Author's response to reviews

Title: Reasons of general practitioners for non-treatment of younger and older patients with newly diagnosed type 2 diabetes mellitus in the United Kingdom: A survey study

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Author's response to reviews: see over
July 21, 2011

Timothy Shipley, PhD
In-house Editor
BMC Endocrine Disorder

Dear Dr. Shipley:

On behalf of my co-authors, I am submitting our revised manuscript. The manuscript has been revised based on the concerns and questions raised by the reviewers. We appreciate the efforts of the reviewers and feel that the edits based on their reviews has strengthened the manuscript. Responses to the reviewers' comments can be found on the following pages and within the manuscript.

We look forward to the journal's decision. Please let us know if you require any additional information.

Sincerely,

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A. Editorial comments:
Please clarify whether or not ethical approval was obtained for your study. If so please provide details of the review board that provided approval in the methods section of your manuscript, if not please let us know why the study was exempt.

Response: According to the guidelines developed by the National Research Ethics Service (NRES), our study did not require Research Ethics Committee review for the following reasons. The study was a non-randomized physician survey including a brief retrospective chart review conducted by the participating physicians. The study did not involve any contact with patients or interventions. Both patients and participating physicians were completely de-identified in data collection and analysis.

http://www.nres.npsa.nhs.uk/applications/guidance/research-guidance/?entryid62=66984

B. Reviewer's report
Title: Reasons of general practitioners for non-treatment of younger and older patients with newly diagnosed type 2 diabetes mellitus in the United Kingdom: A survey study
Version: 1 Date: 12 May 2011
Reviewer: Petra Denig
Reviewer's report:
This is an interesting subject, since we have limited insight in patient-age effects on treatment decisions.

Major points:
1. Maybe I misunderstood but from the methods/results it seems that the age selection (<65 or >65) was not made at the time of the diagnosis. This should have been the criterion since the aim is to understand reasons for not initiating therapy in younger and older patients with NEWLY diagnosed type 2 diabetes. By selecting patients on their age at some arbitrary later point gives a time-biased population. The older patients have a longer duration of diabetes, and were consequently partly also younger (<65) when they were diagnosed. This should be corrected and groups should be compared based on their age at diagnosis.

Response: Physicians were asked to select patients who were <65 and ≥65 years of age at time of diagnosis (not at time of survey). This has been clarified in the Methods section (page 6).

2. It is stated in the Discussion that ‘Older patients in this study were more likely to have pre-existing microvascular and cardiovascular conditions, which appeared to impact the GPs’ decisions on treatment’. It seems that the time-bias (see above) interferes with making such statements. The data were collected at a later point: ‘The following data were abstracted from the patient's charts: demographics, comorbidities, medication use, laboratory measurements, and vital signs’ so I assume that comorbidities was not necessarily pre-existing but could have started after the diagnosis T2DM?
Response: Please see response to comment 1 above – patients were selected based on their age at diabetes diagnosis. Regarding comorbidities and medication use, physicians were asked if their patients were "ever" diagnosed with a given condition and whether they were taking medication to treat that condition. Therefore, the condition may have been pre-existing or could have occurred after diabetes diagnosis. It is important to note that the purpose of collecting these data was to understand the potential factors influencing physician's decision not to treat with antihyperglycemic agents (AHAs) since diabetes diagnosis. Collecting only baseline data would not have provided a complete picture including conditions post diabetes diagnosis.

3. The GPs originated from the Kantar Health Physician Panel from which a random sample was invited to take part in the survey. It is, however, not clear how many participated in the Panel and whether this constitutes a selected GP population. Next, 358 of the eligible GP participated but how many were eligible (response rate). Possible selection bias should be discussed!

Response: More detail on the panel, GP selection and participants, and planned patient sample size was included in the Methods. Acknowledgment of selection bias was added to the limitations of the study (page 7).

4. A comprehensive list of 36 possible reasons for non-treatment with antihyperglycaemic agents was provided to GPs. Where did this list come from? Any validation or support that it is a comprehensive list? How was the grouping made? I was surprised by, for example, finding risk of side effects in the Comorbidity/polypharmacy and not in Factors related to antihyperglycaemic agents. Similar, why is cognitive burden not in the Patient-Related Reasons instead of drug related factors. Please reconsider the categories and explain the methods used for this categorisation.

Response: The survey was developed based on extensive interviews with a panel of practicing endocrinologists and epidemiologists who were also academic researchers. Interviews included discussions about treating older versus younger patients, scenarios where patients are not treated with AHAs for at least 6 months after initial diabetes diagnosis and relevant reasons related to decision of no AHA treatment. After the survey was drafted accordingly, it was presented to each panel member for further review and comment, and they were asked to confirm that the reasons list was comprehensive, and given the opportunity to modify reasons or remove non-relevant items (page 7).

In the survey, reasons were provided under subheadings (not shown) that provided context for physicians. In the case you mention, for example, "risk of side effects" was under the heading "polypharmacy" (please note that under the heading, "Factors related to Antihyperglycemic agents", specific side effects related to AHA use were also listed, i.e., hypoglycemia, weigh gain, fluid retention, etc). Similarly, "Cognitive burden of therapy administration too high for patient" was actually under the subheading "Issues with therapy management" and was considered an AHA-related factor, rather than a patient-related factor (i.e., the patient did not decide the cognitive burden was too high). The authors agree that interpretation of the reasons can be improved, and have made changes to both text and table to clarify (page 20).
Minor essential points:

5. I find the question posed not clear: ‘in younger and older patients’ may suggest that there is also a middle category of patients (not young and not old). It would be helpful to include the age cutpoint in the question.

Response: We added the age cut points to the last paragraph of the Introduction to increase clarity on the age groups (page 5).

6. Could the authors also provide some underpinning for their choice of the 65-year cutpoint?

Response: During survey development interviews with practicing physicians and epidemiologists, they were asked at what age they considered their patients to be "older" in terms of disease management. While most stated that these decisions were generally made on an individual basis and dependent on patient health, there was agreement that 65 years was the most reasonable cut point.

7. More attention should be given to the current debate on age and (less) intensive treatment in the introduction. Only in the discussion it is stated that NICE recommends treatment targets between 6.5% and 7.5% depending on the extent of pre-existing comorbid conditions and agreement with the patient. This is quite essential for this study!

Response: The Introduction was modified to keep the focus on treatment of type 2 diabetes and the association between age and treatment initiation. We removed text describing the intensive glycemic control and outcomes to avoid any confusion it may cause (page 5). In addition, we focus the Discussion on age issues related to our study findings (pages 10-12).

8. GPs documented relevant patient data via the internet using an electronic data capture form. As I understand, this implies that the GPs self-selected and self-reported the data. Was there any validation that these were random patients and that the data abstraction reports were complete & correct? If not, this should at least be discussed as limitation.

Response: Physicians self selected patients based on the pre-specified inclusion and exclusion criteria, and the data completeness was checked. However, there was neither randomization nor validation of data abstraction, except for built-in logical checks of the data. This information was added as a limitation (page 13).

9. In the results it is stated ‘The proportion of patients with their most recent HbA1c measurement above their GP-reported HbA1c threshold was higher (p=0.002) in the younger patients (14.3%) compared to the older patients (10.4%).’ A finding which is also discussed. This seems, however, a skewed comparison since the threshold was for initiating therapy and not for intensifying therapy.

Response: Physicians were asked, "What is the threshold HbA1c level for this patient to start therapy?" The reported threshold value was then compared to patient's most recent (post diabetes diagnosis) HbA1c at time of the survey when the AHA therapy had not initiated yet. The point
here is that some patients had exceeded the physician stated threshold for treatment initiation, but were still untreated.


Response: In the Discussion, we included an additional reference (Parnes et al. Diabetes Care 2004) evaluating physicians' reasons for not starting or changing medication in their patients despite elevated HbA1c (pages 10-12). Our research question is unique compared with the articles provided by the reviewer in that we are addressing GPs' reasons for no treatment initiation for at least 6 months after initial diabetes diagnosis. The suggested articles are addressing the effect of clinical measurements on treatment decisions for multiple metabolic risk factors.

Response: We appreciate this criticism and modified the Discussion (pages 10-14).

12. The focus of the conclusion is on safety but also patients burden/comorbidity is seen as a problem. This could be better acknowledged.

Response: We appreciate this critique and modified the conclusion to include burden on the patient as another factor influencing treatment decisions in older patients (pages 11-12).

13. There is a partial update on the NICE guideline 66 (guideline 87) – update for reference 3.

Response: While we appreciate the recent update to the NICE guidelines (#87) in late 2010, the NICE guideline 66 was most relevant to the time period assessed in our survey (Nov 2009 – Jan 2010).
C. Reviewer's report
Title: Reasons of general practitioners for non-treatment of younger and older patients with newly diagnosed type 2 diabetes mellitus in the United Kingdom: A survey study

Version: 1 Date: 24 June 2011
Reviewer: Louis Kuritzky
Reviewer's report:
I much enjoyed reading your manuscript about understanding reasons why GPs do not initiate treatment for newly diagnosed diabetics.

1. I think that an introductory statement suggesting cardiovascular/macrovascular/mortality benefits for glucose control are lacking. Indeed, our own (United States) FDA requires newly approved diabetes drugs to include the following statement (verbatim): "There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with ________ or any other antidiabetic drug."

Response: We appreciate this comment, but based on a comment from another reviewer we removed the text related to intensive glycemic control and outcomes to keep the focus of the paper on age and treatment initiation (page 5).

2. Although the text was easy to read and enjoyable, I believe there is a great deal more information in the tables that might merit inclusion in the text. For instance, when describing the group ages as either <65 or >65, one might initially think that the groups could--at least conceptually--be quite similar in age, yet the table clearly shows a MAJOR age difference in the two groups. I suggest expanding the text modestly to include some more of the highlights contained within the table.

Response: We added the mean age at diagnosis for the patient subgroups to the Results section of the text (page 8). We prefer to refer to the results in general terms in the text and allow the reader to review the tables for the specific results. Otherwise, there is increased repetition of results within the paper.

3. Finally, the graphic text (Bar graphs) were difficult to discern because colors were so close...if it will be published in dramatic color difference, fine, but otherwise maybe use hatching/cross-hatching/designs to make bars in graphs easily distinguished.

Response: Figure was updated to help better distinguish the groups (page 22).

4. Finally, GPs might be a bit taken aback by this assessment, as if the failure to initiate treatment were always poor practice. Might not there be at least a paragraph acknowledging that delay in treatment IS sometimes a rational choice? Given that we remain unable to prove that tight glucose control saves lives, I do respect the philosophy of those who wish to tread gently on the ground of seniors, patients with complex medical regimens, patients who would simply rather not take additional meds, patients who object to a particular med side effect, or patients who (for whatever reason) might be perceived as having transitory reasons for dysglycemia, such as systemic glucocorticoid treatment.
Response: We agree that the decision to initiate treatment is dependent upon many factors including clinical-, patient-, and systematic-related ones. We highlight this in the Discussion on page 12. In addition, the physicians selected patients who had to be untreated for at least 6 months following their diagnosis. Therefore, these patients had established type 2 diabetes and were not hyperglycemic for a transitory reason.