

## Impact of baseline characteristics on the effects of GLP-1 receptor agonists on cardiovascular events in people with type 2 diabetes: a meta-analysis

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### Citation

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### Review question

Do baseline characteristics have an impact on the effects of glucagon-like peptide 1 (GLP-1) receptor agonists on major adverse cardiovascular events (MACE) in individuals with type 2 diabetes?

### Searches

We will systematically search the PubMed and Embase databases using a pre-defined search strategy, for relevant trials which are reported in English, without date restrictions.

### Types of study to be included

All randomized, controlled, event-driven, cardiovascular outcome trials.

### Condition or domain being studied

This meta-analysis will assess the effects of GLP-1 receptor agonists in reducing MACE in adult individuals with type 2 diabetes and different baseline characteristics.

### Participants/population

Adults with type 2 diabetes.

### Intervention(s), exposure(s)

Any of the GLP-1 receptor agonists (including but not limited to lixisenatide, liraglutide, semaglutide, exenatide, albiglutide, and dulaglutide). We will not consider doses and administration routes of drugs as effect modifiers.

### Comparator(s)/control

Active or placebo control.

### Main outcome(s)

Major adverse cardiovascular events (MACE), a composite of death from cardiovascular causes, nonfatal myocardial infarction (MI), or nonfatal stroke.

### \* Measures of effect

At the end of follow up, using hazard ratios (HRs) as reported by individual studies.

### Additional outcome(s)

None.

### \* Measures of effect

Not applicable.

### Data extraction (selection and coding)

The studies retrieved via the databases will be assessed for relevance according to the titles and abstracts, and then those potentially eligible studies will be assessed for final eligibility against the inclusion/exclusion criteria.

Two authors will then independently extract pre-specified data from the studies selected for inclusion using a standardized Excel data extraction sheet. The pre-specified data to be extracted contain study design, intervention characteristics, baseline characteristics of interest, study outcomes deriving from different subgroups, and risk of bias assessment results.

Any disagreements relevant with data extraction will be resolved through discussion with a third author.

### Risk of bias (quality) assessment

Two authors will independently assess risk of bias using the Cochrane risk of bias tool.

Any disagreements relevant with risk of bias assessment will be resolved through discussion with a third author.

### Strategy for data synthesis

We will perform random-effects meta-analysis in Stata (version 15.1) to estimate pooled hazard ratios (HRs) and 95% confidence intervals (CIs) based on trial-level survival data (i.e., HRs and 95% CIs from individual studies).

Heterogeneity across the studies eligible for inclusion will be estimated using the  $I^2$  test.

Moreover, random-effects meta-regression will also be used to explore subgroup effects.

### Analysis of subgroups or subsets

Subgroup analyses will be conducted according to the following seven baseline characteristics:

1. Sex: Female, Male
2. Duration of diabetes:  $\geq 10$  yr,  $< 10$  yr
3. History of congestive heart failure: Yes, No
4. Prior MI or stroke: Yes, No
5. Antihyperglycemic oral agent therapy: Yes, No
6. Insulin therapy: Yes, No
7. DPP-4 inhibitor therapy: Yes, No.

Moreover, the possible studies with slightly different grouping criteria used for subgroup analyses will be excluded for sensitivity analyses.

### Contact details for further information

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### Organisational affiliation of the review

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### Type and method of review

Intervention, Meta-analysis, Systematic review

### Anticipated or actual start date

10 December 2019

**Anticipated completion date**

01 April 2020

**Funding sources/sponsors**

None.

**Conflicts of interest**

None known

**Language**

English

**Country**

China

**Stage of review**

Review Ongoing

**Subject index terms status**

Subject indexing assigned by CRD

**Subject index terms**

MeSH headings have not been applied to this record

**Date of registration in PROSPERO**

28 April 2020

**Date of first submission**

10 December 2019

**Stage of review at time of this submission**

<b>Stage</b>	<b>Started</b>	<b>Completed</b>
Preliminary searches	Yes	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

*The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.*

*The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.*

**Versions**



28 April 2020

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**PROSPERO**

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