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Effect of GLP-1 receptor agonists on upper gastrointestinal endoscopy outcomes: a systematic review and meta-analysis

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Abstract

Background Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) delay gastric emptying, raising concerns about potential aspiration risk during upper gastrointestinal (GI) endoscopy. We conducted a systematic review and meta-analysis to evaluate the effect of GLP-1 RA therapy on procedural outcomes in patients undergoing upper GI endoscopy.

Methods We searched Medline and Cochrane library up to July 2025 without restrictions. Eligible studies evaluated patients undergoing upper GI endoscopy, comparing those taking GLP-1 RAs with those who were not. Outcomes of interest were the incidence of retained gastric contents (RGC), bronchopulmonary aspiration, and procedure discontinuation. Pooled estimates are expressed as odds ratios (ORs) with 95% confidence intervals (CIs), using a random-effects meta-analysis with inverse variance weighting.

Results Twenty-four observational studies, predominantly retrospective, met the inclusion criteria: these comprised 184,707 participants, of whom 59,095 were taking GLP-1 RAs. Mean age was 58.7 years, 48.8% were women, and 51.2% had type 2 diabetes. Use of GLP-1 RAs was associated with higher rates of RGC (OR 4.82, 95%CI 3.66-6.35) and procedure discontinuation (OR 3.93, 95%CI 2.42-6.39) compared with control treatment. In contrast, the incidence of aspiration events was similar between groups (OR 1.1, 95%CI 0.84-1.48). Results remained consistent in a sensitivity analysis based on propensity score matching to control for confounders.

Conclusions GLP-1 RA therapy is associated with a greater incidence of RGC and higher rates of endoscopy termination, but not with a higher risk of aspiration. Adjusting the fasting duration, rather than routinely discontinuing GLP-1 RAs, may represent a reasonable management approach.

Keywords Upper gastrointestinal endoscopy, glucagon-like peptide-1 receptor agonists, systematic review, meta-analysis

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Introduction

Following their approval, glucagon-like peptide-1 receptor agonists (GLP-1 RAs) have become one of the most widely used drug classes for the management of type 2 diabetes (T2D) [1]. Their widespread adoption has also been fueled by their proven efficacy in promoting weight loss among individuals with obesity, irrespective of diabetes status [2,3]. In addition, emerging evidence of potential therapeutic benefits in other conditions, including chronic kidney disease, neurodegenerative disorders and metabolic dysfunction-associated steatotic liver disease, is expected to expand their clinical indications [4,5].

GLP-1 receptor activation in the gastrointestinal (GI) tract reduces GI motility, thereby delaying gastric emptying. As a result, nausea, vomiting and abdominal discomfort are among the most commonly reported adverse effects in individuals treated with these agents [6]. The delayed gastric emptying

associated with GLP-1 RAs has raised concerns for patients undergoing upper GI endoscopy, due to the potential risk of aspiration during sedation. In June 2023, the American Society of Anesthesiologists (ASA) issued a consensus-based guidance recommending that GLP-1 RAs be withheld prior to procedures [7]. In view of the limited evidence, the American Gastroenterological Association (AGA) released a clinical practice update advocating for an individualized, risk-based approach to the preprocedural management of these agents [8]. More recently, a multisociety clinical practice guidance document emphasized the importance of shared decision-making regarding GLP-1 RA management, while also highlighting the paucity of evidence on the optimal perioperative approach [9].

Likewise, recent observational studies could not establish a clear link between the preprocedural use of GLP-1 RAs and an increased risk of pulmonary aspiration during upper GI endoscopy [10,11]. To clarify this potential association and provide a comprehensive synthesis of the available evidence, we conducted a systematic review and meta-analysis assessing the effect of GLP-1 RA use on procedural outcomes in patients undergoing upper GI endoscopy.

Materials and methods

This systematic review and meta-analysis were conducted according to a prespecified protocol registered in PROSPERO (registration no. CRD420251167356). We report our methods and results in line with the PRISMA and MOOSE statements (Supplementary Tables 1 and 2) [12,13].

Eligibility criteria

We included comparative studies (randomized controlled trials or observational studies) that enrolled adult participants (aged >18 years) undergoing upper GI endoscopy, irrespective of indication. Eligible studies compared patients receiving GLP-1 RAs with those not on GLP-1 RA therapy. For semaglutide, both oral and injectable formulations were considered. We also included studies that recruited participants receiving tirzepatide. The primary outcome of interest was the incidence of retained gastric content (RGC), defined as the presence of any amount of either solid or liquid material in the stomach during endoscopy. Secondary outcomes of interest were the incidence of bronchopulmonary aspiration and rates of procedure discontinuation. We excluded non-comparative studies and studies not reporting at least 1 outcome of interest. In addition, we excluded studies comparing patients receiving GLP-1 RAs with those having discontinued GLP-1 RA therapy prior to endoscopy.

Information sources and study selection

We searched Medline via PubMed and the Cochrane Database from inception to July 7, 2025, without language or publication type restrictions. The search strategy combined free-text terms and controlled vocabulary, as presented in Supplementary Tables 3 and 4. To identify additional eligible studies, we manually screened the reference lists of relevant systematic reviews. We did not search conference proceedings from relevant scientific meetings, or contact study authors for additional information.

Search results were imported into reference manager software (Endnote, Clarivate Analytics), and duplicate records were removed. Two reviewers working independently assessed record eligibility initially at title and abstract level and then in full text. Any disagreements during the study selection process were resolved by a third reviewer. The study selection process was performed using the Covidence web application (Covidence systematic review software, Veritas Health Innovation).

Data extraction and risk of bias assessment

Two reviewers working independently extracted data from eligible studies using predesigned and pilot-tested forms. Extracted information included study characteristics, participant baseline characteristics and outcomes of interest. For studies that included participants undergoing combined upper GI endoscopy and colonoscopy, we preferentially extracted data specific to patients who underwent upper endoscopy alone, given the confounder of preprocedural colonoscopy preparation. In cases of multiple publications with potentially overlapping cohorts, we extracted data from the full text publication that provided the largest amount of information. Any disagreements during the data extraction process were resolved either through discussion between the original reviewers or by a senior reviewer.

Two reviewers independently assessed the risk of bias of the included studies, using the Risk of Bias in Non-randomized Studies – of Interventions, Version 2 (ROBINS-I v.2) tool [14]. Notably, all studies included in this systematic review and meta-analysis were observational. The assessment focused on the following domains: bias due to confounding, bias in classification of interventions, bias in the selection of participants included in the study (or in the analysis), bias due to deviations from intended interventions, bias due to missing data, bias arising from measurement of the outcome, and bias in selection of the reported result. Details on risk of bias judgments are presented in the electronic supplementary material. Any disagreements during the risk of bias assessment were resolved either through discussion between the original reviewers or by a senior reviewer.

Statistical analysis

All outcomes are reported as odds ratios (ORs) along with 95% confidence intervals (CIs). Given the expected between-study heterogeneity, we conducted a random-effects meta-analysis using inverse variance weighting. Between-study

variance (Tau^2) was estimated using the Restricted Maximum Likelihood (REML) method [15,16]. When at least 3 studies were available and Tau^2 was greater than zero, the Hartung-Knapp-Sidik-Jonkman (HKSJ) method was applied to calculate confidence intervals for the pooled effect estimates [15,16]. In cases with only 2 studies, or where Tau^2 was estimated as zero, the confidence intervals for the pooled effect estimates were calculated based on the Wald-type method [15]. Statistical heterogeneity was assessed using the chi-squared (χ^2) test (with a significance threshold of $P<0.10$) and the I^2 statistic, with I^2 values exceeding 50% indicating substantial heterogeneity [16]. Studies with zero events in both arms were excluded from the meta-analysis. For the main analyses, we calculated prediction intervals (PIs) to quantify the expected range of effects in future studies. When at least 10 studies were included in the meta-analysis, we assessed publication bias through visual inspection of funnel plots [17]. All analyses were performed using RevMan Version 7.2.0.

Additional analysis

To assess the robustness of our findings and explore potential sources of heterogeneity we performed several sensitivity analyses. For all outcomes we conducted sensitivity analyses including only studies that: i) employed propensity score matching at baseline to control for confounders; ii) recruited solely participants with T2D; iii) were at low risk for bias; and iv) were published in full text. For the primary outcome, we conducted a *post hoc* analysis pooling adjusted ORs from primary studies, and a subgroup analysis based on the specific GLP-1 RA agent used. These additional analyses were not feasible for the incidence of aspiration, given the limited number of studies with available data.

One reviewer assessed the certainty in effect estimates from main analyses following the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach using the online GRADEpro Guideline Development Tool software [18]. We took into consideration the following domains: study design, risk of bias, inconsistency, indirectness, imprecision, and publication bias.

Results

Search results

Fig. 1 depicts the study selection process. In total, 255 records were screened at title and abstract level, of which 58 were reviewed in full text. Ultimately, 24 records describing 24 studies with 181,770 participants were included in the systematic review and meta-analysis [11,19-41]. During the full-text screening process, 3 studies were excluded because of concerns about overlapping cohorts [10,42,43].

Study and participant characteristics

The main characteristics of the included studies are presented in Table 1. Most studies were published between 2023 and 2025, and originated predominantly from the United States. Eight studies (33.3%) were identified solely as conference abstracts [20,21,25,29,30,32,33,39]. The majority of included studies were single-center, employing a retrospective design. Included studies mainly focused on participants undergoing elective procedures. Recruitment periods across studies spanned from 2005-2024. Fifteen studies (62.5%) applied propensity score matching for multiple variables (including age, T2D, body mass index [BMI] and sex) to ensure balanced baseline characteristics between groups [11,19-23,26,28,30,31,35,37-40]. Fasting protocols prior to procedures were largely unavailable across the included studies, and when reported, they were inconsistent. Supplementary Table 5 summarizes the fasting durations and dietary instructions as provided in the included studies. Among the 181,770 participants 59,098 (32.5%) were receiving GLP-1 RAs, 88,698 (48.8%) were females and 93,101 (51.2%) had T2D. Among studies with available data, the average mean age and BMI were 58.7 years and 33.0 kg/m^2, respectively. Among participants treated with GLP-1 RAs, 10,387 (17.6%) received dulaglutide, 8352 semaglutide (14.1%), 7428 liraglutide (12.6%), and 518 (0.8%) tirzepatide. For the remaining 32,413 participants, the specific GLP-1 RA used was not reported.

RGC

Twenty studies, including 5619 participants in the GLP-1 RA group and 45,299 participants in the control group, reported rates of RGC [19-21,23,25-36,38-41]. The overall incidence of RGC was 11.0% among GLP-1 RA users and 2.7% in the control group. Treatment with GLP-1 RAs was associated with higher odds of RGC compared with controls (OR 4.82, 95%CI 3.66-6.35; I^2=63%) (Fig. 2). Results remained consistent when prediction intervals were applied (95% PI 1.95-11.88) Similarly, findings were robust in a sensitivity analysis restricted to studies employing propensity score matching to adjust for baseline confounders (OR 3.79, 95%CI 2.96-4.84; I^2=10%) (Supplementary Fig. 1). Comparable results were observed in an analysis limited to studies enrolling only participants with T2D (OR 4.09, 95%CI 3.06-5.45; I^2=0%) (Supplementary Fig. 2). When synthesis was restricted to studies at low risk of bias or full-text publications, the effect estimates remained consistent with those of the primary analysis (Supplementary Figs. 3 and 4 respectively). The odds of RGC were similar across different GLP-1 RAs regimens, ranging from 3.48 for liraglutide to 4.35 for semaglutide (Supplementary Fig. 5). A meta-analysis of adjusted ORs yielded similar estimates to our main findings (OR 3.23, 95%CI 2.33-4.47; I^2=70%) (Supplementary Fig. 6).

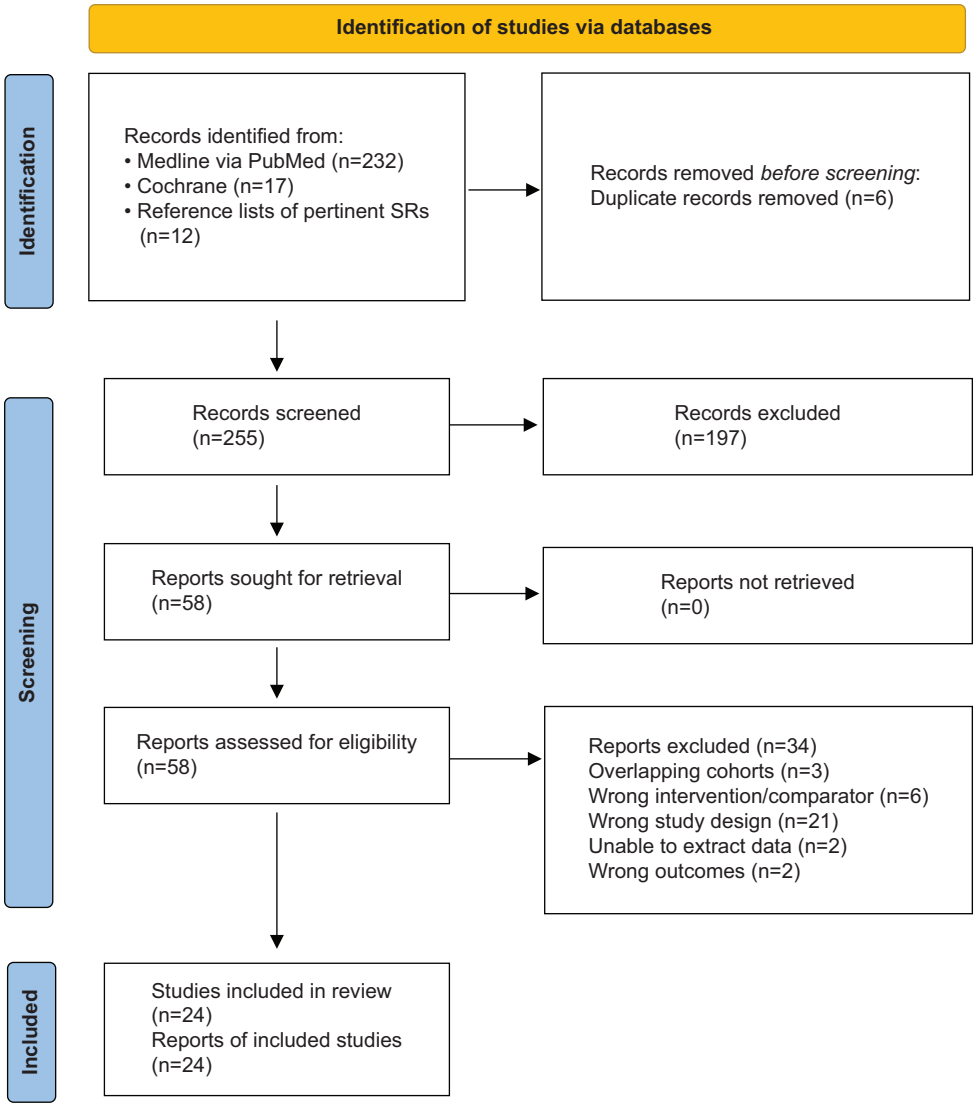

Figure 1 Flow diagram of the study selection process
SRs, systematic reviews
Source: Page MJ, et al. BMJ 2021;372:n71. doi: 10.1136/bmj.n71.

Aspiration

Thirteen studies, including 55,751 participants in the GLP-1 RA group and 113,240 participants in the control group, reported data on aspiration events [11,20-22,24,26,32,34-38,41]. The overall incidence of aspiration was 0.4% among GLP-1 RA users and 0.1% in the control group. Six studies were excluded from the meta-analysis as they had zero events in both arms [20,21,24,26,35,36]. The pooled analysis showed no significant difference in the odds of aspiration between the GLP-1 RA and control groups (OR 1.11, 95%CI 0.84-1.48; I^2=9%) (Fig. 3). Results remained consistent when prediction intervals were applied (95%PI 0.76-1.63). Similar findings were observed in a sensitivity analysis restricted to studies employing propensity score matching to adjust for baseline confounders (OR 1.08, 95%CI 0.76-1.54; I^2=17%) (Supplementary Fig. 7), studies enrolling only participants with T2D (OR 0.94, 95%CI 0.71-1.25; I^2=0%) (Supplementary Fig. 8), studies at low risk for bias (OR 1.09, 95%CI 0.82-1.46; I^2=12%) (Supplementary Fig. 9), and studies published as full text (OR 1.11, 95%CI 0.80-1.53; I^2=10%) (Supplementary Fig. 10). Across individual agents, the rates of aspiration were 0.2% for semaglutide, 0.5% for liraglutide and 0.4% for dulaglutide.

Procedure discontinuation

Eleven studies, including 28,453 participants in the GLP-1 RA group and 87,879 participants in the control group, reported rates of procedure discontinuation [11,20,21,23,24,27,29,30,34,36,40]. The overall incidence of procedure discontinuation was 1.0% among GLP-1 RA users and 0.3% in the control group. One

Table 1 Baseline characteristics of included studies

Author, year [ref.]	Design, Centers	Recruitment Period	Publication type	Study arms	Sample size	Mean age	Mean BMI	Females (%)	T2D (%)	Semaglutide (%)	Liraglutide (%)	Dulaglutide (%)	Tirzepatide (%)
Abu-Freha 2024 [19]	Retrospective multicenter	2020-2023	Full text	GLP-1	1671	60.2	NR	1006 (60.2)	1141 (68.3)	1077 (64.5)	392 (23.5)	202 (12.0)	0 (0)
				No GLP-1	1671	60.9	NR	1006 (60.2)	1141 (68.3)				
Alkabbani 2024 [11]	Retrospective multicenter	2016-2023	Full text	GLP-1	24817	59.9	NR	15794 (63.6)	24817 (100)	5489 (22.1)	6604 (26.6)	9184 (37.0)	375 (1.5)
				No GLP-1	18537	59.8	NR	11815 (63.7)	18537 (100)				
Ayoub 2024 [20]	Retrospective single center	2010-2022	Abstract	GLP-1	101	55.4	38.9	82 (81.2)	101 (100)	NR	NR	NR	NR
				No GLP-1	104	55.1	38.5	84 (80.7)	104 (100)				
Bahdi 2024 [21]	Retrospective single center	2018-2023	Abstract	GLP-1	174	62.0	30.8	115 (66.1)	140 (80.5)	91 (52.3)	25 (14.4)	50 (28.7)	6 (3.4)
				No GLP-1	148	63.0	31.2	91 (61.5)	148 (100)				
Barlowe 2025 [22]	Retrospective multicenter	2005-2021	Full text	GLP-1	15119	54.7	NR	9018 (60.0)	15119 (100)	NR	NR	NR	NR
				No GLP-1	14407	56.7	NR	7448 (52.0)	14407 (100)				
Chapman 2024 [23]	Retrospective single center	2017-2023	Full text	GLP-1	84	53.9	40.7	60 (71.4)	73 (86.9)	20 (24.0)	14 (17.0)	41 (49.0)	7 (8.0)
				No GLP-1	84	54	31.2	58 (69.0)	71 (84.5)				
Dev 2025 [24]	Retrospective multicenter	2018-2023	Full text	GLP-1	1179	60.4	32.9	611 (51.8)	1000 (84.8)	529 (44.9)	155 (13.1)	402 (34.1)	72 (6.1)
				No GLP-1	32096	56.5	27.3	16744 (52.2)	6999 (21.8)				
Elliott 2024 [25]	Retrospective NR	2020-2023	Abstract	GLP-1	155	NR	NR	NR	155 (100)	NR	NR	NR	NR
				No GLP-1	532	NR	NR	NR	532 (100)				
Garza 2024 [26]	Retrospective single center	2018-2023	Full text	GLP-1	306	60.3	33.1	151 (49.0)	269 (88.0)	111 (36.0)	49 (19.0)	108 (35.0)	12 (4.0)
				No GLP-1	306	61	32.6	152 (50.0)	268 (88.0)				
Gonzaga 2024 [27]	Retrospective single center	2023	Full text	GLP-1	73	56.7	34	52 (71.0)	53 (72. 6)	37 (50.7)	NR	22 (30.1)	11 (15.1)
				No GLP-1	973	54	28.1	623 (64.0)	131 (13.5)				
Gu 2025 [28]	Retrospective single center	2022-2023	Full text	GLP-1	152	57.8	34.4	NR	78 (51.3)	152 (100)	0 (0)	0 (0)	0 (0)
				No GLP-1	152	57.2	35.5	NR	78 (51.3)				
Hernandez 2024 [29]	Retrospective single center	2022-2023	Abstract	GLP-1	109	NR	NR	NR	NR	NR	NR	NR	NR
				No GLP-1	949	NR	NR	NR	NR				
Karlson 2024 [30]	Retrospective NR	2015-2023	Abstract	GLP-1	433	NR	NR	NR	NR	NR	NR	NR	NR
				No GLP-1	208	NR	NR	NR	NR				
Kobori 2023 [31]	Retrospective single center	2020-2022	Full text	GLP-1	205	69.3	NR	42 (20.5)	205 (100)	40 (19.5)	69 (33.7)	90 (43.9)	0 (0)
				No GLP-1	205	71	NR	51 (24.9)	205 (100)				

(*Contd...*)

Table 1 (*Continued*)

Author, year [ref.]	Design, Centers	Recruitment Period	Publication type	Study arms	Sample size	Mean age	Mean BMI	Females (%)	T2D (%)	Semaglutide (%)	Liraglutide (%)	Dulaglutide (%)	Tirzepatide (%)
Markley 2024 [32]	Retrospective single center	2020-2023	Abstract	GLP-1	47	53.4	32.9	34 (72.3)	23 (48.9)	NR	NR	NR	NR
				No GLP-1	324	49.3	26.9	189 (55.3)	28 (8.6)				
Meluban 2024 [33]	Retrospective NR	2022-2023	Abstract	GLP-1	65	NR	NR	NR	NR	39 (60.0)	6 (9.2)	17 (26.2)	3 (4.6)
				No GLP-1	2045	NR	NR	NR	NR				
Nadeem 2024 [34]	Retrospective single center	2019-2023	Full text	GLP-1	922	57.1	36.4	558 (61.0)	756 (82.0)	NR	NR	NR	NR
				No GLP-1	34261	53.9	30.5	20191 (59.0)	5407 (16.0)				
Nasser 2024 [35]	Retrospective single center	2023	Full text	GLP-1	23	61.5	32.3	13 (56.5)	19 (82.6)	NR	NR	NR	NR
				No GLP-1	46	61.8	31.4	26 (56.5)	9 (19.6)				
Panchal 2025 [36]	Retrospective single center	2022-2023	Full text	GLP-1	360	59.7	33	210 (58.3)	245 (68.1)	191 (31.9)	28 (4.7)	120 (20.0)	20 (5.6)
				No GLP-1	238	59	33.3	157 (66.0)	135 (56.7)				
Peng 2024 [37]	Retrospective multicenter	2005-2024	Full text	GLP-1	12267	NR	NR	NR	NR	NR	NR	NR	NR
				No GLP-1	12267	NR	NR	NR	NR				
Quinn 2025 [38]	Retrospective multicenter	2022-2023	Full text	GLP-1	470	56.5	36.1	341 (72.6)	350 (74.5)	288 (61.3)	53 (11.3)	112 (23.8)	11 (2.3)
				No GLP-1	470	56	28.8	273 (58.1)	97 (20.6)				
Rizvi 2024 [39]	Retrospective single center	2021-2023	Abstract	GLP-1	217	59	NR	137 (63.1)	NR	217 (100)	0 (0)	0 (0)	0 (0)
				No GLP-1	2429	54.2	NR	1439 (59.2)	NR				
Stark 2022 [40]	Retrospective single center	2015-2020	Full text	GLP-1	59	64	33	10 (17.0)	57 (97.0)	1 (2.0)	22 (37.0)	33 (56.0)	0 (0)
				No GLP-1	118	66	33	7 (6.0)	116 (98.0)				
Wu 2024 [41]	Retrospective single center	2019-2023	Full text	GLP-1	90	63.2	34.3	56 (62.0)	62 (69.0)	70 (70.7)	11 (12.2)	6 (6.6)	1 (1.1)
				No GLP-1	102	57.3	33.9	54 (53.0)	25 (25.0)				

The control group in the study by Alkabbani *et al*. was receiving SGLT-2 inhibitors. Barlowe *et al*. conducted a 3-arm study comparing GLP-1 RAs, DPP4 inhibitors and opioids. Given the effect of opioids in the gastrointestinal tract, we used data only from the first 2 groups. In the study by Dev *et al*., 3.2% of procedures were conducted in hospitalized patients, while 23.9% of participants underwent either endoscopic retrograde cholangiopancreatography, enteroscopy, or upper endoscopic ultrasound

BMI, body mass index; GLP-1, glucagon-like peptide 1; T2D, type 2 diabetes; NR, not reported

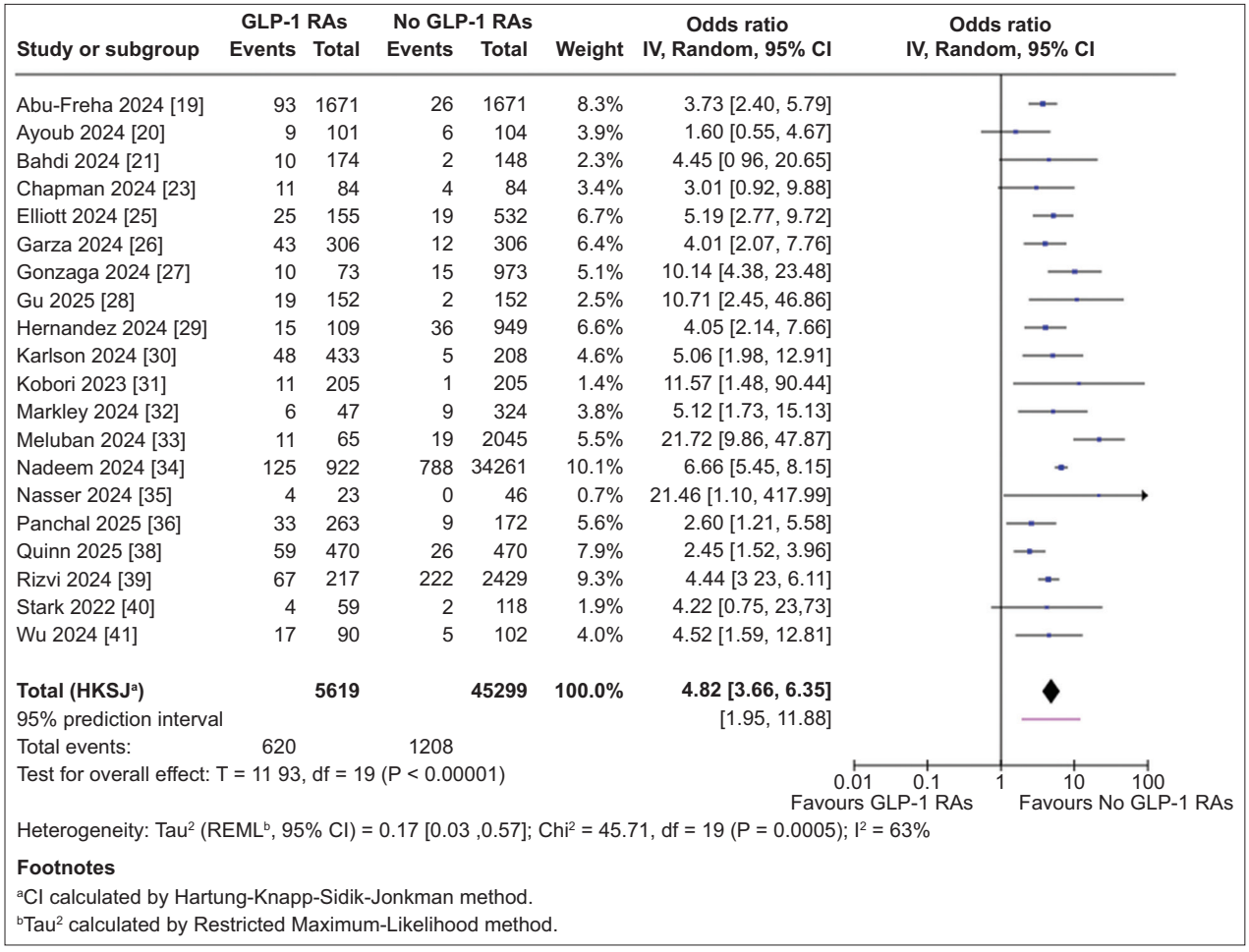

Figure 2 Meta analysis results for GLP-1 RAs vs. No GLP-1 RAs for incidence of retained gastric content
GLP-1 RAs, glucagon-like peptide 1 receptor agonists; CI, confidence interval

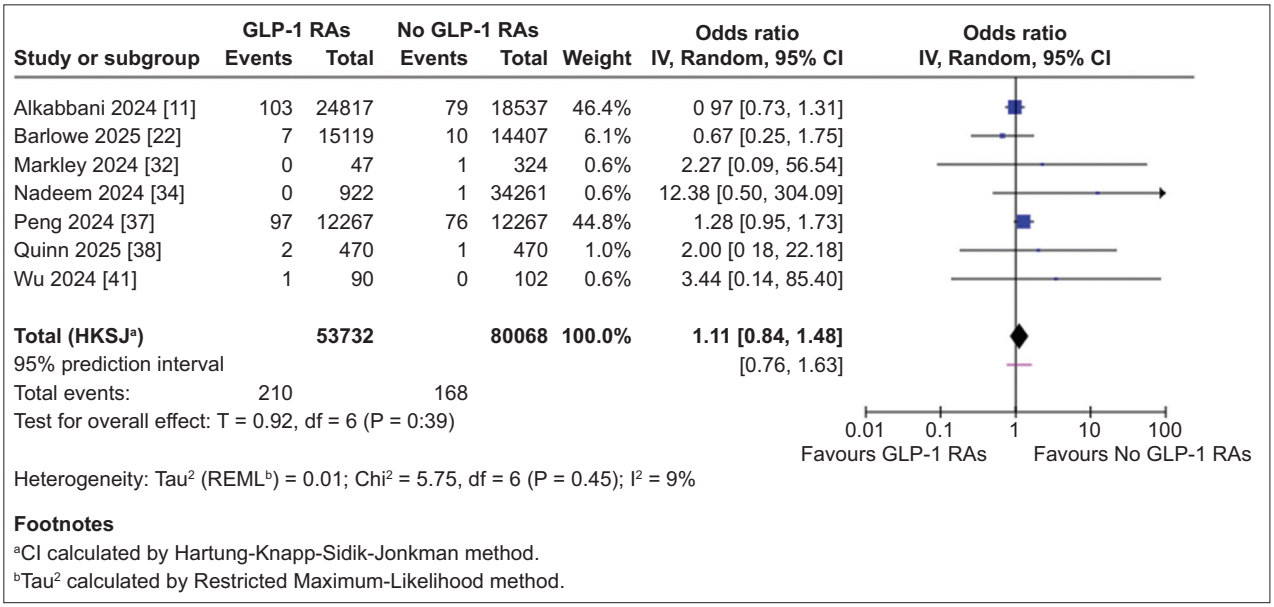

Figure 3 Meta analysis results for GLP-1 RAs vs. No GLP-1 RAs for incidence of aspiration
GLP-1 RAs, glucagon-like peptide 1 receptor agonists; CI, confidence interval

study was excluded from the meta-analysis as it had zero events in both arms [40]. Procedure discontinuation was more likely to occur in GLP-1 RA users compared to controls (OR 3.93, 95%CI 2.42-6.39; I^2=53%) (Fig. 4). Results remained consistent when prediction intervals were applied (95%PI 1.16-13.38). Similar findings were observed in a sensitivity analysis based on propensity score matching, presence of T2D, low risk of bias and full-text publication (Supplementary Figs. 11-14, respectively).

Risk of bias and publication bias assessment

Most studies were at low risk for bias for the primary outcome (Supplementary Table 6). Four studies raised serious concerns over bias, mainly due to residual confounding [20,21,25,33]. Four additional studies published as conference abstracts were at moderate risk for bias, mainly due to concerns related to missing data [29,30,32,39]. Supplementary Tables 7 and 8 present the risk of bias assessment for the incidence of aspiration and procedure discontinuation, respectively. Visual inspection of funnel plots did not suggest the presence of small-study effect bias for RGC or procedure discontinuation rates (Supplementary Figs. 15-16). Owing to the limited number of studies reporting aspiration events, a respective analysis for this outcome could not be performed.

Grading of evidence

The confidence in the effect estimates for all outcomes was rated as very low (Supplementary Table 9). This was primarily due to imprecision in the effect estimates, arising from the limited number of events in both groups across all outcomes, particularly for the incidence of aspiration. In addition, the certainty of evidence was downgraded by 1 level because all available data were derived from observational studies.

Discussion

In this systematic review and meta-analysis, we assessed the effect of GLP-1 RA use on the risk of RGC, aspiration and procedure discontinuation in patients undergoing upper GI endoscopy. Our findings indicate that GLP-1 RA users are more likely to experience RGC (OR 4.82, 95%CI 3.66-6.35) or an aborted upper GI endoscopy (OR 3.93, 95%CI 2.42-6.39). This association remained consistent across multiple sensitivity analyses, including studies employing propensity score matching at baseline and those primarily involving participants with T2D. Moreover, the odds of RGC were comparable across different GLP-1 RAs. Notably, despite the increased risk of RGC, GLP-1 RA use was not associated with a higher incidence of aspiration. The absence of a statistically significant difference between groups in terms of aspiration, should be interpreted cautiously, given the small number of events in the groups (0.4% among GLP-1 RA users and 0.1% in the control group). Furthermore, these estimates derive from observational studies; therefore, the potential for residual confounding remains, despite the use of various methods in the primary studies to control for measured confounders.

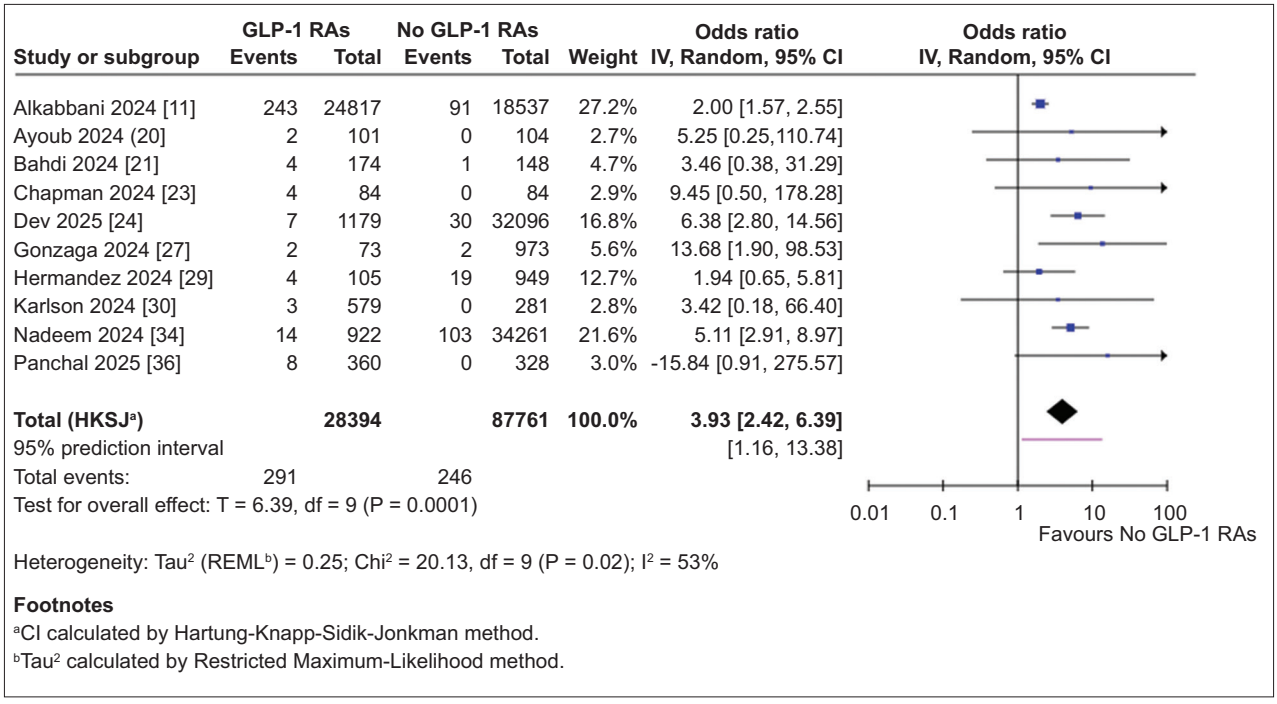

Figure 4 Meta analysis results for GLP-1 RAs vs. No GLP-1 RAs for incidence of procedure discontinuation
GLP-1 RAs, glucagon-like peptide 1 receptor agonists; CI, confidence interval

The confidence in our estimates was rated as very low, mainly because of the small number of events across all outcomes.

This systematic review and meta-analysis provide an updated summary of the available evidence on the effect of GLP-1 RA use on outcomes related to upper GI endoscopy. We included 24 studies, comprising more than 180,000 participants, while accounting for potential cohort overlap. The analysis adhered to rigorous methodological standards consistent with the latest Cochrane recommendations [15], and the robustness of the findings was confirmed through multiple sensitivity analyses. We evaluated the risk of bias using the recently revised ROBIN-I v.2 tool and assessed the certainty in our estimates using robust methodology.

Nevertheless, certain limitations should be acknowledged. Moderate to substantial heterogeneity was observed in most primary analyses, especially for the incidence of RGC (I^2=63%). This heterogeneity was notably reduced in sensitivity analyses that included only propensity score-matched studies (I^2=10%), suggesting that differences in methodological approaches were major contributors to the variability across effect estimates. Additional heterogeneity may have arisen from variations in fasting protocols, patient selection criteria and procedural sedation practices across studies. Moreover, the definition and grading of RGC were not uniform among the included studies. In our study, all types and grades of RGC were pooled together; this approach may have further contributed to the observed heterogeneity. In addition, 8 of the 24 studies (33%) were identified solely as conference abstracts; thus, a thorough evaluation of participant characteristics and applied methodology was not possible. However, sensitivity analyses excluding these studies yielded similar results to our main findings, supporting the robustness of our results across all main outcomes despite the inclusion of several studies published solely in abstract form.

Our findings are generally in line with previously published pertinent meta-analyses [44-48]. Facciorusso *et al* analyzed 13 studies including 84,065 participants and reported higher odds of RGC (OR 5.56, 95% CI 3.35-9.23) and procedure discontinuation (OR 5.13, 95%CI 3.01-8.75) among GLP-1 RA users compared with controls, while rates of aspiration did not differ significantly between groups (OR 1.75, 95%CI 0.64-4.77) [44]. Similarly, Abdulraheem *et al* synthesized 20 studies involving 164,222 participants and found comparable estimates, again showing no increase in aspiration events among GLP-1 RA users [45]. Consistent conclusions were also reached by Singh *et al* and Baig *et al*, who reported an increased risk of RGC and procedure discontinuation in GLP-1 RA users, without a corresponding increase in aspiration risk [47,48].

While our pooled estimates align with prior analyses, our study builds upon the existing literature through several methodological advantages. In contrast to all previously published meta-analyses, we provide prediction intervals to convey the expected range of effects in future studies, thereby enhancing the clinical interpretability of our results. Furthermore, whereas several previous systematic reviews and meta-analyses relied on the Newcastle–Ottawa Scale [44,46-48], we evaluated methodological quality using the updated ROBINS-I v.2 tool, allowing for a more comprehensive and methodologically rigorous assessment of bias in non-randomized studies of interventions. Moreover, in contrast to Abdulraheem *et al*, Singh *et al* and Tan *et al*, we formally appraised the certainty in our pooled estimates using the GRADE methodological framework, thereby strengthening the interpretability and clinical credibility of our results. Interestingly, 3 previous meta-analyses identified a protective effect of concurrent colonoscopy against RGC among GLP-1 RA users [45-47]. This observation may be attributed to the prolonged fasting period required for colonoscopy preparation, which typically involves a clear liquid diet the day before the procedure. Supporting this interpretation, quantitative evidence indicates that GLP-1 RA therapy is associated with an approximately 36-minute delay on solid-phase scintigraphy and no significant differences in modalities reflective of liquid emptying [49].

In its position statement, the American Society for Gastrointestinal Endoscopy recommends withholding GLP-1 RAs on the day of the procedure for patients on daily formulations, and for 1 week in those receiving weekly dosing [50]. This approach is supported by a multicenter study involving 815 participants on GLP-1 RAs, which reported significantly lower rates of RGC among patients who withheld GLP-1 RAs before the procedure compared with those who did not (4.4% vs. 12.7%, P<0.001) [51]. However**,** in a cohort study including 629 bariatric patients, Jirapinyo *et al* observed no significant difference in the rates of early termination of upper endoscopy (1.4% vs. 0%, P=0.36) or RGC (6.4% vs. 2.7%, P=0.36) between patients who continued vs. those who discontinued GLP-1 RA therapy [52]. Taking this further, Santos *et al* evaluated the impact of varying preprocedural semaglutide interruption intervals on RGC during upper endoscopy [53]. Based on their findings, discontinuation of semaglutide for more than 21 days in patients with ongoing GI symptoms, and more than 14 days in asymptomatic individuals, was associated with comparable RGC rates to non-semaglutide users.

Withholding GLP-1 RAs in patients with obesity but without diabetes may pose fewer concerns, whereas interruption in patients with diabetes warrants more caution. Previous studies have identified poorly controlled diabetes and hyperglycemia as independent risk factors for gastric retention, suggesting that such patients may benefit from a prolonged (24 h) preprocedural liquid diet [9,51]. Phan *et al*, reported that, for every 1% increase in hemoglobin A1c, there was a 36% increase in the odds of retained food, after adjusting for medication type and GLP-1 RA withholding status [51]. Other factors that should be considered include the phase of GLP-1 RA therapy. Patients in the maintenance phase appear to be at lower risk of delayed gastric emptying compared to those who have recently undergone dose escalation [9]. Moreover, patients on weekly GLP-1 RA regimens are more likely to experience GI symptoms suggestive of gastric retention, in a dose-dependent manner, than those receiving daily formulations [9].

When clinical concern for RGC exists on the day of the procedure, such as in patients presenting with nausea, bloating, or abdominal discomfort despite prior GLP-1 RA discontinuation, point-of-care gastric ultrasound may be utilized to assess aspiration risk [54]. In such cases, a shared decision-making approach should be adopted, weighing the benefits and risks of proceeding with rapid sequence induction and tracheal intubation under general anesthesia to mitigate aspiration risk,

vs. postponing or canceling the procedure [9]. It should also be noted that, in patients with persistent GI symptoms, even longer GLP-1 RA interruption intervals (exceeding 1 week) may be necessary to reduce the risk of RGC [53].

The current evidence regarding the impact of GLP-1 receptor agonists on upper GI endoscopy-related outcomes is largely based on observational, retrospective studies. Accordingly, prospective studies are urgently needed to generate higher-quality data, though their feasibility may be limited by the low incidence of key outcomes, necessitating large sample sizes. Most existing studies have excluded patients with neurological disorders, gastroparesis or surgically altered GI anatomy, populations in whom the true risk of RGC and aspiration may be greater. This underscores the need for further investigation in these higher-risk subgroups. Furthermore, the majority of available data derive from patients undergoing elective procedures, while hospitalized individuals were generally excluded. As a result, the generalizability of current findings to inpatient settings remains uncertain. Finally, most of the available evidence pertains to participants receiving semaglutide, liraglutide or dulaglutide, with only limited data currently available for tirzepatide.

In conclusion, data from observational studies suggest an increased risk of RGC and procedure discontinuation among patients receiving GLP-1 RAs who undergo upper GI endoscopy, although there is no clear evidence of an elevated risk for aspiration. Therefore, an individualized risk assessment with adjustment of fasting duration, rather than routine discontinuation of GLP-1 RAs prior to upper GI endoscopy, may represent a reasonable approach for these patients.

Summary Box

What is already known:

- Glucagon-like peptide-1 receptor agonists (GLP-1RAs) are widely used for the management of diabetes
- The delayed gastric emptying associated with GLP-1 RAs has raised concerns for patients undergoing upper gastrointestinal (GI) endoscopy, due to the potential risk of aspiration during sedation
- Observational studies have yielded inconsistent findings regarding whether preprocedural use of GLP-1 RAs increases the risk of pulmonary aspiration during upper GI endoscopy

What the new findings are:

- Treatment with GLP-1 RAs is associated with higher odds of retained gastric content during upper GI endoscopy compared with controls
- Procedure discontinuation is more likely to occur in GLP-1 RA users compared to controls
- GLP-1 RA use is not associated with higher rates of aspiration during upper GI endoscopy

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Supplementary material

Electronic supplementary material

Risk of bias assessment using ROBINS-1 v.2

Domain 1 — Bias due to confounding (Variant A: baseline confounding only)

1. 1 Did the authors control for all the important confounding factors for which this was necessary?

Answer Y/PY if appropriate baseline control was used (e.g., stratification, regression, matching, standardization, IPW/ propensity scores) for all important confounders (age, sex body mass index, diabetes); WN if most were controlled and any residual is unlikely to be substantial; SN if ≥1 important confounder that should have been controlled was not; NI if insufficient information (e.g., abstract only).

1. 2 If Y/PY/WN to 1.1: Were confounding factors that were controlled for (and for which control was necessary) measured validly and reliably by the variables available in this study?

If Y/PY/WN to 1.1: Answer Y/PY almost always.

1. 3 If Y/PY/WN to 1.1: Did the authors control for any post- intervention variables that could have been affected by the intervention?

If Y/PY/WN to 1.1: Answer N/PN if no post-intervention variables were controlled; Y/PY if such post-intervention variables were controlled (over-adjustment); NI if unclear.

1. 4 Did the use of negative controls, quantitative bias analysis, or other considerations, suggest serious unmeasured confounding?

Answer N/PN if no evidence of unmeasured confounding; Y/PY if negative controls/quantitative bias analysis suggest serious unmeasured confounding; NA if not applicable.

Domain 2 — Bias in classification of interventions

2. 1 Did assignment of participants to the intervention group or the comparator group rely on events or measurements that occurred after the start of follow up?

Answer Y/PY if group assignment used post-start events; N/PN if classification was pre-start; NI if unclear.

2. 2 If Y/PY to 2.1: Were participants included in the comparator group until they fulfilled the definition of the intervention (or vice versa)?

If Y/PY to 2.1: Answer SY if impact substantial; WY if not substantial; N/PN if not; NI/NA if unclear.

2. 3 If N/PN to 2.1: Was all information used to classify intervention and comparator groups recorded at or before the time the interventions started?

If N/PN to 2.1: Answer Y/PY if classification data pre-start (e.g., prescription records); N/PN if recall; NI/NA as appropriate.

2. 4 Was classification of intervention status influenced by knowledge of the outcome or risk of the outcome?

Almost always Answer N/NP

2. 5 If N/PN to 2.1 and WY/N/PN/NI 2.4: Was intervention status classified correctly for all, or nearly all, participants?

If N/PN to 2.1 and WY/N/PN/NI to 2.4: Answer Y/PY if classification accurate for most; WN if small misclassification; SN if substantial; NI if unclear; NA if not applicable.

Domain 3 — Bias in selection of participants

3. 1 (=2.1) Did assignment of participants to the intervention group or the comparator group rely on events or measurements that occurred after the start of follow up?

Answer same as **2.1**

3. 2 If Y/PY to 3.1: Were participants excluded after the start of follow-up because they did not meet the definition of either the intervention or the comparator?

If Y/PY to 3.1: Answer Y/PY if exclusions occurred post-start; N/PN if not; NI/NA if unclear.

3. 3 Were start of follow up and start of intervention the same for most participants?

Answer Y/PY if start of follow-up aligns with intervention; N/PN if not; NI/NA if unclear.

3. 4 If N/PN to 3.3: Is the effect of intervention expected to be constant over the time period studied?

Answer Y/PY always

3. 5 Was selection of participants into the study (or into the analysis) based on participant characteristics observed after the start of intervention (additional to the situations addressed in 3.1 and 3.3)?

Answer Y/PY if selection used post-intervention characteristics; N/PN if pre-start only; NI if unclear.

3. 6 If Y/PY to 3.5: Were the post-intervention variables that influenced selection likely to be associated with intervention?

If Y/PY to 3.5: Answer Y/PY if post-intervention variables associated with intervention; N/PN if not; NI/NA as appropriate.

3. 7 If Y/PY to 3.6: Were the post-intervention variables that influenced selection likely to be influenced by the outcome or a cause of the outcome?

If Y/PY to 3.6: Answer Y/PY if variables linked to outcome; N/PN if not; NI/NA as appropriate.

3. 8 If Y/PY to 3.2, N/PN 3.4 or Y/PY to 3.7: Is it likely that the analysis corrected for all of the potential selection biases identified in 3.1-3.2, 3.3-3.4 or 3.5-3.7 above?

Answer Y/PY if analysis corrected selection bias (e.g., IPW, clone-censor-weight); N/PN if not; NI/NA if unclear.

3. 9 If N/PN to 3.8: Did sensitivity analyses demonstrate that the likely impact of the potential selection biases identified in 3.1-3.2, 3.3-3.4 or 3.5-3.7 above was minimal?

If N/PN to 3.8: Answer Y/PY if sensitivity analyses show minimal impact; N/PN if not; NI/NA if unclear.

3. 10 If N/PN to 3.9: Were potential selection biases identified in 3.1-3.2, 3.3-3.4 or 3.5-3.7 above sufficiently severe that the result should not be included in a quantitative synthesis?

If N/PN to 3.9: Answer Y/PY if selection bias so severe exclusion needed; N/PN/NI otherwise.

Domain 4 — Bias due to deviations from intended interventions

4. 1. Was the study undertaken in an experimental context?

Answer N/NP always.

4. 2. If Y/PY to 4.1: Did participants deviate from the intended intervention as a result of the processes of recruiting and engaging them in the study?

If Y/PY to 4.1: Answer Y/PY if study processes caused deviations; N/PN otherwise

4. 3. If Y/PY to 4.1: Did study personnel consciously or unconsciously undermine implementation of the intended interventions?

If Y/PY to 4.1: Answer Y/PY if personnel undermined intervention; N/PN if consistent with normal practice

4. 4. If Y/PY/NI to 4.2 or 4.3: Were these deviations from intended intervention likely to have affected the outcome?

If Y/PY/NI to 4.2/4.3: Answer Y/PY if deviations affect outcome; N/PN if not; NI/NA as appropriate.

4. 5. Was an appropriate analysis used to estimate the effect of assignment to intervention?

Answer Y/PY if analysis includes all regardless of deviations; WN if minor exclusions; SN if exclusions likely bias; NI if unclear.

Domain 5 — Bias due to missing data

5. 1 Were complete data on intervention status available for all, or nearly all, participants?

Answer Y/PY if near-complete intervention data; N/PN if not; NI if missingness unreported.

5. 2 Were complete data on the outcome available for all, or nearly all, participants?

Answer Y/PY if near-complete outcome data; N/PN if not; NI if missingness unreported.

5. 3 Were complete data on important confounding variables available for all, or nearly all, participants?

Answer Y/PY if near-complete confounder data; N/PN if not; NI if unreported.

5. 4 If N/PN/NI to 5.1, 5.2 or 5.3: Is the result based on a complete case analysis?

If N/PN/NI to 5.1–5.3: Answer Y/PY if complete case analysis; N/PN if not; NI/NA if unclear.

5. 5 If Y/PY/NI to 5.4: Was exclusion from the analysis because of missing data (in intervention, confounders or the outcome) likely to be related to the true value of the outcome?

If Y/PY/NI to 5.4: Answer Y/PY if missingness related to outcome; N/PN if not; NI/NA if unclear.

5. 6 If Y/PY/NI to 5.5: Is the relationship between the outcome and missingness likely to be explained by the variables in the analysis model?

If Y/PY/NI to 5.5: Answer Y/PY if explained by model variables; WN if minor residual; SN if major; NI if unclear.

5. 7 If N/PN to 5.4: Was the analysis based on imputing missing values?

If N/PN to 5.4: Answer Y/PY if imputation used; N/PN if not; NI if unclear.

5. 8 If Y/PY to 5.7: Is it reasonable to assume that data were 'missing at random' (MAR) or 'missing completely at random' (MCAR)?

If Y/PY to 5.7: Answer Y/PY if MAR/MCAR assumption reasonable; N/PN if not; NI if unclear.

5. 9 If Y/PY to 5.8: Was imputation performed appropriately?

If Y/PY to 5.8: Answer Y/PY if imputation appropriate; WN if minor issues; SN if poor; NI if unclear.

5. 10 If N/PN/NI to 5.7: Was an appropriate alternative method used to correct for bias due to missing data?

If N/PN/NI to 5.7: Answer Y/PY if alternative method used (e.g., IPW, FIML); WN if minor bias; SN if poor; NI/NA if unclear.

5. 11 If PN/N/NI to 5.1, 5.2 or 5.3 AND (Y/PY/NI to 5.5 OR (Y/PY to 5.8 AND WN/SN/NI to 5.9) OR WN/SN/NI to 5.10): Is there evidence that the result was not biased by missing data?

If concerns remain: Answer Y/PY if sensitivity analyses show no bias; N/PN if not; NI/NA if unclear.

Domain 6 — Bias in measurement of the outcome

6. 1 Could measurement or ascertainment of the outcome have differed between intervention groups?

Answer N/NP always.

6. 2 Were outcome assessors aware of the intervention received by study participants?

Answer N/PN if blinded/objective; Y/PY if assessors aware; NI if unclear.

6. 3 If Y/PY/NI to 6.2: Could assessment of the outcome have been influenced by knowledge of the intervention received?

If Y/PY/NI to 6.2: Answer SY if large impact; WY if small; PN/N if unlikely; NI if unclear.

Domain 7 — Bias in selection of reported result

7. 1 Was the result reported in accordance with an available, pre-determined analysis plan?

Almost always answer **'Yes'** ("**Changes** to analysis plans that were made **before unblinded outcome data** were available, or that were clearly unrelated to the results (e.g., due to a broken machine making data collection impossible) **do not raise concerns** about bias in selection of the reported result.)

Perhaps answer **'No'** in cases of post-hoc analyses

7. 2. multiple outcome measurements (e.g., scales, definitions, time points) within the outcome domain?

Answer N/PN always due to the nature of the outcomes (retained gastric content, aspiration, procedure abortion).

7. 3. multiple analyses of the data?

To answer this question check for consistency between Methods and Results in terms of:

- Type of outcome analysis

'No' if there is consistency between Methods and Results (usually the case for pre-defined outcomes)

'Yes' if there is not consistency between Methods and Results

'No Information' for non pre-defined outcomes

7. 4. multiple subgroups?

Answer N/PN always if subgroup analysis is clinically relevant/in line with methods section

Supplementary Table 1 PRISMA checklist

Section and Topic	Item #	Checklist item	Location where item is reported
		TITLE	
Title	1	Identify the report as a systematic review.	1
		ABSTRACT	
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	2
		INTRODUCTION	
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	3
Objectives	4	Provide an explicit statement of the objective (s) or question (s) the review addresses.	3
		METHODS	
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	4
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	4
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Appendix
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	4
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	4,5
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g., for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	4
	10b	List and define all other variables for which data were sought (e.g., participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	4,5
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool (s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	5
Effect measures	12	Specify for each outcome the effect measure (s) (e.g., risk ratio, mean difference) used in the synthesis or presentation of results.	5
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g., tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	5
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	5
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	5
	13d	Describe any methods used to synthesize results and provide a rationale for the choice (s). If meta-analysis was performed, describe the model (s), method (s) to identify the presence and extent of statistical heterogeneity, and software package (s) used.	5
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g., subgroup analysis, meta-regression).	6
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	6
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	5
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	6

(*Contd...*)

Supplementary Table 1 (*Continued*)

Section and Topic	Item #	Checklist item	Location where item is reported
		RESULTS	
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	6
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	6
Study characteristics	17	Cite each included study and present its characteristics.	7,8
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Appendix
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g., confidence/credible interval), ideally using structured tables or plots.	7,8
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	7,8
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g., confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	7,8
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	7,8
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	7,8
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	7,8
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	8,9
		DISCUSSION	
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	9
	23b	Discuss any limitations of the evidence included in the review.	9,10
	23c	Discuss any limitations of the review processes used.	9,10
	23d	Discuss implications of the results for practice, policy, and future research.	10-12
		OTHER INFORMATION	
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	1
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	3
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	NA
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	1
Competing interests	26	Declare any competing interests of review authors.	1
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	1

Supplementary Table 2 MOOSE checklist

Item No	Recommendation	Reported on Page No
	Reporting of background should include	
1	Problem definition	3
2	Hypothesis statement	3
3	Description of study outcome (s)	4
4	Type of exposure or intervention used	4
5	Type of study designs used	4
6	Study population	4
	Reporting of search strategy should include	
7	Qualifications of searchers (eg, librarians and investigators)	NA
8	Search strategy, including time period included in the synthesis and key words	Appendix
9	Effort to include all available studies, including contact with authors	4
10	Databases and registries searched	4
11	Search software used, name and version, including special features used (eg, explosion)	4
12	Use of hand searching (eg, reference lists of obtained articles)	4
13	List of citations located and those excluded, including justification	Figure 1
14	Method of addressing articles published in languages other than English	4
15	Method of handling abstracts and unpublished studies	4
16	Description of any contact with authors	4
	Reporting of methods should include	
17	Description of relevance or appropriateness of studies assembled for assessing the hypothesis to be tested	4
18	Rationale for the selection and coding of data (eg, sound clinical principles or convenience)	4
19	Documentation of how data were classified and coded (eg, multiple raters, blinding and interrater reliability)	NA
20	Assessment of confounding (eg, comparability of cases and controls in studies where appropriate)	4,5
21	Assessment of study quality, including blinding of quality assessors, stratification or regression on possible predictors of study results	4
22	Assessment of heterogeneity	5,6
23	Description of statistical methods (eg, complete description of fixed or random effects models, justification of whether the chosen models account for predictors of study results, dose-response models, or cumulative meta-analysis) in sufficient detail to be replicated	5
24	Provision of appropriate tables and graphics	6-9, appendix
	Reporting of results should include	
25	Graphic summarizing individual study estimates and overall estimate	6-9
26	Table giving descriptive information for each study included	Table 1
27	Results of sensitivity testing (eg, subgroup analysis)	6-9, appendix
28	Indication of statistical uncertainty of findings	6-9, appendix
	Reporting of discussion should include	
29	Quantitative assessment of bias (eg, publication bias)	8
30	Justification for exclusion (eg, exclusion of non-English language citations)	Figure 1
31	Assessment of quality of included studies	8
	Reporting of conclusions should include	
32	Consideration of alternative explanations for observed results	10-12
33	Generalization of the conclusions (ie, appropriate for the data presented and within the domain of the literature review)	10-12
34	Guidelines for future research	10-12
35	Disclosure of funding source	1

Supplementary Table 3 Search strategy, Medline via PubMed

#	Search term
1	Glucagon-Like Peptide 1[MeSH Terms]
2	(glp-1) OR (glp1) OR (glp 1)
3	(semaglutide) OR (dulaglutide) OR (liraglutide) OR (exenatide) OR (tirzepatide)
4	1-3/OR
5	endoscopy
6	4 AND 5

Supplementary Table 4 Search strategy, Cochrane library

#	Search term
1	MeSH descriptor: [Glucagon-Like Peptide 1] explode all trees
2	(semaglutide) OR (dulaglutide) OR (liraglutide) OR (exenatide) OR (tirzepatide)
3	#1 OR #2
4	endoscopy
5	#3 AND #4

Supplementary Table 5 Fasting duration and dietary instructions in included studies

Author, year [ref.]	Fasting duration and dietary instructions
Abu-Freha 2024 [19]	NR
Alkabbani 2024 [11]	NR
Ayoub 2024 [20]	NR
Bahdi 2024 [21]	24-hour liquid diet before the procedure (applicable to colonoscopy only?)
Barlowe 2025 [22]	NR
Chapman 2024 [23]	NPO > 10 hours for solids NPO for 2 hours for liquids
Dev 2025 [24]	Fasting from solid food for 8 hours before the procedure Clear liquids for 2 hours before the procedure
Elliott 2024 [25]	NR
Garza 2024 [26]	Fasting period of minimum 7 hours (for upper endoscopy). Restricted, clear liquid diet the day before and fasting from solids for at least 30 hours (for concurrent colonoscopy)
Gonzaga 2024 [27]	2 hours fasting for clear liquids 6 hours fasting for solids
Gu 2025 [28]	Fasting at midnight before the procedure
Hernandez 2024 [29]	NR
Karlson 2024 [30]	NR
Kobori 2023 [31]	Fasting ≥ 12 hours prior to the procedure
Markley 2024 [32]	NR
Meluban 2024 [33]	NR
Nadeem 2024 [34]	NR
Nasser 2024 [35]	NR
Panchal 2025 [36]	Fasting for at least 8 hours
Peng 2024 [37]	NR
Quinn 2025 [38]	Fasting for ≥ 2 hours for clear fluids Fasting for ≥ 8 hours for solids
Rizvi 2024 [39]	NR
Stark 2022 [40]	NR
Wu 2024 [41]	Fasting for ≥ 8 hours

NOS Nil per os: NR: not reported

Supplementary Table 6 Risk of bias assessment for the incidence of retained gastric content

Author [ref.]	Year	Bias due to confounding	Bias in classification of interventions	Bias in selection of participants into the study (or analysis)	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of the outcome	Bias in selection of the reported result	Overall
Abu-Freha *et al* [19]	2024	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Ayoub *et al* [20]	2024	SERIOUS	LOW	LOW	SERIOUS	MODERATE	LOW	LOW	SERIOUS
Bahdi *et al* [21]	2024	SERIOUS	MODERATE	LOW	MODERATE	MODERATE	LOW	LOW	SERIOUS
Chapman *et al* [23]	2024	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Elliott *et al* [25]	2024	SERIOUS	MODERATE	LOW	MODERATE	MODERATE	LOW	LOW	SERIOUS
Garza *et al* [26]	2024	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Gonzaga *et al* [27]	2024	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Gu *et al* [28]	2025	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Hernandez *et al* [29]	2024	LOW	LOW	LOW	LOW	MODERATE	LOW	LOW	MODERATE
Karlson *et al* [30]	2024	LOW	LOW	LOW	LOW	MODERATE	LOW	LOW	MODERATE
Kobori *et al* [31]	2023	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Markley *et al* [32]	2024	LOW	LOW	LOW	LOW	MODERATE	LOW	LOW	MODERATE
Meluban *et al* [33]	2024	SERIOUS	LOW	LOW	LOW	MODERATE	LOW	LOW	SERIOUS
Nadeem *et al* [34]	2024	LOW	MODERATE	LOW	LOW	LOW	LOW	LOW	MODERATE
Nasser *et al* [35]	2024	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Panchal *et al* [36]	2025	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Quinn *et al* [38]	2025	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Rizvi *et al* [39]	2024	LOW	LOW	LOW	LOW	MODERATE	LOW	LOW	MODERATE
Stark *et al* [40]	2022	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Wu *et al* [41]	2024	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW

Supplementary Table 7 Risk of bias assessment for the incidence of aspiration

Author [ref.]	Year	Bias due to confounding	Bias in classification of interventions	Bias in selection of participants into the study (or analysis)	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of the outcome	Bias in selection of the reported result	Overall
Alkabbani *et al* [11]	2024	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Barlowe *et al* [22]	2025	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Markley *et al* [32]	2024	LOW	LOW	LOW	LOW	MODERATE	LOW	LOW	MODERATE
Nadeem *et al* [34]	2024	LOW	MODERATE	LOW	LOW	LOW	LOW	LOW	MODERATE
Peng *et al* [37]	2024	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Quinn *et al* [38]	2025	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Wu *et al* [41]	2024	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW

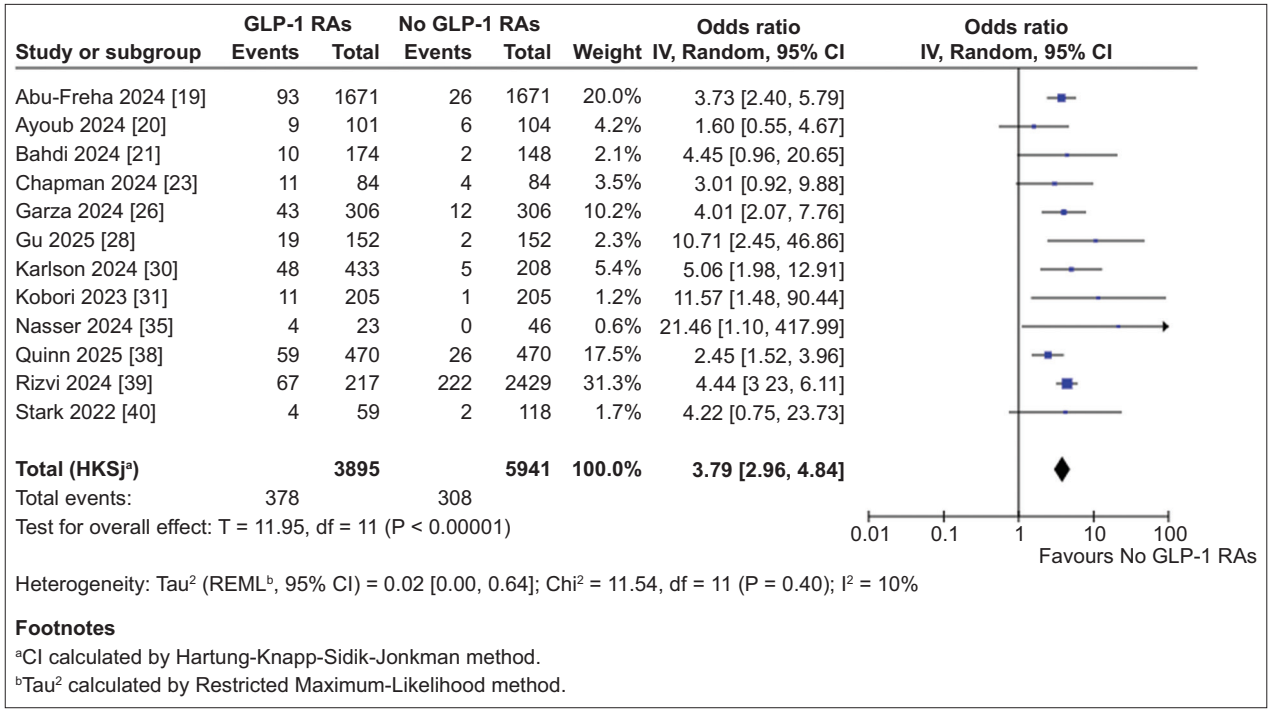
Supplementary Table 8 Risk of bias assessment for the incidence of procedure discontinuation

Author [ref.]	Year	Bias due to confounding	Bias in classification of interventions	Bias in selection of participants into the study (or analysis)	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of the outcome	Bias in selection of the reported result	Overall
Alkabbani *et al* [11]	2024	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Ayoub *et al* [20]	2024	SERIOUS	LOW	LOW	SERIOUS	MODERATE	LOW	LOW	SERIOUS
Bahdi *et al* [21]	2024	SERIOUS	MODERATE	LOW	MODERATE	MODERATE	LOW	LOW	SERIOUS
Chapman *et al* [23]	2024	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Dev *et al* [24]	2025	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Gonzaga *et al* [27]	2024	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW
Hernandez *et al* [29]	2024	LOW	LOW	LOW	LOW	MODERATE	LOW	LOW	MODERATE
Karlson *et al* [30]	2024	LOW	LOW	LOW	LOW	MODERATE	LOW	LOW	MODERATE
Nadeem *et al* [34]	2024	LOW	MODERATE	LOW	LOW	LOW	LOW	LOW	MODERATE
Panchal *et al* [36]	2025	LOW	LOW	LOW	LOW	LOW	LOW	LOW	LOW

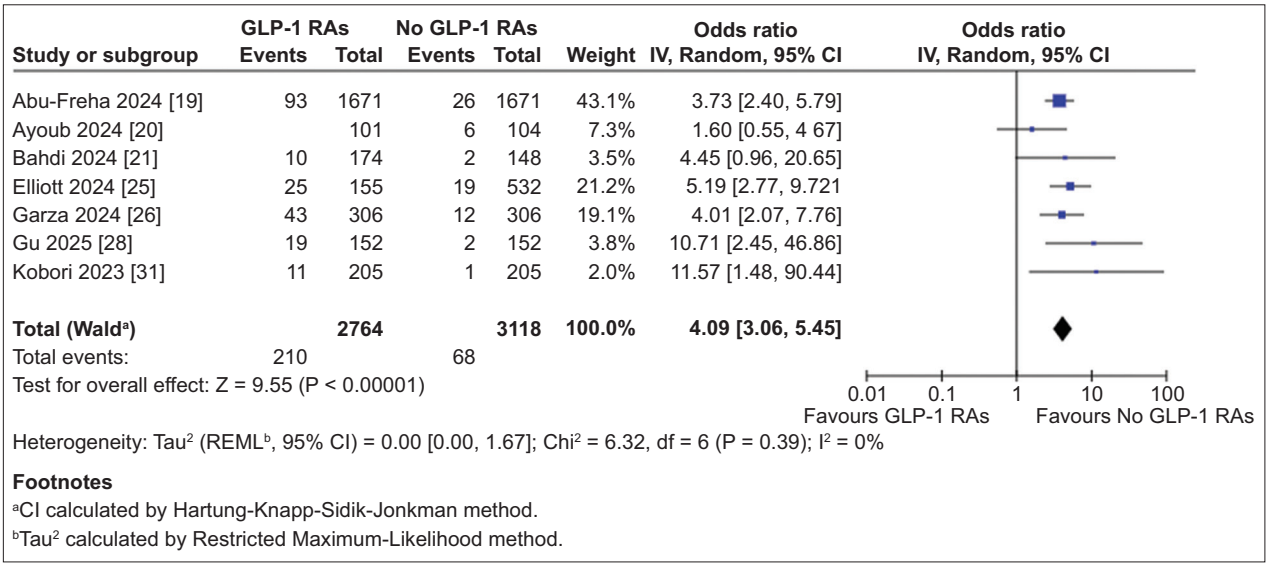
Supplementary Table 9 Certainty in effect estimates for primary analyses

Certainty assessment							No of patients		Effect		Certainty
No of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	[Intervention]	[Comparison]	Relative (95% CI)	Absolute (95% CI)	
						Retained gastric content					
20	Non-randomised studies	Not serious	Serious[a]	Serious[b]	Very serious[c]	Strong association all plausible residual confounding would suggest spurious effect	620/5619 (11.0%)	1208/45299 (2.7%)	**OR 4.82** (3.66 to 6.35)	90 more per 1,000 (from 64 more to 122 more)	⊕◯◯◯ Very Low
						Aspiration					
7	Non-randomised studies	Not serious	Not serious	Serious[b]	Very serious[c]	All plausible residual confounding would suggest spurious effect, while no effect was observed	210/53732 (0.4%)	168/80368 (0.2%)	**OR 1.11** (0.84 to 1.48)	**0 fewer per 1,000** (from 0 fewer to 1 more)	⊕◯◯◯ Very Low
						Procedure discontinuation					
10	Non-randomised studies	Not serious	Serious[d]	Serious[b]	Very serious[c]	Strong association all plausible residual confounding would suggest spurious effect, while no effect was observed	291/28394 (1.0%)	246/87761 (0.3%)	**OR 3.93** (2.42 to 6.39)	**8 more per 1,000** (from 4 more to 15 more)	⊕◯◯◯ Very Low

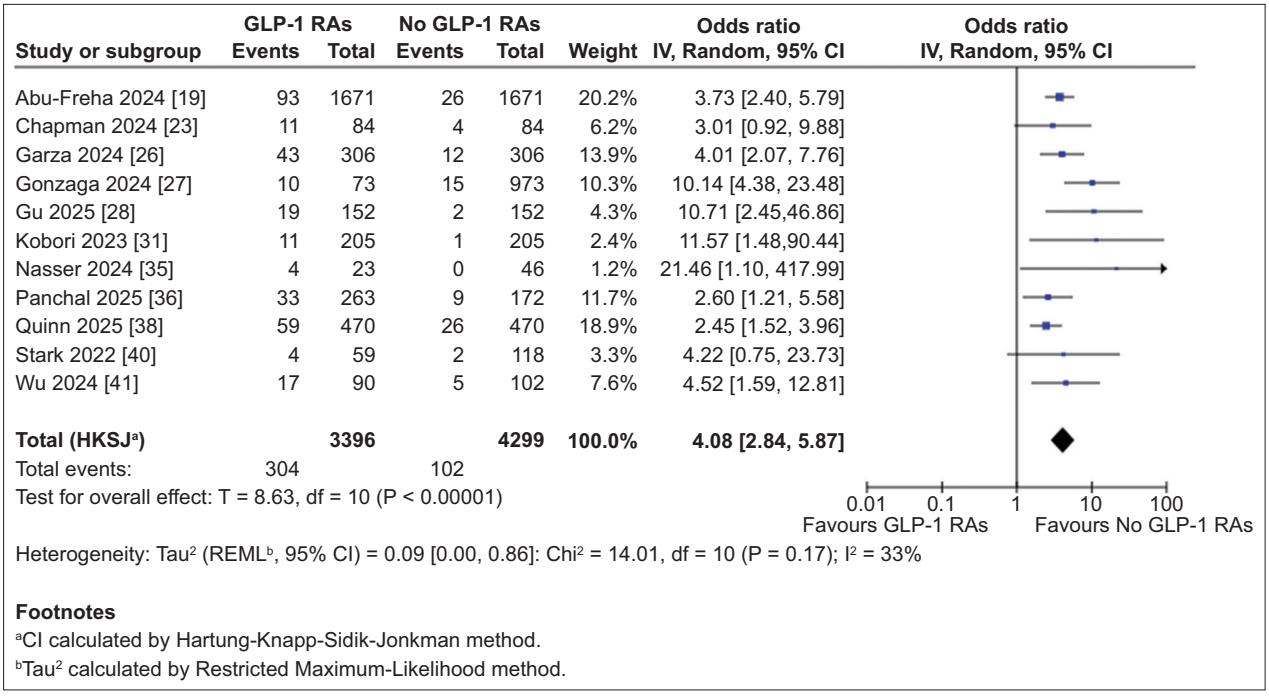
a. Increased heterogeneity in main analysis (Figure 2). b. Mainly due to differences in fasting protocols among studies and inclusion/exclusion criteria. c. Mainly due to the limited number of events in both arms.
d. Increased heterogeneity in main analysis (Figure 4). e. Downgrade by 1 level for all outcomes because of study design



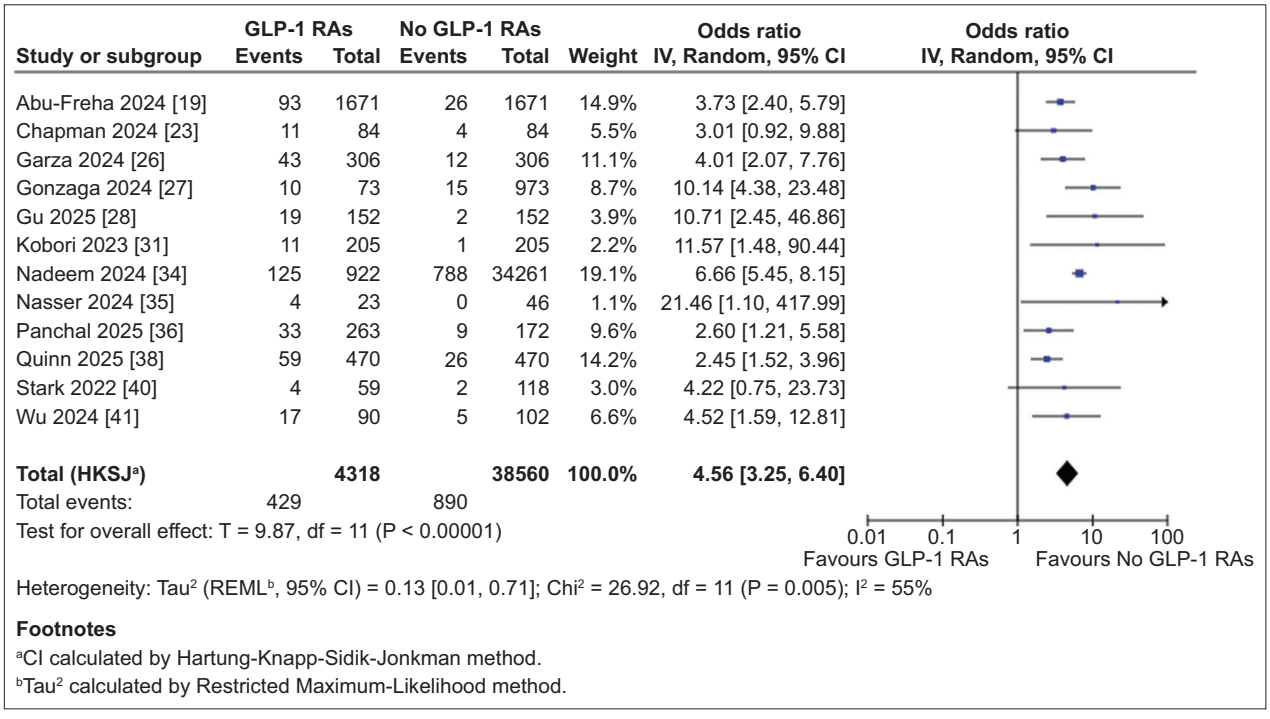
Supplementary Figure 1 Sensitivity analysis restricted to studies employing propensity score matching to control for baseline confounders: Retained gastric content
GLP-1 RAs, glucagon-like peptide 1 receptor agonists; CI, confidence interval



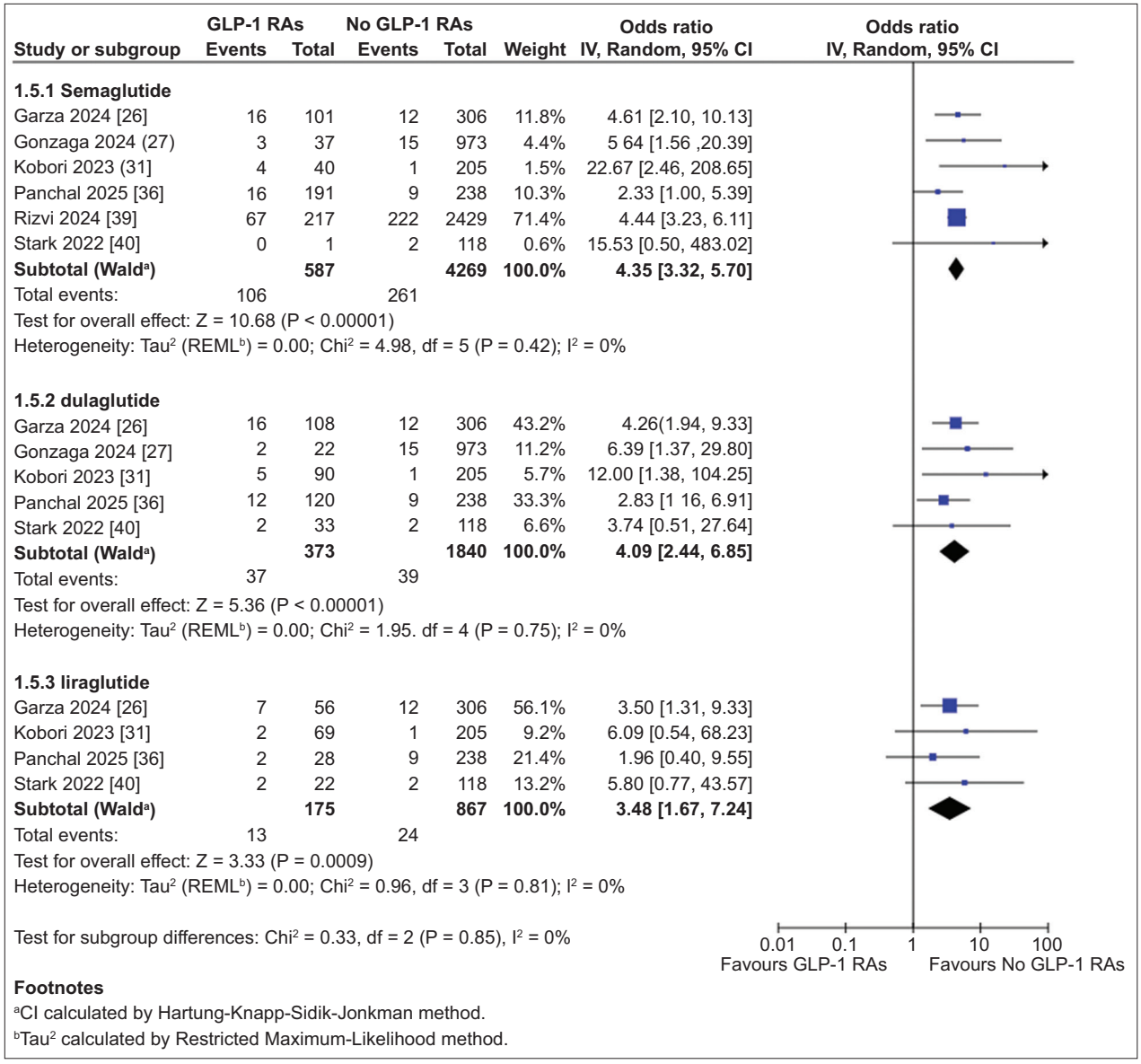
Supplementary Figure 2 Sensitivity analysis restricted to studies enrolling only participants with type 2 diabetes: Retained gastric content
GLP-1 RAs, glucagon-like peptide 1 receptor agonists; CI, confidence interval



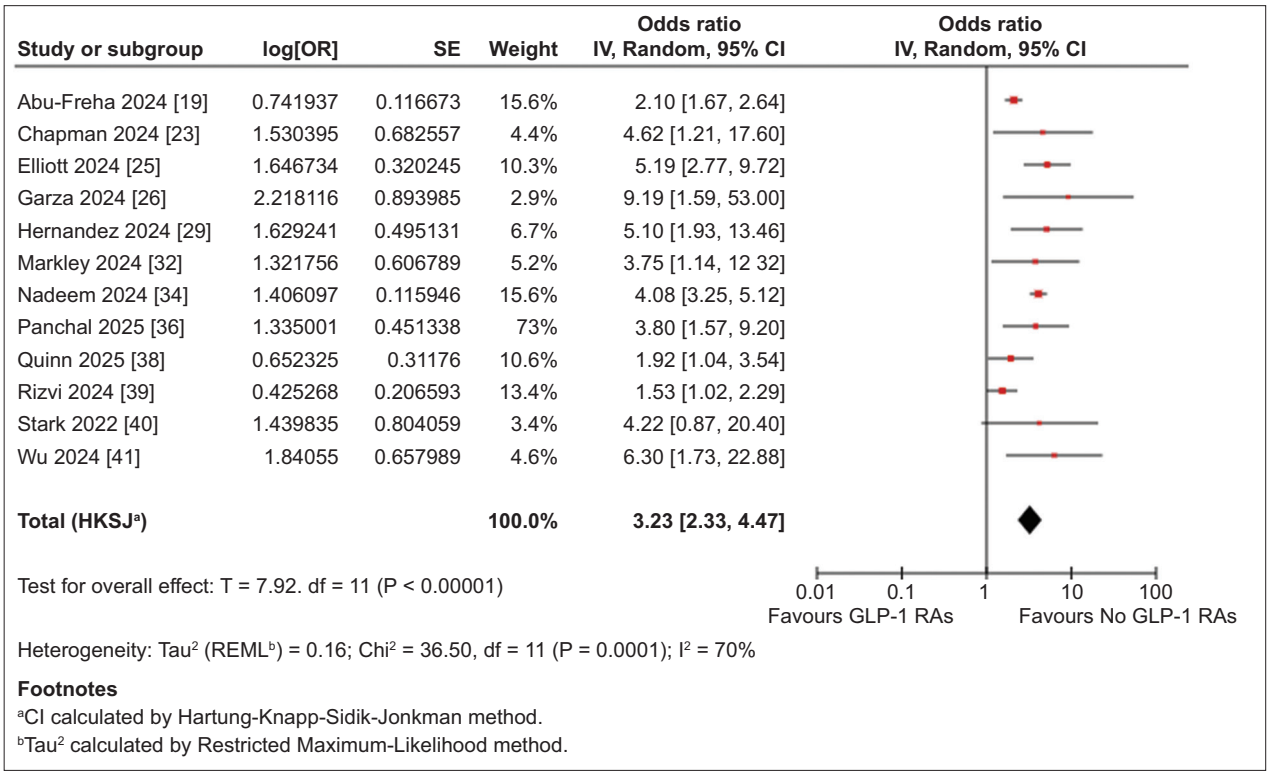
Supplementary Figure 3 Sensitivity analysis including only studies at low risk of bias: Retained gastric content
GLP-1 RAs, glucagon-like peptide 1 receptor agonists; CI, confidence interval



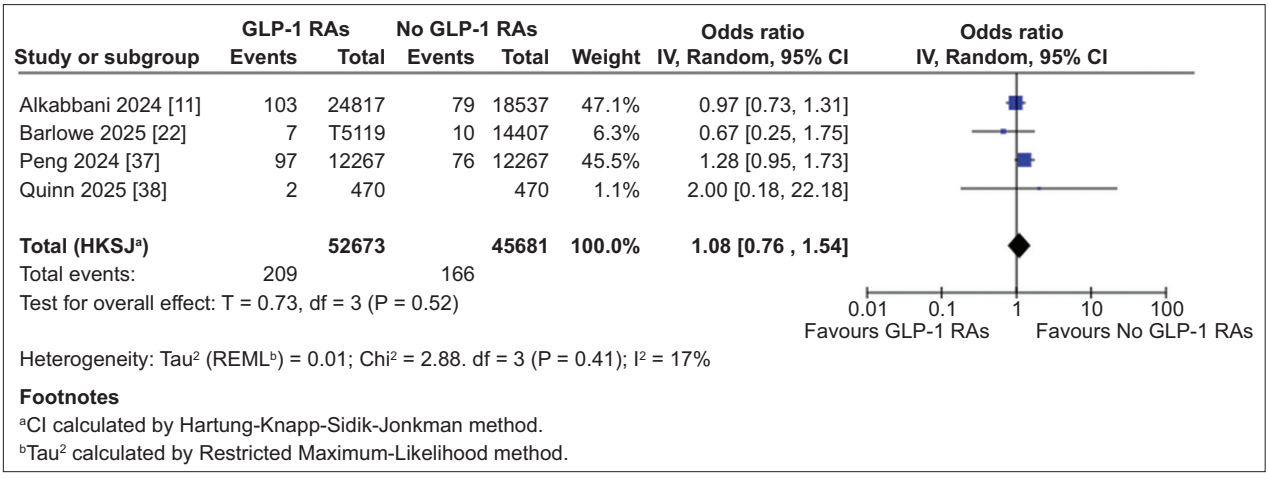
Supplementary Figure 4 Sensitivity analysis including only studies published as full texts: Retained gastric content
GLP-1 RAs, glucagon-like peptide 1 receptor agonists; CI, confidence interval



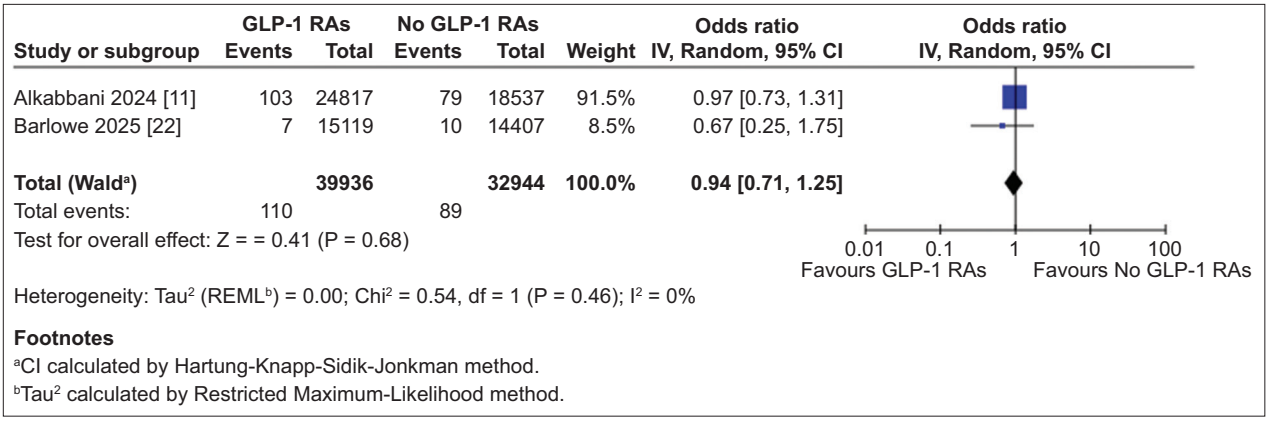
Supplementary Figure 5 Subgroup analyses based on the different GLP-1 RAs: Retained gastric content
GLP-1 RAs, glucagon-like peptide 1 receptor agonists; CI, confidence interval



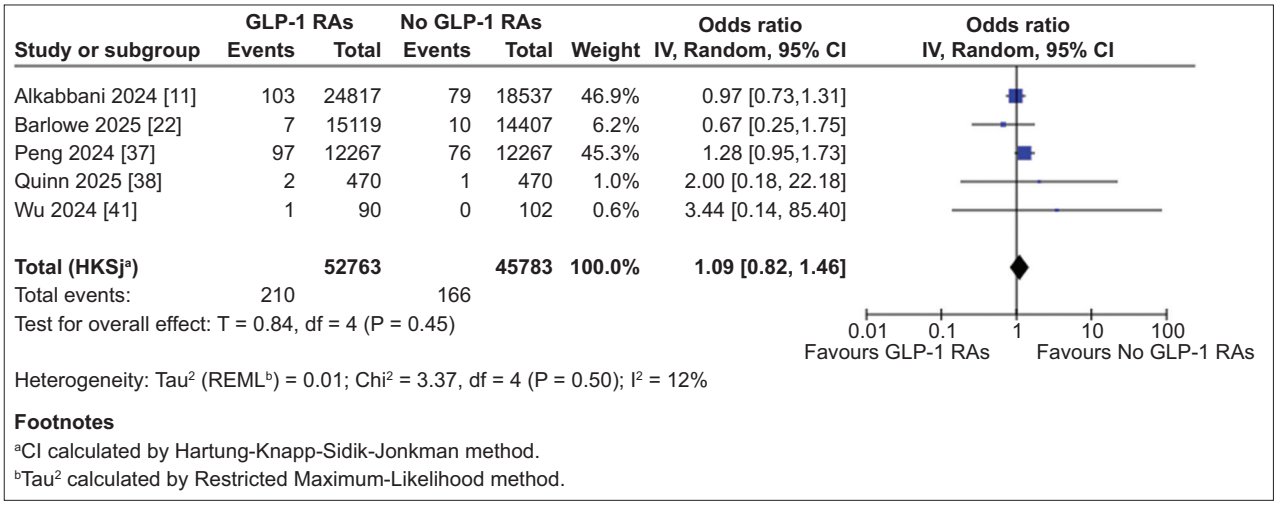
Supplementary Figure S6 Meta analyses of adjusted odds ratios: Retained gastric content
GLP-1 RAs, glucagon-like peptide 1 receptor agonists; CI, confidence interval



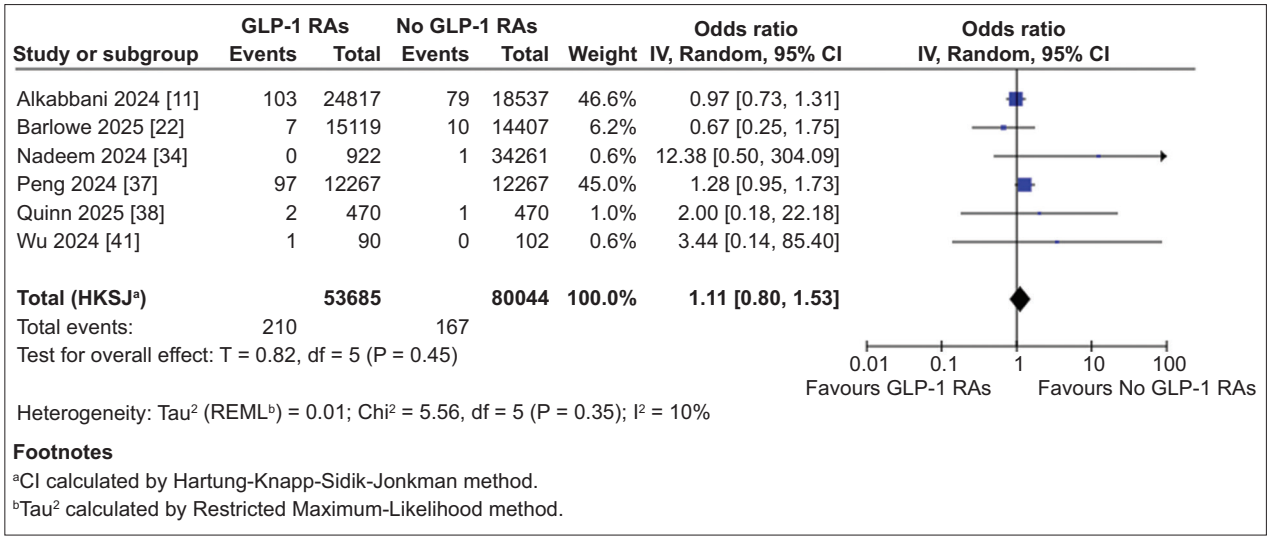
Supplementary Figure 7 Sensitivity analysis restricted to studies employing propensity score matching to control for baseline confounders: Aspiration
GLP-1 RAs, glucagon-like peptide 1 receptor agonists; CI, confidence interval



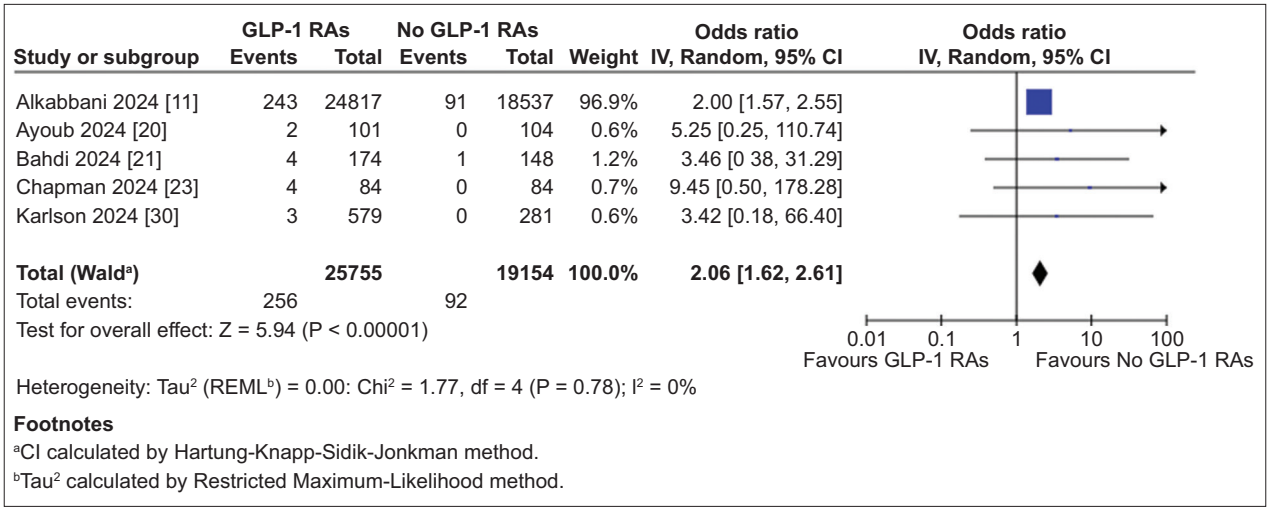
Supplementary Figure 8 Sensitivity analysis restricted to studies enrolling only participants with type 2 diabetes: Aspiration
GLP-1 RAs, glucagon-like peptide 1 receptor agonists; CI, confidence interval



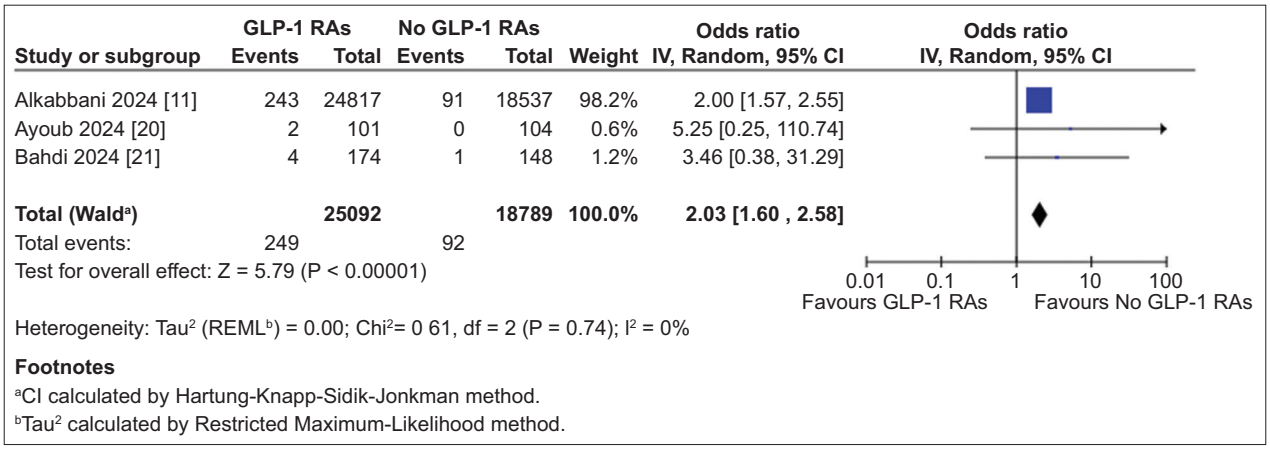
Supplementary Figure 9 Sensitivity analysis including only studies at low risk of bias: Aspiration
GLP-1 RAs, glucagon-like peptide 1 receptor agonists; CI, confidence interval



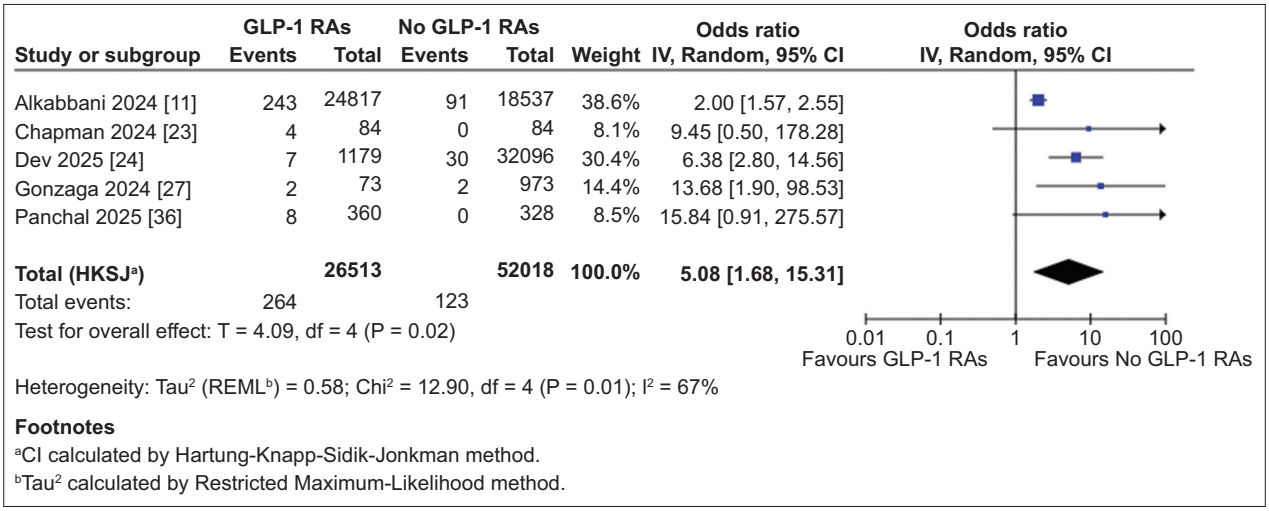
Supplementary Figure 10 Sensitivity analysis including only studies published as full texts: Aspiration
GLP-1 RAs, glucagon-like peptide 1 receptor agonists; CI, confidence interval



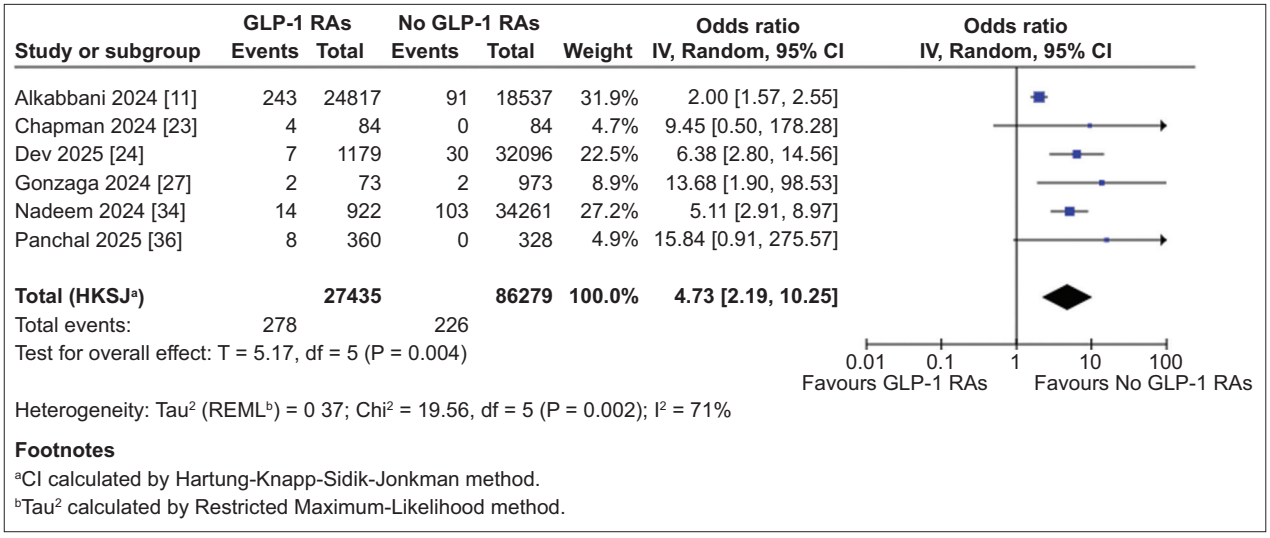
Supplementary Figure 11 Sensitivity analysis restricted to studies employing propensity score matching to control for baseline confounders: Procedure discontinuation
GLP-1 RAs, glucagon-like peptide 1 receptor agonists; CI, confidence interval



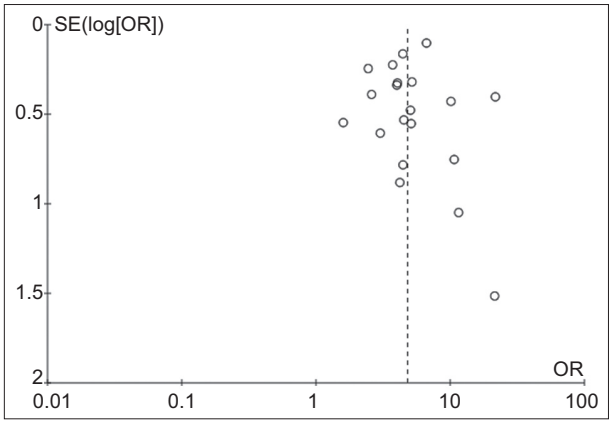
Supplementary Figure 12 Sensitivity analysis restricted to studies enrolling only participants with type 2 diabetes: Procedure discontinuation
GLP-1 RAs, glucagon-like peptide 1 receptor agonists; CI, confidence interval



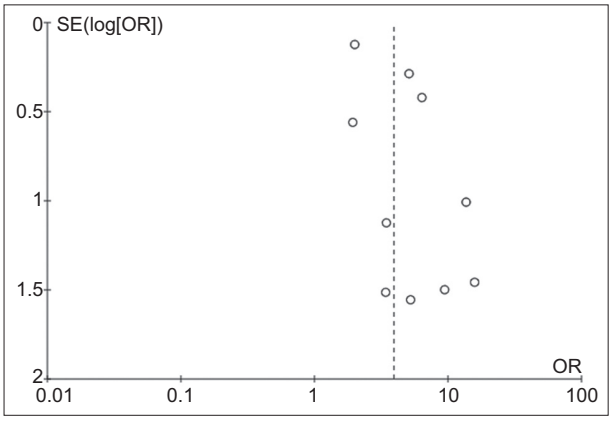
Supplementary Figure 13 Sensitivity analysis including only studies at low risk of bias: Procedure discontinuation
GLP-1 RAs, glucagon-like peptide 1 receptor agonists; CI, confidence interval



Supplementary Figure 14 Sensitivity analysis including only studies published as full texts: Procedure discontinuation
GLP-1 RAs, glucagon-like peptide 1 receptor agonists; CI, confidence interval



Supplementary Figure 15 Funnel plot for incidence of retained gastric content
SE, standard error; OR, odds ratio



Supplementary Figure 16 Funnel plot for incidence of procedure abortion
SE, standard error; OR, odds ratio