Author's response to reviews

Title: A novel method for measuring patients’ adherence to insulin dosing guidelines : Introducing indicators of adherence

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Version: 2 Date: 27 October 2008

Author's response to reviews:

Dear Editor,

Thank you for your comments on our article submitted for the journal of Medical Informatics and Decision Making.

We revised the article and clarified sections commented by reviewers Michael Albisser, and David Cavan. We changed the title of the article thank to Michael Albisser who noted that it was somewhat misleading. In fact, the objective of this study is to propose a method for quantifying patients’ conformance to insulin dosing guidelines.

Here are details of revisions we made to the manuscript in reply to Michel Albisser’s report.

• The reviewer noted that the title was somewhat misleading. We changed the title to “A novel method for measuring patients’ adherence to insulin dosing guidelines : Introducing indicators of adherence”.

• The reviewer stated that the study was retrospective. We added in the discussion that although we used a locked database in the current article, the same method could be applied for an online database to monitor patients’ adherence. In fact, we had already mentioned this in our conclusions.

• The reviewer demanded authors to clarify why they elected to use guidelines adapted to Actrapid and Regular insulin when the patients’ prescription is for Lispro insulin before meals. Our study was non-interventional, and the authors used the guideline which was actually taught to patients without electing it. In fact, in 2006, AJD used the same guideline for both patients under treatment with Humalog (lispro) and Lantus (glargine) and patients under treatment with
NovoRapid (aspart) and Lantus (glargine). A specific guideline was developed for the former group afterwards. While we added these explanations in the discussion, we kindly remind that our method is valid independently from the choice of the guideline.

- The reviewer raised a question about a decision algorithm that may add a new dimension to the guidelines, and suggested making further analysis on the rich dataset provided along with the article. While we find the idea of great clinical interest, it is not in the scope of this article to explore possible mathematical algorithms for providing decision support for insulin adjustment. In fact, this is the subject of our ongoing work, which will be presented in a future article.

Here are details of revisions we made to the manuscript in reply to David Caven's report.

- The reviewer stated that no data were presented on the resulting capillary blood glucose values to show whether the actual dose given was appropriate or effective, apart from data from one subject. This is a legitimate question. However, adding the data from all patients would put the emphasis on the clinical data, whereas we desired to focus primarily on our proposed method and indicators. Authors came to the conclusion that this section has already caused confusion about the article’s main goal, and therefore they decided to omit it. We hope to be able to discuss this aspect thoroughly in our future work. In the introduction, we re-phrased the main goal of the article to clarify we do not want to focus on the data, but on the methods.

- The reviewer stated that the high discrepancy between actual and guideline doses called into question the validity of the guideline. In the discussion, we added that the real adherence rate to the guideline would be the AA plus RA rate, which was 75% and was comparable to other study results [Ref 14]. Even if the discrepancy is high, this will not invalidate our method or indicators, because their role is to quantify these discrepancies. Contrarily, the fact that our method is not dependent to the guideline used, permitted us to find some shortcomings of the guideline (The discussion about the shortcomings of this specific guideline are out of scope of this article).

- The reviewer stated that the guideline reasoning relies on the previous day’s experience to determine the dosage, and concluded that this might not be appropriate. He used the example of a hypoglycemia the previous day, which would have been resulted from exercise or reduced carbohydrate intake. In our guideline, provided along with the article in a mini-site, it is stated that for a hypoglycemia could be taken into account for decisions, it had to be an “unexplained” hypoglycemia. Any hypoglycemia caused by exercise or reduced carbohydrate intake would not affect the dosing decision on the next day, because it is “explained”. Young diabetics learn this very well, and in real life conditions, physicians were not surprised by the way the guideline proposed to dose the insulin. In any way, this would not invalidate our method or our
indicators, because their role is to compare actual and guideline doses.

- We do agree with the reviewer that carbohydrate intake is the most important factor determining blood glucose levels. We emphasized in methods on the fact that patients’ daily carbohydrate intake was constant and fixed in advance by AJD nutritionists; this is why the guideline did not deal with carbohydrate intake as a variable. However, thank to our study this aspect was added afterwards in the next version of the guideline of AJD.

- The reviewer noted that the authors’ conclusion that actual doses might have been more appropriate than the guideline dose negated the usefulness of a system which would record deviation from the guidelines. Although we omitted the section of comparing actual doses with guideline doses to focus on the main goal of the article, by showing this instance (which was exceptional as we could see it for the example patient in figure 4) we would rather conclude that a guideline is hardly applicable for all patients and all situations. In any way, if our method is capable of showing that actual doses are more appropriate than the guideline doses for a given guideline, shows its very usefulness. This shows that the method is efficient in evaluating objectively both the patients and the guideline.

We hope these revisions increase the clarity and readability of our article, and we hope it is accepted for publication in your journal.

Yours Sincerely,

Dr Massoud Toussi,

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