INPLASY

Infection risk in inflammatory bowel disease patients treated with vedolizumab: a systematic review and meta-analysis

INPLASY202660022

doi: 10.37766/inplasy2026.6.0022

Received: 5 June 2026

Published: 5 June 2026

Zhang, L; Hao, X; Cui, Y; Yan, W; Shang, K; Zhang, X.

Corresponding author:
Lidan Zhang

574891114@qq.com

Author Affiliation:
College of Acupuncture and Tuina, Changchun University of Chinese Medicine, Changchun 130117, China.

ADMINISTRATIVE INFORMATION

Support - This work was supported by the Sixth Batch of National Training Program for Outstanding Clinical Talents in Traditional Chinese Medicine (Grant No. 2025256), the 2025 College Student Innovation and Entrepreneurship Training Program Project (Grant No. 202510199002), and the 2024 College Student Innovation and Entrepreneurship Training Program Project (Grant No. S202410199053).

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202660022

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 5 June 2026 and was last updated on 5 June 2026.

INTRODUCTION

Review question / Objective To evaluate the infection risk associated with vedolizumab (VDZ) in patients with inflammatory bowel disease (IBD) and to compare its safety with tumor necrosis factor inhibitors (TNFis), ustekinumab (UST), and placebo.

Rationale Inflammatory bowel disease (IBD) is a chronic immune-mediated gastrointestinal disorder, and biological agents have become first-line therapy for moderate-to-severe IBD. Vedolizumab (VDZ), an intestine-selective anti-α4β7 integrin antibody, is widely used in clinical practice, but its infection risk remains controversial due to conflicting results from existing studies. Previous systematic reviews have limitations such as small sample sizes, incomplete coverage of infection subtypes, and insufficient comparative data with newer biologics. With the publication of new clinical and real-world data up to December 2025, an updated meta-analysis is urgently needed to clarify VDZ-associated infection risk, characterize subgroup differences, and provide evidence for rational clinical medication and safety monitoring.

Condition being studied Inflammatory bowel disease (IBD) refers to immune-mediated chronic inflammation of the gastrointestinal tract, consisting mainly of Crohn's disease (CD) and ulcerative colitis (UC). Its pathogenesis is complex, involving intestinal mucosal immune dysfunction, abnormal activation of innate and adaptive immunity, intestinal flora imbalance, genetic predisposition, and environmental factors. The primary therapeutic goals for IBD management are

to induce and maintain clinical remission, prevent complications, and improve patient quality of life.

METHODS

Search strategy A systematic search was conducted in five electronic databases from inception to December 31, 2025: PubMed, Web of Science, Ovid MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL). Search terms included Medical Subject Headings (MeSH) and free-text words: Vedolizumab, Anti-alpha 4 beta 7 integrin antibody, Inflammatory Bowel Disease, Crohn's Disease, Ulcerative Colitis, Infection, Infectious complication, Adverse event, Safety, etc. These terms were combined using Boolean operators (AND/OR), and the search strategy was adapted to the specific syntax of each database. Additionally, the reference lists of included studies and relevant systematic reviews/meta-analyses were manually screened to identify additional eligible studies. EndNote X9.1 software was used to manage search results; duplicate records were first removed using the software's built-in deduplication function, followed by manual verification. The complete database-specific search strings are provided in Supplementary Material 2 of the manuscript.

Participant or population (1) Study population: Patients diagnosed with IBD (CD or UC) based on internationally recognized criteria (Montreal classification and World Gastroenterology Organisation global guidelines).
(2) No restrictions on age, sex, disease duration, or prior treatment history, unless the study focused exclusively on pregnant/lactating women or patients with severe comorbidities without pre-planned subgroup analysis.
(3) All included patients received vedolizumab monotherapy or combination therapy with immunosuppressants (azathioprine, mercaptopurine, or methotrexate).

Intervention Patients receiving vedolizumab (VDZ) monotherapy or VDZ combination therapy (with immunosuppressants including azathioprine, mercaptopurine, or methotrexate), with clearly reported VDZ dosage, administration route, and treatment duration. The standard intravenous VDZ regimen was 300 mg at week 0, week 2, week 6, and then every 8 weeks thereafter.

Comparator Studies with comparator groups receiving tumor necrosis factor inhibitors (TNFis), ustekinumab (UST), or placebo were included for head-to-head comparative safety analysis.

Study designs to be included Randomized controlled trials (RCTs), prospective cohort studies, retrospective cohort studies, and case-control studies.

Eligibility criteria Inclusion criteria
(1) Full-text articles published in English.
(2) Complete data on the number of infection events and total sample size.
(3) Infectious events were clearly defined and reported, including overall infection, site-specific infections (respiratory tract, gastrointestinal, skin and soft tissue, genitourinary, systemic invasive, opportunistic), and severe infections.
(4) All infection outcomes were standardized according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.
Exclusion criteria
(1) Literature type: Reviews, case reports, commentaries, letters to the editor, conference abstracts, and preclinical studies (in vitro or animal studies).
(2) Duplicate publications or studies with overlapping populations; only the most comprehensive and detailed study was retained.
(3) Studies with missing infection-related data that could not be supplemented even after contacting the corresponding authors.
(4) Studies focusing exclusively on pregnant/lactating women or patients with severe comorbidities without pre-planned subgroup analysis.

Information sources (1) Electronic databases: PubMed, Web of Science, Ovid MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL).
(2) Manual search: Reference lists of included studies and relevant systematic reviews/meta-analyses.
(3) Corresponding authors: Contacted via email to request supplementary data for studies with incomplete information.

Main outcome(s) (1) Overall infection incidence in VDZ-treated IBD patients, presented as pooled proportion with 95% confidence interval (CI).
(2) Site-specific infection incidences (respiratory tract, digestive system, genitourinary system, skin and soft tissue, systemic invasive, nervous system, musculoskeletal, ocular, pathogen-specific, and other infections).
(3) Comparative infection risk between VDZ and TNFis, UST, or placebo, presented as pooled risk ratio (RR) with 95% CI.

Additional outcome(s) (1) Subgroup-specific infection incidences stratified by disease type (CD

vs. UC), study design, geographic region, follow-up duration, publication year, study scope, and patient age group.
(2) Sources of heterogeneity identified via meta-regression analysis.
(3) Publication bias assessment results using funnel plots and Egger's test.
(4) Sensitivity analysis results to evaluate the robustness of pooled estimates.

Data management Two independent researchers extracted data from all included studies using a standardized data extraction form. Inter-reviewer agreement was calculated using Cohen's kappa coefficient, with disagreements resolved by consensus or adjudication by a third senior investigator. Extracted data included basic study information, patient characteristics, treatment regimens, and outcome measures. EndNote X9.1 software was used to manage literature search results and deduplication. All extracted data were stored in a standardized electronic database for subsequent statistical analysis.

Quality assessment / Risk of bias analysis (1) Non-randomized studies (cohort and case-control studies): Methodological quality was assessed using the Newcastle-Ottawa Scale (NOS), which includes three domains: Study Group Selection (4 points), Group Comparability (2 points), and Outcome Assessment (3 points), with a maximum total score of 9 points. Studies with an NOS score ≥6 were deemed high quality and included in the final analysis.
(2) Randomized controlled trials (RCTs): Methodological quality was assessed using the Cochrane Risk of Bias Tool 2.0 (RoB 2.0), which evaluates five key domains: randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Each domain was rated as low risk, some concern, or high risk of bias.

Strategy of data synthesis Meta-analysis was performed using R software (version 4.2.2) with the meta and metafor packages.
(1) Proportion meta-analyses: Infection incidence with 95% CI was used as the effect size indicator. The optimal transformation method was selected based on normality assessment of raw proportions and four common transformations (log, logit, arcsine, Freeman-Tukey double arcsine). All proportion meta-analyses employed restricted maximum likelihood (REML) random-effects models with Knapp-Hartung adjustment to account for small sample sizes and extreme heterogeneity. 95% prediction intervals were calculated to quantify the range of true effect sizes expected in future studies.
(2) Comparative safety analyses: Risk ratios (RR) with 95% CIs were pooled from head-to-head studies comparing VDZ with TNFis, UST, or placebo.
(3) Heterogeneity assessment: Statistical heterogeneity was assessed using the Cochrane Q test and I^2 statistic. A $P<0.05$ in the Q test indicated significant heterogeneity, and the I^2 statistic quantified the magnitude of heterogeneity.
(4) Publication bias: Evaluated using funnel plots and Egger's linear regression test. The trim-and-fill method was applied to correct the pooled effect size if significant bias was detected.
(5) All statistical tests were two-tailed, with a significance level of $\alpha=0.05$ (95% confidence level).

Subgroup analysis Subgroup analyses were conducted to explore potential sources of heterogeneity according to the following factors:
(1) Publication year (≤2020 vs. >2020)
(2) Study design (RCTs, prospective cohort, retrospective cohort, other designs)
(3) Study scope/organization type (single-center, national multicenter, multinational multicenter, global large-scale, nationwide registry)
(4) Predominant patient age group (adult, pediatric, elderly)
(5) Geographic region (Asia, Europe, North America, Global/multinational)
(6) Follow-up duration (short-term ≤6 months, medium-term 7–12 months, long-term >12 months)
(7) Disease type (Crohn's disease vs. ulcerative colitis).

Sensitivity analysis Sensitivity analysis was performed by sequentially excluding one study at a time to evaluate the influence of individual studies on the pooled effect size. The stability of the results was assessed by comparing the pooled estimates before and after each exclusion.

Language restriction Only full-text articles published in English were included in the review.

Country(ies) involved China (All authors are affiliated with Changchun University of Chinese Medicine, Changchun, China).

Other relevant information (1) This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines.

(2) The manuscript is currently in the author proof stage for publication in Frontiers in Medicine (DOI: 10.3389/fmed.2026.1806488).
(3) Supplementary materials include detailed search strategies, study quality assessment results, baseline characteristics of included studies, and additional forest plots, which will be deposited to FigShare and receive a DOI upon publication.

Keywords comparative safety; infection risk; inflammatory bowel disease; meta-analysis; vedolizumab.

Dissemination plans (1) The results will be formally published in the peer-reviewed journal Frontiers in Medicine.
(2) The findings will be presented at national and international academic conferences in the field of gastroenterology and inflammatory bowel disease.
(3) All study data, code, and supplementary materials will be made publicly available through the journal's website and FigShare repository to ensure transparency and reproducibility.

Contributions of each author

Author 1 - Lidan Zhang - Visualization, Project administration, Validation, Formal analysis, Data curation, Supervision, Methodology, Software, Conceptualization, Investigation, Writing – original draft.
Author 2 - Xiaogang Hao - Conceptualization, Investigation, Software, Writing – original draft.
Author 3 - Yidan Cui - Validation, Formal analysis, Data curation, Methodology, Writing – original draft.
Author 4 - Wenjian Yan - Conceptualization, Investigation, Software, Writing – original draft.
Author 5 - Kun Shang - Conceptualization, Software, Funding acquisition, Writing – review & editing, Investigation, Resources, Project administration, Validation, Visualization.
Email: 13596191172@163.com
Author 6 - Xin Zhang - Project administration, Resources, Data curation, Visualization, Funding acquisition, Investigation, Validation, Conceptualization, Methodology, Formal analysis, Writing – review & editing, Software.
Email: zhangxin@ccucm.edu.cn