Author/s:
Elkin, J;Rele, S;Sumithran, P;Hii, M;Thuraisingam, S;Spelman, T;Phan, T;Choong, P;Dowsey, M;Shadbolt, C

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Review Article

# Association between glucagon-like peptide-1 receptor agonist use and peri-operative pulmonary aspiration: a systematic review and meta-analysis

**Jasmin Elkin, Siddharth Rele, Priya Sumithran, Michael Hii, Sharmala Thuraisingam, Tim Spelman, Tuong Phan, Peter Choong, Michelle Dowsey** and **Cade Shadbolt**

## Summary

**Introduction** Glucagon-like peptide-1 receptor agonists are known to delay gastric emptying; however, the association between glucagon-like peptide-1 receptor agonist use and peri-operative pulmonary aspiration risk is not known. This systematic review and meta-analysis aimed to summarise the evidence on whether glucagon-like peptide-1 receptor agonist exposure is associated with pulmonary aspiration or increased residual gastric content in fasted patients undergoing procedures requiring anaesthesia or sedation.

**Methods** We searched six databases for studies assessing peri-operative pulmonary aspiration or residual gastric contents in fasted patients or volunteers who were using any form of glucagon-like peptide-1 receptor agonist. Pooled odds ratios were estimated for each outcome using random effects meta-analysis. Certainty of evidence for each outcome was assessed using the GRADE framework.

**Results** Of 9010 screened studies, 28 observational studies were included. In a meta-analysis of nine studies involving 185,414 patients and 471 cases of pulmonary aspiration, glucagon-like peptide-1 receptor agonist exposure was not associated with pulmonary aspiration (OR 1.04, 95%CI 0.87–1.25, low certainty of evidence). In a meta-analysis of 18 studies involving 165,522 patients and 3831 cases of residual gastric contents, glucagon-like peptide-1 receptor agonist exposure was associated with an increased risk of residual gastric contents despite appropriate fasting (odds ratio 5.96, 95%CI 3.96–8.98, low certainty of evidence). In a meta-analysis of five studies involving 1706 patients and 208 cases of residual gastric contents, withholding at least one dose of glucagon-like peptide-1 receptor agonist before a procedure was associated with lower odds of residual gastric contents (odds ratio 0.51, 95%CI 0.33–0.81, very low certainty of evidence).

**Discussion** Patients using glucagon-like peptide-1 receptor agonists are at increased risk of presenting for anaesthesia with residual gastric contents, though the available evidence does not indicate that this translates to an increased risk of pulmonary aspiration.

For full author affiliations, see end of article
Correspondence to: Cade Shadbolt
Email: cade.shadbolt@unimelb.edu.au
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X: @UniMelbMDHS

## Introduction

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are used widely for the management of obesity and type 2 diabetes [1]. This group of drugs slows the rate of post-prandial gastric emptying [2–4] and there have been recent case reports of patients who are taking these drugs before surgery having pulmonary aspiration or increased residual gastric contents despite appropriate fasting [5–14]. This has led various professional organisations to acknowledge that patients taking these drugs may be at an increased risk of pulmonary aspiration or regurgitation during the peri-operative period [15–18]. In response, safety-related warnings regarding pulmonary aspiration risks in patients undergoing elective procedures were added to GLP-1 RA labels in November 2024 [19]. A further safety update was issued by the Medicines and Healthcare products Regulatory Agency in January 2025, emphasising the widespread nature of these concerns [20].

Currently, multi-societal consensus statements across the UK, USA and Australia support a shared decision-making approach for minimising risk among patients using GLP-1 RAs [18, 21, 22]. However, there remains variation in the specific interventions recommended in these consensus statements. Some professional bodies recommend considering withholding GLP-1 RAs before surgery but emphasise that there is limited evidence available about the effectiveness of this strategy [16, 21–23]. Moreover, concerns have been raised about the risks associated with requiring an extended period of withdrawal, which may result in worsening glycaemic control among patients managing type 2 diabetes [18, 21, 24, 25]. Alternative strategies, including changing pre-operative fasting guidance, using prokinetic drugs and implementing routine point-of-care ultrasound to mitigate risk, have been suggested, but their effectiveness also remains uncertain [21, 26].

Previous systematic reviews have examined the risk of pulmonary aspiration or residual gastric contents among patients using GLP-1 RAs, but they have been limited to patients undergoing endoscopic procedures [27–29] or those temporarily exposed to GLP-1 RAs during the immediate peri-operative period [30]. To address uncertainty, this systematic review aimed to summarise the available evidence on whether GLP-1 RA exposure is associated with pulmonary aspiration or increased residual gastric contents in fasted patients undergoing procedures requiring anaesthesia or sedation. This review also aimed to synthesise the evidence on whether withholding GLP-1 RAs is associated with reductions in the risk of pulmonary aspiration or the presence of residual gastric contents in fasted patients.

## Methods

We conducted a systematic review and meta-analysis and reported it according to the PRISMA statement and meta-analyses of observational studies in epidemiology (MOOSE) reporting guidelines [31, 32]. Deviations and clarifications to the initial protocol are shown in online Supporting Information Table S1.

We searched MEDLINE, Embase, Web of Science and Cochrane Central on 19 March 2024 and updated this search on 13 January 2025 (online Supporting Information Appendix S1). The search was limited to studies published from 2005 onwards, as this was the year of the first approval of a GLP-1 RA by the US Food and Drug Administration. The clinicaltrials.gov and World Health Organisation registries were searched on the same dates for information on unpublished or ongoing studies. Forward and backwards citation tracking of included studies was last updated on 14 January 2025 using an automated online platform that has been described previously [33].

Randomised controlled trials and observational studies were included if they reported on the association between pre-operative GLP-1 RA use and the risk of pulmonary aspiration in fasted patients undergoing anaesthesia or procedural sedation, or residual gastric contents in fasted patients undergoing procedures requiring anaesthesia or procedural sedation, or in healthy volunteers who had fasted for at least 6 h from solid foods and at least 2 h from clear liquids, in accordance with standard pre-operative fasting requirements [34].

Studies were not included if fasting duration was not reported, except for studies involving elective procedures where fasting was assumed to be a requirement. We did not include studies which measured post-prandial gastric emptying rate (e.g. scintigraphy) rather than residual gastric content in the fasted state, and studies where the GLP-1 RA was commenced in the immediate peri-operative period (i.e. within 14 days before the procedure or outcome measurement). Non-English studies and conference abstracts were not included. When multiple studies were derived from overlapping samples, each study was included in the narrative summary, though only the study with the lowest risk of bias across all six domains was included in pooled estimates. When the same study was reported across multiple publications, only the most recent publication was included. Ongoing or completed studies without published results were identified during screening

but not included in the quantitative synthesis. Studies were screened independently and in duplicate by two authors (JE and SR) using the Covidence systematic review software (Covidence, Melbourne, VIC, Australia), with disagreements adjudicated by a third author. Reasons for not including studies were reported, and study authors were contacted to provide further information if eligibility was unclear.

Pulmonary aspiration included direct measures of peri-operative pulmonary aspiration or postoperative respiratory complications that were directly attributed to aspiration (e.g. aspiration pneumonitis). Estimates based on pulmonary complications more generally did not meet this outcome definition. While the inclusion of pulmonary complications that were not explicitly linked to pulmonary aspiration may have provided additional capture of sub-clinical cases of aspiration, the value of such a broad definition as a surrogate for aspiration risk has not been established. Residual gastric content included gastric residue identified via direct visualisation during endoscopy of the upper gastrointestinal tract or gastric contents identified via ultrasound. Individual outcome definitions as described by the study authors are presented in online Supporting Information Tables S2 and S3.

Trial characteristics and outcome data were extracted independently and in duplicate by two authors (JE and CS), with disagreements adjudicated by a third author, using a structured data extraction template. Adjusted odds ratios (OR) were the preferred effect estimates included in the meta-analyses of both outcomes. For estimates relating to aspiration, adjusted measures of relative risk (RR) were treated as adjusted ORs, as odds approximate risk for low event rates [35]. When adjusted estimates were not reported, unadjusted ORs were calculated from the reported number of aspiration events in patients with and

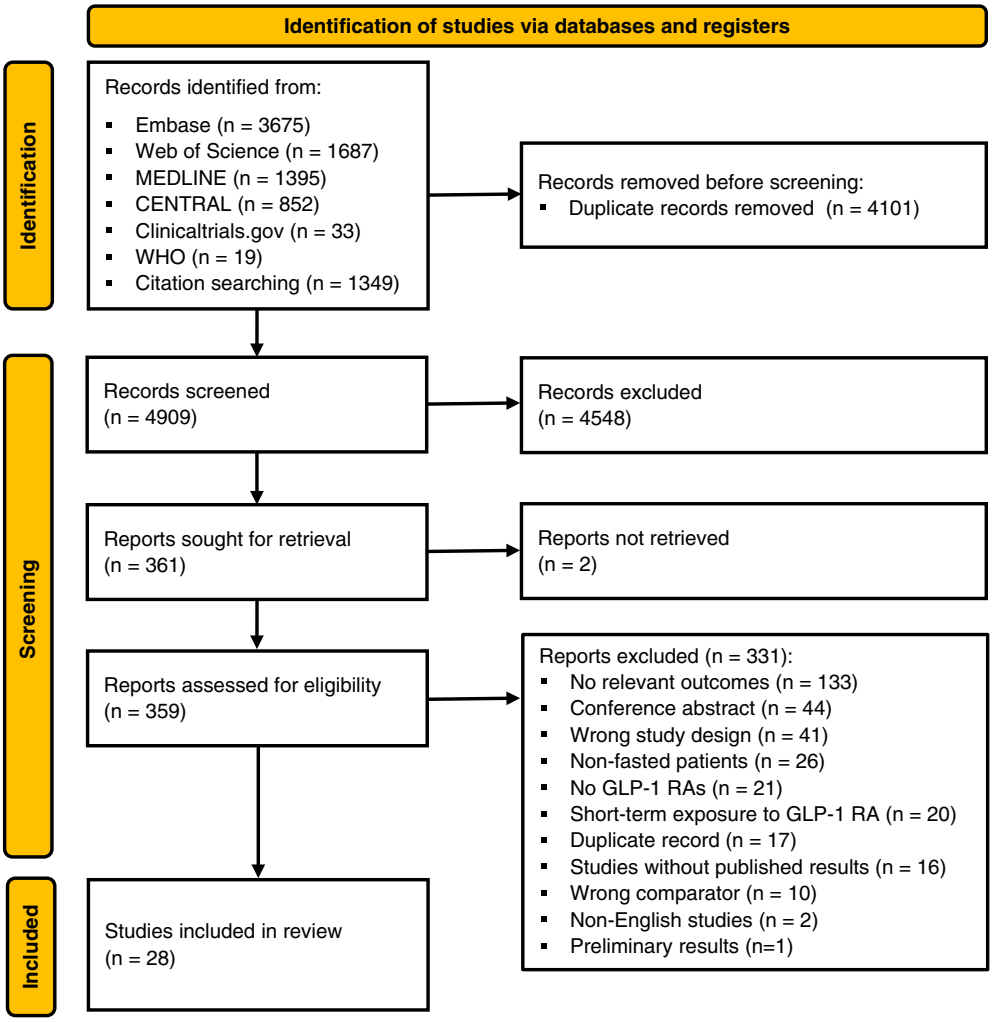


**Figure 1** Study flow diagram. GLP-1 RA, glucagon-like peptide-1 receptor agonist.

without GLP-1 RA exposure. For studies with no events in at least one group, we added a continuity correction value to both groups that was inversely proportional to the sample size of the other study group [35, 36]. For estimates relating to residual gastric contents, adjusted RRs were not treated as analogous to ORs, as this is a more common outcome. Study authors were contacted to provide adjusted ORs if multivariable analyses were reported alongside other measures of effect (online Supporting Information Table S4). When adjusted ORs could not be obtained, unadjusted ORs were calculated directly from the reported number of patients with residual gastric contents in exposed and unexposed groups.

Risk of bias assessment was conducted independently and in duplicate by two authors (JE and CS) for each effect estimate rather than once per study [37], with disagreements adjudicated by a third author. For studies examining the association between pre-operative GLP-1 RA exposure compared with no exposure and the risk of pulmonary aspiration or residual gastric contents, we used a modified quality in prognosis studies tool [38, 39]. For estimates of the association between withholding at least one dose of GLP-1 RA and the study outcomes, we used the ROBINS-I tool. In line with ROBINS-I recommendations, studies judged to be at critical risk of bias were not included in the meta-analyses [40]. For each of the included studies, bias due to confounding was evaluated by consideration of adjustment for important variables, including age; sex; BMI; diabetes; ASA physical status; drugs associated with delaying gastric emptying; and comorbidities.

Effect estimates for pulmonary aspiration and residual gastric contents were pooled separately. Pooled odds ratios and 95%CI were calculated via random effect meta-analysis using the restricted maximum likelihood heterogeneity variance estimator [41, 42]. Heterogeneity was assessed by estimating the $I^2$ statistic. Funnel plots were assessed visually for evidence of small study bias, and the robustness of estimates to worst-case publication bias was assessed by conducting meta-analyses of only non-affirmative studies (i.e. studies with confidence intervals that overlap the null value) [43]. Overall certainty of evidence for each pooled

**Table 1** Characteristics of included studies. Values are number.

| | **Pulmonary aspiration n = 11** | **Residual gastric content n = 20** |
|---|---|---|
| **Country** | | |
| Brazil | 1 | 4 |
| Canada | 1 | 0 |
| Israel | 0 | 1 |
| Japan | 0 | 1 |
| USA | 9 | 14 |
| **Population** | | |
| OGD | 6 | 15 |
| OGD and/or colonoscopy | 1 | 0 |
| Mixed endoscopy procedures | 1 | 1 |
| Mixed surgical procedures | 2 | 2 |
| Total knee arthroplasty | 1 | 0 |
| Healthy volunteers | 0 | 2 |
| **Data collection** | | |
| Prospective | 0 | 5 |
| Retrospective | 11 | 15 |
| **Exposure type** | | |
| Any GLP-1 RA | 9 | 14 |
| Once-weekly GLP-1 RA only | 0 | 1 |
| Once-weekly semaglutide | 2 | 3 |
| Once-daily or once-weekly semaglutide | 0 | 2 |
| **GLP-1 RA for diabetes only** | 4 | 2 |
| **Assessed time since last dose** | 0 | 5 |

OGD, oesophagogastroduodenoscopy; GLP-1 RA, glucagon-like peptide-1 receptor agonist.

estimate was evaluated in line with the non-contextualised approach of the GRADE recommendations, which accounts for risk of bias; inconsistency; indirectness; imprecision; and publication bias [44]. All statistical analyses were performed using the meta, metafor and PublicationBias packages in R statistical software (Version 4.3.2, R Core Team, Vienna, Austria) [45, 46].

Two prespecified subgroup analyses were performed according to the type of GLP-1 RA (i.e. studies limited to once-weekly formulations vs. studies not limited to once-weekly formulations) and indication for GLP-1 RA (i.e. studies limited to patients with diabetes vs. studies not limited to patients with diabetes). We performed a post hoc subgroup analysis comparing studies limited to patients

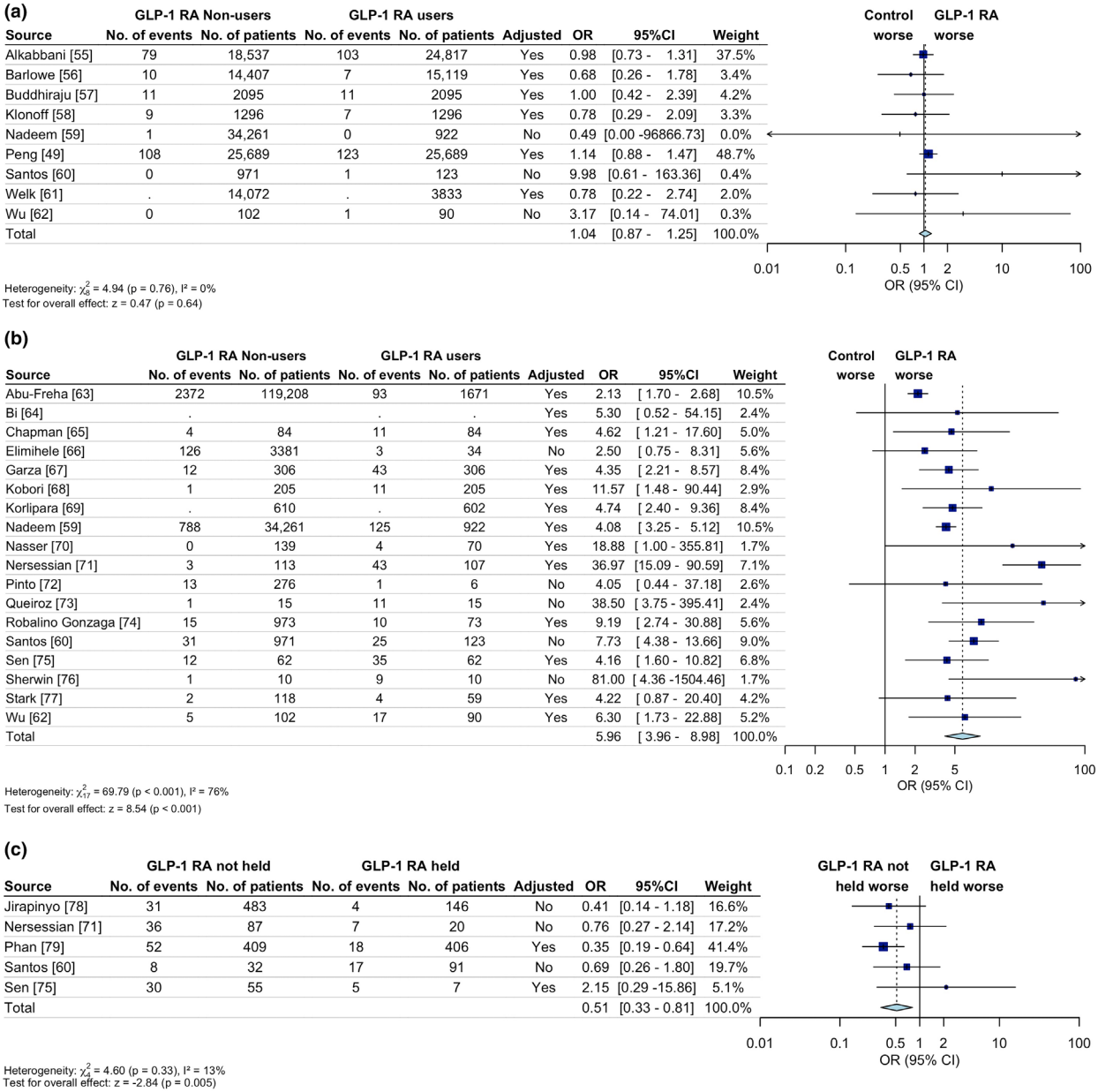


**Figure 2** Forest plots for (a) pulmonary aspiration; (b) residual gastric content; and (c) withholding GLP-1 RAs and residual gastric contents. Dark blue boxes represent individual study odds ratios. The size of the boxes is proportional to study weight; whiskers represent the confidence intervals; light blue diamonds represent the overall pooled odds ratio and 95%CI; dotted vertical lines indicate pooled odds ratios. Event rates were not reported by Welk 2024 for pulmonary aspiration, and Bi 2021 and Korlipara 2024 for residual gastric content. GLP-1 RA, glucagon-like peptide-1 receptor agonist.

undergoing oesophagogastroduodenoscopy with all other studies to examine whether the absence of association between GLP-1 RA exposure and pulmonary aspiration could be explained by altered intra-operative management following direct visualisation of residual gastric contents. We also performed a post hoc analysis comparing studies limited to healthy volunteers with all other studies. To examine the extent to which our main analysis was impacted by varying degrees and methods of adjustment, we performed a post hoc sensitivity analysis by pooling unadjusted estimates from studies included in our main meta-analyses.

## Results

The literature search identified 9010 records (Fig. 1) from which 28 observational studies involving 466,373 patients were included in the meta-analysis (online Supporting Information Table S5). Sixteen studies that were ongoing or completed without published results at the time of the final search are summarised in online Supporting Information Table S6.

Eleven retrospective studies assessed pulmonary aspiration in 335,876 patients (Table 1), with a median (IQR [range]) number of patients per study of 29,526 (3391–39,268 [192–118,646]). Pulmonary aspiration events were identified from electronic medical records or administrative claims data (online Supporting Information Table S2). Of three studies examining patients undergoing similar procedures from the same administrative database [47–49], only one was included in the meta-analysis.

Nine studies were included in the meta-analysis for pulmonary aspiration (Fig. 2). These examined 185,414 patients, of which 471 cases of pulmonary aspiration were identified (Table 2). Pre-operative exposure to GLP-1 RAs was not associated with pulmonary aspiration (OR 1.04, 95% CI 0.87–1.25). Evaluation of indirectness suggested potential concerns due to a large proportion of studies restricted to endoscopic procedures or patients with diabetes (Table 2). Visual inspection of funnel plot asymmetry did not indicate small study effects (online Supporting Information Figure S1). Sensitivity analysis restricted to non-affirmative studies was not performed due to an absence of affirmative studies. Subgroup analysis of studies limited to healthy volunteers was not performed due to an absence of studies restricted to this population. All other subgroup analyses were consistent with the primary analysis (online Supporting Information Figures S2–S4). Overall risk of bias was moderate to high (online Supporting Information Table S7). For most studies, bias was largely attributed to incomplete adjustment for important prespecified confounders (online Supporting Information Table S8). Among the six studies that adjusted for potential confounders, most accounted for age; sex; and diabetes, but adjustment for BMI; ASA physical status; drugs; and comorbidities was inconsistent across studies. Despite this, sensitivity analysis of unadjusted ORs was consistent with the primary analysis (online Supporting Information Figure S5). Overall certainty of evidence was low (Table 2).

Twenty studies, including 166,966 patients, assessed residual gastric content (Table 1), with a median (IQR [range]) number of patients per study of 346 (188–1058 [20–120,879]). Residual gastric contents were identified via retrospective review of patient medical records for 15 studies involving endoscopic procedures, with the remaining five studies having measured residual gastric content prospectively using gastric ultrasound (online Supporting Information Table S3).

Eighteen studies were included in the meta-analysis for residual gastric content (Fig. 2). These examined 165,522 patients, of which 3831 had residual gastric contents (Table 2). Pre-operative GLP-1 RA exposure was associated with higher odds of residual gastric contents (OR 5.96, 95% CI 3.96–8.98); however, this estimate was impacted by substantial heterogeneity (Fig. 2). Although our certainty of evidence was increased due to the large effect, evaluation of indirectness suggested potential concerns due to a large proportion of studies restricted to endoscopic procedures (Table 2). Visual inspection of funnel plot asymmetry indicated that small study effects may have inflated this estimate (online Supporting Information Figure S6), though a sensitivity analysis restricted to non-affirmative studies indicated that our pooled estimate was robust to even worse-case publication bias (OR 3.38, 95%CI 1.49–7.68) (online Supporting Information Figures S7 and S8). Subgroup analysis indicated that GLP-1 RA exposure had a stronger association with residual gastric content in studies of patients who had not undergone an upper gastrointestinal endoscopic procedure compared with studies in other populations (online Supporting Information Figure S9). Despite this, both subgroups showed a large effect in the same direction. A stronger association with residual gastric contents was also found in the subgroup analysis of studies of healthy volunteers compared with other populations. However, the subgroup of healthy volunteers only included two small studies (online Supporting Information Figure S10). No other subgroup effects were identified (online Supporting Information Figures S11 and S12). Overall risk of bias was predominantly high (online Supporting Information Table S9). For most studies, bias was largely attributed to high concerns with

**Table 2** Summary of findings and GRADE assessment. Values are number, proportion (fraction) or effect size (95%CI).

| Comparison | Outcome | Number of patients (studies) | Event rate control | Event rate exposure | Odds ratio (95% CI) | Absolute risk difference (95% CI) | Risk of bias |
|---|---|---|---|---|---|---|---|
| GLP-1 RA exposure vs. control | Pulmonary aspiration | 185,414 (9)[†] | 0.2% (218/111,430) | 0.3% (253/73,984) | 1.04 (0.87–1.25) | 1 more per 10,000 (3 fewer to 5 more) | Serious |
| GLP-1 RA exposure vs. control | Residual gastric contents | 165,522 (18)[‡] | 2.1% (3386/160834) | 10.0% (445/4439) | 5.96 (3.96–8.98) | 93 more per 1000 (57 more to 141 more) | Very serious |
| GLP-1 RA held vs. not held* | Residual gastric contents | 1706 (5) | 14.7% (157/1066) | 7.6% (51/670) | 0.51 (0.33–0.81) | 7 fewer per 100 (9 fewer to 2 fewer) | Very serious |
| **Comparison** | **Outcome** | **Inconsistency** | **Indirectness** | **Imprecision** | **Publication bias** | **Large effects** | **Certainty of evidence** |
| GLP-1 RA exposure vs. control | Pulmonary aspiration | Not serious | Serious | Not serious | Not serious | No upgrade | Low |
| GLP-1 RA exposure vs. control | Residual gastric contents | Serious | Serious | Not serious | Not serious | Upgrade | Low |
| GLP-1 RA held vs. not held* | Residual gastric contents | Not serious | Serious | Not serious | Not serious | No upgrade | Very low |

[†]Three studies from the same administrative database assessed similar procedures. To avoid double counting, the study with the lowest risk of bias across all six domains was included in the meta-analysis. Thus, only nine studies on pulmonary aspiration were included.
[‡]One study did not report event rates for patients using GLP-1 RAs; therefore, the total number of patients is greater than the sum of the control and exposure groups.
*Control group is patients who did not withhold GLP-1 RA before a procedure; exposure group is patients who withheld GLP-1 RA for at least one dose before a procedure.

study participation, outcome measurement and incomplete adjustment for important prespecified confounders (online Supporting Information Table S10). Among the 13 studies that adjusted for potential confounders, most accounted for age; sex; and diabetes, but adjustment for BMI; ASA physical status; drugs; and comorbidities was inconsistent. Despite this, sensitivity analysis of unadjusted ORs was consistent with the primary analysis (online Supporting Information Figure S13). Overall certainty of evidence was low (Table 2).

Five observational studies assessed the association between the time since the last dose of GLP-1 RAs and residual gastric contents (Table 1). These examined 1706 patients who were using GLP-1 RAs, of whom 208 had residual gastric contents (Table 2). Two examined a cohort using either weekly or daily dosed formulations, and the remaining studies were restricted to cohorts using weekly formulations (online Supporting Information Table S11).

All five studies were included in the meta-analysis of time since last dose of GLP-1 RA and residual gastric content (Fig. 2). Withholding at least one dose of GLP-1 RA before a procedure was associated with lower odds of residual gastric content (OR 0.51, 95%CI 0.33–0.81). However, evaluation of indirectness suggested potential concerns due to more than half of the studies being limited to oesophagogastroduodenoscopy procedures. Visual inspection of funnel plot asymmetry indicated that small study effects may have inflated this estimate (online Supporting Information Figure S14). Sensitivity analysis restricted to non-affirmative studies indicated that the direction of the pooled estimate remained robust to even worse-case publication bias, though the wider confidence intervals from this sensitivity analysis included the null value (OR 0.67, 95%CI 0.38–1.18) (online Supporting Information Figures S15 and S16). Subgroup analysis of GLP-1 RA indication and healthy volunteers was not performed due to an absence of studies restricted to patients with diabetes or healthy volunteers. No other subgroup effects were identified (online Supporting Information Figures S17 and S18). Overall risk of bias across studies analysed was serious (online Supporting Information Table S12). Key concerns were attributed to potential bias due to residual confounding, participant selection and outcome measurement. Of the five included studies, only two accounted for potential confounders. Given this, the sensitivity analysis of unadjusted ORs was consistent with the primary analysis (online Supporting Information Figure S19). Overall certainty of evidence was very low (Table 2). No studies measured the association between the time since last dose of GLP-1 RA and pulmonary aspiration.

## Discussion

In this systematic review and meta-analysis, we assessed data from 28 observational studies involving 466,373 patients to evaluate the relationship between GLP-1 RA use and the risk of peri-operative pulmonary aspiration among patients undergoing elective procedures. Our findings indicate that patients using GLP-1 RAs before an elective procedure are at a higher risk of presenting with residual gastric contents compared with those not using GLP-1 RAs. Despite this, the available evidence does not indicate that pre-operative GLP-1 RA use is associated with an increased risk of peri-operative pulmonary aspiration, and the relationship between withholding GLP-1 RAs before surgery and aspiration risk remains unstudied. Our analysis suggests that patients who withheld at least one dose of their GLP-1 RA before surgery were less likely to present with residual gastric contents compared with maintaining a regular dosing schedule, though this evidence was derived from five small observational studies that are inherently vulnerable to bias due to residual confounding. Importantly, available studies did not examine the potential risks of withholding these drugs, such as glycaemic instability or abrupt increases in blood pressure [50]. Given the absence of direct evidence from randomised controlled trials relating to such risks, the very low certainty of the available evidence and the small absolute risk of pulmonary aspiration following appropriate fasting, it remains unclear if withholding GLP-1 RA drugs is warranted before elective procedures.

These findings may provide some degree of reassurance to both patients and clinicians about the risk of pulmonary aspiration among patients using GLP-1 RAs before elective procedures. However, some caution is warranted due to the low certainty of the available evidence. Moreover, due to the low incidence of pulmonary aspiration, our pooled estimates were compatible with an increase in pulmonary aspiration risk of up to ≥ 5 cases per 10,000 procedures, which may be considered clinically important given the severity of this complication. Despite this, high rates of residual gastric contents among these patients may be a cause for concern, independent of any assumed association with pulmonary aspiration risk. Gastric content may complicate procedures that require clear stomach visualisation, such as gastroscopy, potentially leading to aborted procedures due to inadequate gastric clearance. Aborted procedures expose patients to unnecessary anaesthetic risks while also affecting the efficient use of healthcare resources adversely [51].

Consequently, these findings indicate that tailored guidance on the peri-operative management of GLP-1 RAs may be warranted for procedures reliant on an empty stomach, even in the absence of heightened pulmonary aspiration risk.

This review highlights the need for targeted research exploring the risks and benefits of strategies for managing GLP-1 RA drugs before elective procedures. While several observational studies were identified by our search of ongoing studies, it is unclear whether the findings from additional observational studies will add to the current evidence in a way that alters clinical practice. Importantly, two ongoing randomised controlled trials focusing on pre-operative management of GLP-1 RAs were identified. One is assessing the effect of withholding GLP-1 RAs on aspiration and increased residual gastric content risk (NCT06533527), and the other is assessing the effectiveness of a 24-h clear liquid diet for reducing residual gastric contents (NCT06654219). Such trials are needed urgently to assess the efficacy and safety of these approaches and of alternative strategies, such as the use of promotility drugs or assessing pulmonary aspiration risk with pre-operative gastric ultrasound [26]. Updates to this review will be warranted once more data are available from randomised controlled trials, as such evidence will be critical to informing recommendations presented in future clinical practice guidelines. Further to this, given the fast-accumulating evidence in this area, pre-specified trial sequential analysis may allow researchers to determine when additional studies are no longer likely to impact conclusions drawn from existing studies [52]. In addition, future reviews could be enriched by including additional secondary outcomes, such as adverse events or postoperative outcomes, which could provide a more comprehensive understanding of the benefits and risks associated with the use of GLP-1 RAs before elective procedures.

The findings of this review should be interpreted within the context of some limitations. First, there was heterogeneity in how outcomes were described across the included studies. This included differences in measurement methods, such as using endoscopy vs. gastric ultrasound to assess gastric contents, and differences in outcome definitions, such as distinguishing between pulmonary aspiration and aspiration pneumonitis. Second, all included studies assessing pulmonary aspiration were conducted retrospectively, which makes them inherently vulnerable to underreported cases or unmeasured confounding. Third, the available evidence is drawn largely from populations undergoing oesophagogastroduodenoscopy, a procedure that is unique insofar as it allows for intra-operative management to be altered following direct visualisation of residual gastric contents. While this may limit the applicability of our findings to patients undergoing most types of elective procedures, the clinical interpretation of the findings was consistent across subgroup analyses of studies limited to patients undergoing oesophagogastroduodenoscopy. Fourth, information on the duration, dosage and timing of GLP-1 RA use was not described due to inconsistent reporting across included studies. It is unclear if variation in these factors could have affected the interpretation of pooled estimates. Fifth, an absence of studies with pre-registered protocols raises concerns about potential selective analysis and reporting, though findings appeared to be largely robust to publication bias. Sixth, none of the studies were judged to be at a low risk of bias, which is reflected in the overall certainty of the evidence being low to very low. Finally, we excluded two potentially eligible studies that were not published in English [53, 54]. It is unclear if this exclusion is likely to have altered our findings.

This systematic review and meta-analysis found that patients using GLP-1 RAs are at increased risk of presenting for surgery with residual gastric contents, though this does not necessarily indicate an increased risk of pulmonary aspiration. The available evidence to support withholding GLP-1 RAs before surgery is derived from a small number of observational studies and is impacted by a high degree of uncertainty. Given the uncertainty of evidence and absence of randomised controlled trials, ongoing research is needed to evaluate the risks and benefits of different strategies for managing these drugs during the peri-operative period.

## Author affiliations

Jasmin Elkin,[1] Siddharth Rele,[1] Priya Sumithran,[2,3] Michael Hii,[1] Sharmala Thuraisingam,[1] Tim Spelman,[1] Tuong Phan,[4] Peter Choong,[1] Michelle Dowsey,[1] and Cade Shadbolt,[1]

1 Department of Surgery, The University of Melbourne, St Vincent's Hospital Melbourne, Fitzroy, VIC, Australia

2 Department of Surgery, School of Translational Medicine, Monash University, Melbourne, VIC, Australia

3 Department of Endocrinology and Diabetes, Alfred Health, Melbourne, VIC, Australia

4 Department of Critical Care, The University of Melbourne, St Vincent's Hospital Melbourne, Fitzroy, VIC, Australia

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in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. PS is a council member of the Australian and New Zealand Obesity Society; a member of the Obesity Collective leadership group; and is a co-author on manuscripts with a medical writer provided by Novo Nordisk and Eli Lilly. CS received research support for investigator-initiated studies, paid to his institution, from Eli Lilly. MD received research support for investigator-initiated studies, paid to her institution, from Eli Lilly. PC received research support for investigator-initiated studies from Medacta, Eli Lilly, Medibank Private; royalty fees from Kluwer; consultancy fees from DePuy, Surgeon advisory board, Stryker Corporation, Johnson and Johnson, and Medacta; is on the Editorial Board for EFORT Reviews and Journal of Clinical Medicine, and is an international corresponding editor for JAAOS International. JE was supported to conduct this work by an Australian Government Research Training Program Scholarship. Open access publishing facilitated by The University of Melbourne, as part of the Wiley - The University of Melbourne agreement via the Council of Australian University Librarians.

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## Supporting Information

Additional supporting information may be found online via the journal website.

**Appendix S1.** Search strategies.
**Table S1.** Protocol deviations and clarifications.
**Table S2.** Outcome definitions for pulmonary aspiration.
**Table S3.** Outcome definitions for residual gastric content.
**Table S4.** Data requested from study authors.
**Table S5.** Characteristics of included studies.
**Table S6.** Unpublished studies.
**Table S7.** Modified quality in prognosis studies tool assessment of pulmonary aspiration.
**Table S8.** Adjusted variables in included studies assessing pulmonary aspiration.
**Table S9.** Modified quality in prognosis studies tool assessment of residual gastric contents.
**Table S10.** Adjusted variables in included studies assessing residual gastric contents.
**Table S11.** Studies assessing withholding at least one GLP-1 RA dose before a procedure on residual gastric contents.
**Table S12.** Risk of bias assessment.
**Table S13.** GRADE assessment.
**Figures S1–S19.** Funnel plots, sensitivity and subgroup analyses.