Author's response to reviews

Title: The high-cost, type 2 diabetes mellitus patient: an analysis of managed care administrative data

Authors:

Juliana L Meyers (jmeyers@rti.org)
Shreekant Parasuraman (shreekant.parasuraman@astrazeneca.com)
Kelly F Bell (kelly.bell@bms.com)
John P Graham (john.graham@bms.com)
Sean D Candrilli (scandrilli@rti.org)

Version: 2 Date: 28 October 2013

Author's response to reviews: see over
October 28, 2013

Professor Olivier Bruyère
Editor-In-Chief
Archives of Public Health

Dear Professor Bruyère:

Enclosed is a manuscript resubmitted for your consideration for publication in Archives of Public Health. The manuscript is an original research article titled, “The high-cost type 2 diabetes mellitus patient: an analysis of managed care administrative data” by Juliana Meyers, Shreekant Parasuraman, Kelly Bell, John Graham, and Sean Candrilli. The manuscript is 48 double-spaced pages in length, including 3 pages of references. Additionally, the manuscript includes 4 tables and 2 figures.

Responses to the reviewer comments are provided at the end of this cover letter.

The manuscript describes a retrospective analysis of patients with type 2 diabetes mellitus in a commercial claims database. Specifically, high-cost (HC) type 2 diabetes mellitus (T2DM) patients were identified and compared with patients with type 2 diabetes mellitus who were not high-cost. Given the rising health care costs in the United States, identifying patients who could be considered HC is of significant interest to health care payers. Previous studies have identified HC patients in other disease areas (e.g., acute coronary syndromes), but to our knowledge, no retrospective analysis has been published that examines HC patients with T2DM.

All data used in this analysis were from the LifeLink database. RTI International’s Institutional Review Board determined that this study met all criteria for exemption, as the data were retrospective, pre-existing, and de-identified.

This work has not been previously published, nor is it under consideration for publication elsewhere. Portions of this study were presented at the Academy of Managed Care Pharmacy’s 24th Annual Meeting and Exposition in 2012 in San Francisco, California.

All authors have read and approved this manuscript for submission to Archives of Public Health. All authors contributed to the study concept, data analysis, and manuscript preparation. This study was funded and conceived by AstraZeneca. The study design was developed in consultation with AstraZeneca, and results were reviewed by AstraZeneca. AstraZeneca did not influence interpretation of results, and the manuscript was reviewed by
AstraZeneca prior to publication. Juliana Meyers and Sean Candrilli are employees of RTI Health Solutions, a research organization hired by AstraZeneca to conduct the analysis. Shrekkant Parasuraman is an employee of AstraZeneca, and Kelly Bell and John Graham are employees of Bristol-Myers Squibb.

Please address all correspondence to the following author:

Juliana Meyers  
RTI Health Solutions  
200 Park Offices Drive  
Research Triangle Park, NC 27709  
Telephone: +1.202.506.6944  
Fax: +1.919.541.7222  
E-mail: jmeyers@rti.org

The authors hereby consent to transfer copyright to Archives of Public Health upon publication. We welcome any suggestions regarding the manuscript and look forward to receiving your feedback. Thank you for your consideration.

Sincerely,

Juliana Meyers, MA  
Associate Director, Health Economics  
RTI Health Solutions  
200 Park Offices Drive  
Research Triangle Park, NC 27709  
Telephone: +1.202.506.6944  
Fax: +1.919.541.7222  
E-mail: jmeyers@rti.org
Responses to Reviewer Comments

Reviewer 1

Abstract (Conclusion): The conclusion should be rewritten in relation to the objectives of the paper (to assess the predictors of being a high-cost patient). The last sentence of the abstract is not related to the content of the article and should be deleted. The authors have not discussed and reviewed current approaches.

We have removed the last sentence of the abstract and added the following sentence to address the objectives of the manuscript, “Patients were significantly more likely to be HC if they had comorbid conditions, a diagnosis of obesity, or used insulin.”

Page 9: I would suggest deleting discussion in the heading.

We have removed the words “and discussion” from the heading.

In the introduction, the authors explain that identifying the patients with high-costs could be of significant interest to health care payers because interventions could be developed that would focus on patients who are likely to become HC. A discussion surrounding this remark is needed in the discussion of the article. Have any existing intervention been shown to be more effective in patients with high CCI, for example?

We have added a paragraph to the discussion section to further describe the implications of this study and the potential steps health plans may take to reduce health care costs. Specifically, the following text has been added “A previous study examining Medicare patients with T2DM found that interventions aimed at diabetes have not differed based on comorbid illness burden. Our analysis found that patients with a higher comorbidity burden and more concomitant conditions were significantly more likely to be HC. Therefore, from the perspective of a payer, one practical implication of the present analysis is that it may make sense to provide those patients who have the most comorbidities and concomitant conditions (i.e., those patients who are at the greatest risk of being HC) with additional patient care tailored at treating the comorbidity or concomitant condition (e.g., weight loss programs for obese patients).

The implications of the study findings should also be extensively discussed. It is not clear what to do with these results. What are the recommendations for health care
providers? To focus on patients with high-costs? Or to develop effective treatments in high-cost patients? Or others?

This text has been added to the discussion section of the manuscript: “The goal of this study was to provide payers with a means of identifying patients who are at increased risk for becoming HC, using real-world data. Once these patients are identified, personalized interventions could be developed that may decrease the likelihood of the patient becoming HC. Interventions might include extra office visits for comorbid conditions, structured weight loss programs, or increased pharmacotherapy for glucose controls. Economic evaluations to examine the cost benefit structure of developing such interventions would be informative.”

Reviewer 2

The authors stated that they used data from January 1, 2005 to December 31, 2010 as the time window to identify patients who had at least two diagnoses of T2DM. Subsequently, qualified patients were followed for 1 year. On page 6, second paragraph, the authors stated that “To allow for adequate follow-up time….patients were required to have at least 12 months of continuous post-index date observation.” If the window for the index date was between January 1, 2005 and December 31, 2010 as indicated by the authors, then shouldn’t the authors have another year of data that extends to December 31, 2011? If not, then the time window to identify patients (index date) should end at December, 2009 for the last patient to be identified and then followed till December 31, 2010. Please clarify.

We have provided further clarification in the manuscript regarding the period of time when patients were selected (i.e., January 1, 2005, through December 31, 2009) and the period of time when data were available (i.e., January 1, 2005, through December 31, 2010).

The strong predictors for high-cost T2DM patients that the authors identified in the study including: higher CCI score, renal impairment, obesity, hypertension and, receipt of insulin. Knowingly, these health conditions are all associated with high healthcare costs or, will result in high-costs due to comorbidities. There is ample information on this in the existing literature. Hence, the implication of the study or the contribution of this paper to the literature may be marginal.
While literature exists showing that patients with more comorbidities incur higher health care costs, to our knowledge no study has been conducted looking at drivers of health care costs specifically in a diabetes population. Furthermore, the conclusions drawn from this study are based upon a large, real-world population. Clinical trials frequently exclude patients with comorbid conditions; however, there is little information available on such HC patients.

Additionally, Hartmann (2013) found that while the main driver for health care costs was inpatient admissions, the reason for the admission varied by patient sex and age, highlighting the facts that HC patients require care tailored to their unique situation and that no single intervention exists that will reduce health care costs among all patients.

In addition to adding the words “real-world” in key places in the manuscript (e.g., first sentence of the conclusions section), we have also added the following paragraph to the discussion section: “Hartmann examined patients in the top decile of health care spending, using German health insurance information. Consistent with our analysis, Hartmann found that the highest health care expenses for patients were incurred in the inpatient sector, with over 80% of all HC patients having at least one hospital admission (compared with 74.2% in our analysis). Additionally, Hartmann found that the reasons for the hospitalization differed based on patient age and sex, which further highlights the facts that HC patients require care tailored to their unique situation and that no single intervention exists that will reduce health care costs among all patients.”

The introduction was not well structured with regard to the specific research question: The introduction provides abundant information on the diabetes and related therapies and costs (which in any case are very well known), but does not present enough background information with regard to predictors of high-cost patients.

Given that the readership may include practitioners who do not have extensive experience with diabetes patients, we have left the background regarding diabetes as is.

Furthermore, to our knowledge there are limited published data documenting predictors of being an HC patient. Previous studies have been conducted for cardiovascular conditions and for all insured persons, but to our knowledge this is the first study to date to examine predictors of HC patients in a diabetes population. We discuss the paucity of HC data in a diabetes population in the penultimate paragraph of the introduction section.
In the methods section, please provide further details as to how the predictors were chosen, for instance, what constructive steps the authors used to determine the set of predictors?

Baseline demographic data were included as independent variables in the regression equation, as these have repeatedly been shown to be associated with costs. Furthermore, we looked at clinical characteristics, given what data are available in the data set. We have updated the text describing the independent variables to make this clear.

Also, we have added a sentence to the limitations section saying that additional factors that we could not observe likely also would predict the risk of being an HC patient. Specifically the following text has been added: “Logistic regression model specifications were limited to the data available, and additional predictors of being an HC patient may exist (e.g., increased glycated hemoglobin value).”

Please clarify how are the missing data were handled in this claims data analysis.

Missing data were reported where applicable in the unadjusted analysis (i.e., patient demographics, health plan, and payer type). In the regression analysis examining factors associated with being an HC patient, 28,100 patients with missing age, gender, health plan, or health payer information were excluded from the analysis. This text has been included as a footnote to Table 2 as well as in the methods section.

The authors discussed and analyzed costs for groups who were top 10% of cost distribution as well as those who were top 20% of cost distribution, however, the abstract only mentioned the group who were top 10% of cost distribution. Please revise and provide more complete information in abstract.

We agree that these additional data are interesting and should be included in the manuscript; however, we are at the word limit in the abstract and unable to include this information there as well.

Page 6, paragraph 2, line 11: “The mean CCI score, along with the number and percentage of patients with a score<2 or >2, was reported.” please provide reasons behind using CCI=2 as the cut-off point.
The CCI = 2 was chosen as the cut-off point because approximately half the sample had a CCI = 0 or 1, and about half the sample had a CCI of 2 or more. This can be seen in the results tables.

Page 6, paragraph 2, last sentence: “Furthermore, to obtain the largest possible sample size of patients with T2DM, we did not require patients to have received a diabetic medication....” With a sample as large as 1.72 million, sample size (power) should not be a problem, so more strict inclusion criteria (e.g. patients with at least two diagnoses of T2DM + have received at least one diabetic medication) may be more appropriate for this study.

We have conducted a sensitivity analysis limiting the study population to the 926,180 patients who received an antidiabetic medication (i.e., an oral antidiabetic or insulin). In this subpopulation of treated T2DM patients, those with costs greater than $22,646 comprised the top 10th percentile (vs. $19,922 in the overall T2DM population), while patients with costs greater than $12,349 comprised the top 20th percentile (vs. $10,580 in the overall T2DM population). We found that there were no differences in patient demographics between the overall study sample and those patients who received antidiabetic medication. Having a CCI score greater than or equal to 2 was the strongest predictor of being an HC patient (OR = 4.862; \( P < 0.0001 \)), followed by a renal impairment diagnosis (OR = 2.369; \( P < 0.001 \)), an obesity diagnosis (OR = 1.991; \( P < 0.0001 \)), or receipt of insulin (OR = 1.897; \( P < 0.001 \)). Patients in the top 10% of the cost distribution accrued approximately $53,917 more in health care costs versus patients in the bottom 90% of the cost distribution (vs. $51,794 in the overall T2DM population), with the largest difference in costs attributable to inpatient stays. Additionally, patients in the top 10% of the cost distribution accrued costs of over $5.5 billion, which represented 54.1% of all costs accrued by the treated T2DM population (vs. 57.3% among all T2DM patients). Patients in the top 20% of the cost distribution accrued costs of over $7.0 billion, which represented 69.0% of all costs accrued by the treated T2DM population (vs. 72.3% among all T2DM patients). Text has been added to the discussion section reviewing the sensitivity analysis conducted as well as highlighting the key findings described in this paragraph.

Page 7, first paragraph, I suggest the authors revise the sentence “All-cause costs were examined (rather than T2DM-related costs)...” to statements indicating that both types of costs were examined in their analyses. Since the authors analyzed both all-cause costs and T2DM-related costs in the study, that sentence was misleading.
This sentence was referring specifically to the HC and NHC subgroup analyses. In these subgroup analyses, only the all-cause costs were examined to place patients in either the HC or the NHC cohort. We have reworded this sentence as follows to make this clearer, “For this analysis examining HC and NHC T2DM patients, all-cause costs were examined (rather than T2DM-related costs) because many patients likely had coexisting conditions (e.g., hypertension or renal impairment) that were T2DM related but that may not have been coded as such in the claims.”

Page 7, last sentence: “Because we wished to evaluate underlying comorbidity burden independent of T2DM, comorbidities corresponding to T2DM were removed from the CCI score”. Why??

Because all patients in the study sample had a diagnosis of T2DM, including diabetes in the CCI score would inflate the score for all patients by the same factor. We have rewritten this sentence as follows to further clarify, “Because all patients in the study had a diagnosis of T2DM and because we wished to evaluate underlying comorbidity burden independent of T2DM, comorbidities corresponding the T2DM were removed from the CCI score (i.e., we did not want the CCI to be inflated for all patients).”

The result section can be significantly shortened. For example, the first paragraph (from line 4 to 15) discussing results for top 20% seemed that the authors used the exact same sentences as in the second paragraph on page 11 discussing results for top 10%. It looks very redundant. The same issue applies for the second paragraph on page 12 and the second paragraph on page 13.

We have significantly revised the results section, and the repeated text is no longer present.

The discussion was weak. The authors used more than half of space to repeat the results and did not adequately discuss the implication of the findings and important limitations of the study.

We discuss important limitations of the study on page 19. We have added two sentences to the limitations to further discuss the limitations of the database (i.e., that no information was available on blood glucose or glycated hemoglobin values so the effect of glucose control on costs could not be assessed and that it was not feasible to assess the effect of an intervention [e.g., change in diabetes medication] on costs).
We have also added two new paragraphs comparing our results to previous studies. Results of a sensitivity analysis looking at treated T2DM patients also have been added to this section. A new paragraph also has been added to the end of the discussion section, which discusses the implications of the study.

MINOR ESSENTIAL REVISIONS

Page 4, last paragraph, please provide a reference for the information given on medical costs.

A reference has been added to the information given on medical costs.

Page 12, paragraph 2, line 1, “Health care costs related to T2DM were, on average, $2,997 more…” Please clarify and revise the “$ 2,997”. Did the authors mean “$3,780-$803=2,977” instead?

Thank you for catching this typographical error. The number should be $2,977; this change has been made in the manuscript.

Page 24, table 1, Male=50.12% > Female=49.78% in Top 10% group, however, Male=47.84% < Female=52.15% in Top 20% group. It is a little abnormal here, please re-check them.

These numbers have been double-checked and are correct.

Page 27, table 1, for Top 10% group, diabetes without chronic complications=98.74% and diabetes with chronic complications=26.24%, 98.74% +26.24% >1? Why? The same for the Top 20% group. Please re-check them.

These categories are not mutually exclusive. Patients may have had diagnoses of both diabetes without chronic complications and diabetes with chronic complications.

Page 29, table 2, compared with older patients (55+ years), younger patients are more likely to be higher-cost? It does not make sense and it is contrary to table 1, in which older patients have a much higher percent in high-cost group.

In Table 1, the mean (SD) age of patients in the top 10% of costs was 57.5 (12.9) years, while the mean (SD) age of patients in the bottom 90% of costs was 57.6 (14.8) years (which makes the mean age of patients in the bottom 90% of costs slightly higher than the
mean age of patients in the top 10% of costs). Additionally, the percentage of patients aged
greater than 65 years was 22.8% in the top 10% of costs and 29.5% in the bottom 90% of
costs. Using these results, the data presented in Table 1 support the regression results
presented in Table 2.