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LETTER

Response to "Letter to the Editor Regarding: Patient Preferences for Glucagon-like Peptide-1 (GLP-1) Receptor Agonist Treatment of Type 2 Diabetes Mellitus in Japan: A Discrete Choice Experiment"

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Dear Editor,

We would like to thank you for the opportunity to respond to the issues raised in the letter related to our publication [1] and to provide details of the methodology to address the concerns. In the letter, the author noted concerns about the cardiovascular (CV) outcome risk reduction value used for the semaglutide 0.50 mg profile. The author also requested clarification and disclosure of the references related to attribute levels.

The author is correct that the CV outcome risk reduction for the semaglutide 0.50 mg profile (26% versus placebo) was based on combined data for the 0.50 and 1.0 mg doses reported in the primary publication of SUSTAIN-6 by Marso et al. [2]. This was in accordance with the primary outcome of the study and to support noninferiority and superiority testing. As presented in the appendix of Marso et al., and noted in the letter, CV risk reduction was not significant for either dose independently (23% [$p = 0.13$] for semaglutide 0.50 mg and 29% [$p = 0.06$] for semaglutide 1.0 mg) [2], which was expected because the study was not powered or intended to assess the doses separately.

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Table 1 Attributes, levels, and sources for the discrete choice experiment

Attribute	Level	Represents	Reference
Method of administration	Multi-dose prefilled pen, used with disposable injection needles, with dose adjustment possible	Semaglutide 0.50 mg	Ozempic® prescribing information at the time of study conduct
	Single-dose, disposable prefilled pen, with no dose adjustment possible	Dulaglutide 0.75 mg	Trulicity® prescribing information at the time of study conduct
HbA1c change	On average, patients achieve a 1.9% reduction in HbA1c level	Semaglutide 0.50 mg	Seino et al. [6]
	On average, patients achieve a 1.6% reduction in HbA1c level	Intermediate level	Not applicable
	On average, patients achieve a 1.4% reduction in HbA1c level	Dulaglutide 0.75 mg	Miyagawa et al. [7]
CV risk reduction	26% reduction of risk in cardiovascular diseases (heart attack, stroke, death due to cardiovascular diseases)	Semaglutide 0.50 mg	Marso et al. [2]
	No data for the benefit or risk in cardiovascular diseases (heart attack, stroke, death due to cardiovascular diseases)	Dulaglutide 0.75 mg	None available
Weight change	On average, patients have a 2.2 kg weight loss	Semaglutide 0.50 mg	Seino et al. [6]
	On average, patients have a 1.1 kg weight loss	Intermediate level	Not applicable
	On average, patients do not have any weight loss	Dulaglutide 0.75 mg	Miyagawa et al. [7]
Common side effects	On average, 1 out of 9 patients will experience transient nausea	Semaglutide 0.50 mg	Seino et al. [6]
	On average, 1 out of 12 patients will experience transient nausea	Intermediate level	Not applicable
	On average, 1 out of 19 patients will experience transient nausea	Dulaglutide 0.75 mg	Miyagawa et al. [7]

By contrast, providing the uncertainty (95% confidence intervals) around the predicted choice probability for the semaglutide 0.50 mg profile versus the dulaglutide 0.75 mg profile would have strengthened our conclusions and might have alleviated the author's concern. Uncertainty around estimates from patient preference studies should be provided to help interpret results and inform patient-centered benefit–risk assessments [3]. The confidence interval around the predicted choice probability was small (78% [95% confidence interval, 74–82%]), supporting the conclusion that the large majority of participants preferred the semaglutide 0.50 mg profile.

To address the concern of the author about using a 26% CV risk reduction for the semaglutide 0.50 mg profile, we conducted an additional sensitivity analysis for the predicted choice probability. Using a 23% CV risk reduction, the predicted choice probability was 76% (95% confidence interval, 71–80%) in favor of the semaglutide 0.50 mg profile, which is close to the original value and supports the robustness and validity of our original conclusion.

Additional relevant data have been published since the discrete choice experiment was performed. SUSTAIN-7, a head-to-head randomized clinical trial, showed that hemoglobin A1c (HbA1c) and body weight were reduced significantly more with semaglutide 0.50 mg than with dulaglutide 0.75 mg [4]. This was confirmed in a network meta-analysis among patients with type 2 diabetes mellitus in Japan [5]. The REWIND study showed that dulaglutide 1.5 mg reduces cardiovascular risk compared to placebo, although this dosage is still not currently approved in Japan.

Finally, to address the request for clarification and disclosure of the references related to attribute levels, we provide them as Table 1.

Respectfully,
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process, as a letter this article underwent review by a member of the journal's editorial board.

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