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Comparison of subcutaneous GLP-1 receptor agonists, semaglutide and dulaglutide, on HbA1c and weight loss outcomes: A systematic review

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Abstract

Background: The aim of this systematic review was to ascertain whether semaglutide is more effective than dulaglutide on outcomes of glycosylated haemoglobin (HbA1c) and weight loss in adults. The objectives were to identify studies that compared the subcutaneously administered formulations of the two drugs, compare changes in outcomes stated, analyse the data and evaluate each drugs' effectiveness and determine which drug is more effective at achieving the outcomes.

Methods: Studies were eligible for inclusion if they were published up to December 2023, written in the English language and involved adult participants only. Studies were excluded if they were of a qualitative methodology, contained paediatric samples, those that involved other subtypes of diabetes mellitus, including gestational diabetes and studies that investigated only semaglutide or dulaglutide. Two electronic databases, Medline and Embase, were searched up to 31 December 2023 for published studies with at least 3-month follow-up that compared semaglutide and dulaglutide on the outcomes of changes in HbA1c and weight. Included studies were assessed for risk of bias using the Cochrane Collaboration risk-of- bias tool v2.0 and the Risk of Bias in Non-randomised studies of Interventions tool, as appropriate. Data on the outcomes were then considered for appropriateness for statistical analyses. All included studies were deemed unsuitable for statistical analyses due to inconsistencies of implied data distributions and use of statistical methods and were therefore synthesised using descriptive statistics and a narrative analysis.

Results: A total of 3 studies (1343 participants) met the inclusion criteria, where study 1 was a non- randomised cohort study, and study 2 and 3 were randomised controlled open-label studies. Statistical analysis was unable to be conducted without reducing the validity of the analysis, due poor use of statistics overall within all the studies. As a result, a narrative analysis was conducted. Both semaglutide and dulaglutide were shown to reduce HbA1c and weight from baseline, with semaglutide showing overall greater reductions in both HbA1c and weight reduction. Overall, participants on semaglutide were more likely to experience adverse events and discontinue treatment due to this. However, dulaglutide was

found to have higher rates of serious adverse events and death related to treatment than semaglutide.

Conclusions: Evaluation of the three studies showed that both GLP1-RAs are effective at reducing HbA1c and weight, with semaglutide achieving greater reductions in both outcomes overall. However, more robust and long-term studies needed on real-life populations to better determine the real-world, long-term efficacy and safety of these drugs. In addition, it was concluded that more needs to be done to increase research proficiency in healthcare, especially in the field of statistics. Better training should be sought on the conduction of statistical analyses and reporting of research, such as the reporting of normalised data, so readers and future systematic reviews may make robust comparisons between studies.

Keywords: Diabetes mellitus | GLP-1 receptor agonists | Semaglutide | Dulaglutide | HbA1c | Weight loss

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