Authors' Reply to Dr Malerbi: "Insulin Glargine in a Brazilian State: Should the Government Disinvest?"

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Dear Editor,

We thank Dr. Malerbi for his comments regarding the systematic review [1]: "Insulin Glargine in the Brazilian State: Should the Government disinvest? An Assessment Based on a Systematic Review". [2]. In particular, we thank Dr Malerbi for pointing out the recently published ORIGIN study [3] clarifying the situation regarding insulin glargine and its neutral effects on the development of cancer following the previous observations of Hemkens et al and Jonasson et al [4,5]. This will be welcomed by patients.

However, we were concerned by his comments that we 'seem to have prepared their review with the primary motivation of justifying – both on administrative and juridical grounds – the denial from the government to dispense insulin analogues to those diabetic patients who need them'. This is because the rationale for undertaking this review within a public health system with finite resources was the following:
a) Substantial increase in the expenditure on insulin glargine in the State of Minas Gerais in recent years – facilitated by a 536% difference in costs between insulin glargine and NPH insulins [2]
b) Published reviews from World-renowned organisations including the WHO [6], the Cochrane Collaboration [7,8], NICE (UK) [9,10], IQWiG (Germany) [11] and the Canadian Agency for Drugs and Technologies in Health [10] showed at best only minor health gain from long-acting insulins vs. standard (NPH) insulins
c) There are concerns with the independence of panel members who have produced national or international guidelines for patients with diabetes in the past [12]

Consequently, we believed there was a need to undertake a robust systematic review to ascertain the potential value of insulin glargine in the State of Minas Gerais. In addition, use the combined outcome measures of glycated haemoglobin as well as episodes of hypoglycaemia [2] alongside adverse effects and outcomes on microvascular and macrovascular end-organs in the review to document all key aspects of insulin therapy.

The study used a validated methodology for the preparation of Systematic Reviews and the principles of preparing this review were rigorously respected in the methodology [2]. Consequently, the review was developed based on best available scientific evidence and methodologies. We prepared the review with the primary motivation of summarising the available evidence accurately and reliably, in order to provide the best information for clinicians and policy makers to judge risks, benefits, and harms caused by the use of insulin glargine. In view of this, appearing to contradict the comments of Dr Malerbi.

Our findings are further endorsed by the consistency of our results with the published reviews already mentioned [6-11] as well as those of Singh et al [13], Monami et al [14], and REBRATS [15]. We are not aware of any more recent studies that would contest our findings. Dr Malerbi comments that 'Insulin analogues are better insulins' but without supplying any references/ published RCTs to support this statement. Consequently, we would still argue that the available robust published evidence (according to acknowledged Systematic Review techniques) would suggest the documentation of any health gain for long-term analogues insulins vs. NPH insulins is weak, inconsistent and presents conflict of interest. We believe this is an important point to be considered in the debate of public financing in a resource constrained scenario, especially in underdeveloped and developing countries. It is also relevant that high income countries such as Germany and UK have restricted the use of long acting insulins on the basis of their limited perceived value versus NPH insulins in the majority of patients. This is particularly important since in the UK the cost of insulin glargine is only twice that of NPH insulins versus the current 536% difference in the State of Minas Gerais[2,10]. Larger and better conducted studies are needed to support either the incorporation or delisting of insulin glargine at premium prices vs. NPH insulins. In the meantime, the authorities in the State of Minas Gerais should seek a price reduction for the continued reimbursement, similar to the situation in for instance Germany [5].

Finally, it should be emphasized once again that the authors of the study do not have conflicts of interest that might affect the study design or the outcomes given the rigorous process used and the consistency of our findings with other published meta analyses and reviews from many national and international organisations and academic units. Consequently, we are perturbed and concerned by the inference from Dr Malerbi and hope our explanation addresses this.

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