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The incidence of chronic drug-induced liver injury: A systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Formal screening of search results against eligibility criteria.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 7 August 2025 and was last updated on 7 August 2025.

INTRODUCTION

Review question / Objective As the incidence of drug-induced liver injuriy gradually increases, the incidence of chronic drug-induced liver injury may also change. The reported rates of chronicity vary among different studies. This study aims to analyze the incidence of chronic drug-induced liver injury, providing valuable epidemiological evidence to guide clinical practice and offering important follow-up and testing information for patients with high-risk factors for chronicDILI.

Condition being studied Drug-induced liver injury (DILI) refers to abnormal liver function caused by drugs and their metabolites, or by food additives or chemical agents.Drug-induced liver injuriey presents as acute conditions and have a good prognosis. However, certain drug-induced liver injury may become chronic DILI even after stopping the suspected causative drugs. There are currently no studies specifically focused on the incidence of chronic drug-induced liver injury.

METHODS

Search strategy Three researchers will conduct searches in PubMed, Web of Science, Embase and Cochrane library databases from their respective inception dates to 11 July 2025 using the following search terms: ("Chemical and Drug Induced Liver Injury" OR "Hepatitis, Toxic", "Drug-Induced Liver Disease" OR "DILI" OR "drug-induced hepatotoxicity" OR "drug-induced liver damage" OR "drug-induced chronic liver failure" OR "idiosyncratic drug-induced liver injury") AND ("Incidence" OR "Epidemiology" OR "frequency" OR "Follow-Up Studies" OR "Cohort Studies" OR "Prospective Studies" OR "Retrospective Studies"). No limits will be applied to the search.

Participant or population Patients diagnosed with drug-induced liver injury.

Intervention No intervention measures.

Comparator No comparator.

Study designs to be included All selected articles will meet the following inclusion criteria according to the PICOS acronym: Participants (P): Patients diagnosed with drug-induced liver injury (DILI); Intervention (I): not applicable; Comparison (C): not applicable; Outcome (O): prevalence of chronic drug-induced liver or relevant data from which the prevalence of chronic drug-induced liver injury could be estimated; Study design (S): cohort studies with accessible data published in a peer-reviewed, English-language journal.

Eligibility criteria All selected articles will meet the following inclusion criteria according to the PICOS acronym: Participants (P): Patients diagnosed with drug-induced liver injury (DILI); Intervention (I): not applicable; Comparison (C): not applicable; Outcome (O): prevalence of chronic drug-induced liver or relevant data from which the prevalence of chronic drug-induced liver injury could be estimated; Study design (S): cohort studies with accessible data published in a peer-reviewed, English-language journal. Exclusion criteria encompassed studies where DILI was attributed to non-drug-related factors, and those with a follow-up duration of less than six months. To ensure accuracy, any disagreements that arose during the study selection process will be resolved by consensus among the three independent researchers or through discussion with the corresponding author.

Information sources Three researchers will conduct searches in PubMed, Web of Science, Embase and Cochrane library databases from their respective inception dates to 11 July 2025.

Main outcome(s) A random-effects model will be applied to estimate the pooled incidence of chronic DILI. To explore potential sources of heterogeneity, subgroup analyses and meta-regression analyses will be performed. Subgroup analyses will be stratified by geographic region, sample size, study type, and quality assessment. Publication bias will be assessed using funnel plots and Egger's test. Sensitivity analyses will be conducted by sequentially excluding individual studies to evaluate the robustness of the pooled estimates.

Quality assessment / Risk of bias analysis The quality of cohort studies will be assessed using the Newcastle–Ottawa Scale (NOS), which evaluates three domains: selection of study groups, comparability of groups, and ascertainment of exposure or outcome. The NOS uses a star-based scoring system, where higher scores indicate better quality. Studies scoring 0–3, 4–6, and 7–9 stars were classified as low, medium, and high quality, respectively. Discrepancies and uncertainties in scoring will be resolved through discussion with the corresponding author.

Strategy of data synthesis A random-effects model will be applied to estimate the pooled incidence of chronic DILI and its corresponding 95% confidence intervals (CIs). Heterogeneity across studies will be assessed using the I^2 statistic, $I^2 > 50\%$ indicating substantial heterogeneity.

Subgroup analysis To explore potential sources of heterogeneity, subgroup analyses and meta-regression analyses were performed. Subgroup analyses will be stratified by geographic region, sample size, study type, and quality assessment.

Sensitivity analysis Publication bias will be assessed using funnel plots and Egger's test. Sensitivity analyses will be conducted by sequentially excluding individual studies to evaluate the robustness of the pooled estimates. All statistical tests will be two-tailed, and a P value < 0.05 was considered statistically significant.

Country(ies) involved China.

Keywords chronic drug-induced liver injury, meta-analysis,incidence.

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