Reviewer’s report

Title: Biphasic Insulin Aspart 30 vs. NPH plus Regular Human Insulin in Type 2 Diabetes Patients; A Cost-Effectiveness Study

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Reviewer: Katarzyna Kissimova-Skarbek

Reviewer's report:

This is a well performed and presented cost-effectiveness study, which compares two medical interventions of treatment persons with T2DM with two types of insulin: Biphasic Insulin Aspart 30 (BIAsp 30) and NPH plus Regular Human Insulin (NPH/Reg) in single-center, parallel-group, randomized, open-label clinical trial.

Authors concluded that treating persons with T2DM with BIAsp 30 is more effective in almost all outcomes measured in the study (among others, in terms of experiencing less frequently hypoglycemic events than the group receiving human insulin and achieving improved health related quality of life). In addition, treatment with BIAsp 30 caused in the analyzed period less total costs than in the group treated with NPH/Reg. As a result BIAsp 30 insulin was found to be cost-saving in the trial groups. A cost-effectiveness and cost-utility framework was used correctly, but details of costs calculations methods were not sufficiently presented (reference article was given) and some clarifications are needed. The study is appropriately situated in the context. The manuscript is well written and the objectives, interventions, and results are clearly described. The conclusions appear to be robust.

The methods applied are appropriate and mostly well described.

Effectiveness data: Authors should state which value set have been used to convert the health states derived by the EQ-5D-3L instrument to a single score (between 1 and 0). In the absence of a set of Iranian national population-based utility weights, probably a set of utility weights for a population that most closely approximates it have been selected, or in the absence of a suitable candidate - the most robust valuation set (the UK TTO set).

Costs: The mean direct costs (medical and non-medical) and production lost during trial period of 48 weeks have been presented. Some clarifications of the costs estimation methods are
necessary. From the published paper, where the costs calculation methods are explained (and Authors are referring to) is not clear if the production lost is calculated considering only the working age time lost or entire time lost due to T2DM; is there unemployment rate in the Iran economy used to correct the real production lost to the society? what is the method of valuation time lost for someone being on disability retirement? It seems (from the paper Authors have referred to) that indemnity claims are also applied (which are rather transfer payments, not costs) instead of average wage in the economy.

Statistical analyses: Data base is not available to reviewer; however the statistical analyses chosen seem appropriate. I am not able to see calculations, but I have one recommendation to the table 3: please present results as "mean frequency of hypoglycemic events per 100 person-years" instead of "mean frequency of hypoglycemic events reported as percent per person year". Please look at the results in table 5, where the same values are named as: "Hypoglycemia event per person year".

Discussion section: The limitations of the study and the transferability of the results to the entire Iranian population are not discussed, adding these will be valuable for this paper.

Please note, I have proposed some correction entered in the manuscript as comments.

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.

Yes

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 am able to assess the statistics

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

Acceptable

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During past five years for a period of three years (2009 - 2011) I was an employee of the International Diabetes Federation (IDF). IDF is supported financially by several commercial entities including NovoNordisk. The insulin of this company is a subject of economic evaluation by the manuscript I am reviewing. I declare that no competing interests exist.

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