Reviewer's report

Title: Severe hypoglycemia symptoms, antecedent behaviors, immediate consequences and association with glycemia medication usage: secondary analysis of the ACCORD Clinical Trial data

Version: 2 Date: 7 March 2012

Reviewer: Susan Braithwaite

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Discretionary revisions:

A category of interest for Table 3 would be “sulfonylurea + metformin”. On table 3, under the rows for the categories “metformin, TZD” and “metformin,sulfonylurea, TZD”, the footnote says “regardless of other medications.” Does this mean insulin was possibly included in those rows (I don’t think so, but the footnote should be clarified to state exclusion of insulin)?

Not only the choice of medication, but differences in dosage of insulin necessary to achieve the glycemic targets and the overall ratio of insulin to carbohydrate (for the insulin users) were differences not captured by the the assessments conducted in the paper. Some comment about insulin dose would be of interest.

On the assumption that higher insulin doses were used to aim at lower glycemic targets in the intensive group, it would be expected, for the comparion between “just sensitizer” vs “just insulin,” that the effect on HR for the intensive group would be more striking. However, it appears that the opposite was true. The HR for “just sensitizer” vs “just insulin” was more strikingly low for the standard group (Table 4).

The discussion on avoidance of hypoglycemia of course in 2012 is being read in the days of increased use of incretin-based therapies and declining favor for thiazolidinediones. In the discussion, the authors state that the more frequent use of oral medications in the standard group suggests that these medications should be considered, in those experiencing severe hypoglycemia. In tables 5a and 5b there is a passing mention of incretin therapy. Why do the authors not discuss exenatide, if that drug was in use during the study by some participants?

The paper is extremely well written.

Level of interest: An exceptional article

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

I declare that I have no competing interests.