete were.”

Response: We changed what to of and deleted were (see Methods / Video recordings / second sentence, p.7).

27. “Methods / data analysis / first sentence: change practice nurse to practice nurses”.

Response: We changed practice nurse to practice nurses (see Methods / Data analysis / first sentence, p.8).

28. “methods / data analysis / fourth sentence: delete ‘the’ between as and practice and delete ‘s’ from insurances.”
Response: We removed ‘the’ between as and practice and removed ‘s’ from insurances (see Methods / Data analysis / fourth sentence, p.8).

29. “Methods / data analysis / second paragraph / second sentence: change ‘patients without cardiovascular nor endocrine diseases’ to ‘patients with neither cardiovascular nor endocrine diseases’.”
Response: We changed ‘patients without cardiovascular nor endocrine diseases’ to ‘patients with neither cardiovascular nor endocrine diseases’ (see Methods / Data analysis / second paragraph / second sentence, p.8).

30. “Results / costs / first sentence: insert ‘were’ after each %.”
Response: We inserted ‘were’ after each % (see Results / Costs / first sentence, p.10).

31. “Discussion / 4th paragraph/ second sentence: needs to be reworded. How about: ‘Positive . . . as well as negative . . . outcomes are relevant’.”
Response: We reworded the text as follows: Positive (i.e. high prescribing behaviour of cardiovascular medication results in higher survival rates and less adverse effects) as well as negative (no difference in health outcomes between FPs with a high or a low prescribing behaviour of cardiovascular medication) outcomes are relevant (see Discussion / fourth paragraph / second sentence, p.13).

32. “Conclusion / 3rd sentence: insert ‘to determine’ between needed and whether.”
Response: We inserted ‘to determine’ between needed and whether (see Conclusion / third sentence, p.15).

“Discretionary Revisions”
1. “It would be helpful to more clearly specify throughout the article that the study is focusing on cardiovascular primary preventive activities (to distinguish from secondary prevention).”
Response: We specified more clearly throughout the article that the study is focusing on cardiovascular primary preventive activities.

2. “It would be helpful to provide the total time spent on CVD preventive activities (i.e. frequency of preventive activities per week x time spent on each activity, by discipline). This would help to put the magnitude of time spent into the context of total FP activity.”
Response: The total time spent on CVD primary preventive activities in FP per 1 fte discipline per year is 47 hours, 30 hours, and 41 hours for the general practitioner, the health care assistant and practice nurse respectively. See the tables A-D below for more detail information. We are prepared to put these results in an appendix if the Editor agrees on this.

Table A: Frequency of primary preventive activities in family practice to prevent cardiovascular diseases in the Netherlands in 2009, in amount per week per discipline.

<table>
<thead>
<tr>
<th></th>
<th>family history</th>
<th>lifestyle history</th>
<th>cardiovascular risk profiling</th>
<th>blood pressure measurement</th>
<th>a blood test related activity</th>
<th>lifestyle counselling</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP</td>
<td>6.6</td>
<td>6.5</td>
<td>4.0</td>
<td>16.7</td>
<td>4.3</td>
<td>6.2</td>
</tr>
<tr>
<td>HCA</td>
<td>2.5</td>
<td>2.9</td>
<td>2.4</td>
<td>10.5</td>
<td>5.2</td>
<td>3.6</td>
</tr>
<tr>
<td>PN</td>
<td>3.9</td>
<td>5.4</td>
<td>4.0</td>
<td>13.1</td>
<td>2.8</td>
<td>9.5</td>
</tr>
</tbody>
</table>

Note: GP = general practitioner; HCA = health care assistant; PN = practice nurse

Table B: Duration of primary preventive activities in family practice to prevent cardiovascular diseases in seconds.

<table>
<thead>
<tr>
<th></th>
<th>family history (sec)</th>
<th>lifestyle history (sec)</th>
<th>cardiovascular risk profiling (sec)</th>
<th>blood pressure measurement (sec)</th>
<th>a blood test related activity (sec)</th>
<th>lifestyle counselling (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>23.7</td>
<td>24.1</td>
<td>244</td>
<td>105.7</td>
<td>71.1</td>
<td>46.1</td>
</tr>
</tbody>
</table>

Table C: Time spent on primary preventive activities in family practice to prevent cardiovascular diseases in the Netherlands in 2009, in minutes per week per discipline.

<table>
<thead>
<tr>
<th></th>
<th>family history (min/wk)</th>
<th>lifestyle history (min/wk)</th>
<th>cardiovascular risk profiling (min/wk)</th>
<th>blood pressure measurement (min/wk)</th>
<th>a blood test related activity (min/wk)</th>
<th>lifestyle counselling (min/wk)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP</td>
<td>2.6</td>
<td>2.6</td>
<td>16.1</td>
<td>29.4</td>
<td>5.2</td>
<td>4.8</td>
</tr>
<tr>
<td>HCA</td>
<td>1.0</td>
<td>1.2</td>
<td>9.8</td>
<td>18.5</td>
<td>6.1</td>
<td>2.8</td>
</tr>
<tr>
<td>PN</td>
<td>1.6</td>
<td>2.2</td>
<td>16.3</td>
<td>23.1</td>
<td>3.3</td>
<td>7.3</td>
</tr>
</tbody>
</table>

Note: GP = general practitioner; HCA = health care assistant; PN = practice nurse

Table D: Time spent on primary preventive activities in family practice to prevent cardiovascular diseases in the Netherlands in 2009, in hours per year per discipline.
<table>
<thead>
<tr>
<th></th>
<th>family history (hours/yr)</th>
<th>lifestyle history (hours/yr)</th>
<th>cardiovascular risk profiling (hours/yr)</th>
<th>blood pressure measurement (hours/yr)</th>
<th>a blood test related activity (hours/yr)</th>
<th>lifestyle counselling (hours/yr)</th>
<th>total (hrs/yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP</td>
<td>2.0</td>
<td>2.0</td>
<td>12.3</td>
<td>22.5</td>
<td>4.0</td>
<td>3.7</td>
<td>46.5</td>
</tr>
<tr>
<td>HCA</td>
<td>0.8</td>
<td>0.9</td>
<td>7.5</td>
<td>14.2</td>
<td>4.7</td>
<td>2.1</td>
<td>30.2</td>
</tr>
<tr>
<td>PN</td>
<td>1.2</td>
<td>1.7</td>
<td>12.5</td>
<td>17.7</td>
<td>2.5</td>
<td>5.6</td>
<td>41.2</td>
</tr>
<tr>
<td>Total</td>
<td>4.0</td>
<td>4.5</td>
<td>32.4</td>
<td>54.4</td>
<td>11.2</td>
<td>11.4</td>
<td>117.9</td>
</tr>
</tbody>
</table>

Note: GP = general practitioner; HCA = health care assistant; PN = practice nurse

3. “Change risk factor modifications to risk factor modification throughout document (I think latter sounds better).”

Response: We changed risk factor modifications to risk factor modification throughout the manuscript.

4. “The categories of patient characteristics and FP characteristics are provided in Table 5, but I think it would be helpful to include these in the methods section too.”

Response: We included the categories of patient characteristics and FP in the methods section; see Methods / Data analysis / second paragraph / fourth sentence, pp. 8-9 or the following text: Multilevel analyses were conducted to investigate whether differences in prescription of cardiovascular medication for each patient group could be explained by family practice characteristics (urbanisation and practice type) and/or by patients’ characteristics (age, gender, living in a disadvantaged neighbourhood (i.e. a geographically localised community within a larger city, town or suburb that contained a large proportion of people with a low social economic status), and insurance type).

Reviewer #2 Gary McLean

“Major Compulsory Revisions.”

1. “The paper explores spending on cardiovascular preventive activities and prescribing of primary cardiovascular medication (PPCM) in Dutch family practices. However, my main issue is that there is no attempt to evaluate whether spending on one impacts on the other (i.e. does higher spending on cardiovascular preventive activities reduce prescribing and vice versa). There is already a considerable literature on variation on prescribing in CVD prescribing and reasons for this. The authors should therefore either add weight to their paper by combing the two issues under study here or explain in more detail why they have not or cannot do this and why in it's present form the study is important and should in published in relation to other literature in the field.”
Response: We agree with the reviewer that it is valuable to obtain insight whether higher spending on cardiovascular preventive activities may reduce prescribing and vice versa. We used a mixed methods design, which consisted of three parts: i) a questionnaire among family practices (FPs); ii) video recordings of hypertension-, cholesterol- and/or endocrine-related general practitioner visits; and iii) the database of Netherlands Information Network of General Practice. Although there was an overlap in the FPs used for the three different approaches, this overlap was too small to give reliable insight whether higher spending on cardiovascular preventive activities reduced prescribing and vice versa. We mentioned this point as a recommendation to the manuscript; see Discussion, fourth paragraph, p.13.

We realised that there was already a considerable literature on variation on prescribing in CVD prescribing. However, the strength of our study is that it focused on the variation on cardiovascular medication prescriptions that are for primary prevention (i.e., cardiovascular medication aimed at a determinant of cardiovascular disease for people with neither cardiovascular nor endocrine diseases). To date information is lacking how much general practitioners differ in prescribing behaviour regarding primary preventive cardiovascular medication. Additionally, our study gives a comprehensive overview of spending on cardiovascular primary preventive activities in FPs, which is quite innovative and crucial for health policy development and evaluation. Therefore, we are convinced that our study contains valuable information to the readers. We specified more clearly throughout the article that the study is focusing on cardiovascular primary preventive activities.

2. “There authors should define in more detail what is meant by PPCM what drugs were used and why.”

Response: Primary preventive cardiovascular medication (PPCM) is defined as cardiovascular medication (i.e., all kind of beta blockers and statins) aimed at a determinant of cardiovascular disease for people without cardiovascular or endocrine diseases (i.e. diabetes (types 1 and 2) and disorders of lipid metabolism (e.g. hypercholesterolemia)); see Methods / Database of Netherlands Information Network of General Practice / p.7. However, other (primary) preventive cardiovascular medication exists. Aspirin, for example, can be used as a (primary) preventive cardiovascular medication as well. However, this medication is also used as an analgesic to relieve minor aches and pains, as an antipyretic to reduce fever, and as an anti-inflammatory medication. Therefore for practical reasons we focused on statins and beta blockers only. We added our focus on statins and beta blockers only as a limitation to the manuscript, and mentioned that the costs of total spending on primary preventive
cardiovascular medication may therefore be an underestimation; see Discussion, fifth limitation, p.14.

3. “The authors should answer how the possible disparancy between costs and volume might impact of their findings for prescribing.”

We have interpreted this comment as: ‘do different trends for costs and volume of prescriptions for PPCM have an impact on our statement that ‘total costs of cardiovascular primary preventive activities in FPs such as blood pressure measurements and lifestyle counselling are relatively low compared to the costs of PPCM’. We do think they have, but not such that our conclusions have to be altered. In the Netherlands important PPCM like simvastatin and pravastatin have gone out of patent before 2005 (the starting point of our study). This has had a profound impact upon the costs of statins. Total volume of statins prescribed rose with 49% over 2005-2009, while total costs fell with 7%. For beta blocking agents both costs and volume rose with 12% over this period (source: Dutch health insurance Board www.gipdatabank.nl). Without the pricefall in statins, the relative costs of primary preventive activities in FPs would even have been lower compared to the costs of PPCM than is currently the case.

4. “The authors should define in more detail what is meant by disadvantaged neighbourhood and outline other factors not accounted for which might impact on variations on prescribing such as ethnicity.”

Response: A disadvantaged neighbourhood means a geographically localised community within a larger city, town or suburb that contained a large proportion of people with a low social economic status; see Methods / Data analysis / second paragraph / p.9. Although we took into account different factors that might have an impact on variations in prescribing (e.g., age, gender, neighbourhood), there may be other factors for which we did not account for such as ethnicity and marital status. We added this point as a limitation to the manuscript; see Discussion, fourth limitation, p.14.

Reviewer #3 Ngiap Chuan Tan

1. “Is the question posed by the authors well defined? The focus is on expenditure on “cardiovascular preventive activities” in Dutch FP. However the authors are not explicit in defining what constitute “cardiovascular preventive activities”, which should be done clearly
in the background description. Do “cardiovascular preventive activities” encompass both primary prevention and secondary prevention activities? Is this a universally acceptable definition or one that is drawn up by the authors, which is also acceptable? Whilst measuring blood pressure for the healthy population is a form of primary prevention activity, prescribing anti-hypertensive medication will likely be secondary prevention of patients already at risk of cardiovascular complication. Instead of grouping them together, the authors may consider if there is any merit of cost analysis for each component. Secondary prevention activities are likely to incur higher cost, as it also includes blood pressure measurement, lifestyle counseling, consultation and medication. The authors define cost expenditure on medication as those spent largely on statins and antihypertensive drugs. Shouldn’t anti-platelet medications such as aspirin and the more costly clopidogrel be included in computing the cost of the PPCM?”

Response: Our study is focusing on cardiovascular primary preventive activities only. All data collected about the six activities (blood pressure measurement; cardiovascular risk profiling; a blood test related activity; family history; lifestyle history; and lifestyle counselling) as well as the data about prescription of primary preventive cardiovascular medication (PPCM) agreed with primary prevention. PPCM is defined as cardiovascular medication aimed at a determinant of cardiovascular disease for people with neither cardiovascular nor endocrine diseases. We specified more clearly throughout the article and in the title that the study is focusing on cardiovascular primary preventive activities.

We defined expenditure on medication as those spent on statins and beta blockers. However, we agree with the reviewer that other (primary) preventive cardiovascular medication exists. Aspirin, for example, can be used as a (primary) preventive cardiovascular medication as well. However, this medication is also used as an analgesic to relieve minor aches and pains, as an antipyretic to reduce fever, and as an anti-inflammatory medication. Therefore for practical reasons we focused on statins and beta blockers only. We added our focus on beta blockers and statins only as a limitation to the manuscript, and mentioned that the costs of total spending on primary preventive cardiovascular medication may therefore be an underestimation; see Discussion, fifth limitation, p.14.

2. “Are the methods appropriate and well described? The reviewer would like to applaud the authors for taking on the challenge of executing a mix-methods study, which is commendable. The authors should elaborate on the following:
2a. The questionnaire relies on self-reporting of the FP and answers were based on estimates of the “cardiovascular preventive activities”. These are potentially areas of bias and the authors reported them as a study limitation. What is the number of FPs in LINH? How do the authors select the 80 FPs? Randomized or purposeful sampling? Why 80? Any power calculation?

Response: Each year the ‘Netherlands Information Network of General Practice’ (LINH-DB) contains 80 family practices (FPs). So there was one questionnaire for each of these 80 practices in the network in 2009. This network takes into account the representativeness regarding practice type, urbanisation and the software system that is used. The sample of practices originates from the mid 1990’s; eighty FPs are sufficient to make disease-related conclusions at the Dutch national level. Practices participate on a voluntary basis. The LINH database holds longitudinal data on morbidity, prescribing, and referrals, based on the routine electronic patient records that are kept by the participating practices. In order to enable longitudinal analyses, changes in the set of participating practices are kept to a minimum. There is a waiting list for practices to participate in the network. When a practice quits participating in the network, a new practice is invited, taking into account the representativeness of the network regarding practice type, urbanisation, and software system that is used. These FPs are spread throughout the Netherlands and are representative of all Dutch FPs. Practices that are allowed to the network have successfully completed a three month test period in which their recording behaviour is monitored. We added these details to the manuscript; see Methods / Questionnaire, second paragraph, p.6.

2b. Mining the database was carried out only on FPs with complete data sets. This is another area of bias and the authors should explain for such selection. Those FP with incomplete data sets, do they have different prescribing behavior? Is this why there is considerable “heterogeneity” in prescribing behavior of PPCM between FPs?”

Response: To investigate the prescription of primary preventive cardiovascular medication in FPs, we had to include FPs with complete data sets over the whole period 2005-2007. Namely, cardiovascular treatment of patients who had consulted their general practitioner for cardiovascular problems in 2005-2007 was not regarded of primary preventive nature. From the FPs with complete data sets, 41 percent was a single handed practice, and 46% of the FPs had a practice location in a (very) strongly urbanised area (i.e., this was quite similar to the Dutch national situation of FPs with 42% single handed practices and 48% located in a (very) strongly urbanized area). Nevertheless, we cannot rule out that FPs with incomplete data sets
may have different prescribing behaviour than FPs with incomplete data sets. We added this point as a limitation to the manuscript; see Discussion, sixth limitation, p.14.

3. “Are the data sound? There are limitations in such study that we can recognize but they should be specified in the discussion. The authors have discussed some assumptions but may consider include some of the suggestions as above.”

Response: We have specified the limitations of the study more clearly in the discussion including the suggestions of the reviewer mentioned above. See Discussion, final paragraph, pp. 13-14.

4. “Does the manuscript adhere to the relevant standards for reporting and data deposition? Yes”

Response: Due to the positive assessment of the reviewer, we did not revise this point.

5. “Are the discussion and conclusions well balanced and adequately supported by the data?

5a. The discussion can be improved if the definition of “cardiovascular preventive activities” is made clearer and it will also impact on the conclusion and recommendation. The authors can be more explicit as to what new information does this paper add to medical literature.

Response: We specified more clearly in the discussion (and throughout the article) that the study is focusing on cardiovascular primary preventive activities. The strength of our study is that it focused on the variation on cardiovascular medication prescriptions that are for primary prevention (i.e., cardiovascular medication aimed at a determinant of cardiovascular disease for people with neither cardiovascular nor endocrine diseases). To date information is lacking how much general practitioners differ in prescribing behaviour regarding primary preventive cardiovascular medication. Additionally, our study gives a comprehensive overview of spending on cardiovascular primary preventive activities in FPs, which is quite innovative and crucial for health policy development and evaluation. Therefore, we are convinced that our study contains valuable information to the readers. We were more explicit as to what new information does this paper add to medical literature; see Discussion, sentences 1 and 2, page 12, and Conclusion, p.15.

5b. Even if there is considerable “heterogeneity” in prescribing behavior of PPCM between FPs, as reported by the authors, what is the implication in clinical care and healthcare expenditure? Is this an issue, apart from the many factors that can affect such prescribing
behavior? The authors themselves put up both sides of the arguments (are there references for the "positive and negative outcomes", but ultimately does it matter at all?)

**Response:** In the health care system there are not enough health care resources to meet all of the health needs that people have, so we have to choose which needs are met and which are not met. As the population ages the annual costs of CVD and other diseases (e.g. osteoporosis, cancer) are likely to increase. From a societal point of view it is important to spend the money as efficient as possible to receive the most benefit for the society. For example, if a relatively low prescribing behaviour of cardiovascular medication may achieve similar health outcomes compared with a relatively high prescribing behaviour, probably important cost savings can be reached on the prescription of cardiovascular medication. Therefore, positive (i.e. high prescribing behaviour of cardiovascular medication results in higher survival rates and less adverse effects) as well as negative (no difference in health outcomes between FPs with a high or a low prescribing behaviour of cardiovascular medication) outcomes are relevant. A positive outcome justifies the expenditure on cardiovascular medication from a societal perspective. A negative outcome indicates that important cost savings may be achieved by reassessing the prescription of cardiovascular medication, because a relatively low prescribing behaviour of cardiovascular medication may achieve similar health outcomes compared with a relatively high prescribing behaviour; see Discussion, p.13.

Differences in PPCM prescribing behaviour between FPs that is not explained by patient’s or practice’s characteristics may indicate under-treatment. From a patient-care perspective it is important to have insight into these differences. Under-treatment justifies an increase in resources, whereas over-treatment indicates inefficiency. Another relevant implication for clinical practice is that our research shows that the current guideline is interpreted differently. Improvement of the current guideline may be useful, especially for primary prevention, for which the discrepancy between family practices is considerable; see Discussion, p.13.

6. “Are limitations of the work clearly stated? Are limitations of the work clearly stated? Limitations can be expanded, as deliberated above.”

**Response:** We have specified the limitations of the study more clearly in the discussion including the suggestions of the reviewer mentioned above. See Discussion, final paragraph, pp. 13-14.

7. “Do the authors clearly acknowledge any work upon which they are building, both published and unpublished? Yes.”
Response: Due to the positive assessment of the reviewer, we did not revise this point.

8. “Do the title and abstract accurately convey what has been found? Yes”
Response: Due to the positive assessment of the reviewer, we did not revise this point.

9. “Is the writing acceptable? Grammatically the authors perhaps should refrain from beginning the sentence with “Also” (“Background”, page 3, para 3, line 5, “discussion” page 10, para 2, line 2) and “Especially” (“Conclusion”, page 12, line 5). “Background”, page 3, para 3, line 2: “a comprehensive” rather than “an”. “Cost”, page 8, line 2, a verb should be inserted between “39.8% practice costs…”60.2% personnel…”
Response: We changed the text as suggested by the reviewer. Additionally, a native English speaker has checked and corrected the English language throughout the revised paper.

Associate Editor's Comments
"This is an interesting paper using a number of sources to estimate the costs and workload of primary prevention in family practice. The referees have raised a number of points and made suggestions that could improve the paper, and I would be grateful if you could respond to these."

1. “Of particular importance, in my view, is to be clearer about what is included as primary prevention. My reading is that treatment of hypertension is included, but the statement on page 6 that treatment of patients for 'cardiovascular problems' were not regarded is confusing as I would include patients with hypertension in this group.”
Response: Cardiovascular primary preventive activities are defined as preventive activities (e.g. prescribing of blood-pressure-lowering drugs, or lifestyle counselling) aimed at a determinant of cardiovascular disease for people without CVD (see Background / second paragraph, p.4). We agree that the statement of page 6 “that treatment of patients for 'cardiovascular problems' was not regarded” is confusing. We rephrased this sentence into “Cardiovascular treatment of patients who had consulted their general practitioner for cardiovascular or endocrine diseases in 2005-2007 was not regarded of primary preventive nature” (see Methods / Database of Netherlands Information Network of General Practice, pp. 7-8).
2. “Similarly the phrase ’unrecognised CVD’ on page 5 is misleading; do you mean without established CVD?”

Response: We agree that the phrase ‘unrecognised CVD’ is misleading. We replaced this phrase by ‘without established CVD’; see Background / second paragraph, p.4.

3. “It is also not clear whether the videotapes excluded patients with established cardiovascular disease.”

Response: We assumed that the time spent on a blood pressure measurement, a blood test related activity, or lifestyle counselling, did not differ between primary and secondary prevention. Therefore, we included all recorded hypertension-, cholesterol- and endocrine-related visits for further analyses. We added more detail information to the manuscript; see Methods / Video recordings, final paragraph, p.7.

4. “I agree that you should state what is meant by endocrine, and why patients with these conditions were excluded.”

Response: ‘Endocrine diseases’ consisted of diabetes (types 1 and 2) and/or disorders of lipid metabolism (e.g. hypercholesterolemia). Patients with these conditions were excluded, because the focus of the manuscript is on primary prevention. Primary prevention focuses on patients without cardiovascular diseases and/or endocrine diseases, because in that case - according the Dutch guidelines - the use of measures belongs to regular care; see Methods / Database of Netherlands Information Network of General Practice; p.8.

5. “The 3rd para of background asserts that medication prescribed in primary prevention ’may be not always strictly needed' but this is not referenced.”

Response: The Dutch multidisciplinary guideline for cardiovascular risk management recommends that people without a history of CVD or endocrine disease complaints should receive primary prevention interventions such as lifestyle recommendations, blood pressure measurements or blood tests if there is a positive family history, clear overweight, or a patient’s request (Dutch Institute for Healthcare Improvement CBO. The Dutch multidisciplinary guideline for cardiovascular risk management. [http://www.cbo.nl/Downloads/217/rl_cvm_200.pdf]). This guideline recommends cardiovascular risk profiling if (i) the systolic blood pressure (SBP) is 140 mmHg or higher, (ii) the total cholesterol (TC) is 6.5 mmol/l or higher, or (iii) if the combination age (men ≥ 50 year, women ≥ 55 year) and smoking exists. The decision to prescribe medications for people without a history of CVD or
endocrine disease complaints depends not only on the estimated risk of CVD, the SBP, and TC/ high density lipoprotein cholesterol’-ratio, but also on patient’s preferences. (The Dutch multidisciplinary guideline for cardiovascular risk management. [http://www.cbo.nl/Downloads/217/rl_cvrm_2006.pdf]). We added these sentences and reference to the manuscript; see Background / third paragraph, third paragraph, pp. 4-5, and Reference list.

6. “Finally, table 3 needs annotation, and I am not convinced of the value of figure 2.”
Response: We gave annotation to Table 3 and removed Figure 2.

7. “Requesting copyediting: We have read through your manuscript and feel that the quality of written English is not suitable for peer review. We advise you to seek the assistance of a fluent English speaking colleague, or to have a professional editing service correct your language. Please ensure that particular attention is paid to the abstract.”
Response: A native English speaker has checked and corrected the English language throughout the revised paper.

8. “Requesting proof of ethics committee approval: Experimental research that is reported in the manuscript must have been performed with the approval of an appropriate ethics committee. Research carried out on humans must be in compliance with the Helsinki Declaration (http://www.wma.net/e/policy/b3.htm), and any experimental research on animals must follow internationally recognized guidelines. A statement to this effect must appear in the Methods section of the manuscript, including the name of the body which gave approval, with a reference number where appropriate.”
Response: The study protocol adheres to the Dutch privacy legislation, approved by the Dutch Data Protection Authority. However, approval by a medical ethics committee was not required for this observational study, because the study did not interfere with a GPs usual work as process and patients were not confronted with whatever project-related intervention. (see Methods / Video recordings, p.7). Patient's consent included the use of the video recordings for communication research and was formulated in such a general way as to allow secondary analyses at a later state. The studies were carried out according to Dutch privacy legislation. The privacy regulation was approved by the Dutch Data Protection Authority. Our research did comply with the Helsinki Declaration. This same procedure was accepted for a publication in this journal (Noordman, J., Verhaak, Dulmen, S. van. Discussing patient’s
lifestyle choices in the consulting room: analysis of GP-patient consultations between 1975 and 2008. BMC Family Practice 2010, 11:87) and for a publication in Family Practice (Noordman, J., Verhaak, P., Beljouw, I. van, Dulmen, S. van. Consulting room computers and their effect on GP patient communication: comparing two periods of computer use. Family Practice 2010; 27: 644-651). We added more details to the manuscript; see Methods / Video recordings, p.7 or the following text: The study protocol adheres to the Dutch privacy legislation, approved by the Dutch Data Protection Authority. However, approval by a medical ethics committee was not required for this observational study, because the study did not interfere with a GPs usual work as process and patients were not confronted with whatever project-related intervention. Our research complied with the Helsinki Declaration. All participating general practitioners and patients filled in an informed consent form before the recording of the consultation.