PRISMA 2020 Checklist

Efficacy and Safety of Oral Small-Molecule GLP-1 Receptor Agonists in Type 2 Diabetes and Obesity: A Systematic Review with Targeted Meta-analyses of Orforglipron and Danuglipron

Page MJ, McKenzie JE, Bossuyt PM, et al. PRISMA 2020. BMJ 2021;372:n71. Page locations refer to the accompanying Orforglipron_Manuscript_Clean.pdf (17 pages), finalized 5 November 2026; supplementary tables refer to the revised supplement. Section and table identifiers remain applicable to the Word manuscript.

Section/Topic	Item #	Checklist item	Location (page)	Notes
TITLE				
Title	1	Identify the report as a systematic review.	p. 1	
ABSTRACT				
Abstract	2	See the PRISMA 2020 for Abstracts checklist (structured summary).	pp. 1-2	Structured Background/Methods/Results/Conclusions abstract
INTRODUCTION				
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	p. 2	
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	p. 2	
METHODS				
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	p. 3	
Information sources	6	Specify all databases, registers, and other sources searched, and the date each was last searched.	p. 3; Table S1	
Search strategy	7	Present the full search strategy for at least one database, including filters and limits used.	Table S1	Full multi-database strategies summarized narratively; complete strings held as Supplementary Table S1 (referenced, not reproduced in main text)
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria, including number of reviewers, and use of automation tools.	p. 3	
Data collection process	9	Specify methods used to collect data, including number of reviewers, and processes for obtaining data from investigators.	p. 3	
Data items	10a	List and define all outcomes for which data were sought.	pp. 3-4; Dataset S2	HbA1c, body weight, discontinuation, GI AEs, hepatic signals, MACE
Data items	10b	List and define all other variables for which data were sought (e.g., participant/intervention characteristics, funding sources); describe assumptions made.	Dataset S2	

Study risk of bias assessment	11	Specify the methods used to assess risk of bias, including number of reviewers and tools used.	p. 3; pp. 7-8; Table 2	Cochrane RoB 2
Effect measures	12	Specify for each outcome the effect measure(s) used in the synthesis or presentation of results.	pp. 3-4	Adjusted treatment differences for continuous outcomes; risk ratios for the specified safety comparisons.
Synthesis methods	13a	Describe processes for deciding which studies were eligible for each synthesis.	pp. 3-4; Table S3	
Synthesis methods	13b	Describe methods for preparing data for presentation or synthesis.	pp. 3-4; Dataset S2	
Synthesis methods	13c	Describe methods for tabulating or visually displaying results.	Figures 1-2c; Tables 1-4	
Synthesis methods	13d	Describe methods for synthesizing results and, if meta-analysis was done, the model, method to identify heterogeneity, and software used.	pp. 3-4; Tables S2-S4	REML, DL and common-effect estimates; Wald, HKSJ and modified HKSJ intervals; Q, I squared and tau squared.
Synthesis methods	13e	Describe methods to explore possible causes of heterogeneity among study results (e.g., subgroup analysis, meta-regression).	pp. 3-4; Table S2	Separate molecules, phases, populations and comparators; no formal meta-regression with small k.
Synthesis methods	13f	Describe sensitivity analyses to assess robustness of synthesized results.	Table S2; Dataset S2	Alternative models and CI methods; original two-trial weight subset; leave-one-out outputs in Dataset S2.
Reporting bias assessment	14	Describe methods used to assess risk of bias due to missing results in a synthesis.	p. 11	Fewer than ten trials per contrast; reporting-bias limits are explicit. Sponsor and primary-publication evidence are distinguished.
Certainty assessment	15	Describe methods used to assess certainty (confidence) in the body of evidence for an outcome.	pp. 10-11; Table 3	GRADE, for HbA1c and body weight only
RESULTS				
Study selection	16a	Describe results of search and selection process, from records identified to studies included, ideally with a flow diagram.	pp. 4-6; Figure 1	

Study selection	16b	Cite studies that might appear eligible but were excluded, and explain why.	pp. 4-5; original screening file	The supplied record categories and linked reports are reported explicitly. A separate full-text exclusion bibliography was not reconstructed; the original screening workbook is supplied for traceability.
Study characteristics	17	Cite each included study and present its characteristics.	pp. 6-7; Table 1	
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	pp. 7-8; Table 2	
Results of individual studies	19	For all outcomes, present summary statistics for each group and effect estimates/CI, ideally with a structured table or plot.	pp. 8-13; Dataset S2	
Results of syntheses	20a	Briefly summarize characteristics and risk of bias among studies contributing to each synthesis.	pp. 7-12	
Results of syntheses	20b	Present results of all statistical syntheses; if meta-analysis, summary estimate, CI, and heterogeneity measures.	pp. 8-12; Figures 2a-2c	
Results of syntheses	20c	Present results of investigations of heterogeneity among study results.	pp. 9-10; Table S2	
Results of syntheses	20d	Present results of sensitivity analyses.	Table S2; Dataset S2	Sensitivity results supplied in Table S2 and Dataset S2.
Reporting biases	21	Present assessments of risk of bias due to missing results for each synthesis.	p. 11	No reliable quantitative small-study-effects test with these few trials; no assertion that registration excludes selective reporting.
Certainty of evidence	22	Present assessments of certainty in the body of evidence for each outcome.	pp. 10-11; Table 3	
DISCUSSION				
Discussion	23a	Provide a general interpretation of results in the context of other evidence.	p. 13	
Discussion	23b	Discuss limitations of the included studies.	p. 14	
Discussion	23c	Discuss limitations of the review processes used.	p. 14; Table S3	
Discussion	23d	Discuss implications of results for practice, policy, and future research.	p. 14	
OTHER INFORMATION				

Registration and protocol	24a	Provide registration information, including register name and registration number, or state that the review was not registered.	p. 1; p. 3	PROSPERO CRD420261508176
Registration and protocol	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	PROSPERO CRD420261508176; no separate full protocol	Full protocol document referenced as not separately prepared beyond the PROSPERO record
Registration and protocol	24c	Describe and explain any amendments to information provided at registration or in the protocol.	pp. 3-4 and 14; Table S3	Dose-specific phase 3 pooling; omitted ACHIEVE-1 weight contrast corrected; added sensitivity analyses and restored selected safety pooling; ACHIEVE-4 disposition corrected. See Table S3.
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders.	p. 14	
Competing interests	26	Declare any competing interests of review authors.	p. 15	
Availability of data, code and other materials	27	Report which of the following are publicly available: template data collection forms, data extracted from included studies, analytic code, other materials used in the review.	p. 15; Dataset S2	Revised aggregate inputs, arm-level counts, source locations and executable Python code supplied as Dataset S2.

Item 16b: the supplied record-level screening workbook is retained for traceability. A separate full-text exclusion bibliography was not reconstructed. Sensitivity analyses (13f and 20d) are now supplied in Table S2 and Dataset S2. All locations refer to the revised manuscript.