Author's response to reviews

Title: The influence of population characteristics on variation in general practice based morbidity estimations

Authors:

Catharina van den Dungen (karin.van.den.dungen@rivm.nl)
Nancy Hoeymans (nancy.hoeymans@rivm.nl)
Hendriek C. Boshuizen (hendriek.boshuizen@rivm.nl)
Marjan van den Akker (marjan.vandenakker@maastrichtuniversity.nl)
Marion C.J. Biermans (m.biermans@elg.umcn.nl)
Kees van Boven (cvboven@hetnet.nl)
Henk J. Brouwer (h.j.brouwer@amc.uva.nl)
Robert A. Verheij (r.verheij@nivel.nl)
Margot W.M. de Waal (m.w.m.de_waal@lumc.nl)
Francois G. Schellevis (f.schellevis@nivel.nl)
Gert P. Westert (g.westert@iq.umcn.nl)

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Author's response to reviews: see over
Dear Editor,

Before we start to explicate the revisions we made in reaction to the comments of the reviewers, we first have to explain some overall changes in the results and discussion. When we went through all analysis and results, we discovered an error in the basic file, which we used for all analysis. This error has been corrected and all analyses have been redone. This resulted in slightly larger effects of socio-demographic characteristics SES, ethnicity and urbanization degree on morbidity estimations, and subsequently in slightly larger changes in the variations among GPRNs (MOR) after adjustment for these socio-demographic factors. Because of these differences, the tables and text in the results and discussion are adjusted. However, the overall conclusions that the characteristics do not explain the large differences in morbidity estimations among networks or practices did not change.

We also checked the English language.

In the next section we will justify the changes made in the article because of re-analysis.

<table>
<thead>
<tr>
<th><strong>Results –section</strong></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Line 218 to 226</td>
<td>The exact figures are changed</td>
</tr>
<tr>
<td>Line 226 to 228</td>
<td>The category of ethnicity has been changed to 50% or more</td>
</tr>
<tr>
<td>Line 250</td>
<td>The MOR of prevalence rates of diabetes mellitus has been changed to MOR\textsubscript{network} 1.20(1.08-1.61) and MOR\textsubscript{practice} 1.49(1.43-1.53)</td>
</tr>
<tr>
<td>Line 255-256</td>
<td>The prevalence rates of COPD do not show an MOR&gt;1.40 anymore and have removed from the results description</td>
</tr>
<tr>
<td>Line 262</td>
<td>Gender does not contribute significantly to the estimation of morbidity rates of COPD. Therefore we added (except gender in COPD)</td>
</tr>
<tr>
<td>Line 266-268</td>
<td>Changes in MOR became slightly larger after reanalysis. We added the sentence: “In most diseases the MOR seems to decrease after adjustment for population characteristics, although for some diseases, the MOR even increased.”</td>
</tr>
<tr>
<td>Line 271</td>
<td>Changes in 95%CI in incidence rates of depression, (1.00-2.77)</td>
</tr>
<tr>
<td>Line 344-349</td>
<td>After reanalysis the results showed larger effects of socio-demographic characteristics on morbidity estimations in prevalence rates than in incidence rates. We discussed this effect here. “The effects of socio-demographic characteristics are larger for prevalence rates and therefore we see more changes in variation among networks after adjustments. For example, SES and ethnicity significantly contribute to the prevalence of diabetes mellitus in patients (results not shown), and MOR declines from 1.20(1.08-1.61) to 1.13(1.04-1.39). Despite the small changes in variation after adjustment, differences among GPRNs and practices still remain large.”</td>
</tr>
<tr>
<td>Line 361</td>
<td>The largest percentage of urbanization level was now 85%, but the conclusion stayed the same.</td>
</tr>
</tbody>
</table>
Author’s response to the feedback of reviewer Dulcie McBride

Title: The influence of population characteristics on variation in general practice based morbidity estimations
- Version: 1 Date: 7 June 2011

Overall Comments
We would like to thank the reviewers for your comments. Overall, the feedback has been very useful to improve our paper. Most comments have been fully adapted and assimilated in the new version.

Abstract
1. Does ‘listed’ need to be in inverted commas?
2. Are the brackets around fully in (fully) understood necessary?
3. Define SES before using the abbreviation
Correct observations, we deleted the inverted commas, line 36 (also in the main text of the article, line 192), defined SES first (line 38) and removed the brackets around fully (line 78).

4. “The differences in socio-economic status, urbanization level and ethnicity are substantial.” – suggest add explanation of which differences, e.g. between networks, practices, disease prevalence?
The focus of the paper is the differences in morbidity estimations among networks. To clarify this part and emphasize our focus, we rephrased it into; “The differences in SES, urbanization level, and ethnicity distribution among the networks’ practice populations are substantial” (line 42-43)

5. “Adjusting for these differences in patient populations did however not decrease the variation in morbidity estimations” – the grammar is a little difficult to follow in this sentence
We rephrased the sentence to; “The variation in morbidity rate estimates among networks did not decrease after adjusting for these socio-demographic characteristics”. (line 43-45)

Methodology
6. “To gain more insight in possible explanations for these differences in morbidity rates, we investigate to which extent variation is reduced if age, gender, SES, urbanization level,” – should this be to “what extent” not “which extent”
Yes, but this sentence has been removed, this part has been changed because of the remarks at point 12.

Tables
8. Need a definition of 95% BI (or should that read CI?) correct, we meant the confidence interval. Changed in tables 2, 3 and 4.
Results
9. “The total study population consisted of 480,038 persons in 111 practices with an average age of 38.6 years” – is the average mean or median? Mean age, we changed it in the text (line 219)

10. “(MORnetwork= 1.08 (1.00-1.34) not significant)” – suggest changing “not significant” to a p-value. The p-value is 0.19, which is added to the text (line 243).

11. “This indication is more visibly in incidence figures (10 out of 13) in comparison to prevalent figures (5 out of 10).” “visibly” should be “visible” and explain what the 10 out of 13 and 5 out of 10 refer to. It refers to the amount of incidence and prevalent diseases this indication is visible. We changed this in the text. “This is visible in incidence rates of 10 out of 13 diseases and in prevalence rates of 6 out of 10 diseases.” (Line 247-248).

Background
12. The hypothesis is generally referred to throughout this section but at no point does the hypothesis appear to be explicated stated. My assumption is that as the distribution of various socio-demographic factors varies between GPRNs the hypothesis is that the incidence and prevalence of certain diseases will be higher in those GPRNs with a greater proportion of patients living in urban/deprived areas, for example. The hypothesis needs to be clearly stated.

We agree that the hypothesis should be more expressed in the end of the background. We take the view that because of the great diversity of the hypotheses for all diseases, incidence versus prevalence and the influence of all population characteristics it is impossible to state all hypotheses. For example in case of ethnicity, persons from non-western countries are more susceptible for diabetes, but coronary heart diseases are more common in native Dutch people. We also think that for our main goal to explain why morbidity estimations differ among different networks, the precise mechanism or tendency of the influence of the population characteristic is less important. Therefore we chose to rephrase the last part of the background, but we still stated the hypothesis in more general terms. “We hypothesize that adjusting for differences in age, gender, SES, urbanisation level, and ethnicity among networks will reduce the variation among networks and therefore partly explain the differences in morbidity estimations among GPRNs.” (Line 105-108)

Methodology
13. It should be explained which codes are used to define to the diseases. Are just diagnostic codes used – thereby implying that tests were required or referral to secondary care may have been necessary to get the diagnosis. There is evidence that referrals to secondary care vary by socio-demographic factors. Or are the authors also looking at symptom codes in which case is there the possibility that some patients have been missed, particularly with generic conditions such as “back problem” which may be written in free-text sections of databases and not have an ICD-10 code.

Earlier research showed that the best way to deal with some diseases, because of registration habits, was to combine different codes (Report no. 431501017 - R. Gijsen, H. Verkleij, P.H. Dijkstraeus et al. Disease specific comparison of recorded morbidity in four general practice registration networks: An analysis on behalf of VTV-1997 - august 1997 in Dutch). In case of back problems, a combination of different complaint and diagnostic codes is used. In table 2 we added a column with the specific ICPC-1 codes used in the analysis. The networks used in this research do not work with free-text information (line 117-118), because of privacy rules.
We used the ICPC coded information about the different diseases, except for one network that works with E-read codes (line 144-148).

Furthermore, the general practitioners in these networks have been trained to use classification codes and they receive feedback about their registration quality. To diagnose some diseases the GP needs additional information from diagnostic tests, specialists etc., and this information, received from external parties, is considered and if relevant recorded in the electronic patient record. And in that case the information is included in the database (line 148-150).

14. Further explanation would be useful around incidence and prevalence of disease. Are incident cases the first episode ever recorded for a patient or the first episode in that year? Incident cases of chronic diseases represent the first time a patient has been diagnosed with the disease. Incident cases of acute illnesses represent the first time a patient has an episode that year. In this research we count the number of patients which had at least one new episode that year and not the number of episodes. More sub acute diseases, like back problems which can be acute or chronic, the assessment is made by the physician. Does the GP considers the episode to be ‘new’, the episode is counted as an incident case, if the GP believes the complaint fits an existing episode we consider this a prevalent case. This is now also explained in the text (lines 153-156).

15. Many readers will not be familiar with this SES score so some mention of its validity is necessary. The rationale for grouping the quintiles into three categories is needed. Again, the validity of the methods for defining urbanisation level would be useful. And again, many readers may not be familiar with ‘non-western immigrants’ as a definition of ethnicity and further explanation may be necessary along with its validity and the rationale for distinguishing the four categories.

The SES indicator is based on real observations in every postal code area in the Netherlands. It does not represent the SES of every individual living in that postal code, but we also know that high SES people living in a low SES neighborhood are in a less fortunate position than high SES persons living in a high SES neighborhood. We assume the SES indication is valid, because we found significant contributions of SES in our research according to what is expected. For example, low SES was related to more diabetes mellitus and COPD as reported in other studies. (lines 170-175)

We understand that it is not clear why we first grouped the SES scores into 5 parts, but for analysis needed to retain more power in our analyses, and therefore we eventually recodes SES into 3 parts. (lines 175-178)

The urbanization level is based on the actual number of addresses in a postal code area and is widely used and recognized to be a valid way to determine urbanization level in the Netherlands. (Lines 178-179)

Furthermore, we added the definition of non-western immigrants to make clear what we mean by this term. The four categories are based on discriminative ground combined with the occurrence of the percentages in the Netherlands and certainty of the person in question is of non-western origin. Most postal areas have 0-9% immigrants, a person living in such an area is likely to be of Dutch native origin. Persons living in an <50% area have a higher probability to be of non western origin, but more change of being of Dutch native origin than people living in >=50% areas. The last category is >=70% of the people are of non western origin, there are no postal areas in our analysis where >=90% non western immigrants live. (lines 183-188)
**Analyses**

15. Suggest an explanation of why picked the two models including adjusting for age and gender together rather than models adjusting for each socio-demographic variable separately and then together. We also analyzed the socio-demographic variables in separate models, but the influence of the variables separately did not change the conclusions. The focus of our study is to investigate the variation in morbidity estimations among different GPRNs. Furthermore SES, ethnicity and degree of urbanization all three contribute to better morbidity estimates, leaving out one of them is not meaningful. If we want to explain the variation among GPRNs we think single variable models do not contribute to a better understanding.

**Results**

16. Socio-demographic characteristics and differences in morbidity - this paragraph may need clarifying as it starts by suggesting that socio-demographic factors contribute significantly to morbidity estimates for some of the diseases (results not shown) but then goes on to state that only small changes in variation in morbidity estimates are observed after adjustment for these characteristics. The analysis showed a significant contribution of some socio-demographic characteristics to several morbidity estimates, but the effects were mostly very small. These effects are too small to contribute important changes in the overall estimation of morbidity in networks and therefore do not explain the differences among networks. The estimations became slightly more precise as the 95%CI became (in most cases) smaller. But we understand this is not properly explained in our article and therefore we added some explanation in the discussion and give some additional information in the results section (results section 261-274, discussion section 332-349). See also the answer by remark 21.

17. The same paragraph notes that “minor decreases” in MORs were observed for most diseases – suggest that an explanation of the significance or lack of significance of these decreases is included. We did not statistically compare the differences between the different models, but the magnitude of the variation of the different models fitted the CI’s of the other models. For that reason we concluded that the influence of the socio-demographic does not contribute to explaining the differences in morbidity estimations among networks. If we look at the exact MOR-figure we see small changes in MOR which show in most cases a decrease, but we cannot proof this is a real decrease because of the large CI.

**Discussion**

18. “For these diseases, differences were large between practices as well as between networks, indicating that diseases that are more difficult to diagnose are more susceptible for variation, partly due to diagnostic differences among GPs.” – another alternative is that they are more susceptible to different ways of coding and recording and some population groups may be more likely to present than others with these conditions. We sure believe that there are more reasons for variations for different diseases. Coding and recording aspects are important, partly we overcome this influence by including different codes together (as in the example of neck and back problems) (lines 145-147) and we only use ‘episode based’ data, because recording in ‘problem based’ data is different. Furthermore GPRNs have quality checks for recording. A general practice that delivers data with a low quality will not be included in the database for that specific year. A shortcoming of using GPRN data is that we only have information about patients who seek medical help. To give these other possibilities for differences a proper place in our discussion we added some sentences in the discussion (lines 295-298, 302-303, 310-313, 313-322, 326-330).
19. “In this context it is also interesting to investigate the differences between strict and more interpretable registration rules on variation among practices.” – what is meant by registration rules? This probably needs some further explanation here. We changed expression to recording rules, because we think this is easier to understand. Networks are build for specific goals, for example to provide a sampling source for research or to measure morbidity in the population. To design the best database for the purpose of the network GPs have to keep to specific registration or recording rules (line 67-69). For a better understanding we added more information about these rules and differences in the text (line 315-321), but for more detailed information we refer to another article (Dungen vdC, Hoeymans N, Gijsen R, Akker vdM, Boesten J, Brouwer H, et al. What factors explain the differences in morbidity estimations among general practice registration networks in the Netherlands? A first analysis. European Journal of General Practice. 2008;14(suppl 1):53-62.).

20. “Osteoarthritis is a chronic disease, but since health care cannot always provide effective treatment patients do not necessarily contact their GP each year. These differences in registration rules may explain some of the variation in prevalence rates among GPRNs.” – there is also evidence that presentation and frequency of presentation to primary care for osteoarthritis is related to a number of socio-demographic characteristics. This is correct, but we have no indication this is different for different networks because the incidence figure of osteo-arthritis shows almost no variation among networks (the variations among networks are not significant for the incidence rates, see table 2). To give a better understanding we explained this in the discussion, lines 309-314.

21. “Overall, the relations found seem to be legitimate. For example, low SES was related to higher morbidity rates of diabetes mellitus and in COPD high SES was related to lower morbidity rates (results not shown) [20]. Although direct measures are more precise, the contribution to explaining the differences in morbidity estimations was very small.” – again more explanation and discussion would be useful about why this is the case as it appears contradictory. The fact that socio-demographic characteristics contribute to a better estimation of morbidity rates, it feels contradictory this does not explain the differences among networks or networks. Our explanation is that the effect of the population characteristics on morbidity estimations in our study is too small to make a difference in the overall situation and variations between networks. In some diseases we see a pattern in concordance with what we expected: less variation among GPRNs after adjustment, but the differences are small. Also most MOR estimations of all three models lie within the confidence intervals of all three models, and therefore we conclude that it does not explain the differences.

To explain these considerations we added some explanation to the text, in the results section we describe that only small changes are visible (lines 264-266), in the discussion we added “This finding seems contradictory, but there are just small differences in age and gender distribution among GPRNs and therefore only small changes are possible” (lines 335-337), “The influence of SES, ethnicity and urbanization level is also limited, despite the large differences in distribution among GPRNs. We believe this to be the case due to little power, because of the small numbers of patients diagnosed with a disorder in comparison to the ‘healthy’ people. Furthermore if the socio-demographic characteristics significantly contribute to an improved morbidity estimation, as for example SES and ethnicity in back and neck problems (results not shown), this effect is too small to actually change MOR. The effects of socio-demographic characteristics are larger for prevalence rates and therefore we see more
changes in variation among networks after adjustments. For example, SES and ethnicity significantly contribute to the prevalence of diabetes mellitus in patients (results not shown), and MOR declines from $1.20 (1.08-1.61)$ to $1.13 (1.04-1.39)$. Despite the small changes in variation after adjustment, differences among GPRNs and practices still remain large (lines 338-349)
Author’s response to the feedback of reviewer Daiki Kobayashi
Title: The influence of population characteristics on variation in general practice based morbidity estimations
Version: 1 Date: 27 June 2011

Reviewer’s report:
Thank you for your feedback, we added more explanation in the text as a result of following points.

1. In Page 5, the authors used six GPRNs to analyze. Did these six databases represent general Dutch population? More explanation, such as how many databases are there in Dutch, how different these databases from all databases, and why these six databases were elected, may be needed.
In the Netherlands we have about twelve networks. One network differs from the rest because it contains whole patient records instead of coded information and therefore morbidity figures cannot be directly estimated from episodes in the database. The information of one network has been incorporated in another network which we have used in this research. One network could not provide morbidity information on time. Two networks were not selected because they only have problem list based data, which we excluded because of the known estimation differences with episode based information.
We added more clarification about this topic into the text:
“To our knowledge, this is the first study to investigate the influence of socio-demographic characteristics on the variation of morbidity estimates among ‘episode based’ GPRNs. The distribution of age and gender in the different network populations corresponds reasonably well to the Dutch general population.” (lines 352-355)
“The differences in ethnicity and urbanization level are much larger among networks, which is caused by the fact that most networks operate regionally and the distribution of these characteristics is not equally distributed between regions in the Netherlands. Therefore we think adjusting for these characteristic is essential.” (lines 356-359)
“Other Dutch GPRNs did not want to participate or were not able to deliver their data on time. Dutch GPRNs differ from each other, but the distribution of the population characteristics in different GPRNs was broad and therefore we think considering other GPRNs would not have changed our conclusion.” (lines 384-387)

2. In Page 12-13, the authors concluded that this study showed that one of the factors could not explain these differences. However, some of diseases seemed different after adjusted in Table 3, such as Gastrointestinal tract infection. Although I know that it may be difficult to compare models before adjusted with those after adjusted statistically, it may need the definition that the factors could not explain these differences. Thank you for your perceptivity, because the variation among networks is substantial in gastrointestinal tract infection and should be bold. Because of this error, we checked all other values and we noticed one or two other faults. Now the significant and insignificant figures are correctly presented in the tables.

We also rephrased parts in the text to make clear that some variations among GPRNs seem to increase after adjusting for socio-demographic characteristics. See lines 266-268 and 344-349.