Colorectal cancer risk in ulcerative colitis: an updated population-based systematic review and meta-analysis

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Summary

Background Patients with ulcerative colitis (UC) face a heightened risk of colorectal cancer (CRC), though the estimated risk levels differ across UC populations. This study aims to provide updated, population-based estimates of CRC incidence, standardised incidence ratios (SIR), and prevalence in patients with UC.

Methods We searched PubMed, Embase, and Cochrane Library to April 12, 2025, for population-based studies on patients with UC reporting CRC risk. Study quality was assessed using the Newcastle–Ottawa Scale. The primary outcome was CRC risk in UC, evaluated through incidence, SIR, and prevalence. A random-effects model was used for meta-analysis, and meta-regression evaluated the impact of study characteristics. Publication bias was assessed using funnel plots and statistical tests. PROSPERO: CRD42025634800.

Findings From 7991 records, 13 population-based studies involving 161,157 patients with UC were included. Most studies were conducted in Europe, with others from North America and Asia. All studies were of good quality, with scores greater than 5 on the NOS quality assessment scale. The pooled CRC incidence was 1.47 per 1000 person-years (95% CI 1.30–1.67; $I^2 = 66.2\%$), the SIR was 2.48 (95% CI 1.64–3.76; $I^2 = 91.7\%$), and the prevalence was 1.54% (95% CI 1.14–1.99; $I^2 = 96.1\%$). Subgroup analyses revealed similar CRC risk in male (SIR 2.14, 95% CI 0.85–5.38) and female (SIR 2.20, 95% CI 1.52–3.19) patients and an increased risk with extensive colitis, with an SIR of 3.95 (95% CI 2.56–6.09).

Interpretation This systematic review and meta-analysis provides population-based estimates of CRC risk in patients with UC, based on high-quality studies with rigorous methodology. The results offer reliable reference values for incidence, SIR, and prevalence, which are applicable to the broader UC population and relevant to clinical decision-making and public health planning. Nonetheless, substantial heterogeneity across studies and limited geographic representation—particularly from Asia, South America, Africa, and Oceania—highlight the need for additional population-based research in underrepresented regions to improve the global applicability of CRC risk estimates in UC.

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Keywords: Ulcerative colitis (UC); Colorectal cancer (CRC); Epidemiology

Introduction

In the 21st century, inflammatory bowel disease (IBD), which includes ulcerative colitis (UC) and Crohn's disease (CD), has emerged as a global health challenge, with a prevalence exceeding 0.3%.[1] Patients with IBD are at a higher risk of developing colorectal cancer (CRC).[2] A milestone meta-analysis published by Eaden et al.[3] in 2001 reported a CRC incidence rate of

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Research in context

Evidence before this study

We conducted an initial comprehensive search of PubMed, Embase, and the Cochrane Library from database inception to April 12, 2025, without language restrictions, to identify existing evidence on colorectal cancer (CRC) risk among patients with ulcerative colitis (UC). Our search terms included ("inflammatory bowel disease" OR "ulcerative colitis") AND ("carcinoma*" OR "cancer*" OR "neoplasia*" OR "neoplasm*" OR "tumor*"), limiting the results to systematic reviews and meta-analyses. Four notable meta-analyses were identified: A landmark meta-analysis by Eaden et al. (2001) reported an incidence rate of 3 per 1000 person-years (pys) and a prevalence of 3.7% among patients with UC, providing a foundational estimate. Jess et al. (2012) reported a pooled standardized incidence ratio (SIR) of 2.4 based on population-based cohorts, highlighting increased CRC risk compared to the general population; Lutgens et al. (2013) found a lower pooled SIR of 1.7 based on similar cohorts. Conversely, Castaño-Milla et al. (2014) reported a declining CRC incidence rate of 1.58 per 1000 pys, suggesting improvements in surveillance and management strategies.

Added value of this study

Our meta-analysis adds distinct value by exclusively synthesizing data from population-based cohorts, thereby providing risk estimates that accurately reflect the general population of patients with UC. This is the first systematic review and meta-analysis to simultaneously report all three primary measures of CRC risk—incidence, SIR, and prevalence—offering a comprehensive and multi-dimensional understanding of CRC risk. We employed rigorous methodological approaches, including selecting the most recent or longest-follow-up studies from overlapping cohorts, systematic data extraction, and quality assessment using the Newcastle–Ottawa Scale, ensuring high reliability and robustness of our pooled estimates. Notably, 62% (8/13) of included studies were published from 2016 onwards, allowing us to present contemporary risk data that aligns closely with current clinical practices and management strategies for patients with UC.

Implications of all the available evidence

Our findings show a pooled CRC incidence rate of 1.47 per 1000 pys, an SIR of 2.48, and a prevalence of 1.54% among patients with UC. By integrating high-quality, up-to-date population-based studies, our meta-analysis provides a relevant benchmark for clinicians and policymakers to guide surveillance intervals and risk stratification efforts. The inclusion of predominantly recent cohorts ensures that the estimates reflect contemporary treatment and surveillance practices. Nonetheless, most included studies originated from Europe and North America, with limited data available from Asia, South America, Africa, and Oceania. Future research should address this gap by conducting large-scale, population-based cohort studies in underrepresented regions to improve global estimates of CRC risk in UC and support equitable preventive strategies across diverse healthcare settings.

3 per 1000 person-years (pys) and a prevalence of 3.7% among patients with UC. Subsequently, a 2012 meta-analysis by Jess et al.[4] based on population-based cohorts, estimated a pooled standardised incidence ratio (SIR) of 2.4. Lutgens et al. 2013 meta-analysis[5] reported a pooled SIR of 1.7 based on similar cohorts. Further evidence from a 2014 meta-analysis by Castaño-Milla et al.[6] revealed a decline in CRC incidence rate to 1.58 per 1000 pys. These meta-analyses primarily utilised data aggregated from diverse study types, including single-center studies, referral centers, population-based cohorts, private practices, surveillance programs, and histology series. Estimates derived from population-based cohorts, which reflect the broad spectrum of disease, are essential for guiding informed service planning and resource allocation; with the widespread use of immunosuppressive and biologic agents as well as advancements in CRC surveillance programs,[7] updating CRC risk estimates in population-based UC cohorts has become imperative.

Consequently, we performed this systematic review and meta-analysis, focusing strictly on population-based patient cohorts, to update the estimation of the incidence, SIR, and prevalence of CRC in patients with UC.

Methods

Search strategy and selection criteria

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.[8] Moreover, this study followed a priori-created protocol registered on the International Prospective Register of Systematic Reviews, PROSPERO (CRD42025634800). Available from https://www.crd.york.ac.uk/PROSPERO/view/CRD42025634800.

A thorough search was performed in PubMed, Embase, and Cochrane Library from their inception until Apr 12, 2025. The search strategy utilised a mix of MeSH terms and keywords, as outlined in Supplementary Table S1, to comprehensively identify relevant studies. No grey literature sources or trial registries were searched, and unpublished studies were not included.

We included population-based studies in which the diagnosis of UC adhered to internationally recognized standards,[9–11] and CRC was identified through clinical, endoscopic, histopathological, or radiological methods. Eligible studies focused on cohorts of patients with UC, reporting the incidence and prevalence of CRC, as well

as follow-up durations, or providing sufficient data for these calculations. Only full-text articles published in English were considered, and studies were required to include a UC cohort of at least 300 patients. Studies were excluded if they only offered information on IBD without distinguishing UC-specific data, or if only an abstract was available. For studies utilising the same cohort, the selection prioritized the most recent publication or the one with the longest follow-up duration.

In this study, we defined three primary measures to evaluate CRC risk in patients with UC: a: Incidence was defined as the number of new CRC cases among patients with UC without CRC at baseline, divided by the total person-time (person-years) at risk; b: Standardised incidence ratio (SIR) was defined as the ratio of observed CRC cases in the UC cohort to the number of CRC cases expected in the general population, standardised for age, sex, and calendar time; c: Prevalence referred to the proportion of patients with UC who had a diagnosis of CRC at any point during the study period, calculated as the total number of CRC cases divided by the total number of patients with UC (including those with and without CRC). These definitions follow standard epidemiological principles and were consistently applied during data extraction and analysis.

The collected study reports were imported into an EndNote library (EndNote 20.6), where duplicates were identified and removed. Reviewers ZLC and ZXH independently screened titles and abstracts to identify relevant studies. The full texts of these articles were then reviewed to assess eligibility based on the pre-established criteria. In cases of disagreement or uncertainty, a third reviewer (ZSL) was consulted to resolve the issue.

The extracted data included the first author's name, publication year, country or area, study conducted period, the number of patients with UC, median follow-up time, the duration of follow up, the number of CRC cases, CRC incidence rate, the cumulative CRC incidence rate, SIR, and prevalence rate of CRC in UC. The two reviewers (ST, XT) independently extracted the data and cross-checked the results for consistency. Discrepancies were resolved through discussion, with a third reviewer (XHW) making the final decision if consensus was not achieved.

Data analysis
Two researchers (ZLC, ZXH) independently evaluated the methodological quality of each included study using the Newcastle–Ottawa Scale (NOS) for cohort studies. The NOS allocates up to 4 points for selection, 2 points for comparability, and 3 points for exposure/outcome (Supplementary Table S2). Thus, a score of 9 indicates the highest quality.[12]

The primary outcomes were the incidence, SIR, and prevalence of CRC. For incidence, we extracted the number of new CRC cases and total person-years (pys) of follow-up; when pys were not reported, they were estimated by multiplying the number of patients with UC at risk by the mean follow-up duration. Incidence rates were assumed to follow a Poisson distribution and were log-transformed for variance stabilization before pooling. For SIR, we used the reported estimates and 95% confidence intervals to derive standard errors on the log scale via standard methods. For prevalence (defined as the proportion of CRC cases among patients with UC), the Freeman-Tukey double arcsine transformation was applied to stabilize variance given the low proportions observed.

Pooled analyses for all outcomes were performed using the DerSimonian and Laird random-effects model, with pooled estimates back-transformed to the original scale. Heterogeneity was assessed using Cochran's Q test and quantified by I^2. Sensitivity analyses, meta-regression (examining region, cohort size, median follow-up time), and publication bias tests (Begg's and Egger's) were conducted in Stata 18.

Role of the funding source
The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding authors (ZSL and XHW) had full access to all the data in the study and had final responsibility for the decision to submit the manuscript for publication.

Results
The initial search identified 7991 articles, of which 773 were duplicates. After reviewing the titles and abstracts of the remaining 7218 articles, 7159 were excluded. After reviewing the full texts of the remaining 59 studies, 46 were excluded due to the following reasons: three studies involved an entirely selected population, eight were non-population-based, nine reported only IBD data without detailed UC information, two reported incomplete data on UC, and 24 involved overlapping cohorts. The systematic review ultimately included 13 studies.[13–25] A partial overlap exists between the studies by Olén et al.[15] and Söderlund et al.[22] but both were retained, as Söderlund uniquely reported cumulative incidence data not available in Olén for the overlapping Swedish population. The literature screening process is presented in Fig. 1. All studies were of good quality, with scores greater than 5 on the NOS quality assessment scale (Supplementary Table S3).

The 13 included population-based studies, published between 2000 and 2024, collectively reported 161,157 UC cases, of which 2048 were detected as CRC. The majority of these studies were conducted in Europe, specifically in Hungary,[13] Denmark,[15] Sweden,[15,22] the United Kingdom,[16] Norway,[19] the Netherlands,[20] Italy,[25] and other unspecified European countries.[21] Three studies were conducted in North America, specifically in
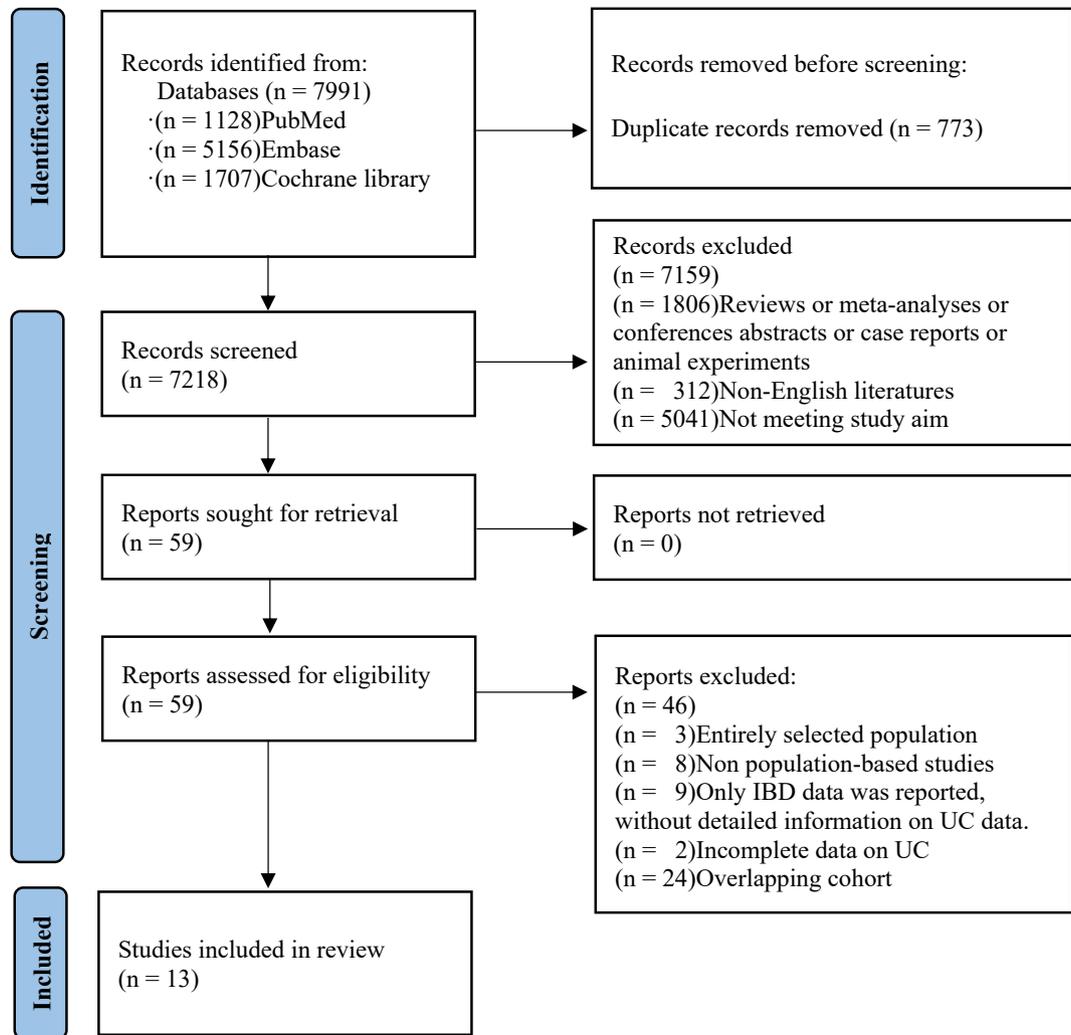
Fig. 1: Flowchart of study identification and selection. Flowchart summarizing the process of study identification, screening, eligibility assessment, and final inclusion in the systematic review and meta-analysis.

the United States[17,23] and Canada,[24] while two studies originated from Asia, specifically China[14] and South Korea.[18] Detailed study characteristics are presented in Table 1.

Incidence of CRC in UC
Analysis of 13 studies revealed that the incidence of CRC in patients with UC ranged from 0.74 to 2.79 per 1000 pys. In a combined analysis, the incidence rate was found to be 1.47/1000 pys (95% CI 1.30–1.67) with significant heterogeneity between the studies (I^2 = 66.24%, p < 0.0001; Fig. 2). There was no significant change in the pooled incidence estimates after the sequential exclusion of any study. Meta-regression analyses indicated that region, cohort size, median follow-up time were not significantly associated with the risk. The funnel plot (Supplementary Figure S1), along with

Begg's test (p = 0.43) and Egger's test (p = 0.69), indicated an absence of publication bias.

Of the 13 studies, four[13,20,22,23] documented the cumulative incidence of CRC in patients with UC. The cumulative incidence of CRC increased over time, ranging from 0.5% to 0.9% at 10 years, 2.5%–3.5% at 20 years, 4.6%–6.5% at 30 years (Table 2).

SIR of CRC in UC
In the meta-analysis of SIR for the risk of CRC in patients with UC, eight studies[13,14,17,20,22–25] reported or allowed the calculation of overall SIR, with values ranging between 0.71 and 8.38. The pooled overall SIR was found to be 2.48 (95% CI 1.64–3.76) with significant heterogeneity among the studies (I^2 = 91.67%, p < 0.0001; Fig. 3). There was no significant change in the pooled SIR estimates after the sequential exclusion

Author	Year	Country or area	Study conducted period	The number of UC	Median follow-up Time (years) and The duration of follow up (pys[a])	The number of CRC	Incidence (/1000 pys)	The cumulative CRC incidence	Standardised Incidence Ratio (SIR)	Prevalence (%)
Wetwittayakhlang[13]	2024	Veszprem Province, Hungary	1997–2020	1370	17 years 23,290 pys	41	1.76	10 year: 0.9% (95% CI: 0.6–1.2); 20 year: 3.5% (95% CI: 2.8–4.2); 30 year: 6.5% (95% CI: 5.4–7.6);	Incidence 2.02 (95% CI: 10.1–12.1) Male 2.01 (95% CI: 1.38–3.12); Female 1.95 (95% CI: 1.23–3.08); Extensive colitis 3.77 (95% CI: 2.41–5.91);	2.99
Zhang[14]	2022	China	1998–2018	869	7 years 6083 pys	17	2.79		Incidence 8.38 (95% CI: 5.79–12.30);	1.96
Olén[15]	2020	Denmark & Sweden	1969–2017	96447	13 years 1,039,672 pys	1336	1.29			1.39
King[16]	2020	UK	2000–2017	37793	6.4 years 242,407 pys	328	1.35			0.87
Samadder[17]	2019	Utah, USA	1996–2011	4421	9.4 years 41,642 pys	61	1.46		Incidence 5.2 (95% CI: 3.9–6.6); Male 7.1 (5.0–9.1); Female 2.9 (1.4–4.4);	1.38
Jung[18]	2017	Korean	2011–2014	9785	2.2 years 21,048 pys	31	1.47		Male 2.14 (1.31–3.30); Female 2.95 (1.47–5.29);	0.32
Hovde[19]	2017	South-Eastern region, Norway	1990–2013	519	21 years 10,899 pys	14	1.28			2.70
van den Heuvel[20]	2016	Netherlands	1991–2011	1644	8.8 years 16,193.5 pys	12	0.74	5 y: 0.2%; 10 y: 0.5%; 15 y: 1.5%;	Incidence 0.71 (95% CI: 0.37–1.24); Male 0.53 (0.19–1.16); Female 1.07 (0.39–2.34); Extensive colitis 1.89 (0.51–4.84);	0.73
Katsanos[21]	2011	European	1993–2009	445	15 years 6675 pys	8	1.20			1.80
Söderlund[22]	2009	Sweden	1954–2004	4125	24 years 99,000 pys	135	1.36	10 year: 0.9%;[b] 20 year: 2.5%; 30 year: 4.6%;	Incidence 2.7 (95% CI: 2.3–3.2); Extensive colitis 5.6 (95% CI: 4.4–7.0);	3.27
Jess[23]	2006	Minnesota, USA	1940–2001	378	12.6 years 5567 pys	6	1.08	5 year: 0%; 15 year: 0.4% (95% CI: 0.0–1.5); 25 year: 2.0% (95% CI: 0.0–4.9);	Incidence 1.1 (95% CI: 0.4–2.4); Extensive colitis 2.4 (95% CI: 0.6–6.0);	1.59
Bernstein[24]	2001	Canada	1984–1997	2672	7.4 years 19,665 pys	49	2.49		Incidence 2.46 (95% CI: 1.83–3.25);	1.83
Palli[25]	2000	Italy	1978–1997	689	11 years 7579 pys	10	1.32		Incidence 1.79 (95% CI: 0.85–3.28);	1.45

(Note: UC, ulcerative colitis; CRC, colorectal cancer; Extensive colitis: Inflammation extending beyond the splenic flexure, including subtotal or total colonic involvement. [a]Person-years. [b]Judged from Fig. 1 in Söderlund et al.[22]).

Table 1: Study characteristics.
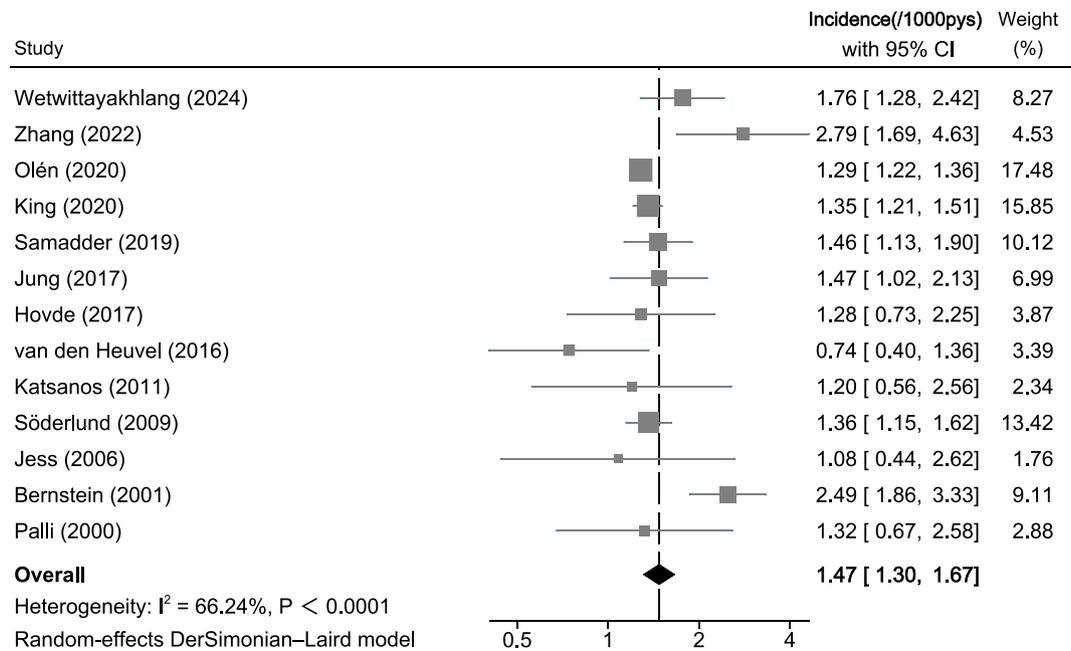
Fig. 2: Pooled incidence rate of colorectal cancer in patients with ulcerative colitis. Forest plot presenting the pooled incidence rate of colorectal cancer among patients with ulcerative colitis, expressed as cases per 1000 person-years. Error bars represent 95% confidence intervals.

of any study. Meta-regression analyses revealed no significant association between the SIR and factors including region, cohort size, median follow-up time. Due to the inclusion of fewer than 10 studies in the meta-analysis, a visual inspection of funnel plots for bias was not feasible.[26]

Four studies[13,17,18,20] provided sex-specific CRC risk estimates in UC, yielding a pooled SIR of 2.20 (95% CI 1.52–3.19) for females (I^2 = 32.59%, p = 0.22; Supplementary Figure S2) and 2.14 (95% CI 0.85–5.38) for males (I^2 = 93.95%, p < 0.0001; Supplementary Figure S3). Additionally, four studies[13,20,22,23] assessed CRC risk based on disease extent, finding a pooled SIR of 3.95 (95% CI 2.56–6.09) for extensive colitis (I^2 = 55.96%, p = 0.08; Supplementary Figure S4).

Prevalence of CRC in UC
The prevalence of CRC in patients with UC, as reported in the 13 studies included, ranged from 0.32% to 3.27%. A pooled analysis found a prevalence rate of 1.54% (95% CI 1.14–1.99), with significant heterogeneity among

studies (I^2 = 96.14%, p < 0.0001; Fig. 4). Sequential removal of each study did not materially affect the pooled incidence estimates. In meta-regression analyses, we evaluated the impact of region, cohort size, median follow-up time on CRC risk in UC. The median follow-up time was the only factor significantly linked to CRC risk (p < 0.0001; Fig. 5). Due to significant heterogeneity in the overall analysis, assessing publication bias through funnel plot asymmetry was deemed inappropriate.[26]
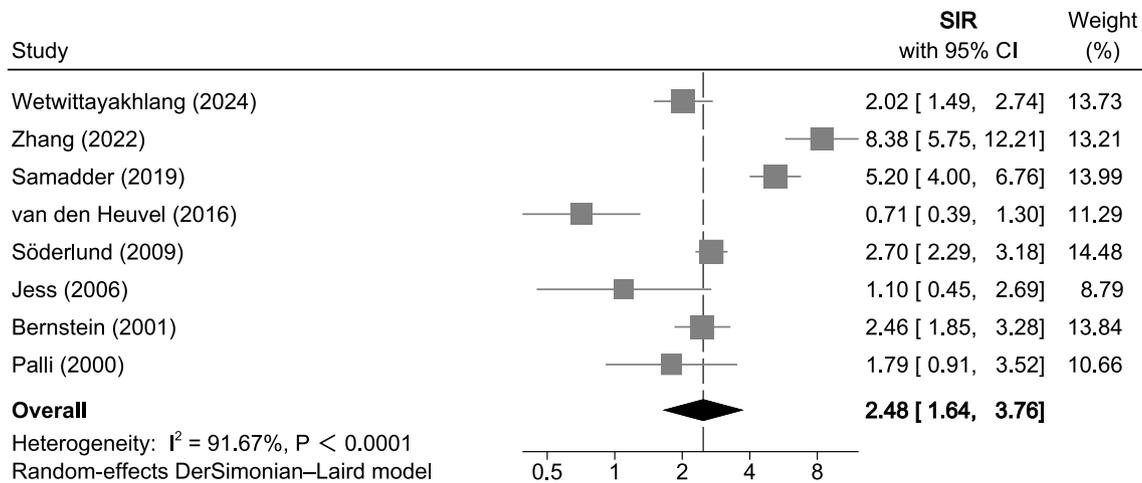
To assess the potential impact of overlapping cohorts, we conducted a sensitivity analysis by excluding either Olén et al.[15] or Söderlund et al.[22] The pooled estimates for incidence and prevalence remained consistent, supporting the overall robustness of our findings (Supplementary Table S4).

Discussion
Our meta-analysis revealed a pooled CRC incidence of 1.47 per 1000 pys, an SIR of 2.48, and a prevalence of

Author	Cumulative incidence of CRC (%)					
	5 years	10 years	15 years	20 years	25 years	30 years
Wetwittayakhlang[13]	–	0.9%	–	3.5%	–	6.5%
van den Heuvel[20]	0.2%	0.5%	1.5%	–	–	–
Söderlund[22]	–	0.9%	–	2.5%	–	4.6%
Jess[23]	0%	–	0.4%	–	2.0%	–

Table 2: Cumulative incidence of CRC according to duration of UC.

Study			SIR with 95% CI	Weight (%)
Wetwittayakhlang (2024)			2.02 [1.49, 2.74]	13.73
Zhang (2022)			8.38 [5.75, 12.21]	13.21
Samadder (2019)			5.20 [4.00, 6.76]	13.99
van den Heuvel (2016)			0.71 [0.39, 1.30]	11.29
Söderlund (2009)			2.70 [2.29, 3.18]	14.48
Jess (2006)			1.10 [0.45, 2.69]	8.79
Bernstein (2001)			2.46 [1.85, 3.28]	13.84
Palli (2000)			1.79 [0.91, 3.52]	10.66
Overall			**2.48 [1.64, 3.76]**	

Heterogeneity: I^2 = 91.67%, P < 0.0001
Random-effects DerSimonian–Laird model

0.5 1 2 4 8

Fig. 3: Pooled standardized incidence ratio (SIR) of colorectal cancer in patients with ulcerative colitis. Forest plot showing the pooled standardized incidence ratio (SIR) of colorectal cancer in patients with ulcerative colitis compared to the general population. Error bars represent 95% confidence intervals.

1.54%. These values are lower than those reported by Eaden et al.[3] in 2001 (incidence: 3 per 1000 pys; prevalence: 3.7%) but align closely with more recent meta-analyses by Castaño-Milla et al.[6] in 2014 (incidence: 1.58 per 1000 pys) and Jess et al.[4] in 2012 (SIR: 2.4; prevalence: 1.6%). Importantly, our study reflects an updated synthesis of population-based data from the past decade, with 8 out of the 13 included studies (62%) published in 2016 or later. This emphasis on more recent, large-scale cohorts provides contemporary evidence on CRC risk in patients with UC in the context of evolving treatment strategies and surveillance practices. Notably, van den Heuvel et al. (2016),[20] one of the included studies, reported a CRC SIR of 0.71 (95% CI 0.37–1.24) in a Dutch UC cohort, suggesting that improved surveillance and management may substantially reduce CRC risk even in high-risk populations.

Study	CRC	Total UC		Prevalence(%) with 95% CI	Weight (%)
Wetwittayakhlang (2024)	41	1,370		2.99 [2.15, 3.97]	7.71
Zhang (2022)	17	869		1.96 [1.13, 3.00]	6.97
Olén (2020)	1,336	96,447		1.39 [1.31, 1.46]	9.45
King (2020)	328	37,793		0.87 [0.78, 0.96]	9.40
Samadder (2019)	61	4,421		1.38 [1.06, 1.75]	8.85
Jung (2017)	31	9,785		0.32 [0.21, 0.44]	9.18
Hovde (2017)	14	519		2.70 [1.46, 4.29]	5.91
van den Heuvel (2016)	12	1,644		0.73 [0.37, 1.21]	7.96
Katsanos (2011)	8	445		1.80 [0.74, 3.27]	5.57
Söderlund (2009)	135	4,125		3.27 [2.75, 3.84]	8.81
Jess (2006)	6	378		1.59 [0.53, 3.14]	5.19
Bernstein (2001)	49	2,672		1.83 [1.36, 2.38]	8.48
Palli (2000)	10	689		1.45 [0.67, 2.50]	6.52
Overall				**1.54 [1.14, 1.99]**	

Heterogeneity: I^2 = 96.14%, P =< 0.0001
Random-effects DerSimonian–Laird model

0 1 2 3 4

Fig. 4: Pooled prevalence of colorectal cancer in patients with ulcerative colitis. Forest plot summarizing the pooled prevalence of colorectal cancer among patients with ulcerative colitis. Error bars represent 95% confidence intervals.
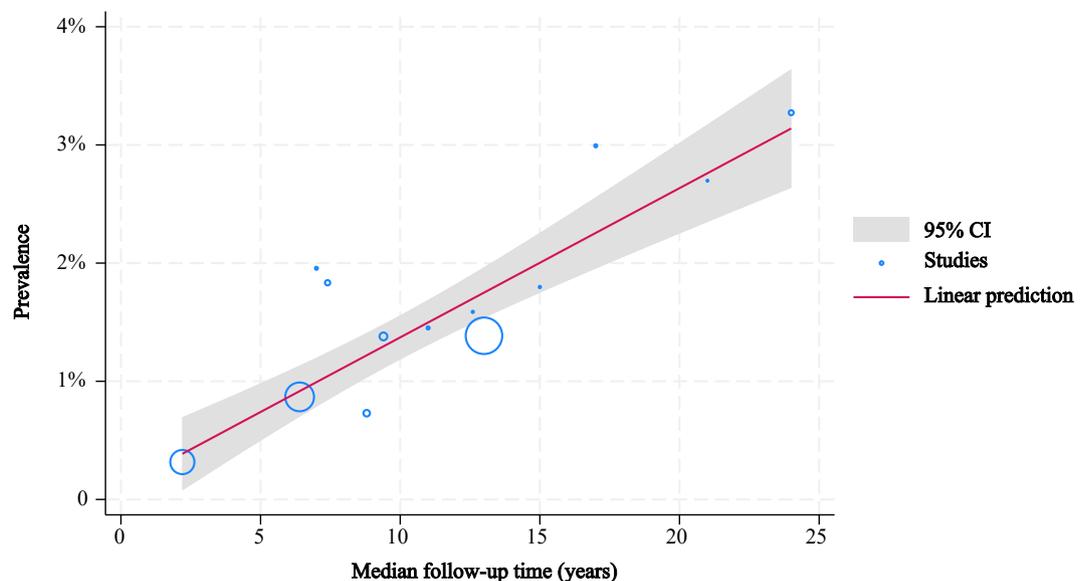
Fig. 5: Meta-regression analysis of CRC prevalence in UC by median follow-up time. Bubble plot illustrating the relationship between colorectal cancer prevalence and median follow-up time among patients with ulcerative colitis. Each circle represents an individual study, with circle size proportional to the weight of the study in the meta-analysis.

For extensive colitis, our meta-analysis found a pooled SIR of 3.95, consistent with the SIR of 4.8 reported by Jess et al.[4] in 2012, further supporting that a more extensive disease distribution significantly increases CRC risk in patients with UC. In terms of sex-specific risk, however, our findings differ from those of Jess et al.[4] in 2012, who reported SIRs of 1.9 for females and 2.6 for males. In contrast, our meta-analysis found similar SIRs for females and males (2.20 vs 2.14, respectively), with no significant difference between the sexes. Notably, while our subgroup analyses included sex and extent of disease—two commonly reported risk modifiers—other established CRC risk factors such as PSC, prior dysplasia, or family history of CRC were not consistently reported across the included population-based studies. As highlighted in the comprehensive meta-analysis by Wijnands et al.[27] in 2021, these factors play a significant role in risk stratification. However, the limited availability of stratified SIR or incidence data precluded their inclusion in our quantitative synthesis. This underscores the need for future population-based studies to report CRC outcomes stratified by key clinical risk factors to enhance personalized surveillance strategies.

Additionally, our meta-regression analysis indicated a significant association between the median follow-up time and CRC prevalence (p < 0.0001). Visualization using a bubble plot indicated a rising trend over time. This pattern likely reflects the cumulative nature of CRC risk, whereby longer follow-up durations increase the likelihood of cancer detection. These findings highlight the need to account for follow-up length when interpreting prevalence estimates and suggest that future studies should adopt standardised or stratified follow-up periods to improve comparability.

This systematic review and meta-analysis has several notable strengths. First, by focusing strictly on population-based patient cohorts, we ensured that the data accurately represent the general population of patients with UC, providing insights that are highly relevant for clinical practice and public health. The study selection process was rigorous, and when multiple studies were published using the same cohort, the most recent article or the one with the longest follow-up period was chosen, ensuring that the findings reflect the most updated data on CRC risk in patients with UC. Additionally, the use of strict methods for study selection, data extraction, and quality assessment further strengthens the robustness of the results. All included studies were of high quality, as evidenced by their scores on the Newcastle–Ottawa Scale, which adds to the credibility of the findings. The comprehensive and updated data from diverse population-based cohorts enhance the generalizability of the conclusions drawn.

Despite these strengths, this meta-analysis has several limitations. The number of studies included is relatively small, with a majority originating from Europe, while studies from other regions, including Asia, North America, South America, Africa, and Oceania, are either limited or entirely absent. For example, although previous meta-analyses, such as the one by Sawan et al.[28] reported a much lower CRC prevalence of 0.85% in Asian populations, large-scale, population-based studies with extended follow-up periods are still

scarce in this region. Similarly, research from other continents is insufficient, highlighting a significant geographic imbalance. This limited geographic representation restricts our ability to comprehensively assess regional variations in CRC risk among patients with UC. Given the global variations in UC prevalence and CRC risk, more high-quality, population-based studies from underrepresented regions are essential to fill these gaps. Additionally, the small number of studies reporting cumulative incidence and sex-specific data further limits our ability to perform detailed subgroup analyses and understand the nuances of CRC risk in patients with UC.

Another key limitation is the substantial heterogeneity across studies. Despite the rigorous selection of strictly population-based cohorts and the use of meta-regression to explore potential sources of variability, substantial heterogeneity remains. Similar challenges have been reported in prior meta-analyses, such as the landmark study by Eaden et al.[3] (p < 0.0001). Future research with standardised methodologies and larger, more homogenous cohorts is necessary to better understand and reduce this variability.

In conclusion, this systematic review and meta-analysis of population-based cohorts updates CRC risk estimates in patients with UC, showing a pooled CRC incidence of 1.47 per 1000 person-years, an SIR of 2.48, and a prevalence of 1.70%. These estimates are applicable to the broader patient with UC population and can inform the development of preventive strategies for CRC. However, significant heterogeneity and geographic limitations underscore the need for more high-quality, population-based studies, particularly from underrepresented regions, to refine risk estimates and guide global clinical practice.

Contributors
ZSL and XHW conceptualised the study. ZLC and ZXH developed the methods. ZLC and ZXH searched the literature. ST and XT extracted and curated the data. ZLC and ZXH conducted the formal analyses. ZSL and XHW reviewed the data. ZLC and ZXH drafted the manuscript. All authors gave comments and approval on the final version of the manuscript. ZLC, ZXH, XHW, and ZSL had full access to and verified the underlying study data. All authors had final responsibility for the decision to submit for publication.

Data sharing statement
Data generated or analysed in this article are included in the appendix.

Declaration of interests
All authors declare no competing interests. The State Key Laboratory of Digestive Health, provided funding solely to cover article processing charges. The funder had no role in study design, data collection, data analysis, data interpretation, or writing of the manuscript.

Appendix A. Supplementary data
Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2025.103269.

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