

# INPLASY PROTOCOL

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**Conflicts of interest:**  
None declared.

## A meta-analysis of the association between type 2 diabetes and hepatocellular carcinoma in patients with hepatitis B virus

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**Review question / Objective:** In recent years, more and more studies have shown that type 2 diabetes is a risk factor for liver cancer in patients with hepatitis B. The purpose of this study was to accurately evaluate the relationship between type 2 diabetes and hepatocellular carcinoma in patients with hepatitis B.

**Eligibility criteria:** Inclusion criteria: 1. The research method is case-control study or cohort study, and the literature data is complete. The patients with T2DM were divided into the case group, and the patients without T2DM were the control group; 2. The subjects of the study were HBV-infected patients confirmed by laboratory indicators; the diagnosis of liver cancer complied with the diagnostic criteria revised by the Fourth National Conference on Liver Cancer; The diagnosis conformed to the diagnostic criteria for DM developed by the American Diabetes Association (ADA) or the World Health Organization (WHO) in clinical applications discussed at the Sixth National Endocrinology Academic Conference of the Chinese Medical Association; 3. Outcome indicators After multivariate logistic regression analysis, the original Data provide OR values and 95% confidence intervals (95% CI). Exclusion criteria: 1. Repeated publications; 2. Animal and cell studies; 3. Unable to obtain full text, meta-analysis, and literature review; 4. Other types of diabetes were used as exposure factors; Or those that could not be calculated from the literature and those whose data descriptions were not well described.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 01 June 2022 and was last updated on 01 June 2022 (registration number INPLASY202260001).

### INTRODUCTION

**Review question / Objective:** In recent years, more and more studies have shown that type 2 diabetes is a risk factor for liver cancer in patients with hepatitis B. The

purpose of this study was to accurately evaluate the relationship between type 2 diabetes and hepatocellular carcinoma in patients with hepatitis B.

**Condition being studied:** Primary liver cancer is the sixth most common cancer in the world and the third leading cause of cancer-related death, after lung cancer and colorectal cancer. In 2020, there will be 905,677 new cases of liver cancer worldwide and 830,180 deaths. The number of liver cancer patients in my country accounts for more than half of the global liver cancer patients, and it is one of the countries with the heaviest liver cancer burden. Common causes of primary liver cancer include: hepatitis B virus infection or hepatitis C virus infection, aflatoxin, alcoholism, obesity, smoking, etc. In recent years, a large number of cohort studies and case-control studies have explored the relationship between type 2 diabetes and liver cancer, and it is believed that type 2 diabetes is an independent risk factor for liver development. The European Association for the Study of the Liver (EASL) considers diabetes as a risk factor for hepatocellular carcinoma in chronic HBV-infected patients. Clinical studies have also shown that type 2 diabetes is a risk factor for liver cancer in patients with hepatitis B. p: Hepatitis B virus infection; I: Type 2 diabetes; C: no diabetes; O: odds ratio or hazard ratio for the incidence of liver cancer; S: cohort study or case-control study.

## METHODS

**Search strategy:** (((((((Diabetes Mellitus, Type 2[MeSH Terms]) OR (Maturity Onset Diabetes Mellitus[Title/Abstract])) OR (Diabetes Mellitus, Noninsulin Dependent[Title/Abstract])) OR (Non-Insulin-Dependent Diabetes Mellitus[Title/Abstract])) OR (Diabetes Mellitus, Stable[Title/Abstract])) OR (Type 2 Diabetes Mellitus[Title/Abstract])) OR (Diabetes, Type 2[Title/Abstract])) OR (Adult-Onset Diabetes Mellitus[Title/Abstract])) AND (((((((Hepatitis B virus[MeSH Terms]) OR (B virus, Hepatitis[Title/Abstract])) OR (Chronic Hepatitis B[Title/Abstract]) OR (Hepatitis B cirrhosis[Title/Abstract])) OR (Hepatitis B Virus Infection[Title/Abstract])) OR (Hepatitis B cirrhosis decompensated[Title/Abstract])) AND (((((((Liver Neoplasms[MeSH Terms]) OR

(Hepatocellular Cancer[MeSH Terms])) OR (Hepatocellular Carcinoma[Title/Abstract])) OR (Liver Cancer[Title/Abstract])) OR (Liver Neoplasm[Title/Abstract])) OR (Hepatic Cancer[Title/Abstract]))).

**Participant or population:** patients with hepatitis B virus infection.

**Intervention:** Type 2 diabetes.

**Comparator:** No diabetes.

**Study designs to be included:** Cohort study or case-control study.

**Eligibility criteria:** Inclusion criteria: 1. The research method is case-control study or cohort study, and the literature data is complete. The patients with T2DM were divided into the case group, and the patients without T2DM were the control group; 2. The subjects of the study were HBV-infected patients confirmed by laboratory indicators; the diagnosis of liver cancer complied with the diagnostic criteria revised by the Fourth National Conference on Liver Cancer; The diagnosis conformed to the diagnostic criteria for DM developed by the American Diabetes Association (ADA) or the World Health Organization (WHO) in clinical applications discussed at the Sixth National Endocrinology Academic Conference of the Chinese Medical Association; 3. Outcome indicators After multivariate logistic regression analysis, the original Data provide OR values and 95% confidence intervals (95% CI). Exclusion criteria: 1. Repeated publications; 2. Animal and cell studies; 3. Unable to obtain full text, meta-analysis, and literature review; 4. Other types of diabetes were used as exposure factors; Or those that could not be calculated from the literature and those whose data descriptions were not well described.

**Information sources:** CNKI, VIP, Wanfang Database, Pubmed, Embassy, Web of Science and the Cochrane Library.

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**Main outcome(s):** Odds ratio; hazard ratio; risk ratio.

**Author 3 - Xu Huan - Literature quality evaluation, dissertation proofreading.**

**Data management:** Endnote.

**Quality assessment / Risk of bias analysis:**

The Newcastle-Ottawa Scale (NOS) was used to evaluate literature quality, funnel plot was used to analyze publication bias, Begg and Egger methods were used to further verify publication bias, and cut-and-fill method was used to evaluate the impact of publication bias on the results.

**Strategy of data synthesis:** The heterogeneity test was assessed according to the Cochrane manual. When the Q test  $P > 0.1$  and  $I^2 < 50\%$ , it was considered that there was no heterogeneity, and the fixed effect model was used for analysis; otherwise, the random effect model was selected for analysis.

**Subgroup analysis:** Subgroup analysis was performed according to whether the study subjects had liver cirrhosis, study subjects, study sample size, and study methods.

**Sensitivity analysis:** The difference between the combined effect size of the remaining literature after deleting any one of the literatures and the combined effect size when it was not deleted, if the difference is small, the result is stable and reliable; if the difference is large, the result is not robust enough, and the reason needs to be further investigated.

**Language:** No language restrictions.

**Country(ies) involved:** China.

**Keywords:** Hepatocellular carcinoma ; Type 2 diabetes; Hepatitis B virus; Meta-analysis.

**Contributions of each author:**

**Author 1 - Long Siqin - Topic selection, literature retrieval retrieval, screening, data statistics, paper writing, literature quality evaluation.**

**Author 2 - Lv Jiaojian - Data statistics, literature quality evaluation, dissertation proofreading.**