Author's response to reviews

Title: The prevalence and ingredient cost of chronic comorbidity in an Irish elderly population with medication treated type 2 diabetes. A retrospective cross-sectional study using a national pharmacy claims database

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Author's response to reviews: see over
Ms Flory Mae Calumpita  
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United Kingdom  
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Re: MS 9402699187761275

*The prevalence and ingredient cost of chronic comorbidity in an Irish elderly population with medication treated type 2 diabetes. A retrospective cross-sectional study using a national pharmacy claims database.* Miriam P O’Shea, Mary Teeling and Kathleen Bennett

Dear Ms Calumpita,

Thank you for giving my co-authors and I, the opportunity to prepare a revised version of the manuscript entitled “The prevalence and ingredient cost of chronic comorbidity in an Irish elderly population with treated type 2 diabetes: A retrospective cross-sectional study using a national pharmacy claims database”. The layout of the tables in the revised manuscript has been amended to reflect the editor’s comments. The authors would also like to sincerely thank both of the reviewers for their constructive comments and suggestions for this manuscript.
In response to comments made by the first reviewer (John Ford), the following revisions have been made to the revised manuscript;

Major Compulsory Revisions

1. Reviewer’s comment: While the results are interesting they are not unexpected. Therefore to improve the impact, this paper would benefit from a more detailed section in the discussion which outlines the importance of these results and how they might be used by decision makers and economists.

Amendment made: The following sentences were added to the discussion section, pg. 13-14, paragraph 3.

“The results of this study have important clinical implications for both patients and health professionals. There are also substantial economic implications for decision makers responsible for providing the most cost-effective health care. The results of the current study indicate that those with T2DM have greater number of comorbid conditions, both related and unrelated to diabetes, and that these are associated substantial increased cost. Increased education and earlier intervention programme for patients with diabetes are needed so as to avoid the costly consequences of poor adherence and management of their condition. A structured management care programme provided in general practice, in conjunction with a multi-disciplinary team of health professionals, with direct and immediate access to specialist services as required, would facilitate this greatly. In Ireland, this type of programme has been implemented in the Midlands health region for patients with diabetes, and has produced encouraging results [46]. The nationwide implementation of this type of programme could yield an overall improvement in patient management and costs associated with diabetes.”

2. Reviewer’s comment: The authors have used bootstrapping to compare means. Mention of its potential weakness is needed in the discussion, especially in regard to the narrow confidence interval.
Amendment made: The following sentences were added to discussion section, pg. 15, paragraph 1; line 6-11.

“There are limitations to using the bootstrapping methods including the assumption that the distribution of the data from the sample is a reasonable estimate of the population distribution from which it came. Given the very large sample size and the high percentage of the population captured this is unlikely to be a major source of bias. There may also have been some sampling error in the selection of random samples in the bootstrap procedure, but with 2000 samples chosen this is unlikely.”

Minor Essential Revisions

3. Reviewer’s comment: The term “treated T2DM (more accurately “medication treated T2DM”) should be used throughout to make it clear to readers that individuals with diet controlled DM are not included.

Amendment made: The term “treated T2DM” has been replaced with “medication treated T2DM” in the revised manuscript. The term has also been added to the title of the manuscript.

Methods

4. Reviewer’s comments: Appendix 1 was not attached and therefore I was unable to comment on this.

Amendment made: The authors apologise for this error and have included the appendix in this revised version of the manuscript (pg. 26 - 28).

Results

5. Reviewer’s comment: Sentence in the results “The T2DM group was nearly three times more likely to have ≥ 5 comorbid conditions compared to the non T2DM group”. Why was this cut off chosen? Was it pre-specified?
Amendment made: The authors have added two additional sentences to the methods section, to explain the reason behind this cut off. The additional sentences, (pg.8, paragraph 1; lines 1 - 4) read

“The median number of comorbid conditions in the T2DM group was chosen as a proxy measurement to define low (<median) versus high (>=median) comorbidity. The association between T2DM and low versus high comorbidity was subsequently examined using the $\chi^2$ test”.

6. Reviewer’s comment: One of the confidence intervals does not make sense in the discussion. Sentence beginning “The mean annual ingredient cost of comorbidity in the study population with T2DM was significantly higher (€1238.67 95% CI €1238.20 - €1238.14)”. In addition, the word “significantly” should be removed as this may be interpreted as statistical significance.

Amendment made: The authors apologise for this error and have rectified the 95% CI so that it now correctly reads “(€1238.67, 95% CI €1238.20 - €1239.14)”. In addition the word “significantly” was removed from this sentence in the revised manuscript (pg.10, paragraph 2; line 1-3).

7. Reviewer’s comment: There needs to be consistency between the terminology of “sex” and “gender”. Was gender or sex reported in the claims database?

Amendment made: The word “gender” was replaced with the word “sex” throughout the document. The sex of the claimant is documented in the database; this is addressed in the methods section (pg.6, paragraph1; line 3 – 6) of the manuscript in the sentence beginning “In addition to providing details on medications dispensed to eligible individuals, the HSE-PCRS pharmacy claims database also contains demographic information about the claimant such as age, sex and region of residence”.
Discussion

8. **Reviewer’s comment:** Sentence in the discussion beginning “It may, therefore, be beneficial for health professionals to actively manage depression in their patients with diabetes…” Whilst I understand the sentiment behind this statement, it needs re-worded to avoid the implication that health professionals currently passively manage depression

**Amendment:** pg.12, paragraph 2, final sentence. This sentence was re-worded and now reads “It is imperative therefore, that depression in patients with T2DM is recognised and treated given the adverse outcomes associated with such comorbidity”.

9. **Reviewer’s comment:** First sentence of the conclusion needs reworded. The word “burden” needs removed or expanded upon. It is true to say that patients have a greater prevalence of comorbidity, but burden implies that each comorbidity has an equal, and cumulative, burden on a patient’s life. This may not be true. For example, the burden of comorbidity from hyperlipidemia will be less than heart failure. It is true that there is a higher burden of medication costs to the healthcare services.

**Amendment:** pg.15, conclusion section; line 1. The word “burden” was removed from the first sentence of the conclusion and replaced with “prevalence”.

In response to comments made by the second referee (Vicky Head), the following revisions have been made to the manuscript;

**Major essential revisions**

1. **Reviewer’s comments:** More information is required on the coverage of the HSE-PCRS database and implications for the generalisability of the findings. In particular
is there different eligibility / coverage for those aged 65-69 compared to >70s and, if so, how might these affect the findings? Are those covered by the GMS likely to have better/ worse health than those not covered? Are the findings for >70s likely to be more robust and generalisable than those for 65-69 years olds? This point carries through to the first paragraph of the results through to the first paragraph of the results and to the final paragraph in the discussion, where more reflection is required.

Amendments: More information about the HSE-PCRS and the eligibility criteria for the all age groups has been added to the method section. The revised version of the methods section now includes the following description and information about GMS eligibility (pg.5, methods section, paragraph 1: line 3-14):

“The HSE-PCRS database is used primarily to provide financial reimbursement to health care professionals involved in primary care, for the provision of health services and prescription medications under a number of different state provided health care schemes, including the General Medical Services scheme (GMS) [27]. The GMS scheme provides eligible individuals, termed “medical card” patients, with access to free health care, routine dental services and prescription medication [27]. Eligibility for the GMS scheme is based on an individual being ordinarily resident in Ireland and the outcome of a gross income means assessment. The weekly income threshold for GMS scheme eligibility is dependent on the marital status and age of the claimant [27]. Older individuals aged >70 years were automatically entitled to a medical card regardless of their income from July 2001 – Dec 2008 [27]. In 2010, the GMS scheme covered half (50.4%) of the Irish population aged between 65-69 years, and 98.4% of the population aged >70 years or more (based on population estimates) [28, 29].”

This may possibly have an impact on the generalisability of the results and as a result the following sentences have been added to the final paragraph of the discussion (pg.14 -15: paragraph 2, line 8 – 19).

“In addition, the current study was unable to take into account patients with medication treated T2DM who did not meet the eligibility criteria for the GMS
scheme. It is possible that non medical card patients may have received their diabetes medication through other community drug schemes such as the Long Term Illness (LTI) scheme or Drugs Payment Scheme (DPS) or paid for their medications privately. In 2010, medical card holders represented a very high proportion of the Irish elderly population > 70 years (98.4%). It is therefore likely, that the results of the present study represent an accurate account of medication treated T2DM, comorbidity and the associated ingredient cost in this age group. For the age group 65-69 years, only half are eligible for the GMS scheme, which may represent a slightly more deprived and sicker population. Previous research has indicated that medical card holders on average visit their doctor more frequently per year [48] and have poorer health [49] when compared to non medical card holders”.

Minor essential revisions

2. **Reviewer’s comments:** Results, 2nd paragraph and links back to Data Analysis – it is not clear why/ how a chi square test was used to test for the difference between the two medians. The text of the first sentence of the paragraph does not intuitively match the analysis cited. If data has been used for this that is not shown in the tables it would be helpful to see it, and for clarity, more detail on the analysis used may be necessary.

**Amendments:** The following sentences were added to the Data Analysis section of the methods to explain the use of the chi square test in this study (pg. 8, paragraph 1: line 1 – 4)

“The median number of comorbid conditions in the combined group was chosen as a proxy measurement to define low (<median) versus high (>=median) comorbidity. The association between T2DM and low vs. high comorbidity was subsequently examined using the $X^2$ test”.
3. **Reviewer’s comments:** p. 9: final paragraph, the first confidence interval given does not contain the point estimate (presumably this is a typo – should read €1238.20 - €1239.14?). This error is repeated in the abstract.

**Amendment:** pg. 10, paragraph 2: line 1-2. This error has been corrected and the 95% CI now reads €1238.20 - €1239.14. It has also been amended in the abstract (pg.2 results section, line 6-7).

4. **Reviewer’s comment:** Overall while the writing is broadly acceptable, there are numerous errors and the manuscript needs thorough proofreading.

**Amendment:** The revised manuscript has been proof read and spelling and grammatical errors corrected.

Discretionary revisions

5. **Reviewer’s comment:** p2: abstract – first line of the methods might read better “The Irish Health Service Executive Primary Care Reimbursement Service prescription pharmacy database which includes all prescribing to individuals covered by the General Medical Services scheme, was used to identify the study population” . The current text implies those eligible for the GMS were identified from a broader database.

**Amendment:** pg.2: abstract. This sentence was re-written in the revised manuscript to reflect the reviewer’s suggestion.

6. **Reviewer’s comments:** p. 3: Background – projected prevalence increase from 2.8% to 4.8% is not doubling of prevalence as currently stated.

**Amendment:** pg.3, background section, paragraph 1: line 2. The word “doubling” was removed and changed to “increase”.

7. **Reviewer’s comments**: p8: Results, paragraph 2 – the statement “The T2DM group was nearly three times more likely to have ≥5 comorbid conditions…..” could be more correctly stated as “The odds of having ≥5 comorbid conditions were three times higher in the T2DM group….”

**Amendment**: pg. 9, results section, paragraph 2, line 4-6. This sentence was re-written in the revised manuscript to reflect the reviewer’s suggestion.

Yours sincerely,

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