Author's response to reviews

Title: Impact of ethnic-specific guidelines for anti-hypertensive prescribing in primary care in England: a longitudinal study

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Author's response to reviews: see over
London 31st of January 2013

Mr
David Sclar
Journal Editorial Office
BioMed Central

Refer to 2119822237103735 “Impact of ethnic-specific guidelines for antihypertensive prescribing in England primary care: longitudinal study”

Dear David
Thank you for giving the opportunity to revise our article. We appreciate the reviewers´ comments which have allowed us to improve our paper. The answers to their questions are addressed in the appended document.

Thank you again for considering our article and we hope that our manuscript will be appropriate for your journal.

We look forward to hearing from you.

Kings regards,

Lena Barrera
On behalf of authors.
Reviewer's report

Title: "Impact of ethnic-specific guidelines for antihypertensive prescribing in England primary care: longitudinal study"

Version: 1 Date: 21 November 2013

Reviewer: Wee LE Liang En lan

Reviewer's report:
- Major Compulsory Revisions (which the author must respond to before a decision on publication can be reached)

1. There does seem to be an increase in prescribing according to guidelines after the guidelines were issued. However, it is difficult to ascribe this observation solely to the effect of the guidelines, based on the temporal sequence. Given a lack of description about events leading up to the guidelines and their dissemination (e.g. How was information regarding the guidelines disseminated?) we are not clear how much of this change can be attributed to the change in guidelines, and how much of it can be attributed to other factors (e.g. publicity, new trial findings, etc)

Authors’ reply

We agree that different interventions could influence the use of the first line monotherapy recommended treatment over the study period. In fact we reported that black patients have been prescribed calico channels antagonist blockers (CCB) as monotherapy before the introduction of the NICE guidelines. However, we found that after the introduction of the 2006 NICE guidelines there was an additional increase in the use of the first line monotherapy. We therefore associated these late changes in antihypertensive prescribing with the introduction of the 2006 NICE guidelines based on the following statements. We will add some of these statements to the main text of the article. We hope this contribute to clarify the association.

1. The coefficient given for the NICE guidelines was significant after adjusting for the baseline trend and a term for the introduction of BHS guidelines in 2004. The model used for testing was performed as follows:

   1. Firstly, the plot described a stable trend from 1997 to 2004 when the prescription of ACEI continually increased picking up 2007. Hence, the graph suggested that the variations in prescribing may be related to both the introduction of BHS and NICE guidelines.

   2. Secondly I tested whether or not there has been a constant variation over the period by chi2 test for linear trend in STATA. The test is an unadjusted test telling us that there was significant annual increased in the percentage of monotherapy prescribing for each NICE patient group
3. The statistical model was a logistic generalized estimated equations model using individual data. The mathematical formulation was

\[ Y = \beta \ast t + \beta_i \ast BHS + \beta_2 \ast NICE \]

The \( \beta \ast t \) term was used to adjust for the baseline trend of odds ratio prescribing so that the other variations in the trend prescribing could be attributed to the introduction of guidelines. We used a logistic regression because the outcome was measured as binary variable at individual level. The \( \beta_i \ast BHS \) term stands for the period after the introduction of BHS guidelines and the \( \beta_2 \ast NICE \) term stands for the period after the introduction of NICE guidelines.

2. The finding concurs with the variations in the trends reported by the 2010 NICE implementation uptake report. The report analyzed patterns in antihypertensive prescribing in UK general practices (1).

3. At the beginning of the 2006 there was a national campaign promoting two messages, the conjunction of the BHS and NICE recommendations in one guideline and therefore the adoption of an ethnic-age algorithm for antihypertensive prescribing. To our knowledge, other national interventions intend to improve antihypertensive prescribing were not launched at that time. The Quality and Outcomes Framework (QOF), a national pay for performance program, was introduced in 2004 could indirectly motivate the use of antihypertensive medications to improve blood pressure control. However this financial incentive program does not have any particular recommendations on drug therapy prescription.

4. Between January 2006 and April 2006 NICE promoted the guideline extensively which finally was adopted in June 2006.

5. The use of NICE guidelines is based on an implementation programme. It included the availability of the guidelines, IT systems, reminders and education and a learning program.

2. The rationale for the choice of this geographic location is not clear. Extrapolating changes in prescribing patterns in a constituency in London is difficult especially when not much details are given about the makeup, population and other socio demographic factors in this community

**Author`s reply**

The population of Wandsworth is from a diverse ethnic background. According to the 2001 UK census, white people are the highest percentage of the population (77.9%) and this percentage slightly decreased in the 2011 census (71.4%). Population of South Asian origin and black origin increased from 6.9% in 2001 to 10.9% in 2011 and from 9.6% in 2001 to 10.6% in 2011 respectively. Population of mixed origin increased from 3.4% in 2001 to 5.0% in 2011. In total 28.6% of residents were from non-white in 2001. The presence of this ethnically diverse population allowed us to compare variation in prescribing by ethnic group.
We acknowledged that our study could not represent the entire London or UK population as it is an observational study carried out in small area in London. Therefore the extrapolation of the results outside this population may be limited. However our findings were in the line with other studies. In an analysis of 28320 hypertensive patients managed in general practices in Lambeth, London, Schofield et al have reported nearly 50% of hypertensive patients were prescribed with 2006 recommended treatment (2). Additionally, although socio-demographic conditions could influence antihypertensive prescribing, the UK’s National Health Service (NHS) aims to reduce differences in treatment among general practices across the country. UK primary care provides universal access to care to all the population. The guidelines apply to all patients regardless of socio-economic status or area of residency.

3. I would also suggest that the authors include additional components to their work (eg. interviews with general practitioners to better understand some of the rationales behind their clinical choices and also the reasons for divergences from guidelines, if any). Rather than just relying on the retrospective data to project treatment trends, this would result in a fuller and richer treatment of the data

Author’s reply

We definitely consider that the analysis could be improved using information from doctors. However we wanted to illustrate the use of secondary data (clinical registers) for the assessment of clinical practice in primary care. There is a lack of information on the use and effectiveness of hypertension guidelines in routine clinical practice. I searched for studies assessing the impact of the England guidelines on drug therapy prescribing between 1999 and 2012 using MEDLINE and PUBMED sources and found the studies listed in the table below. Therefore our study provided additional evidence on the use of NICE guidelines. It also highlights the need for improving the monitoring of general practitioners' prescribing. What is more, collecting information from doctors could introduce bias in the analysis because the data was collected from 1998 to 2007.

Table 1 Studies conducted in England showing the use of therapeutic recommendations established in the time-related hypertension guidelines between 1999 and 2012

<table>
<thead>
<tr>
<th>Year</th>
<th>Type study</th>
<th>Results related to drug therapy prescription</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>(3) Longitudinal study</td>
<td>55% of patients were prescribed with diuretic or beta-blocker monotherapy. The recommendation established in the guideline.</td>
</tr>
<tr>
<td>2007</td>
<td>(4) Cross sectional survey</td>
<td>62% of GPs reported not choosing the recommend drug despite being aware of the guideline. Between 12% and 25% of GPs considered that there are differences in the lowering pressure effect between antihypertensive drugs though the guideline postulated the opposite statement.</td>
</tr>
<tr>
<td>2011</td>
<td>(5) Cohort study hypertensive patients with stroke</td>
<td>Between 1997 and 2006 the proportion of patients prescribed with guideline drug recommendations increased from 24% to 37%. Overall 31%. Using the recommended treatment was associated with lower recurrence of stroke.</td>
</tr>
<tr>
<td>2010</td>
<td>(1) Analysis of the electronic Prescribing Analysis Cost Tool system</td>
<td>After the 2006 NICE hypertension guidelines there has been an increase in the number of younger&lt;55 years prescribed with ACEI. The usage of calcium channels blockers also increased. There was a reduction in beta-blocker use.</td>
</tr>
</tbody>
</table>
Minor essential revisions:

There are quite a few grammatical errors and spelling errors scattered throughout the manuscript. I list some below, but would advise the authors to thoroughly vet their manuscript again before submission.


   Author’s reply:

   We will use this title.

2. Abstract: Methods
   “28 general practices in Wandsworth, London were conducted” - change “were” to “was”

   Author’s reply

   Amendment accepted

3. Intro, second para:
   Variations in hypertension treatment across primary care practices
   “have additionally documented the gap between guidelines and physician chooses” - change chooses to choices

   Author’s reply

   It will be corrected in the main text as follows: “have additionally documented the gap between guidelines and physician antihypertensive drug preferences”

4. Methods, second para:
   “We defined a patient with an additional cardiovascular comorbidity as one who Had one or more of the following diseases diabetes mellitus” - change to “diseases: diabetes mellitus”

   Author’s reply
Reviewer's report

Title: "Impact of ethnic-specific guidelines for antihypertensive prescribing in England primary care: longitudinal study"

Version: 1 Date: 5 November 2013

Reviewer: Giuliano Tocci

Reviewer's report:
The manuscript by Barrera and coworkers described the main findings of a systematic and comprehensive analysis performed on the general practitioners acting in the district of Wandsworth, London, to evaluate the potential impact of ethnicity on prescriptive recommendations promoted by NICE guidelines in different age groups.

The manuscript is overall well written, the methodology is well described and potential limitations were fully acknowledged. The topic is, in my opinion, of clinical relevance, since it provides useful information on physicians' preferences and attitudes for the clinical management of hypertension in a setting of primary care.

I have only minor comments and some references to propose.

Minor Comments
On page 4, last lines, I do not understand why black individuals were not stratified into two age groups, as well as for non-black subjects. This aspect should be better clarified.

Author's reply

Thank you for the comment. We used the classification of the patient groups established in the 2006 NICE guideline for antihypertensive prescribing. The guideline did not make distinction between age groups for those of black origin. We clarified it in the text.

Do you have any information on blood pressure control rates in patients treated with monotherapy or combination therapy. In other words, the increased proportions of patients on monotherapy observed in the study were only related to the publication of NICE guidelines, or other factors beyond age can be also considered?

Author's reply
We have mentioned that the association between the introduction of the guidelines and drug therapy prescribing was established at the end of the period. The reasons for suggesting the association were addressed above. Additionally we had data showing that the blood pressure control rates have improved over the study period. Because the control of blood pressure is determined by other factors that the introduction of the guidelines, we chose to assess the impact of the guidelines by examining variation in drug therapy prescribing. The prescription of antihypertensive drugs are directly influenced by the guidelines.

Reviewer's report

Title: "Impact of ethnic-specific guidelines for antihypertensive prescribing in England primary care: longitudinal study"
Version: 1
Date: 25 October 2013
Reviewer: Xuefeng Liu Liu

Reviewer's report:
The manuscript was written in a good shape. A longitudinal retrospective study was used to assess the variations in antihypertensive prescribing prior to and post the launched National Institute for Health and Care Excellence (NICE) guidelines. Although the topic has a good health concern, there are a few comments which need to be addressed.

Major comments:
1) Page 4. In the methods section, you mentioned you only included patients with essential hypertension aged 17 years or above. But in the abstract, you said aged 18 years or above. Which one was correct?

Author’s reply

Thank you for the correction. It should be said hypertensive patients aged 18 years or over.

2) In the abstract and methods section of the text, need to make inclusion criteria more clear. It is very confusing to say “A longitudinal retrospective study with 15933 hypertensive patients aged 18 years and over were conducted to assess variations in antihypertensive prescribing between 2000 to 2007”. Since this was a longitudinal study and age for each participant changed with years, you need to point out clearly the cutoff of age 18 years or over in 2007 or at baseline in both abstract and methods section.

Author’s reply

The text will be corrected as follows:
We assessed the variations in antihypertensive prescribing among 15933 hypertensive patients aged 18 years or over in the initial record and registered with 28 general practices in Wandsworth, London in 2007. A longitudinal retrospective study was performed using patient’s records from 2000 to 2007. Logistic models were used to measure variations in the odds of being prescribed the 2006 NICE first line recommended monotherapy among NICE patient groups over the period.
3) What is the end period of the study? Is it 2007? If so, the end of the study is only about one year after the NICE guidelines are launched. I am not sure if physicians in hypertension clinics could accept or use the new guidelines within such a short time period without further training. My concern is why you did not use 2008 or 09 as the end period.

Author´s reply

We showed that the first line monotherapy prescribing recommended in the 2006 NICE guidelines were already used before the introduction of the guidance, particularly in those of black origin. In fact the ethnic-algorithm was proposed by the British Hypertension Society in 2004 (6). What we illustrated is that the introduction of the NICE guidelines increased the use of the recommended therapy. We agree on the benefit of including additional years but our data had no information on 2008 onwards. Then we were only able to examine the impact of the 2006 NICE guidelines over the 18 months of the study period because the guidelines were launched between January and June 2006. Therefore the observed impact may only reflect a short term effect. However the observed prescribing pattern is consistent with the prescribing trend reported by the National implementation uptake report for the management of hypertension (1). The validity of the association also could be enhanced by the GEE models as they allow making comparison between short time periods (7-8).

4) Table 2, look at the columns of newly registered in 2000 and 2007 for younger non-black. Some percentages were not right. Check all estimates in this table.

Author´s reply

The table with the corrections highlighted in red is below.
Minor comments:

5) Page 5 on the top, you included three groups of subjects in the study: black, younger non-black and older non-black. Be more specific to the last two groups (e.g. they included white, Asian, etc).

Author’s reply

We have clarified that the younger non-black and older non-black categories include patients of white, Asian, Other Asian or other ethnic origins.

6) Table 3. The first variable NICE is not clear. Is it NICE guideline? Make it more clear.

Author’s reply

The variable NICE refers to the period after the introduction of the 2006 NICE guidelines. We have now written it more clearly in the table.
7) What does BHS stand for? When you first use it in the text, you should write out the full name and put the abbreviation in the parenthesis for late use.

Author’s reply
The BHS is abbreviation for the British Hypertension Society. We have included the full title in the text.

8) When you say aged 18 year and over, I think it would be better to use aged 18 year or over instead.

Author’s reply
We will correct as aged 18 year or over.

9) There are some minor issues or typos in the text, for example, at the end of the second paragraph on page 3, the word “chooses” was not used correctly. Look over the whole manuscript again to correct them.

Author’s reply
The phrase has now been written as: “Variations in hypertension treatment across primary care practices have additionally documented the gap between guidelines and physician antihypertensive preferences.”
References


