Medical management of hyperglycaemia in type 2 diabetes mellitus. Reply to Woo V [letter] and Eizirik DL [letter]

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Abbreviations

ADA American Diabetes Association

CDA Canadian Diabetes Association

To the Editor: We appreciate Dr Woo's comparison of the Canadian Diabetes Association (CDA) 2008 clinical practice guidelines [1] with the American Diabetes Association (ADA)/EASD consensus algorithm [2], and welcome the opportunity to address the differences that he has identified [3]. The original ADA/EASD consensus algorithm [4] and the subsequent revisions [2, 5] were developed independently by the consensus group and were then presented to the two major diabetes organisations for their review and approval of the process.

We were aware of the CDA guidelines. Dr Woo notes the CDA's process of data review with a 'standardised evidence-based approach' and the participation of 'more than 90 authors and a steering committee of 18', and concludes that the process removed 'as much bias as possible', implying that this approach was superior to our consensus algorithm process. Oddly, he then notes that the CDA committee 'believes' that patients and practitioners deserve more choices' (our emphasis) and notes, with no evidence provided, that 'when basal insulin with an intermediate-acting insulin is used it is *very likely* that more than one injection will be required' (our emphasis). These statements belie the objective methodologies cited by Dr Woo.

More important, in our view, is the 'equal weight' that the CDA gives to all pharmaceutical agents available in Canada. This even-handed approach, presumably designed to provide the flexibility that the CDA believes is important, does not aid practitioners and patients. There are demonstrable differences between these medications in their effectiveness, side-effect profiles, tolerability, ease of use and costs. All these factors were considered in the development of our algorithm, and we think they should influence clinicians' choices. The example cited by Dr Woo, in which he criticises the algorithm for not recommending glibenclamide (also known as glyburide in the USA and Canada), is illustrative. Our consensus algorithm specifically recommends against using glibenclamide, despite its glucose-lowering effectiveness and low cost, since there is a wealth of data that supports a greater risk of hypoglycaemia for glibenclamide compared with other similarly effective and low-cost sulfonylureas [6, 7]. In our opinion, this type of information is highly relevant, and should assist healthcare providers and their patients in the choice of agent. Our goal was to provide useful guidelines on the choice of medications from the many that are available.

Finally, even with the careful evidence-based review carried out by the CDA, we must disagree with their conclusion that the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial [8], the Veterans Affairs Diabetes Trial (VADT) [9] and the Rosiglitazone Evaluated for Cardiac Outcomes and Regulation of Glycemia in Diabetes (RECORD) trial [10] have exonerated rosiglitazone of the safety concern raised in previous meta-analyses. The trials

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were not ‘specifically designed to help address this question’, despite the CDA’s claim to the contrary; only the RECORD study was designed to address the effects of rosiglitazone on cardiovascular disease outcome, and its interim analysis suggested a trend, albeit non-significant, for worse, not better, outcomes with rosiglitazone [10, 11].

We agree with Dr Eizirik’s concern [12] regarding the potential for dualities of interest to influence the development of algorithms such as ours. This issue potentially affects all areas of academic medicine. In the current research environment, where academic investigators participate in pharmaceutical company-supported trials, it is difficult to find individuals with the requisite expertise and experience who do not have dualities of interest. During the selection of the consensus group members and our deliberations, all of our dualities of interest were considered and discussed openly. Although the results of the process do not directly address Dr Eizirik’s concern, we note with some satisfaction that we have received far more complaints regarding our recommendations from the pharmaceutical industry than from individuals concerned with our dualities of interest. We hope that the stated rationale for our choices convinces most readers that the algorithm was developed without the intrusion of any bias, other than the shared bias of the consensus group to provide the best care for patients with type 2 diabetes.

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