International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

The impact of SGLT-2i and GLP-1RA on liver-related events in patients with metabolic dysfunction-associated steatotic liver disease and type 2 diabetes mellitus: a systematic review and network meta-analysis

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ADMINISTRATIVE INFORMATION

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INPLASY registration number: INPLASY202530085

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 March 2025 and was last updated on 20 March 2025.

INTRODUCTION

Review question / Objective The aim of this study is to simultaneously compare the efficacy of novel glucose-lowering drugs (GLDs) on liver-related events in individuals with metabolic dysfunction-associated steatotic liver disease (MASLD) and type 2 diabetes mellitus (T2DM).

Condition being studied The Metabolic dysfunction-associated steatotic liver disease (MASLD), previously referred to as non-alcoholic fatty liver disease (NAFLD), is the most common chronic liver disease worldwide, affecting nearly one-third of the global population, with the prevalence among individuals with type 2 diabetes mellitus (T2DM) exceeding 60%. MASLD individuals with T2DM have a higher lifetime risk of advanced liver disease than those without. While glucose-lowering drugs (GLDs) have been widely evaluated in patients with coexistence of T2DM and MASLD (diabetic MASLD), their comparative efficacy on risk reduction of liver-related events remains unclear. Hence this study will aims to evaluate their efficacy for patients with diabetic MASLD.

METHODS

Participant or population Patients with MASLD and T2DM.

Intervention Glucagon-like peptide-1 receptor agonists (GLP-1RAs), sodium–glucose cotransporter 2 inhibitors (SGLT-2is), or other oral glucose-lowering drugs.

Comparator Glucagon-like peptide-1 receptor agonists (GLP-1RAs), sodium–glucose cotransporter 2 inhibitors (SGLT-2is), or other oral glucose-lowering drugs.

Study designs to be included Cohort studies and case-control studies.

Eligibility criteria Studies were included if they fulfilled the following criteria: (1) involvement of adult patients (≥18 years) with MASLD/MAFLD/MASH or NAFLD/NASH with one of the following cardiometabolic risk factor: obesity, type 2 diabetes, hypertension, hyperlipidemia; (2) comparison of any combination of GLP-1 RAs, SGLT-2is, or other oral GLDs; (3) reporting at least one of the following outcomes: incidence of cirrhosis, HCC, liver decompensation, liver failure, liver transplantation, liver-related death or any other liver-related events; (4) sufficient data should be provided. Studies were excluded if they fulfilled the following criteria: (1) duplicated studies; (2) inappropriate publication types, including abstracts, conference papers, reviews, meta-analyses, and correspondence; (3) studies that did not provide sufficient or reliable data.

Information sources We performed an extensive literature search using PubMed, EMBASE, Cochrane Library, and Web of Science without any language restrictions from inception to February 2025.

Main outcome(s) Liver-related events, defined as a composite occurrence of cirrhosis, HCC, liver decompensation, liver failure, liver transplantation, or liver-related death.

Additional outcome(s) Specific individual liver-related events.

Quality assessment / Risk of bias analysis The Newcastle-Ottawa Scale (NOS), a widely used tool for assessing non-randomized study quality, was used for evaluation.

Strategy of data synthesis Pairwise meta-analysis and network meta-analysis were applied for primary and secondary outcomes.

Subgroup analysis We conducted subgroup analyses for pairwise meta-analyses by study design, region, follow-up duration, sex, diabetic complications, hypertension, insulin use, and obesity for treatment pairs evaluated in at least two studies.

Sensitivity analysis Sensitivity analyses were conducted by limiting the analysis to studies with full covariate adjustments, or studies with a NOS full score.

Country(ies) involved China.

Keywords Metabolic dysfunction-associated steatotic liver disease (MASLD); type 2 diabetes mellitus (T2DM); glucose-lowering drugs (GLDs); liver-related events.

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