Author's response to reviews

Title: Variation in guideline recommendations for chronic heart failure across Europe and their relationship to clinical practice A comparative analysis of guideline content and target versus the IMPROVEMENT survey of prescribing performance in primary care.

Authors:

Heidrun B Sturm (h.sturm@med.rug.nl)
Wiek H van Gilst (w.h.van.gilst@med.rug.nl)
Karl Swedberg (karl.swedberg@hjl.gu.se)
Richard F.D. Hobbs (F.D.R.HOBBS@bham.ac.uk)
Floor M Haaijer-Ruskamp (f.m.haaijer-ruskamp@med.rug.nl)

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Author's response to reviews: see over
Dr. Tikki Pang,
Editor in Chief, BMC Health Services Research

Groningen, April 15, 2005

Subject: Re-submission of manuscript

Dear Sir / Madame,

Please find enclosed our revised manuscript entitled: "Variation in guideline recommendations for chronic heart failure across Europe and their relationship to clinical practice. A comparative analysis of guideline content and target versus the IMPROVEMENT survey of prescribing performance in primary care”.

We would like to thank the reviewers for the constructive comments and revised our manuscript accordingly. Please find details of the revision adjacent to the respective reviewer’s comment below.

Sincerely,

Heidrun Sturm, MD, MPH
Reviewer: Arno Hoes  
Version: 2  
Date: 26 February 2005

Reviewer’s report:  
General  
The report includes an interesting comparison of 15, almost all national, guidelines on heart failure in Europe, with emphasis on therapeutic recommendations. In addition, the guideline recommendations are compared to prescription patterns observed in primary care patients, by using the IMPROVEMENT data.

The paper is relevant for those involved in the therapeutic management of heart failure patients and those interested in the application of clinical guidelines in daily primary care. The paper could be further improved if the authors focused even more on drug therapy and on primary care guidelines (in their comparison with prescribing practice). In addition, the statistical analysis is not fully explained in the current version.

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**Major Compulsory Revisions** (that the author must respond to before a decision on publication can be reached)  
1. The paper would be even more interesting if focus would be entirely on drug therapy for heart failure. For example the parts about the diagnosis of heart failure could be deleted; the more since a useful comparison between guidelines and practice data warrants another full paper.

We thank the reviewer for the suggestion and according to his advice deleted Tab. 4a and related text.

2. Emphasis is, certainly in the second part involving the comparison with IMPROVEMENT data, on primary care. It remains unclear whether in that comparison the recommendations from guidelines applied by GPs (according to the experts) in that particular country were applied. I hope, for example, that the GP guideline and not the CBO guideline was used in the Dutch comparison.

We agree with the reviewer about the importance of this point. Guidelines directed at GPs with different recommendations were the ones in Italy and NL and we had not used the GP guideline in the paper. Analysis of the relationship between recommendation and drug use was done with both guidelines separately. This had no influence on the patterns of the results. The results based on GP-guideline recommendations are now reported in Tab. 3.

3. In the statistical analysis, the comparison data were adjusted for age, gender and NYHA classification. The method applied is not mentioned (multiple logistic regression?). Moreover the reason for this adjustment is not provided. Actually, these factors are unlikely to be confounders, since their association with the contents of the guideline seems very unlikely. To clarify this issue, the authors should provide both adjusted and unadjusted odds ratios.
We apologize for not having been clear enough. We improved the methods section (see also reply to second reviewer). The analysis was done by multivariate logistic regression. We agree with the reviewer, that the independent variable (recommendations) is not influenced by national patient characteristics. However patient characteristics are crucial for treatment decisions and are also taken into account in recommendations. In this case patient characteristics (significant in univariate analysis) were taken into account; because the dependent variable, prescribing, is likely to be influenced by patient characteristics (see methods section, p 6). Univariate and multivariate OR are now provided in Table 3. The trend in results was not changed by multivariate analysis.

4. In my view other potential confounders are of more interest, such as the year of publication of the guideline. The latter is likely to be associated with both the contents of the guideline and the prescription pattern and may thus confound the relationship.

The year of publication is certainly important for both factors. We compared guidelines with different publication time descriptively throughout the results. The relation between timing and content of recommendations was not entirely consistent. The range and mean of publication year of the used guidelines for each group is now also included in table 3. Since the analysis was done on patient level, publication time could not be used as an independent variable in the statistical models (See also answer to reviewer 2)

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**Minor Essential Revisions** (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

In table 3, two odds ratios are given for betablocker use in countries with a restricted indication in the guideline; one with the wider indication and one with no recommendation as the reference category. Using a dummy variable and one reference category (and two odds ratios) would make the findings easier to interpret.

We followed the recommendation of the reviewer. Alternative recommendations were grouped in two categories: guidelines recommending a wider indication were combined with guidelines not specifying the indication for BB-use to: “non-restricted indication”. The second independent variable was: "restricted indication” (see table 3).

Some limitations of the IMPROVEMENT study could be mentioned, since the IMPROVEMENT data are crucial in the comparison between guidelines and practice data. For example, some GP patients in IMPROVEMENT may actually be "managed" at cardiology out-patient clinics and not in primary care.

We thank the reviewer for that suggestion. The limitation section was adapted accordingly.

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**Discretionary Revisions** (which the author can choose to ignore)

Unable to decide on acceptance or rejection until the authors have responded to the

**What next?:**
major compulsory revisions

Level of interest:
An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable
Statistical review: No
Declaration of competing interests:
I declare that I have no competing interests
Reviewer's report:

General

This manuscript addresses the role which national guidelines play in contributing to differences between heart failure management in different nations. Given the magnitude of the clinical problem of heart failure, and the consequent public health interest in optimizing care of heart failure patients, the authors have selected a timely and important topic. Unfortunately, I do not believe that the methods are adequate to answer this question.

We apologize for not having been clear and we hope that we could make the goal of the study more explicit. Contrary to the interpretation of the reviewer, the main goal of this study was not to explain how guidelines influence HF management, but to compare the content of recommendations in different countries and to study if such differences are reflected in national prescribing patterns. We have clarified this point in that the last paragraph of the introduction.

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

Firstly, the authors need to more clearly specify the methods by which recommendations were compared and grouped. This is likely to have been a very subjective process, and the manuscript does not provide adequate detail of how this was conducted, and what principles were invoked to assure consistency in this critical step.

We thank the reviewer for pointing out these deficits. The methods section was changed in order to make the approach more understandable.

Secondly, the authors need to decide how to address the variability in time of publication as a factor influencing the results of the comparison. For example, a guideline published in 1994 might be viewed by practitioners as irrelevant, whereas a guideline from 2003 might not yet have entered broader awareness. This factor might be equally important as the content of the guidelines. In a similar vein, the site of publication and means of dissemination of results might influence the utilization of the guidelines.

We agree with the reviewer that publication time, site of publication and dissemination are important topics and we tried to make our descriptive approach towards those more explicit. We adapted the method section (please see p. 6). In the results section we have included differences in recommendations in relation to the year of publication in a more structured way (please see the highlighted sections throughout the results part and reply to reviewer A. Hoes, section 4). The relation between comprehensiveness, form and target group is also described in the results section. More detailed information about the degree of implementation and acceptance or actual utilization etc was beyond the scope of this study.
Thirdly, the statistical analysis is not clear and needs to be specified in much greater detail. The reader cannot tell how the comparisons were made, nor how "agreement" with the guidelines was determined. Without this information, the results cannot be interpreted with confidence.

The method section was changed to address those deficiencies (see above). Definition of the categories was rephrased and “agreement” was replaced by “identical”.

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**Minor Essential Revisions** (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

Figure 1 contains pairs of horizontal rows for each category, rather than a single stacked row. I cannot find adequate explanation of this in the legend.

Always recommendations concerning one drug are grouped together. Additional legend text was added:
“Recommendations relating to one drug are grouped; corresponding results (percentages of identical, different or not specified recommendations) are shown in adjacent horizontal bars. “

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**Discretionary Revisions** (which the author can choose to ignore)

Given the many factors which stand between the publication of a guideline and the implementation of clinical practice based upon the guideline, the authors might wish to consider any of the following in their revision: where the guidelines were published; whether clinicians were aware of the documents; whether clinicians agreed or disagreed with the documents; whether conflicting guidelines from other nations were available to the clinicians and whether they might have influenced their practice; and whether there was temporal migration of practice patterns independent of the guidelines.

The mentioned factors are very relevant for the uptake of recommendations. However as pointed out above, this study aims to assess whether there is a relation between national agreements about therapy as reflected in national guidelines and prescribing on a national scale. The lack of relationship between national recommendations and national prescribing demonstrates that other factors, including the ones mentioned above, need to be considered when explaining international variation in prescribing (See also above).

**What next?:**

major compulsory revisions Unable to decide on acceptance or rejection until the authors have responded to the

**Level of interest:** An article of limited interest

**Quality of written English:** Needs some language corrections before being published

Language has been checked by a native speaker with experience in publishing.

**Statistical review:** Yes

**Declaration of competing interests:**
I declare that I have no competing interests