International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

Global and regional burden of colorectal cancer potentially related to Helicobacter pylori exposure: A risk attribution modelling study

INPLASY202630116

doi: 10.37766/inplasy2026.3.0116

Received: 30 March 2026

Published: 31 March 2026

Li, Y; Cui, C; Sun, D; Ho, K; Qian, C; Guo, Y; Leung, WK; Shah, SC.

Corresponding author:
Yunhao Li

yunhaoli@connect.hku.hk

Author Affiliation:
Department of Medicine, University of California, San Diego.

ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202630115

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 31 March 2026 and was last updated on 31 March 2026.

INTRODUCTION

Review question / Objective The objective of this study is to systematically evaluate the association between Helicobacter pylori exposure and the risk of colorectal cancer, and to quantify this association through meta-analysis of observational studies. Furthermore, this study aims to estimate the global and regional burden of colorectal cancer potentially related to Helicobacter pylori exposure by integrating pooled effect estimates with population-level exposure prevalence data using a risk attribution modelling framework.

Condition being studied The condition of interest is colorectal cancer, a malignant neoplasm arising from the colon or rectum, which represents a major cause of cancer-related morbidity and mortality worldwide. Colorectal cancer develops through a multistep process involving genetic, environmental, and lifestyle-related factors. Increasing evidence suggests that microbial factors, including Helicobacter pylori, may also play a role in colorectal carcinogenesis. Helicobacter pylori is a Gram-negative bacterium primarily associated with gastric diseases, including gastritis, peptic ulcer disease, and gastric cancer. Its potential involvement in colorectal cancer remains under investigation, with proposed mechanisms including systemic inflammation, alterations in gut microbiota, and immune modulation. This study focuses on evaluating the potential relationship between Helicobacter pylori exposure and colorectal cancer.

METHODS

Participant or population We will include adult populations from observational studies assessing the association between Helicobacter pylori exposure and colorectal cancer risk. Eligible populations include individuals from the general population, screening cohorts, or hospital-based settings, without restriction by sex, ethnicity, or geographic region. Studies focusing exclusively on paediatric populations or specific high-risk genetic

syndromes (e.g., familial adenomatous polyposis, Lynch syndrome) will be excluded.

Intervention The exposure of interest is Helicobacter pylori infection or exposure, as defined by each included study. This may include diagnosis based on serology, urea breath test, stool antigen test, histology, or combinations of these methods. Studies reporting either current or past exposure will be considered.

Comparator The comparator group will consist of individuals without Helicobacter pylori infection or exposure, as defined within each study. Studies comparing different exposure categories (e.g., positive vs negative, or varying levels of exposure) will also be included.

Study designs to be included We will include observational studies, including cohort, case–control, and cross-sectional studies, that report the association between Helicobacter pylori exposure and colorectal cancer risk. Studies must provide effect estimates (e.g., odds ratios, relative risks, or hazard ratios) or sufficient data for their calculation. Randomized controlled trials, if available, will also be considered, although they are expected to be limited in this context.

Eligibility criteria In addition to the PICOS criteria, studies will be included if they meet the following criteria: (1) original observational or interventional studies assessing the association between Helicobacter pylori exposure and colorectal cancer risk; (2) reporting effect estimates (e.g., odds ratios, relative risks, hazard ratios) with corresponding confidence intervals, or providing sufficient data for calculation; and (3) published in peer-reviewed journals. Studies will be excluded if they: (1) are reviews, editorials, case reports, conference abstracts without sufficient data, or animal studies; (2) do not provide extractable or calculable effect estimates; (3) focus on surrogate outcomes (e.g., adenoma only) without reporting colorectal cancer outcomes; or (4) include overlapping populations, in which case the most comprehensive or recent study will be retained. No restrictions will be applied on publication year. Only studies published in English will be included.

Information sources A comprehensive literature search will be conducted in the following electronic databases: PubMed/MEDLINE, Embase, and Web of Science, from inception to the date of search. In addition, we will screen the reference lists of relevant reviews and included studies to identify additional eligible articles. Where necessary, corresponding authors will be contacted for clarification or to obtain missing data.
Grey literature sources, including conference proceedings and preprint servers, will be considered if sufficient data are available. However, only studies with extractable data suitable for quantitative synthesis will be included. The search strategy will combine controlled vocabulary terms (e.g., MeSH and Emtree) and free-text terms related to “Helicobacter pylori” and “colorectal cancer”.

Main outcome(s) The primary outcome is the association between Helicobacter pylori exposure and the risk of colorectal cancer, expressed as pooled effect estimates (odds ratios, relative risks, or hazard ratios) with corresponding 95% confidence intervals. Where appropriate, effect estimates will be harmonised and synthesised using random-effects meta-analysis. Secondary outcomes include subgroup-specific associations according to study design, geographic region, diagnostic methods of Helicobacter pylori, and risk of bias. In addition, pooled effect estimates will be used as inputs for subsequent risk attribution modelling to estimate the proportion of colorectal cancer potentially related to Helicobacter pylori exposure at global and regional levels.

Quality assessment / Risk of bias analysis The risk of bias of included studies will be assessed independently by two reviewers using the Newcastle–Ottawa Scale (NOS) for observational studies (cohort and case–control studies). For cross-sectional studies, a modified version of the NOS will be applied.
The NOS evaluates studies across three domains: selection of participants, comparability of study groups, and ascertainment of exposure and outcomes. Each study will be assigned a score, with higher scores indicating lower risk of bias.
Studies will be categorised as low, moderate, or high risk of bias based on predefined thresholds. Discrepancies between reviewers will be resolved through discussion or consultation with a third reviewer.
Risk of bias assessments will be incorporated into subgroup and sensitivity analyses to evaluate their impact on pooled estimates.

Strategy of data synthesis Effect estimates (odds ratios, relative risks, and hazard ratios) will be extracted and transformed onto a common logarithmic scale. Where necessary, conversions between effect measures will be performed using established methods. Pooled effect estimates will be calculated using a random-effects model, accounting for between-study heterogeneity. The

DerSimonian–Laird estimator with Hartung–Knapp adjustment will be applied to provide more robust confidence intervals.
Statistical heterogeneity will be assessed using the I^2 statistic and Cochran's Q test. Publication bias will be evaluated using funnel plots and Egger's test, where appropriate.

The pooled effect estimates will subsequently be used as inputs for risk attribution modelling. Specifically, a modified population attributable framework will be applied to estimate the proportion of colorectal cancer potentially related to Helicobacter pylori exposure. Monte Carlo simulations will be conducted to propagate uncertainty from both effect estimates and exposure prevalence, generating 95% uncertainty intervals.

All analyses will be conducted using R software.

Subgroup analysis Subgroup analyses will be performed to explore potential sources of heterogeneity. Pre-specified subgroup analyses will include:
(1) Study design (cohort vs case–control vs cross-sectional);
(2) Geographic region (e.g., Asia, Europe, Americas);
(3) Method of Helicobacter pylori assessment (serology vs non-serological methods such as urea breath test, stool antigen, or histology);
(4) Risk of bias or study quality;
(5) Study setting (population-based vs hospital-based).
Where sufficient data are available, subgroup differences will be formally assessed.

Sensitivity analysis Sensitivity analyses will be conducted to assess the robustness of the findings. These will include:
(1) Restricting analyses to studies with low or moderate risk of bias;
(2) Restricting analyses to cohort or population-based studies;
(3) Excluding studies with small sample sizes;
(4) Leave-one-out analysis to evaluate the influence of individual studies on the pooled estimates. In addition, sensitivity analyses will be performed to examine the impact of different assumptions in the risk attribution modelling, including variation in exposure prevalence estimates and alternative model specifications.
Consistency of findings across sensitivity analyses will be used to evaluate the stability and reliability of the results.

Language restriction No.

Country(ies) involved USA, Hong Kong, Netherlands.

Keywords Helicobacter pylori; colorectal cancer; risk factors; meta-analysis; epidemiology; infection-related carcinogenesis; population attributable fraction; risk attribution modelling; global burden; GLOBOCAN.

Contributions of each author
Author 1 - Yunhao Li.
Author 2 - Can Cui.
Author 3 - Dianqin Sun.
Author 4 - Kimberly Ho.
Author 5 - Cong Qian.
Author 6 - Yanyan Guo.
Author 7 - Wai K Leung.
Author 8 - Shailja C Shah.