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SYSTEMATIC REVIEW OPEN ACCESS

Systematic Review: Efficacy, Safety and Metabolic Outcomes of GLP-1 Receptor Agonists in Inflammatory Bowel Disease

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ABSTRACT

Background: Obesity and metabolic disease are increasingly prevalent in patients with inflammatory bowel disease (IBD) and can influence disease activity and treatment outcomes. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are effective for weight loss and metabolic control, yet their safety and effects in IBD remain uncertain as patients with IBD have been excluded from pivotal trials.

Aims: To systematically evaluate the weight-related, metabolic, IBD-specific, and safety outcomes of GLP-1 receptor agonists in adults with IBD.

Methods: We conducted a systematic review according to PRISMA guidelines (PROSPERO CRD42025628850). We searched MEDLINE, Embase, Cochrane Library and ClinicalTrials.gov to 9 September 2025 for studies evaluating GLP-1 RAs in adults with IBD. Primary outcomes were weight-related measures. Secondary outcomes included metabolic parameters, IBD activity, and safety. Risk of bias was assessed using Joanna Briggs Institute (JBI) checklists.

Results: We included 14 studies of which 13 were retrospective cohort studies. Ten reported significant reductions in body weight, BMI, or percent weight loss. Four demonstrated improvements in metabolic markers, including decreased haemoglobin A1c and favourable lipid changes. Across multiple datasets, GLP-1 RA use was not associated with increased IBD exacerbations. Several large registries reported reduced risks of corticosteroid use, hospitalisation and surgery among GLP-1 RA users. Adverse events were primarily gastrointestinal, consistent with non-IBD populations.

Conclusion: GLP-1 RAs appear to be well tolerated in patients with IBD, with observational evidence suggesting potential associations with improved weight, metabolic, and disease-related outcomes. Prospective, IBD-specific studies are required to confirm safety, clarify mechanisms, and define optimal patient selection.

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1 | Introduction

Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), is a chronic immune-mediated disorder with increasing prevalence [1]. Traditionally considered a disease of malnutrition, contemporary cohorts now show that 15% to 40% of adults with IBD are obese and an additional 20 to 40% are overweight, reflecting global obesity trends [2]. This epidemiologic shift has important implications, as obesity is increasingly recognised as a state of chronic low-grade inflammation that may alter IBD risk, phenotype, and therapeutic response [3].

Beyond obesity itself, patients with IBD are at increased risk of metabolic comorbidities, including type 2 diabetes mellitus (T2DM), metabolic syndrome (MetS), and metabolic-associated steatotic liver disease (MASLD). A recent systematic review and meta-analysis estimated the pooled prevalence of MetS in IBD at nearly 20%, with a significantly higher prevalence in UC compared to CD (38% vs. 14%) [4]. Coexistent diabetes is also increasingly recognized, affecting approximately 5% of IBD patients in large cohort studies, and is associated with greater inflammatory activity, reduced quality of life, and increased healthcare utilization [5]. Similarly, MASLD has emerged as one of the most common extraintestinal comorbidities in IBD, with prevalence estimates ranging from 20% to 40%, and is linked to systemic inflammation, corticosteroid exposure, and increased morbidity and mortality [6].

Glucagon-like peptide-1 (GLP-1) is an incretin hormone secreted by intestinal L-cells in response to nutrient intake, with key roles in stimulating insulin release, suppressing glucagon, slowing gastric emptying, and promoting satiety [7]. GLP-1 receptor agonists (GLP-1 RAs) have rapidly advanced as a cornerstone therapy for obesity and type 2 diabetes [8]. Phase 3 trials have demonstrated consistent benefits across glycemic control, weight reduction, and cardiovascular outcomes, positioning GLP-1–based therapies among the most effective pharmacologic options for metabolic disease [9–13]. GLP-1 RAs have shown direct anti-inflammatory effects, by modulating immune cell signalling, preventing the release of reactive oxygen species, and contributing to the maintenance of intestinal mucosal barrier integrity. Preclinical studies also indicate an impact on gut microbiota composition, suggesting convergence between metabolic and inflammatory pathways [14]. Thus, not only do GLP-1–based therapies represent a major advance in chronic disease management but they provide a platform for therapeutic exploration in inflammatory conditions such as IBD.

Despite their efficacy, GLP-1 RAs are associated with gastrointestinal side effects in the general population, most notably nausea, vomiting, diarrhoea, and constipation [9–13, 15, 16]. These adverse events are typically mild to moderate and transient but are among the leading causes of treatment discontinuation. In patients with IBD, this tolerability profile warrants particular attention, as overlapping gastrointestinal symptoms may obscure the distinction between drug side effects and disease activity. Additionally, exacerbation of GI symptoms in IBD patients may lead to a disproportionate decline in oral intake threatening nutrition status and sarcopenia, important determinants of clinical outcomes. Such overlap could complicate clinical assessment, influence perceptions of remission, and potentially affect treatment adherence. Understanding the prevalence, severity, and clinical relevance of these adverse events in IBD populations is therefore essential to guide safe and effective prescribing.

Although patients with IBD are increasingly prescribed GLP-1 RAs for coexisting obesity and diabetes, they have been systematically excluded from most pivotal clinical trials. As a result, data on weight-related, metabolic, IBD-specific, and safety outcomes remain limited and fragmented across retrospective cohorts and case reports. Given the rising prevalence of obesity and metabolic disease in IBD, and the potential for GLP-1 RAs to influence both metabolic and inflammatory pathways, clarifying their role in this population is a pressing clinical priority. While systematic reviews have recently addressed this topic [17–19], most were limited to selected IBD-related outcomes or small subsets of available studies. The present review provides the most up-to-date and comprehensive synthesis to date and evaluates weight-related, metabolic, IBD-specific, and safety outcomes in patients with CD and UC within a unified framework.

2 | Methods

2.1 | Protocol and Search Strategy

This systematic review was designed a priori, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses 2020 guidelines (PRISMA 2020) and PRISMA-S extensions [20, 21]. We searched MEDLINE (Ovid), Embase, the Cochrane Library, and ClinicalTrials.gov. The MEDLINE and other database searches combined controlled vocabulary and free-text terms for IBD and GLP-1–related agents. Grey literature and reference lists from recent systematic reviews [17–19] were manually screened to identify any additional eligible studies. These manual searches were conducted in early September 2025 to capture abstracts published after the final database search period [17–19]. Studies limited to non-IBD immune-mediated diseases, animal models, or unreferenced conference abstracts were excluded. The protocol was prospectively registered in PROSPERO (CRD42025628850) and is publicly available together with the detailed search strategies and analytic plan (https://www.crd.york.ac.uk/PROSPERO/view/CRD42025628850). The original protocol specified searches up to December 2024. An amendment was made prior to data extraction to extend the search period through September 9, 2025, to capture recently published studies. No other modifications to the registered protocol were made.

2.2 | Eligibility Criteria

Eligible studies included randomised or non-randomised interventional trials, prospective or retrospective cohort, case–control or cross-sectional studies, and case series enrolling at least 10 participants. We included adults (≥18 years) with a confirmed diagnosis of CD or UC who were treated with any GLP-1 RA, including agents with combined GIP/GLP-1 activity (e.g., liraglutide, semaglutide, tirzepatide). Acceptable included: (i) IBD patients not exposed to GLP-1 RAs, (ii) non-IBD individuals not

exposed to anti-obesity or anti-diabetic therapies, (iii) patients receiving alternative anti-obesity or anti-diabetic therapies, and (iv) within-subject comparisons before and after GLP-1 RA initiation in single-arm cohorts. The primary outcome was changes in weight-related measures (e.g., percent total weight loss, body-mass index, absolute weight change). Secondary outcomes included metabolic-related measures (e.g., HbA1c, lipids), IBD-specific endpoints (including clinical activity indices, changes in biochemical markers such as CRP and FCP, endoscopic or histologic remission, escalation of IBD therapy, hospitalisation, and surgery), and safety events (including any or serious adverse events, and treatment discontinuation). We excluded animal studies, paediatric populations without extractable data, case reports or case series with fewer than 10 patients, and non-English publications. No date limits were applied.

2.3 | Study Selection and Data Extraction

Records were imported into Covidence. Two reviewers independently screened titles/abstracts, then full texts, using the previously defined eligibility criteria. Disagreements were resolved by consensus or third-reviewer adjudication. Reasons for exclusion at the full-text stage were documented in the PRISMA flow diagram (Figure S1).

Data were extracted for all prespecified outcome domains from each included study using standardised forms in Covidence. This included study characteristics (design, setting, country, enrolment dates), participant demographics and IBD phenotype, GLP-1 RA agent/dose/duration, comparator details, follow-up length. For weight-related outcomes, we collected baseline and follow-up total body weight (TBW), percent TBW loss, and/or body mass index (BMI) where available. For metabolic outcomes, extracted data included haemoglobin A1c, fasting glucose, lipid parameters (total cholesterol, HDL, LDL, triglycerides), and liver enzymes. For IBD activity, we captured clinical indices (Harvey–Bradshaw Index, partial Mayo), biochemical markers (CRP, faecal calprotectin), endoscopic scores (SES-CD, MES), and IBD-related events (treatment escalation, corticosteroid use, hospitalisation, surgery). Safety data included the frequency and type of adverse events and serious adverse events, discontinuation rates, and specific complications (pancreatitis, gallbladder disease, ileus/obstruction, malignancy). Discrepancies were reconciled through discussion and a third reviewer.

2.4 | Effect Measures and Data Synthesis

For each outcome, effect measures were recorded as reported in the original publications. Continuous outcomes (e.g., weight, BMI, metabolic markers, CRP, faecal calprotectin) were summarised using mean or median change from baseline with corresponding standard deviations, interquartile ranges, or 95% confidence intervals where available. Categorical and event-based outcomes (e.g., IBD flare, hospitalisation, surgery, corticosteroid use, adverse events) were extracted as proportions, odds ratios (OR), hazard ratios (HR), or incidence rate ratios (IRR), as reported in each study. Given substantial heterogeneity across studies in design, comparators, and reported outcomes, quantitative pooling was not performed. The included cohorts varied widely in study population (IBD with obesity vs. IBD with type 2 diabetes), control selection (non-IBD, non-GLP-1 users, or pre/post within subject), analytic approach (unadjusted proportions, multivariable HR, or mean change), and follow-up duration (3 months to 7 years). Effect measures were inconsistently reported (e.g., OR, HR, or unadjusted rates) and often without sufficient data for transformation to a common metric. These factors precluded valid statistical pooling without introducing bias or over-precision.

2.5 | Risk of Bias Assessment

Observational studies were appraised with the Joanna Briggs Institute (JBI) critical appraisal tools, with the specific checklist selected according to study design, in accordance with JBI guidance [22, 23]. Each domain was rated independently by two reviewers.

3 | Results

3.1 | Included Studies

After automated removal of duplicate studies, a total of 7271 studies were eligible for title and abstract review (Figure S1). Of these, 352 studies were selected for full text review. Fourteen studies met our inclusion criteria assessing the efficacy and safety of GLP-1 RAs in patients with IBD. Study quality was evaluated with the JBI critical appraisal tools and varied in quality, and no studies were removed due to poor quality (Table S1).

3.2 | Study Populations

As summarised in Table 1,13 studies were retrospective cohort studies, and one was a case–control study [24–37]. Ten were studies conducted in the United States, two in Denmark, one in Spain, and one in Israel. Ten study populations were obtained from administrative databases, and four through outpatient clinics with chart review. Four studies assessed the safety and efficacy of GLP-1 RAs in patients with IBD and obesity, three in patients with IBD and type 2 diabetes, and seven in patients with IBD and obesity or type 2 diabetes. Follow-up time ranged from 3 months to 7 years. Study size was quite variable, ranging from 16 to 61,927 participants [25, 30].

Ten studies included a comparison group, while four were single-arm cohorts without comparators (Table 1). Among the studies with comparators, four compared IBD patients receiving GLP-1 RAs with IBD patients not exposed to GLP-1 RAs, three compared IBD patients on GLP-1 RAs with non-IBD individuals receiving GLP-1 RAs, and three used within-subject designs comparing outcomes before and after GLP-1 RA initiation. One study used three different comparison groups to address their objectives including non-IBD patients on GLP-1RAs, IBD patients who have undergone weight loss surgery, and IBD patients not on GLP-1 RAs [36].

Baseline demographic and clinical characteristics are presented in Table S2. Across studies, the mean or median participant age

TABLE 1 | Characteristics of included studies evaluating GLP-1 receptor agonists in IBD.

Author, year	Country	Study design and setting	Inclusion	Exclusion	IBD population (*n*)	Exposed (*n*) and comparator (*n*)	Follow-up time	Outcomes
Anderson 2024	USA	Retrospective cohort Outpatient clinic with chart review	Confirmed IBD GLP1-RA therapy for at least 30 days (dulaglutide, exenatide, liraglutide, semaglutide or tirzepatide)	NR	UC: 59 CD: 61 TOTAL: 120	Exposed: 120 Comparator: None	1 Year	Primary: Adverse Events, descriptive *n* (%) Secondary: % weight change (SD) (mean), Change in CRP levels
Clarke 2025	USA	Retrospective cohort Administrative database	Adults, obesity with BMI ≥ 30 kg/m^2, diagnosis of IBD, treated with GLP-1RA	No weight recorded between 9 and 15 months post GLP-1RA initiation	UC: 130 CD: 137 IBD-U: 5 TOTAL: 272	Exposed: 272 Pre-GLP-1RA initiation: 272	12 months	Primary: ≥ 5% change in TBW at 12 months, IBD flare within 12 months after initiation Secondary: GI and non-GI AEs, GLP1-RA discontinuation, anti-TNFs on primary outcomes
Desai 2024a	USA	Retrospective cohort Administrative database with propensity matching	IBD: > 18 years of age, UC or CD, at least 1 IBD medication, Obesity ≥ 30 kg/m^2, semaglutide prescription prior to January 1, 2023 Control: No IBD or other autoimmune disease, prescribed semaglutide Semaglutide has second prescription at least 3 months after index prescription	History bariatric surgery, Type 2 DM, baseline weight missing in previous 1 year before semaglutide	UC: 51 CD: 99 TOTAL: 150	Exposed IBD: 150 Non-IBD on semaglutide: 21019/150 after Propensity matching IBD not on GLP-1RA: 150	15 months	Primary: Change TBW from baseline—(6–15 months) Secondary: Efficacy of semaglutide compared with other GLP-1RAs Assess effectiveness of semaglutide compared with other AOMs IBD related complications—steroid use, hospitalisation requiring IV steroids, initiation of advanced therapies, IBD-related surgery, any-cause hospitalisation, any-cause ED

(Continues)

TABLE 1 | (Continued)

Author, year	Country	Study design and setting	Inclusion	Exclusion	IBD population (*n*)	Exposed (*n*) and comparator (*n*)	Follow-up time	Outcomes
Desai 2024b	USA	Retrospective cohort, Administrative database with propensity matching	Adults IBD on GLP-1RA group: UC or CD on IBD-related therapy Type 2 DM RxNorm code for liraglutide, dulaglutide or semaglutide Control: UC or CD on IBD-related therapy, Type 2 DM, RxNorm for other anti-glycemics	Potential exposure to GLP-1RAs, UC with prior history of total colectomy prior to initiation of anti-diabetic medication	UC: 2020 CD: 2116 TOTAL: 4136	UC Exposed: 1010 UC not on GLP-1RA: 1010 CD Exposed: 1058 CD not on GLP-1RA: 1058	3 years	Primary: IBD-specific outcomes (hospitalisation requiring IV steroids, surgery within 3 years) Secondary: Risk of oral steroid use and first time advanced therapy initiation in 3 years. Compare mean FCP between GLP-1RA and control cohorts. Compare risk of hospitalisation requiring IV steroid, IBD related surgery for each GLP-1RA, Risk of hospitalisation requiring IV steroids and IBD-related surgery between GLP1RA and OHA. Risk of SAEs (specifically de-novo gallbladder/biliary disease, acute pancreatitis, gastroparesis, ileus/intestinal obstruction, acute kidney injury, thyroid malignancy)

(Continues)

TABLE 1 | (Continued)

Author, year	Country	Study design and setting	Inclusion	Exclusion	IBD population (*n*)	Exposed (*n*) and comparator (*n*)	Follow-up time	Outcomes
Desai 2025	USA	Retrospective cohort, Administrative database with propensity score matching	IBD: Adults, diagnosis of IBD, initiated on tirzepatide (second prescription of tirzepatide at least 30 days after index prescription) IBD with Weight loss surgery: Adults, diagnosis of IBD, underwent sleeve gastrectomy or roux-en-y-gastric bypass Control: non-IBD and no other autoimmune diseases, prescribed tirzepatide	IBD and Controls: Patients with history of bariatric surgery were excluded IBD with weight loss surgery: RxNorm code for tirzepatide or another GLP-1RA	Total: 274 IBD weight loss surgery: 185 Non-IBD: 274	Exposed IBD: 274 Non-IBD on GLP-1RA: 274 IBD not on GLP-1RA: 274 IBD weight loss surgery, not on GLP-1RA: 185	6–15 months	Primary: evaluate effectiveness of tirzepatide in the IBD and non-IBD cohorts, including Total body weight (TBW) change in Lbs from baseline to 6–16 months after initiation Secondary: Compare effectiveness of weight loss between IBD tirzepatide cohort and IBD weight loss surgery cohort. 1-year risk of IBD-related complications in IBD tirzepatide cohort compared to IBD cohort who did not initiate tirzepatide or another anti-obesity medication, including oral and Intravenous steroid use, advanced therapy initiation, IBD-related surgery, FCP ≥ 250ug/g, CRP ≥ 10 mg/L, any-cause hospitalisation and any-cause emergency department visit
Gorelik 2024	Israel	Retrospective cohort Administrative database	IBD, Type 2 DM, living in Israel	NR	UC: 1883 CD: 1854 TOTAL: 3737	Exposed IBD: 633 IBD not on GLP-1RA: 3104	18 months	Primary: Composite outcome of hospitalisation, surgery, steroid dependency, treatment escalation, death

(Continues)

TABLE 1 | (Continued)

Author, year	Country	Study design and setting	Inclusion	Exclusion	IBD population (*n*)	Exposed (*n*) and comparator (*n*)	Follow-up time	Outcomes
Levine 2024	USA	Retrospective cohort Administrative database	Adult > 18 years, IBD, GLP-1 agonist	No outpatient follow-up within the health system	UC: 97 CD: 100 IBD-U: 27 TOTAL: 224	Exposed: 224 Pre-GLP-1RA initiation: 224	1 year	Primary: IBD-related hospitalisation, surgery, steroid prescription, treatment escalation, or treatment change Secondary: Change in BMI, Hgb A1c, total cholesterol, LDL, HDL
Neilson 2024	Denmark	Retrospective cohort Administrative database	Adults Living in Denmark July 1st 2018, discharge diagnosis with UC or CD prior to July 1st 2018	NR	UC: 41191 CD: 20736 TOTAL: 61927	Exposed: 4430 IBD not on GLP-1RA: 57497	Up to 7 years of follow up Total follow-up time 348,687 person-years	Primary: Time to first diagnosis of ileus, or intestinal obstruction
Pham 2024	USA	Case–Control Database	Case: UC or CD subsequent use of liraglutide, semaglutide, orlistat, phentermine-topiramate, phentermine or naltrexone-bupropion Control: non-IBD matched based on age, gender, baseline BMI, AOM and closest max AOM dose.		UC: 15 CD: 21 TOTAL: 36	Exposed: 36 Non-IBD matched on AOM: 36	12 months	Primary: Change in TBW 12 months Secondary: Side effects, SAEs, IBD flare (change in IBD medication, evidence of endoscopic or radiographic inflammation with increased symptoms, steroid use, hospitalisation, surgery)

(Continues)

TABLE 1 | (Continued)

Author, year	Country	Study design and setting	Inclusion	Exclusion	IBD population (*n*)	Exposed (*n*) and comparator (*n*)	Follow-up time	Outcomes
Ramos Belinchón 2024	Spain	Retrospective cohort Outpatient clinic with chart review	IBD, GLP-1 agonist, BMI ≥ 30 kg/m^2	NR	UC: 7 CD: 9 IBD: 16	Exposed: 16 Compartor: None	6 months	Primary: Change in TBW, ≥ 5% weight reduction at 6 months Secondary: Change in TBW at 3 months, TBW ≥ 10% at 6 months, SAEs, AEs, change in labs (total cholesterol, LDL, HDL, Triglycerides, Glycemia, HbA1c, ALT, AST, Bilirubin, GGT, ALP, FCP, CRP, Creatinine, HBI, pMayo)
Sehgal 2025	USA	Retrospective cohort Hospital database and chart review	Adults, diagnosis of IBD and prescription of GLP-1RA (dulaglutide, semaglutide, liraglutide, exenatide, tirzepatide), regardless of indication for GLP-1RA	Reported active IBD symptoms or had a change in IBD medication (including steroids) within first 3 months of initiation of GLP-1RA, patients that did not have at least 6 months of follow-up data after the prescription of GLP-1RA, patients who were pregnant, active malignancy or presence of ileostomy/colostomy.	UC: 102 CD: 142 TOTAL: 244	Exposed: 244 Comparator: None	3 months	Primary: continuation of GLP-1RA at end of 3 month interval, reason for discontinuation (AEs, IBD Flare, minimal weight loss, polypharmacy) Secondary: change in weight, change in biomarkers (CRP, FCP)

(Continues)

TABLE 1 | (Continued)

Author, year	Country	Study design and setting	Inclusion	Exclusion	IBD population (*n*)	Exposed (*n*) and comparator (*n*)	Follow-up time	Outcomes
St-Pierre 2024	USA	Retrospective cohort Outpatient clinic with chart review	Adults, IBD, prescribed semgalutide or tirzepatide	Diabetes	UC: 12 CD: 24 TOTAL: 36	Exposed: 36 Comparator: None	Median 450 days (IQR 265–564)	Primary: Change in BMI and TBW Secondary: Changes in metabolic parameters (cholesterol, LDL, HDL, triglycerides, HgbA1c, ALT, IBD related biomarkers CRP, FCP), activity (inflammation on endoscopy or imaging, therapy changes), side effects, adverse events
Villumsen 2021	Denmark	Retrospective cohort Administrative database	Alive and living in Denmark with at least two IBD-related recordings within 5 years of entry Adult onset of IBD IBD and Type 2 DM with prescription of anti-diabetic drug following latest diagnosis of IBD or Type 2 DM	Prevalent users of GLP-1-based therapies at study entry	UC: 2791 CD: 960 TOTAL: 3751	Exposed: 982 IBD, non-users of GLP-1RA and/or DPP-4 inhibitors: 2769	Up to 147 months	Primary: Composite need for oral corticosteroid treatment, need for anti TNF treatment, IBD-related hospitalisation, or surgery
Weng 2025	USA	Retrospective cohort, Hospital administrative database	Adults, diagnosis of IBD and GLP-1RA exposure (two filled GLP1 RA prescriptions within 90 day period)	NR	UC: 174 CD: 97 TOTAL: 271	Exposed: 271 Pre-GLP-1RA initiation: 271	12 months	Primary: GI adverse events; ileus or bowel obstruction, bowel surgery, hospitalisation with IBD, escalation of IBD therapy (systematic corticosteroids, cyclosporine, immunomodulators or advanced therapies).

Abbreviations: AE, adverse event; ALP, alkaline phosphatase; ALT, alanine aminotransferase; Anti-TNF, anti-tumour necrosis factor; AOM, anti-obesity medication; AST, aspartate aminotransferase; BMI, body mass index; CD, Crohn's disease; CRP, C-reactive protein; DM, diabetes mellitus; ED, emergency department; FCP, faecal calprotectin; GGT, gamma-glutamyl transferase; GI, gastrointestinal; GLP-1RA, glucagon like protein 1 receptor agonist; HbA1c, haemoglobin A1c; HBI, Harvey Bradshaw index; HDL, high-density lipoprotein; IBD, inflammatory bowel disease; IBD-U, undefined inflammatory bowel disease; IQR, interquartile range; IV, intravenous; LDL, low-density lipoprotein; NR, not reported; OHA, oral hypoglycemic agents; pmayo, partial mayo score; SAE, serious adverse event; SD, standard deviation; TBW, total body weight; UC, ulcerative colitis; USA, United States of America.

ranged from 36 to 63 years, with most cohorts including a higher proportion of women (13/14 studies; range 45.3%–81.3%). Both CD and UC were represented in roughly equal proportions, although not all studies stratified outcomes by disease subtype. Of the six studies reporting biochemical markers of IBD activity, three studies reported high faecal calprotectin (FCP) and CRP levels at baseline. Desai et al. reported a mean CRP of 15.3 (SD 29.1) and FCP of 439 (SD 869) for UC and a mean CRP of 16.1 mg/L (SD 33 mg/L) and FCP of 260 mcg/g (SD 283 mcg/g) for CD [31]. Levine et al. reported a median CRP of 8.8 mg/L (IQR 6.4–22.5 mg/L) [27]. Finally, Sehgal et al. also reported a mean CRP of 10.1 mg/dL (SD 16.6 mg/dL) and FCP of 824.9 mcg/g (SD 2112.7 mcg/g) at baseline [34].

3.3 | GLP-1 Effectiveness

As seen in Table 2, 10 studies reported outcomes on percent total weight loss [24, 28, 30, 33, 37], change in BMI [27, 28, 33, 35] and/or change in TBW [28–30, 34, 36]. All 10 studies reported a decrease in percent weight loss, in BMI and/or TBW by the study endpoint. Two studies did not identify a significant difference in TBW loss between IBD and non-IBD users of GLP-1 RAs [29, 31]. Similarly, Weng et al. did not report a significant difference in BMI between baseline and 12 months after initiation of GLP-1 RA among patients with IBD and reported no difference in change in BMI between IBD type [35]. However, one study reported a significant change in decreased TBW between IBD and non-IBD cohorts on 15 mg tirzepatide dosing, reporting a mean change of −26 lbs. (95% CI −38 to −15) among the IBD cohort and a mean change of −21 lbs (95% CI −29 to −12) among the non-IBD cohort ($p = 0.002$) [36]. Similarly, Pham et al. reported a significant difference in percent change in TBW between cases and controls, with controls having lost 8.1% vs. 6.9% lost in the IBD cases ($p = 0.03$) on anti-obesity medications [37].

3.4 | Changes in Other Metabolic Markers

Four studies reported changes in metabolic markers including haemoglobin A1c, lipids, and liver enzymes, in Table 3 [27, 28, 30, 36]. Levine et al. reported significantly decreased HbA1c levels for both patients with IBD and controls: The IBD group had a decrease in median Hb A1c from 6.5% (IQR 5.9%–7.4%) at baseline to 6.2% (IQR 5.4%–7.0%) at the end of the study ($p = 0.01$) whereas the control group reported 6.6% (IQR 5.9%–8.0%) at baseline to 6.3% (IQR 5.7%–7.6%) at follow-up ($p = 0.03$) [27]. Desai et al. reported a significant difference in the change in HbA1c level between IBD and non-IBD on tirzepatide, reporting a mean HbA1c change of −0.76 (95% CI −0.99 to −0.52) among IBD on tirzepatide and a mean change of −0.88 (95% CI −1.13 to −0.62; $p < 0.0001$) among the non-IBD cohort on tirzepatide. Two studies reported decreases in Hgb A1c levels, although they did not reach significance [28, 30].

Total cholesterol, HDL, LDL were also reported by the four studies (Table 3). Levine and colleagues reported a significant increase in total cholesterol (baseline 169 mg/dL, end of study 177 mg/dL; $p < 0.01$), HDL (baseline 52 mg/dL, end of study 58 mg/dL; $p = 0.03$), and LDL (baseline, 89 mg/dL end of study 89 mg/dL; $p < 0.01$) in the IBD group treated with GLP-1 RAs and no significant change in the control group [27]. Desai et al. reported significant differences when comparing the change in HDL, LDL and triglycerides among IBD and non-IBD patients on tirzepatide. The mean change in HDL among IBD patients on tirzepatide was reported as +1 (95% CI −2.1 to 4.1) and 0.5 (95% CI −3.3 to 2.3) among non-IBD patients on tirzepatide ($p = 0.01$). The mean LDL change among IBD patients on tirzepatide was −5.8 (95% CI −12.8 to −1.20), and non-IBD patients on tirzepatide reported a change of −3.6 (95% CI −11 to 3.8; $p = 0.003$) [36]. Similarly, patients with IBD on tirzepatide experienced significantly greater decreases in triglycerides compared to non-IBD patients on tirzepatide, reporting a change of −33 (95% CI −49.9 to −16.1) among patients with IBD and −16 (95% CI −34.2 to 2.2) among non-IBD patients ($p < 0.0001$) [36]. In contrast, St-Pierre et al. reported a significant difference between baseline and follow-up for HDL among IBD patients (baseline HDL 55.5 to 49 mg/dL at end of study; $p = 0.04$), but no significant changes in total cholesterol, LDL or triglycerides. Ramos Belinchón et al. showed no changes in total cholesterol, HDL, LDL or triglycerides [30]. Two studies reported improvement in liver enzymes as an outcome; however, none showed any statistically significant changes with GLP-1 RA treatment [28, 30].

3.5 | IBD-Related Outcomes

All studies reported outcomes related to IBD activity, assessed through biomarkers (CRP, FCP), clinical indices (HBI, partial Mayo), endoscopic activity, or IBD-related events (Table 4). Five studies compared biomarker changes with GLP-1 RAs, with two studies reporting a significant decrease in CRP levels between baseline and study endpoint among IBD patients [24, 34] while three studies showed stability in biomarkers [27, 28, 30]. Two studies compared FCP at baseline and at the end of the study, and although there was a decrease in the median FCP, it was not statistically significant [30, 34]. No studies included changes in CRP or FCP levels in non-IBD populations.

Clinical indices and endoscopic outcomes were infrequently assessed across studies. In one study, no significant changes were observed in HBI ($p = 0.61$), partial Mayo ($p = 0.67$), SES-CD ($p = 0.35$), or MES ($p = 0.16$) scores following GLP-1 RA initiation, despite significant reductions in CRP [24]. Another study similarly reported no significant changes in HBI ($p = 0.388$) and partial Mayo ($p = 0.089$) [30].

With respect to clinically relevant outcomes, studies comparing the year before and after GLP-1 RA initiation, four studies reported no significant differences in steroid prescriptions, treatment escalation, hospitalizations, or surgeries [24, 27, 33, 35]. Larger administrative cohorts demonstrated potential protective associations. Gorelik et al. reported lower risks of steroid dependence (HR 0.66, 95% CI 0.48–0.99) and hospitalizations (HR 0.74, 95% CI 0.61–0.91) with no significant increase in medication escalation, surgeries and any-cause death between GLP-1 RA users and non-users [26]. Similarly, Villumsen identified reduced incidence rates (IRR) of steroid use (IRR 0.54, 95% CI 0.41–0.70), hospitalizations (IRR 0.73, 95% CI 0.58–0.91), and composite outcomes including anti-TNF initiation, hospitalization, or surgery (IRR 0.52, 95% CI 0.42–0.65) among GLP-1 RA

or DPP-4 inhibitor users [32]. In propensity-matched cohorts, GLP-1 RA use was associated with reduced risks of hospitalization (OR 0.35, 95% CI 0.19–0.67; $p = 0.001$) and surgery (0% vs. 5.9% in controls) with semaglutide [29], and decreased risks of hospitalization (OR 0.48, 95% CI 0.35–0.66, $p < 0.0001$) [36] and surgery (HR 0.55, 95% CI 0.36–0.84) [31]. Overall, findings were heterogeneous, but large population-based studies suggest favorable associations between GLP-1 RA exposure and IBD-related outcomes.

3.6 | Safety in IBD Population

Ten studies reported descriptively on adverse events (AEs) and serious adverse events (SAEs) (Table S3) [24, 25, 28–31, 33–35, 37]. The most common AEs were gastrointestinal, including nausea (2.2%–30.5%), diarrhoea (2.2%–12.5%), constipation (2.9%–25%), abdominal pain (1.1%–14.6%), and bloating (1.1%), with frequencies comparable to non-IBD control groups. In large propensity-matched cohorts, rates of gallbladder disease, pancreatitis, ileus or obstruction, gastroparesis, acute kidney injury, and thyroid malignancy were not increased in IBD compared with non-IBD users [29]. Presence or rates of local skin site reactions were not described in any of the studies. Discontinuation rates in smaller cohorts ranged from 11% to 24%, most frequently due to gastrointestinal intolerance [28, 33, 34]. Three SAEs were attributed to GLP-1 RA therapy: a cerebrovascular event, severe diarrhoea, and one case of pancreatitis, each leading to treatment discontinuation [30, 34, 37]. None of the included studies reported an increased risk of IBD flare directly attributable to GLP-1 RA therapy. Registry-based analyses provided additional reassurance in regard to the risk of ileus: Nielsen identified a reduced risk of ileus or obstruction among IBD GLP-1 RA users compared with non-exposed IBD individuals (HR 0.57, 95% CI 0.36–0.88) [25]. Collectively, the safety profile of GLP-1 RAs in IBD appears consistent with that observed in non-IBD populations.

4 | Discussion

Across diverse study designs and populations, GLP-1 RAs were consistently effective for weight loss, with reductions in BMI or TBW in nearly all cohorts. Improvements in metabolic parameters were also reported, most notably reductions in haemoglobin A1c and, in select studies, favourable changes in lipid profiles. Importantly, GLP-1 RA therapy appeared safe in IBD, with adverse event rates comparable to those reported in non-IBD populations and no evidence of increased risk of disease exacerbation. Instead, several large population-based cohorts suggested potential protective associations, with reduced risks of corticosteroid use, hospitalisation, and IBD-related surgery observed among GLP-1 RA users. Collectively, these findings support both the metabolic and potentially disease-modifying benefits of GLP-1 RAs in patients with IBD. The clinical implications of these findings are increasingly relevant as obesity and metabolic comorbidities become more prevalent in patients with IBD. GLP-1 RAs may be particularly suitable for patients with IBD and obesity, type 2 diabetes, or other features of metabolic syndrome, offering dual benefits on weight, glycaemic control, and potentially disease course.

These findings are broadly consistent with outcomes reported in large phase III clinical trials of GLP-1 RAs in non-IBD populations. In the STEP 1 trial, semaglutide achieved a mean weight reduction of nearly 15% compared with placebo in adults with obesity [10]. Similar magnitudes of effect were demonstrated in SURMOUNT-1, where tirzepatide led to mean weight loss of up to 21% [12] and confirmed in the more recent SURMOUNT-3 and SURMOUNT-4 programs [13]. The SUSTAIN program established durable glycaemic and cardiometabolic benefits of semaglutide in type 2 diabetes, including significant reductions in HbA1c and cardiovascular risk [9]. More recently, the SELECT trial demonstrated reduced major adverse cardiovascular events among overweight and obese patients without diabetes treated with semaglutide [11]. Collectively, these pivotal trials underscore the robust efficacy and safety of GLP-1 RAs in metabolic disease, with weight loss and cardiometabolic improvements comparable to those observed in IBD populations.

Our findings complement and expand upon the recently published meta-analyses on this topic. Bayoumy et al. (2025) synthesised 11 observational studies but pooled data from only four in the meta-analysis, emphasising IBD-related events including hospitalizations, surgery, corticosteroid initiation and advanced therapy initiation [18]. However, even within those datasets, heterogeneity remained moderate to high for several outcomes ($I^2 = 46\%–69\%$), reflecting differences in data source, covariate adjustment, and outcome definitions. In contrast, our review included smaller clinical cohorts, mixed indications (obesity vs. diabetes), and diverse outcome domains (metabolic, inflammatory, and safety endpoints), for which a pooled quantitative estimate was not feasible. Thin et al. (2025) offered a broader immunologic review encompassing non-IBD diseases yet excluded studies addressing metabolic outcomes [17]. Yang et al. (2025) analysed a limited set of cohort studies with comparison groups, largely derived from abstracts and without metabolic or safety detail [19]. Our intent was instead to provide a comprehensive qualitative synthesis that integrates metabolic and disease-specific findings across heterogeneous study designs. This approach allows for a more clinically relevant interpretation of the totality of evidence, while avoiding over-interpretation of pooled results derived from non-comparable cohorts. Moreover, the current review includes three studies not previously captured. Our review provides the most comprehensive synthesis to date, integrating metabolic, inflammatory, and safety endpoints within a consistent analytic framework.

While the primary indication for the use of GLP-1 RAs remains metabolic, emerging data raise the possibility that GLP-1 RAs could exert disease-modifying effects in IBD through anti-inflammatory and gut barrier–stabilising mechanisms. With respect to IBD-specific outcomes, the available evidence suggests that GLP-1 RAs are not associated with an increased risk of disease exacerbation and may in fact confer protective effects. While smaller clinical cohorts have largely shown stable disease activity as measured by biomarkers, symptom indices, and clinical events, several large administrative datasets consistently demonstrated reduced risks of corticosteroid use, hospitalisation, and surgery among GLP-1 RA users. These findings raise the possibility that GLP-1 RAs could influence IBD disease course beyond their metabolic benefits. Mechanistically, GLP-1 RAs exert direct anti-inflammatory actions through modulation

TABLE 2 | Weight outcomes (BMI, total body weight, percent weight loss) in IBD patients treated with GLP-1 receptor agonists.

Author year, dollow-up time	GLP-1RA agent *n* (%)	% weight change			BMI			Change in total body weight		
		IBD/baseline	Comparator/EOS	*p*	Baseline	EOS	*p*	IBD/baseline	Comparator/EOS	*p*
Anderson 2024 1 year follow-up	First GLP-1RA initiated: Dulaglutide 26 (21.7) Exenatide 8 (6.7) Liraglutide 12 (10) Semaglutide 74 (61.7)		% weight loss mean (SD): −3.9 (7.7)							
Clarke 2025 1 year follow-up	All: Semaglutide 120 (44.4) Liraglutide 51 (18.9) Tirzepatide 25 (9.3) Dulaglutide 71 (26.3) Exenatide 5 (1.1)		% TWL, mean (SD) Total: −8.72 (8.98) UC: −8.23 (8.65) CD: −9.0 (9.25) ≥ 5% TWL UC: 61% CD: 60% IBDU: 67%			Change in BMI, mean (SD) Total: −3.26 kg/m^2 (3.60) UC: 3.04 kg/m^2 (3.6) CD: −3.40 kg/m^2 (3.91) IBDU: −5.12 kg/m^2 (4.75)				
Desai 2024a 15 months	IBD: Semaglutide 150 (100) Non-IBD: Semaglutide 150 (100)							Change (95% CI) IBD: −16 lbs (−29.4 to −2.6) UC: −16 lbs (−33.1 to 1.1) CD: −17 lbs (−34.9 to 0.9)	Change (95% CI) Non-IBD: −18 lbs (−30.7 to +1.1) Non-IBD: −16 lbs (−29.8 to −2.1) Non-IBD: −17 (−34.9 to −2.1)	0.24 1.0 0.08
Desai 2025 6–15 months	IBD: Tirzepatide 274 (100) Non-IBD: Tirzepatide 274 (100)								Change in mean (SD) TBW: IBD tirzepatide: −21 lbs (8) Non-IBD tirzepatide: −21 lbs (9) Change in mean (SD) TBW between 6 and 12 months: IBD tirzepatide: −19 (8) Non-IBD tirzepatide: −20 (9) Change in mean (SD) TBW between 12 and 15 months: IBD tirzepatide: −22 lbs (10) Non IBD tirzepatide: −21 (12) Change in mean (SD) TBW: UC: −21 (95% CI −32 to −9) Non IBD tirzepatide: −21 (95% CI −34 to −7) CD: −21 (95% CI −34 to −7) Non-IBD tirzepatide: −20 (95% CI −33 to −6) Change in mean (SD) TBW: IBD tirzepatide: −21 lbs (15) IBD weight loss surgery = −55 lbs (13) Change in mean (SD) TBW with Tirzepatide dose: 15 mg IBD: −26 lbs. (−38 to −15) Non IBD: −21 (−29 to −12) Change in mean TBW with Tirzepatide dose: 5–10 mg IBD: −16 (95% CI −36 to 6) Non-IBD: −10 (95% CI −23 to 3)	$p = 1.00$ $p = -0.67$ $p = 0.46$ $p = 1.00$ $p = 0.52$ $p < 0.0001$ $p = 0.002$ $p = 0.07$

(Continues)

TABLE 2 | (Continued)

Author year, dollow-up time	GLP-1RA agent *n* (%)	% weight change			BMI			Change in total body weight		
		IBD/baseline	Comparator/EOS	*p*	Baseline	EOS	*p*	IBD/baseline	Comparator/EOS	*p*
Levine 2024 1 year follow-up	Semaglutide 148 (66.1) Liraglutide 47 (21.0) Dulaglutide 16 (7.1) Tirzepatide 12 (5.4) Exenatide 1 (0.5)				IBD, median (Q1–Q3): 33.5 kg/m^2 (29.4–37.5) Control, median (Q1–Q3): 36.1 kg/m^2 (31.9–39.6)	IBD, median (Q1-Q3): 31.6 kg/m^2 (28.2–36.2) Control, median (Q1-Q3): 34.4 kg/m^2 (30.1–39.6)	< 0.01 0.03			
Pham 2024 1 year follow-up	Case and matched Control: Liraglutide 9 (25) Semaglutide 10 (27.8) Phentermine-topiramate 3 (8.3) Phentermine 12 (33.3) Naltrexone-bupropion 2 (5.5)	Mean %TBW loss (SD) Case: −6.9 (8.3)	Mean %TBW loss (SD) Control: −8.1 (7)	0.03						
Ramos Belinchón 2024 6 months follow-up	Liraglutide 11 (68.8) Semaglutide 5 (31.3)		Weight loss ≥ 5% at EOS: 58.3% (7/12) Weight loss ≥ 10% at EOS: 16.7 (2/12)					Baseline, Median (Q1–Q3), 92.2 kg (83.42 to 94.6)	EOS, median (Q1–Q3): 81.95 kg (76.62 to 87.67)	0.002
Sehgal 2025 3 months follow-up	All: Dulaglutide: 47 (19) Semaglutide: 131 (54) Liraglutide: 38 (16) Exenatide: 3 (1) Tirzepatide: 5 (2) CD: Dulaglutide: 28 (20) Semaglutide: 76 (54) Liraglutide: 22 (16) Exenatide: 2 (2) Tirzepatide: 3 (2) UC: Dulaglutide: 19 (19) Semaglutide: 55 (54) Liraglutide: 16 (16) Exenatide: 1 (1) Tirzepatide: 2 (2)							Baseline, mean (SD) Total: 102 kg (26.4) CD: 99.3 (23.7) UC: 106 (29.8)	EOS, mean (SD) Total: 97.6 (28.0) CD: 96.6 (24.7) UC: 99.8 (32.3)	0.01 NR NR
St-Pierre 2024 Median 450 days (IQR 265–564) follow-up	Semaglutide or tirzepatide 36 (100)	%TBW GLP-1RA therapy, median (Q1–Q3); −11.5% (−23.1 to −10.3)	Discontinued GLP-1RA, median (Q1–Q3): −1.1% (−5.6 to 3.1)	0.0115	Baseline, median (Q1–Q3): 34.0 kg/m^2 (31.0 to 38.2)	EOS, median (Q1–Q3): 31.0 kg/m^2 (29.0 to 36.1)	< 0.0001		Change from Baseline, median (Q1–Q3) −8.15 kg (−15.9 to −2.2)	< 0.0001 From baseline—last available BMI

(Continues)

TABLE 2 | (Continued)

Author year, dollow-up time	GLP-1RA agent *n* (%)	% weight change			BMI			Change in total body weight		
		IBD/baseline	Comparator/EOS	*p*	Baseline	EOS	*p*	IBD/baseline	Comparator/EOS	*p*
Weng 2025 1 year follow-up	Semaglutide: 57 (57.9) Dulaglutide: 75 (27.7) Tirzepatide: 36 (13.3) Liraglutide: 3 (1.1)				Baseline, median (Q1–Q3): 33.8 kg/m^2 (29.9 to 38.0)	6mo, median (Q1–Q3): 32.6 kg/m^2 (28.1 to 36.7) 12mo, median (Q1–Q3): 33.4 (28.6 to 36.7) Change in BMI: UC, median (Q1–Q3): −1.4 (−2.9 to 0.32) CD: 1.7 (−2.2 to −0.02)	NR 12 months: 0.20 Change in BMI between UC and CD: 0.296			

Abbreviations: BMI, body mass index; CD, Crohn's disease; CI, confidence interval; EOS, end of study; GLP-1RA, glucagon like protein 1 receptor agonist; IBD, inflammatory bowel disease; IBD-U, undefined inflammatory bowel disease; IQR, interquartile range; NR, not reported; SD, standard deviation; T2DM, type 2 diabetes mellitus; TBW, total body weight; UC, ulcerative colitis; %TWL, percent total weight loss.

of immune signalling, inhibition of NF-κB activation, reduction of pro-inflammatory cytokines, and enhancement of intestinal barrier integrity, providing biologic plausibility for a disease-modifying effect [38]. Additional pathways may include favourable shifts in gut microbial composition and attenuation of oxidative stress, further linking metabolic and inflammatory processes. Nonetheless, most available data remain retrospective, and the degree to which GLP-1 RAs exert direct effects on IBD activity requires confirmation in prospective and mechanistic studies.

Safety and tolerability of GLP-1 RAs in IBD populations appear broadly consistent with findings in non-IBD cohorts. Across the included cohorts, gastrointestinal symptoms such as nausea, diarrhoea, and abdominal pain were reported at rates comparable to non-IBD users of GLP-1 RAs and were typically self-limited. None of the included studies demonstrated a temporal association between these symptoms and biochemical or clinical evidence of IBD exacerbation. Although symptom overlap remains a potential diagnostic challenge in practice, current evidence suggests that most gastrointestinal adverse events reflect expected drug tolerability rather than IBD flare. Future prospective studies incorporating concurrent biomarker and symptom tracking will be important to further delineate this distinction. Specific concerns have also been raised regarding their use in stricturing disease or ileal involvement due to the theoretical risk of obstruction or ileus. Notably, data from the Danish registry found no increased risk of obstruction among GLP-1 RA users compared with non-users [25]. Use in perioperative settings has not been systematically evaluated, warranting caution until further evidence is available. Finally, as most patients receiving GLP-1 RAs will remain on concomitant biologics or immunosuppressive therapies, careful attention to tolerability and potential drug–drug interactions is required. One case report of severe hepatotoxicity with azathioprine when combined with semaglutide has been reported [39]. Collectively, these findings suggest that GLP-1 RAs may represent an attractive therapeutic option for selected IBD patients, balancing metabolic benefits with potential IBD-specific advantages; however larger studies are required.

Despite the metabolic benefits observed with GLP-1 RAs, none of the included studies evaluated nutritional status, lean body mass, or sarcopenia-related outcomes in patients with IBD. This represents an important knowledge gap, given that reduced appetite and caloric intake associated with GLP-1 RA therapy could exacerbate malnutrition or loss of muscle mass. There are factors already prevalent and prognostically significant in IBD. Future prospective studies should incorporate comprehensive nutritional and body composition assessments, including measures of muscle mass and function, to determine the balance between metabolic benefits and potential risks of sarcopenia or undernutrition in this population.

This review has several important limitations. All available studies were retrospective in design, with the majority derived from large administrative databases rather than prospectively collected clinical cohorts. Study populations were heterogeneous, encompassing patients treated for diabetes, obesity, or both, which complicates interpretation of outcomes within IBD-specific subgroups. Objective measures of disease activity

TABLE 3 | Changes in metabolic parameters (HbA1c, cholesterol, triglycerides, liver enzymes) with GLP-1 receptor agonist therapy in IBD.

Author Year, follow-up time	Hgb A1c			Total cholesterol			HDL			LDL			Other metabolic markers		
	Baseline	End of study	*p*	Baseline	End of study	*p*	Baseline	End of study	*p*	Baseline	End of study	*p*	Baseline	End of study	*p*
Desai 2025 6–15 months follow-up	IBD tirzepatide, mean (SD): 7.06 (1.55) Non IBD tirzepatide, mean (SD): 7.18 (1.79)	IBD tirzepatide EOS, mean (SD): 6.3 (1.55) Change (95% CI): −0.76 (−0.99 to −0.52) Non IBD tirzepatide: EOS, mean (SD): 6.3 (1.3) Change (95% CI): −0.88 (−1.13 to −0.62)	<0.0001				IBD tirzepatide, mean (SD): 46.3 (16.7) Non IBD tirzepatide, mean (SD): 46 (14.5)	IBD tirzepatide: EOS, mean (SD): 47.3 (15.1) Change (95% CI): +1 (−2.1 to 4.1) Non IBD tirzepatide: EOS, mean (SD): 45.5 (14.5) Change (95% CI): −0.5 (−3.3 to 2.3)	0.01	IBD tirzepatide, mean (SD): 91 (37.3) Non IBD tirzepatide, mean (SD): 92.4 (38.4)	IBD tirzepatide: EOS, mean (SD): 85.2 (34.7) Change (95% CI): −5.8 (−12.8 to 1.20) Non IBD tirzepatide: EOS, mean (SD): 88.8 (37.8) Change (95% CI): −3.6 (−11 to 3.8)	0.003	Baseline triglycerides: IBD tirzepatide, mean (SD): 166 (101) Non IBD tirzepatide, mean (SD): 163 (93.6)	Triglycerides IBD tirzepatide: EOS, mean (SD): 133 (71.5) Change (95% CI): −33 (−49.9 to −16.1) Non IBD tirzepatide: EOS, mean (SD): 147 (92.8) Change (95% CI): −16 (−34.2 to 2.2)	<0.0001
Levine 2024 1 year follow-up	IBD, median (Q1–Q3): 6.5% (5.9 to 7.4) Control, median (Q1–Q3): 6.6% (5.9 to 8.0)	IBD, median (Q1–Q3): 6.2% (5.4 to 7.0) Control, median (Q1–Q3): 6.3% (5.7 to 7.6)	0.01 0.03	IBD, median (Q1–Q3): 169 mg/dL (130 to 189) Control, median (Q1–Q3): 153 mg/dL (125 to 192)	IBD, median (Q1–Q3): 177 mg/dL (151 to 207) Control, median (Q1–Q3): 151 mg/dL (127 to 193)	<0.01 0.85	IBD, median (Q1–Q3): 52 mg/dL (40 to 60) Control, median (Q1–Q3): 45 mg/dL (42 to 61)	IBD, median (Q1–Q3): 58 mg/dL (44 to 66) Control, median (Q1–Q3): 46 mg/dL (39 to 58)	0.03 0.69	IBD, median (Q1–Q3): 79 mg/dL (58 to 108) Control, median (Q1–Q3): 71 mg/dL (54 to 98)	IBD, median (Q1–Q3): 89 mg/dL (69 to 111) Control, median (Q1–Q3): 69 mg/dL (62 to 104)	IBD: <0.01 Control: 0.20			

(Continues)

TABLE 3 | (Continued)

Author Year, follow-up time	Hgb A1c			Total cholesterol			HDL			LDL			Other metabolic markers		
	Baseline	End of study	*p*	Baseline	End of study	*p*	Baseline	End of study	*p*	Baseline	End of study	*p*	Baseline	End of study	*p*
Ramos Belinchón 2024 6 months follow-up	Baseline, median (Q1–Q3): 6.2% (5.5 to 7.8)	EOS, median (Q1–Q3): 5.9% (5.3 to 7.58)	0.14	Baseline, median (Q1–Q3): 193 mg/dL (158 to 225)	EOS, median (Q1–Q3): 148 mg/dL (137 to 195)	0.10	Baseline, median (Q1–Q3): 54 mg/dL (50.5 to 62.5)	EOS, median (Q1–Q3): 42 mg/dL (41 to 52)	0.20	Baseline, median (Q1–Q3): 99 mg/dL (84 to 141)	EOS, median (Q1–Q3): 78 mg/dL (58 to 126)	0.58	Triglycerides, median (Q1–Q3): 139 mg/dL (97 to 197) ALT, median (Q1–Q3): 29.5 IU/L (19 to 40) AST, median (Q1–Q3): 22.5 IU/L (17 to 29) GGT, median (Q1–Q3): 26.5 IU/L (17 to 49) ALP, median (Q1–Q3): 72 IU/L (68 to 91)	Triglycerides, median (Q1–Q3): 127 mg/dL (103 to 200) ALT, median (Q1–Q3): 23 IU/L (15 to 60) AST, median (Q1–Q3): 17.5 IU/L (15.75 to 26.75) GGT, median (Q1–Q3): 26 IU/L (21 to 34) ALP, median (Q1–Q3): 83 IU/L (76 to 90)	0.58 0.67 0.92 0.45 0.67
St-Pierre 2024 Median 450 days (IQR 265–564) follow-up time	Baseline, median (Q1–Q3): 5.45% (5.3% to 5.75%)	EOS, median (Q1–Q3): 5.3% (5.0 to 6.5)	0.0536	Baseline, median (Q1–Q3): 190.5 mg/dL (157.8 to 215)	EOS, median (Q1–Q3): 160 mg/dL	0.0634	Baseline, median (Q1–Q3): 55.5 mg/dL (46.3 to 69.8)	EOS, median (Q1–Q3): 49 mg/dL (44.5 to 53.5)	0.0427	Baseline, median (Q1–Q3): 102.5 mg/dL (75.3 to 121.8)	EOS, median (Q1–Q3): 90.5 mg/dL (76.8 to 11.8)	0.1859	Triglycerides, median (Q1–Q3): 116.5 mg/dL (80.5 to 165) ALT, median (Q1–Q3): 21 U/L (16 to 32)	Triglycerides, median (Q1–Q3): 88.5 mg/dL (67.5 to 109.3) ALT, median (Q1–Q3): 20 U/L (12 to 31)	0.4618 0.8590

Abbreviations: ALP, alakaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; EOS, end of study; GGT, gamma-glutamyl transferase; GLP-1RA, glucagon like protein 1 receptor agonist; HbA1c, haemoglobin A1c; HDL, high-density lipoprotein; IBD, inflammatory bowel disease; IQR, Interquartile range; LDL, low-density lipoprotein; NR, not reported; SD, standard deviation.

TABLE 4 | Effects of GLP-1 receptor agonists on IBD activity (biomarkers, clinical indices, endoscopy) and IBD-related outcomes.

Author year, follow-up time	IBD disease activity			IBD-related outcomes
	Baseline/IBD group	End of study/ comparator	*p*	
Anderson 2024 1 year follow-up	CRP: 12.92 mg/dL HBI: 3.52 pMayo: 1.61 SES-CD: 3.10 MES: 0.67	CRP: 6.38 mg/dL HBI: 3.18 pMayo: 1.54 SES-CD: 2.60 MES: 0.00	0.005 0.61 0.67 0.35 0.16	*IBD-related hospitalizations*: 10 in the year before GLP-1RA initiation and 10 in the year after GLP-1RA initiation ($p = 1.00$)
Clarke 2025 1 year follow-up	NR	NR		*IBD flare (dichotomous composite outcome of IBD-related ED visits or hospitalizations, surgeries, escalation/change of IBD-directed therapy or steroid use)*: 1 year prior to GLP1RA: 29 (16.57%), 1 year after GLP1RA: 23 (13.14%), $p = 0.40$.
Desai 2024a 15 months follow-up	NR	NR		*Oral Steroids*: IBD GLP-1RA, *n* (%): 38 (26.7), IBD control, *n* (%): 44 (30.9). Adjusted OR (95% CI): 0.81 (0.48–1.36), $p = 0.43$ *IV steroids*: IBD GLP-1RA, *n* (%): 10 (7), IBD control, *n* (%): 14 (9.8). Adjusted OR (95% CI): 0.69 (0.29–1.61), $p = 0.39$ *Advanced therapy initiation*: IBD GLP-1RA, *n* (%): 10 (10.3). IBD control, *n* (%): 10 (10). Adjusted OR (95% CI): 1.03 (0.41–2.60), $p = 0.94$ *Any cause hospitalisation*: IBD GLP-1RA, *n* (%): 17 (11.9). IBD control, *n* (%): 39 (27.4). Adjusted OR (95% CI): 0.35 (0.19–0.67), $p = 0.001$ *IBD related surgery*: IBD GLP-1RA, *n* (%): 0 (0), IBD control, *n* (%): 10 (5.9) *Any cause ED*: IBD GLP-1RA, *n* (%): 31 (21.8), IBD control, *n* (%): 33 (23.2). Adjusted OR (95% CI): 0.92 (0.52–1.61), $p = 0.77$

(Continues)

TABLE 4 | (Continued)

Author year, follow-up time	IBD disease activity: Baseline/IBD group	IBD disease activity: End of study/ comparator	IBD disease activity: *p*	IBD-related outcomes
Desai 2024b 3years follow-up	FCP at baseline UC GLP-1RA: 439 μg/g (869) FCP at baseline UC Control: 688 μg/g (878) FCP at baseline CD GLP-1RA: 260 (283) FCP at baseline CD Control: 326 μg/g (435)	FCP at EOS UC GLP-1RA: 324.7 μg/g (533) FCP at EOS UC Control: 369.7 μg/g (624) FCP at EOS CD GLP-1RA: 260 μg/g (391) FCP at EOS CD Control: 324 μg/g (487)	0.67 0.29	*Oral Steroids*: UC GLP-1RA, *n* (%): 331 (32.7), UC Control, *n* (%): 284 (28.1). Adjusted HR (95% CI): 1.12 (0.96–131), $p = 0.14$ CD GLP-1RA, *n* (%): 361 (34.1), CD control, *n* (%): 313 (29.5). Adjusted HR (95% CI): 1.10 (0.95–1.28), $p = 0.19$ *IV steroids*: UC GLP-1RA, *n* (%): 119 (11.7%), UC Control, *n* (%): 93 (9.2%). Adjusted HR (95% CI): 1.21 (0.92–1.59), $p = 0.15$ CD GLP-1RA, *n* (%): 125 (11.8), CD Control, *n* (%): 116 (10.9). Adjusted HR (95% CI): 1.04 (0.80–1.34), $p = 0.75$ *Initiation of Advanced therapy*: UC GLP-1RA, *n* (%): 31 (3.6), UC Control, *n* (%): 36 (4.2). Adjusted HR (95% CI): 0.82 (0.51–1.33), $p = 0.43$ CD GLP-1RA, *n* (%): 50 (6.8), CD control, *n* (%): 39 (5.1). Adjusted HR (95% CI): 1.31 (0.86–2.00), $p = 0.19$ *Total Colectomy*: UC GLP-1RA, *n*: < 10, UC Control, *n* (%): 15 (1.48). Adjusted HR (95% CI): 0.37 (0.14–0.97), $p = 0.03$ *IBD-related Surgery*: CD GLP-1RA, *n* (%): 34 (3.2), CD Control, *n* (%): 116 (10.9). Adjusted HR (95% CI): 0.55 (0.36–0.84), $p = 0.005$ *Composite outcome (IV steroid use and/or Colectomy)*: UC GLP-1RA, *n* (%): 123 (12.1), UC control, *n* (%): 104 (10.2). Adjusted HR (95% CI): 1.12 (0.86–1.45), $p = 0.39$ *Composite outcome (IV and/or IBD related surgery)*: CD GLP-1RA, *n* (%): 154 (14.5), CD Control, *n* (%): 151 (14.2). Adjusted HR (95% CI): 0.97 (0.78–1.22), $p = 0.85$
Desai 2025 6–15 months follow-up	NR	NR		*Intravenous steroids*: IBD tirzepatide, *n* (%): 80 (17.6), IBD control, (%): 69 (15.2), adjusted OR (95% CI): 1.1.9 (0.83–1.69), $p = 0.32$ *Oral steroids*: IBD tirzepatide, *n* (%): 84 (18.5), IBD control, *n* (%): 106 (23.4), adjusted OR (95% CI): 0.74 (0.54–1.02), $p = 0.07$ *New advanced therapy*: IBD tirzepatide, *n* (%): 11 (3.5), IBD control, *n* (%): 16 (4.7), adjusted OR (95% CI): 0.73 (0.33–1.59), $p = 0.43$ *IBD-related therapy*: IBD tirzepatide, *n*: < 10, IBD control, *n*: < 10, adjusted OR (95% CI): N/a, p = N/a *FCP > 250 μg/g*: IBD tirzepatide, *n* (%): 12 (37.5), IBD control: 13 (32.5), adjusted OR (95% CI): 1.47 (0.56–3.86), $p = 0.42$ *CRP ≥ 10 mg/L*: IBD tirzepatide, *n* (%): 33 (32.3), IBD contro, *n* (%) l: 58 (44.2), adjusted OR (95% CI): 0.60 (0.35–1.03), $p = 0.06$ *Any-cause hospitalisation*: IBD tirzepatide, *n* (%): 69 (12.2), IBD control, *n* (%): 126 (22.4), adjusted OR (95% CI) = 0.48 (0.35–0.66), $p < 0.0001$ *Any-cause ED*: IBD tirzepatide, *n* (%): 106 (18.8), IBD control, *n* (%): 117 (20.8), adjusted OR (95% CI) = 0.88 (0.65–1.18), $p = 0.4$

(Continues)

TABLE 4 | (Continued)

Author year, follow-up time	IBD disease activity			IBD-related outcomes
	Baseline/IBD group	End of study/ comparator	*p*	
Gorelik 2024 18 months follow-up	NR	NR		*Steroid Dependency*: 136 events per 1000 patient years (95% CI 132–141), Adjusted HR for GLP-1RA users vs. No GLP-1RA users: 0.66 (95% CI 0.48–0.99) *IBD-related medication escalation*: 37 events per 1000 patient years (95% CI 34–39), Adjusted HR for GLP-1RA users vs. No GLP-1RA users: 0.82 (95% CI 0.59–1.17) *IBD-related hospitalizations*: 174 events per 1000 patient years (95% CI 169–179), Adjusted HR for GLP-1RA users vs. No GLP-1RA users: 0.74 (95% CI 0.61–0.91) *IBD related surgeries*: 14 event per 1000 patient years (95% CI 12–15). Adjusted HR for GLP-1RA users vs. No GLP-1RA users: 0.84 (95% CI 0.47–1.0) *Composite outcome*: 316 events per 1000 patient years (95% CI 309–323). Adjusted HR for GLP-1RA users vs. No GLP-1RA users: 0.74 (95% CI 0.62–0.89) *Death*: 19 events per 1000 patient years (95% CI 18–21). Adjusted HR for GLP-1RA users vs. No GLP-1RA users: 0.72 (95% CI 0.38–1.34)
Levine 2024 1 year follow-up	CRP: 6.9 mg/L (3.1–11.4)	CRP: 5.5 mg/L (2.8–11.6)	0.45	*Steroid Prescription*: 1 year before GLP-1RA, *n* (%): 50 (22.3) 1 year after GLP-1RA, *n* (%): 41 (18.3), $p = 0.27$ *IBD-related medication change or escalation*: 1 year before GLP-1RA, *n* (%): 36 (16.1), 1 year after GLP-1RA, *n* (%): 28 (12.5), $p = 0.34$ *IBD-related hospitalizations*: 1 year before GLP-1RA, *n* (%): 20 (8.9) 1 year after GLP-1RA, *n* (%): 17 (7.6), $p = 0.70$ *IBD-related surgeries*: 1 year before GLP-1RA, *n* (%): 3 (1.3) 1 year after GLP-1RA, *n* (%): 4 (1.8), $p = 1.00$ *Composite outcome*: 1 year before GLP-1RA, *n* (%): 77 (34.4), 1 year after GLP-1RA, *n* (%): 68 (30.4), $p = 0.36$
Nielson 2024 Up to 7 years of follow-up	NR	NR		*Ileus or obstruction*: *N* (%) in GLP-1RA: 21 (0.5%) for 6838 years at risk. *N* (%) in Non-exposed: 1766 (3.1%) for 341,849 years at risk. Adjusted HR (95% CI): 0.57 (0.36–0.88) *Steroid Exposure*: *N* (%) in GLP-1RA: 1237 (27.9). *N* (%) in non-exposed: 14630 (25.4), $p =$ not significant
Pham 2024 1 year follow-up	NR	NR		*Steroids*: 4 *Change in biologic therapy*: 5 *Hospitalisation*: 2 *IBD Flare*: 7 (19.4)

(Continues)

TABLE 4 | (Continued)

Author year, follow-up time	IBD disease activity			IBD-related outcomes
	Baseline/IBD group	End of study/ comparator	*p*	
Ramos Belinchón 2024 6 months follow-up	FCP: 41 μg/g (14–80) CRP: 0.45 mg/ dL (0.4–0.78) HBI: 3 (1–5) Pmayo: 1.286 (0–1)	FCP: 32.7 μg/g (13.8–50.98) CRP: 0 mg/dL (0–1.5) HBI: 4 (2.75–4.25) Pmayo: 1.00 (1–2.23)	0.74 0.66 0.388 0.089	*Increased HBI, n (%)*: 2 (12.5%) *Steroid Prescription, n (%)*: 1 (6.25) oral budesonide
Segal 2025 3 months follow-up	CRP: 10.1 mg/dL FCP: 824.9 μg/g (2112.7)	CRP: 3.0 mg/dL FCP: 234.7 μg/g (530.8)	< 0.01 0.13	*IBD Flare, n (%): 1 (0.4)*
St-Pierre 2024 Median 450 days (IQR 265–564)	CRP mg/L: 3 mg/L (3–6.5)	CRP: 3 mg/L (3–6.5)	0.2081	*Steroid Prescriptions, n (%)*: 1 (2.8%) *Change in IBD therapy, n (%)*: 6 (16.7%)
Villumsen 2021 Up to 147 months follow-up	NR	NR		*Steroids*: Users of GLP-1RA and/or DPP-4 inhibs: 133 events/2813 PY, IR per 1000 PY: 47.3. Non-users: 1238/13,104 PY. IR per 1000PY: 94.5 Adjusted IRR (95% CI): 0.54 (0.41–0.70) *Anti-TNF initiation*: Users of GLP-1RA and/or DPP-4 inhibs: 29/4183 PY, IR per 1000PY: 6.9. Non-users: 213/18,737 PY, IR per 1000PY: 11.4. Adjusted IRR (95% CI): 0.56 (0.32–1.00) *IBD-related hospitalizations*: Users of GLP-1RAs and/or DPP-4 inhibs: 178/2889, IR per 1000PY: 61.6. Non-users: 1445/14,024 PY, IR per 1000PY: 103.0. Adjusted IRR (95% CI): 0.73 (0.58–0.91) *IBD-Related Surgeries*: Users of GLP-1RAs and/or DPP-4 inhibs: 97/3675 PY, IR per 1000PY: 26.4. Non-users: 593/17,456 PY, IR per 1000PY: 34.0. Adjusted IRR (95% CI): 0.79 (0.57–1.09) *Composite outcome*: GLP-1RA and/or DPP-4 inhibs: IR 106.9 per 1000PY. Non-users: IR 242.9/1000PY. Adjusted IRR (95% CI): 0.52 (0.42–0.65)

(Continues)

TABLE 4 | (Continued)

Author year, follow-up time	IBD disease activity			IBD-related outcomes
	Baseline/IBD group	End of study/ comparator	*p*	
Weng 2025 1 year follow-up	NR	NR		*Ileus/bowel obstruction*: 12 months before GLP-1RA, *n* (%): 4 (5.0), 12 months after GLP-1RA, *n* (%): 2 (2.5), $p = 0.683$ *Bowel Surgery*: 12 months before GLP-1RA, *n* (%): 3 (3.8), 12 months after GLP-1RA, *n* (%): 2 (2.5), $p = 0.617$ *IBD Hospitalisation*: 12 months before GLP-1RA, *n* (%): 2 (2.5), 12 months after GLP-1RA, *n* (%): 0 (0), $p = 0.480$ *Systemic Corticosteroids*: 12 months before GLP-1RA, *n* (%): 16 (20.0), 12 months after GLP-1RA, *n* (%): 14 (17.5), $p = 0.831$ *Cyclosporine*: 12 months before GLP-1RA, *n* (%): 0 (0), 12 months after GLP-1RA, *n* (%): 0 (0), $p \geq 0.999$ *Immunomodulators*: 12 months before GLP-1RA, *n* (%): 4 (5.0), 12 months after GLP-1 RA, *n* (%): 1 (1.3), $p = 0.248$ *Advanced Therapy*: 12 months before GLP-1RA, *n* (%): 10 (12.5), 12 months after GLP-1RA, *n* (%): 8 (10), $p = 0.617$

Abbreviations: Anti-TNF, anti-tumour necrosis factor; CD, Crohn's disease; CI, confidence interval; CRP, C-reactive protein; DPP-4, dipeptidyl peptidase 4; ED, emergency department; EOS, end of study; FCP, faecal calprotectin; GI, gastrointestinal; GLP-1RA, glucagon like protein 1 receptor agonist; HBI, Harvey Bradshaw index; HR, hazard ratio; IBD, inflammatory bowel disease; IBD-U, undefined inflammatory bowel disease; IQR, interquartile range; IR, incidence rate; IRR, incidence rate ratio; IV, intravenous; MES, Mayo endoscopic score; NR, not reported; OR, odds ratio; pmayo, partial Mayo score; PY, person years; SD, standard deviation; SESCD, simple endoscopic score for Crohn's disease; UC, ulcerative colitis.

such as endoscopy or histology were rarely reported, limiting the ability to draw firm conclusions about the direct effects of GLP-1 RAs on mucosal inflammation. Finally, residual confounding is likely across all included studies, and the absence of randomised controlled data precludes definitive assessment of causality.

5 | Conclusion

In summary, across available observational studies, GLP-1 RAs are effective for weight loss, improve glycaemic and metabolic outcomes, and appear safe in IBD, with no signal of increased disease activity or exacerbations. Several cohorts have reported associations with lower rates of corticosteroid use, hospitalisation and surgery, though causality cannot be inferred and evidence is limited by retrospective design and heterogeneous populations. Future prospective trials are needed to confirm these findings and clarify safety in specific subgroups.

Author Contributions

Brooke Maracle: data curation, writing – original draft, writing – review and editing, methodology, visualization, formal analysis. **Steven Quan:** data curation, writing – review and editing. **Patrick Hamilton:** data curation, writing – review and editing. **Asma Shaikh:** data curation, writing – review and editing. **Deepan Hazra:** data curation, writing – review and editing. **Diane L. Lorenzetti:** methodology, validation, data curation, writing – review and editing. **Stephanie L. Gold:** writing – review and editing, methodology. **Maitreyi Raman:** writing – review and editing, methodology. **Joëlle St-Pierre:** conceptualization, supervision, writing – review and editing, writing – original draft, methodology, visualization, formal analysis, project administration, investigation.

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Conflicts of Interest

B.M., S.Q., P.H., A.S., D.H., D.L.L. declare no conflicts of interest. S.L.G.: Nestle Nutrition Institute Fellow 2023, Supported by a Crohn's and Colitis Foundation Career Development Award, Medical Board Member of Nutritional Therapy for IBD. M.R.: has served as a speaker for Fresenius Kabi, Pendopharm, a consultant for mBiota, has received education research grant from Abbvie, Pfizer, Organon, Celltrion. J.S.-P. has served as a consultant for Pfizer, Abbvie, Eli Lilly and Pendopharm, and speaker for Takeda.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Figure S1:** PRISMA 2020 flow diagram of study selection for systematic review of GLP-1 receptor agonists in IBD. **Table S1:** Risk of bias assessment of included studies using the Joanna Briggs Institute (JBI) critical appraisal tool. **Table S2:** Baseline demographic and clinical characteristics of IBD patients treated with GLP-1 receptor agonists across included studies. **Table S3:** Adverse events and serious adverse events reported in IBD patients treated with GLP-1 receptor agonists.