Reviewer’s report

Title: What to do with diabetes therapies when HbA1c lowering is inadequate: add, switch, or continue? A MASTERMIND study

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Reviewer: John Wilding

Reviewer's report:

This study attempts to answer the important clinical question - what to do if a patient with T2DM shows an inadequate response to addition of a new therapy to existing treatment? The data suggest that the best strategy is probably to add additional therapy rather than to switch treatment, as this policy does not seem to result in a greater improvement in HbA1c, compared to simply continuing the apparently ineffective treatment.

The study also confirms previous data showing that treatment escalation is often significantly delayed in UK primary care (clinical inertia).

Have the authors considered looking at HbA1c trajectory in the period prior to starting new therapy in this analysis? It is possible that those patients who showed an inadequate response to therapy were in fact on a steeper upward trajectory of HbA1c at the time of addition of the new treatment compared to those who showed an improvement.

The policy of switching therapy with inadequate response could be related to the patient experiencing an adverse event or not tolerating a particular medication rather than an inadequate biological response. Although this information cannot easily be extracted from CPRD data, it would be worth mentioning this in the discussion and if possible investigating if coding consistent with side effects was the reason for switch in some patients?

CPRD data was included from a 2004 to 2017. There have been substantial changes in practice over that time with reduction in use of TZDs (and withdrawal of rosiglitazone), and introduction of several new classes (DPP4i, GLP1RA and SGLT2i). Is there any evidence that the proportion of patients who show inadequate response has changed over time? Could a large number of people switching from rosiglitazone when it was withdrawn have influenced the results?
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Not applicable

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

Yes

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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