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Comparing the risk of gastroparesis following different modalities for treating obesity: semaglutide versus bupropion-naltrexone versus sleeve gastrectomy – a retrospective cohort study

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ABSTRACT

Objective The use of glucagon-like peptide 1 receptor agonists has been associated with gastroparesis, but little is known about the risk of gastroparesis in those with obesity but without type 2 diabetes (T2D), and how that risk compares with other treatment modalities for obesity. This study aims to characterise the relationship between different treatment modalities for obesity and the risk of gastroparesis in a population without pre-existing T2D.

Methods A retrospective cohort study using Merative MarketScan Research Databases of individuals with obesity who underwent treatment with semaglutide, bupropion-naltrexone or sleeve gastrectomy from 1 January 2018 to 31 December 2022. The incidence of gastroparesis diagnosis was evaluated using International Classification of Diseases, Version 10 codes. The risk of gastroparesis was compared between three intervention groups using Cox proportional hazards regression models.

Results Of the 55 460 individuals included, 36 990 (66.7%) were treated with semaglutide, 7369 (13.3%) with bupropion-naltrexone and 11 101 (13.7%) with sleeve gastrectomy. Gastroparesis rates among those treated with semaglutide versus bupropion-naltrexone versus sleeve gastrectomy were 6.5 per 1000 person-years (PY) vs 2.1 per 1000 PY vs 1.1 per 1000 PY, respectively. After adjusting for baseline characteristics, individuals treated with semaglutide had a higher risk of gastroparesis than those treated with bupropion-naltrexone (adjusted HR 3.33, 95% CI 2.27, 4.98) and sleeve gastrectomy (adjusted HR 6.14, 95% CI 3.94, 9.57).

Conclusions There is an increased incidence of gastroparesis among individuals with obesity without T2D who are using semaglutide as compared with bupropion-naltrexone and sleeve gastrectomy. Understanding these potential side effects, though rare, may help guide personalised treatment regimens.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Gastroparesis is a known side effect of glucagon-like peptide 1 agonists, a medication that was primarily used to treat type 2 diabetes (T2D). As indications for this medication have expanded to treatment for obesity, the risk of gastroparesis in a population without diabetes is not well established, and little is known about how this compares to other weight loss interventions.

WHAT THIS STUDY ADDS

⇒ In individuals with obesity and no T2D, those treated with semaglutide had significantly higher risk of developing gastroparesis than individuals treated with bupropion-naltrexone or sleeve gastrectomy.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Understanding the potential side effects of these treatment modalities, though rare, may help individuals and their care teams weigh each treatment's risks and benefits to develop a personalised regimen.

INTRODUCTION

Over the past two decades, the prevalence of obesity in the USA has risen markedly,[1] affecting more than 100 million adults, including over 22 million individuals with severe obesity.[2] There is a wide range of options for the management of obesity, each accompanied by a distinct set of risks and benefits. Lifestyle modifications such as dietary changes and behavioural interventions remain the foundation of obesity management[3]; however, for individuals with inadequate response to lifestyle modifications, antiobesity medications can be added to the regimen.[4 5] Currently, there are six drugs approved by the US Food and Drug Administration for long-term use,[6] and as the demand for the newest drugs grows,[7 8] there has been increasing interest in their potential side effects.[9–11] Recent reports have identified that individuals being treated with glucagon-like

peptide 1 (GLP-1) receptor agonists have increased risks of gastrointestinal side effects, including gastroparesis, which can be debilitating and result in a poor quality of life.[12–14] Conversely, sleeve gastrectomy (SG) has been shown to accelerate gastric emptying.[15] While prior literature has shown these effects in a population that includes individuals with type 2 diabetes (T2D), the relationship between the newest class of GLP-1 agonists (eg, semaglutide) and risk of gastroparesis in a population without diabetes is not well established, and how this risk ultimately compares with the risk of gastroparesis after other weight loss interventions is not clear. This distinction is important as diabetes remains a strong risk factor for the development of gastroparesis,[16 17] and semaglutide may be associated with gastroparesis in a population without known risk factors for the disease, as is suggested in a study which examined its effects in women with polycystic ovary syndrome but without T2D.[18]

We aim to address this gap in knowledge by conducting a retrospective study using data from a large US claims-based dataset. Our primary objective was to compare the risk of gastroparesis among individuals with obesity who did not have T2D and were treated by one of the following interventions: semaglutide, bupropion-naltrexone or SG. Bupropion-naltrexone was selected as comparator because its mechanism differs from semaglutide and should not exert any effects on gastric emptying,[19] while SG was selected to compare the risk after a surgical intervention for weight loss. Our secondary objective was to examine potential risk factors for the development of gastroparesis in those without T2D who were being treated with semaglutide.

METHODS

Data

This study used claims data from the Merative MarketScan Research Databases (Merative, Ann Arbor, Michigan, USA). Formerly known as the Truven MarketScan Databases, this aggregated dataset contains all paid claims and encounter data for over 273 million unique patients and has been effectively applied in other areas of surgical health services research.[20 21] The database includes enrolment, inpatient, outpatient and prescription drug service use, representing the medical experience of insured employees and their dependents.[20] Data management and analysis were conducted from August to November 2024. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology reporting guidelines (online supplemental material (checklist)).[22]

Interventions

Three weight loss interventions were examined: semaglutide, bupropion-naltrexone and SG. Semaglutide and bupropion-naltrexone were identified from national drug classification (NDC) codes in outpatient pharmaceutical claims. The NDCs for semaglutide (Wegovy, Ozempic, Rybelsus) and bupropion-naltrexone (Contrave) were identified in Redbook. Individuals were identified as receiving semaglutide or bupropion-naltrexone treatment if they filled at least one prescription for these medications (regardless of duration or dose). SG was identified in the inpatient admissions and outpatient services claims using common procedure terminology, version 4 and International Classification of Diseases, Version 10 (ICD-10) procedure codes (see online supplemental eTable 1).

Gastroparesis

Gastroparesis was defined as having at least one ICD-10 diagnosis code in an outpatient service or inpatient admission during the study period (see online supplemental eTable 1). Specifically, individuals who had a gastroparesis diagnosis code in the year before the index date were identified as having baseline gastroparesis (see online supplemental eTable 2), and those with at least one gastroparesis diagnosis code at any time after the index date were identified as having gastroparesis in the follow-up period.

Cohort

This study used data from individuals aged 18–64 with a body mass index (BMI) diagnosis of at least 30 kg/m^2 identified from 1 January 2018 to 31 December 2022. Three cohorts were examined based on the intervention type; individuals who had more than one intervention in the study period were excluded. Individuals had to have at least 1 year of continuous enrolment before the intervention and did not have a diagnosis for T2D or gastroparesis in that baseline year (online supplemental eFigure 1).

Statistical analysis

Baseline demographic and health characteristics were compared among individuals treated with bupropion-naltrexone and SG to characteristics of individuals treated with semaglutide. Demographic characteristics examined were age and sex, and health characteristics such as BMI at baseline, and diagnosis of obesity-related comorbidities (dyslipidaemia, gastro-oesophageal reflux disease, metabolic dysfunction-associated fatty liver disease (MAFLD) and pre-diabetes) in the year before the index date (see online supplemental eTable 1).

Next, the rate of gastroparesis per 1000 person-years (PY) of follow-up was calculated. Risk of gastroparesis was compared between the three intervention groups using Cox proportional hazards regression models. Both unadjusted and adjusted models were examined; adjusted models included all baseline characteristics identified above. We also calculated the absolute risk difference at 1 year (per 1000 people), and the number needed to harm. An additional analysis examined the rate of gastroparesis across the specific medications filled in the semaglutide group.

Given the lack of understanding of risk factors for gastroparesis among individuals without T2D, an exploratory analysis was conducted to examine whether any of the demographic or baseline health characteristics examined were significantly associated with the risk of gastroparesis.

A sensitivity analysis was performed to examine the robustness of the definition of gastroparesis. In this analysis, only individuals who had a gastroparesis claim and filled a prescription for a promotility agent after the intervention initiation were defined as having gastroparesis. Promotility agents included are metoclopramide and erythromycin. National drug codes for promotility agents were obtained from Redbook.

Statistical significance was determined using a two-sided p value as well as 95% CI that did not cross 1, and SAS V.9.4 was used to conduct the analysis.

Patient and public involvement

Patients and the public were not involved in the design of this study.

RESULTS

Of the 55 460 individuals who met the inclusion criteria, 36 990 (66.7%) were treated with semaglutide, 7369 (13.3%) were treated with bupropion-naltrexone and 11 101 (13.7%) had an SG procedure (online supplemental eFigure 1). Individuals who had a baseline diagnosis of gastroparesis in the year preceding the index date were excluded, but those prevalences of gastroparesis are described in online supplemental eTable 2: 1.8 per 1000 persons in the SG cohort, 3.2 per 1000 persons in the semaglutide cohort and 2.6 per 1000 persons in the bupropion-naltrexone cohort. Baseline demographic and health characteristics for individuals who were treated with bupropion-naltrexone and who had SG differed substantially from the characteristics of individuals who were treated with semaglutide (table 1).

Average length of follow-up differed between the three treatment groups: 1.0 years, 2.1 years and 2.0 years for individuals treated with semaglutide, bupropion-naltrexone and SG, respectively. Rates of gastroparesis were highest among those who were treated with semaglutide (6.5 per 1000 PY), followed by those treated with bupropion-naltrexone (2.1 per 1000 PY) and lowest for those who had an SG (1.1 per 1000 PY). After adjusting for baseline demographic and health characteristics, individuals treated with semaglutide had significantly higher risk of gastroparesis than those treated with bupropion-naltrexone (adjusted HR (aHR) 3.33, 95% CI 2.27, 4.98) and individuals who had a SG (adjusted HR 6.14, 95% CI 3.94, 9.57) (table 2). When comparing semaglutide with bupropion-naltrexone and semaglutide with SG, 226 and 183 individuals, respectively, would need to be treated with semaglutide for one case of gastroparesis to occur (table 2).

We conducted an additional analysis examining the rate of gastroparesis within the semaglutide group based on the specific semaglutide prescription filled: Ozempic (70%), Wegovy (14%) and Rybelsus (16%) (online supplemental eTable 3). Gastroparesis rates varied across type, with those using Ozempic having the highest rate of gastroparesis (7.2 per 1000 PY) and Rybelsus having the lowest rate of gastroparesis (3.7 per 1000 PY).

In our exploratory analysis of 36 990 individuals treated with semaglutide, we examined the relationship between baseline demographic/health characteristics and risk of gastroparesis (table 3). In the adjusted analyses, the strongest predictors of gastroparesis were baseline MAFLD diagnosis compared with no MAFLD diagnosis (aHR 2.11; 95% CI 1.39, 3.21), BMI between 30 and 34 compared with BMI 40+ (aHR 1.93; 95% CI 1.42, 2.62), baseline gastro-oesophageal reflux disease (GERD) diagnosis compared with no GERD diagnosis (aHR 1.80;

Table 1 Demographic and health characteristics of the study cohorts

Baseline demographic and health characteristics	Semaglutide (N=36 990); n (%)	Bupropion-naltrexone (N=7369)		Sleeve gastrectomy (n=11 101)	
		n (%)	Difference p value*	n (%)	Difference p value*
Age; mean (SD)	45.4 (9.8)	45.7 (10.4)	<0.01	40.8 (10.1)	<0.01
Male sex	10 467 (28.3)	1328 (18.0)	<0.01	2391 (21.5)	<0.01
Baseline BMI; mean (SD)	38.6 (6.1)	37.2 (5.8)	<0.01	42.0 (6.5)	<0.01
Obesity-related comorbidities					
Hypertension	11 087 (30.0)	2731 (37.1)	<0.01	4597 (41.4)	<0.01
Dyslipidaemia	4706 (12.7)	1136 (15.4)	<0.01	1824 (16.4)	<0.01
GERD	1435 (3.9)	399 (5.4)	<0.01	1523 (13.7)	<0.01
MAFLD	1728 (4.7)	260 (3.5)	<0.01	897 (8.1)	<0.01
Pre-diabetes	2122 (5.7)	301 (4.1)	<0.01	523 (4.7)	<0.01

*Reference group=semaglutide.
BMI, body mass index; GERD, gastro-oesophageal reflux disease; MAFLD, metabolic dysfunction-associated fatty liver disease.

Table 2 Rates of gastroparesis and comparisons of rates across interventions

Intervention	Total person-years (PY)	Gastroparesis cases	Rate (per 1000 PY)	HR (95% CI)		Absolute risk difference at 1 year (per 1000)	Number needed to harm
				Crude	Adjusted*		
Comparison 1							
Semaglutide	35 774	233	6.5	2.99 (2.05, 4.39)	3.38 (2.30, 4.95)	4.4	226
Bupropion-naltrexone	15 593	33	2.1	Reference	Reference	Reference	Reference
Comparison 2							
Semaglutide	35 774	233	6.5	5.67 (3.67, 8.71)	5.88 (3.78, 9.16)	5.4	183
Sleeve gastrectomy	21 672	24	1.1	Reference	Reference	Reference	Reference

*Adjusted for age, sex, baseline BMI, baseline comorbidities (hypertension, dyslipidaemia, GERD, MAFLD, pre-diabetes).
BMI, body mass index; GERD, gastro-oesophageal reflux disease; MAFLD, metabolic dysfunction-associated fatty liver disease.

95% CI 1.09, 2.97) and female sex compared with male sex (aHR 1.56; 95% CI 1.14, 2.13)).

Sensitivity analysis

A sensitivity analysis was conducted using a stricter definition of gastroparesis: requiring individuals to have both a diagnosis claim for gastroparesis and to have filled a pharmaceutical claim for a promotility agent. The rate of gastroparesis was significantly lower using this definition, but the risk of gastroparesis remained significantly higher among those who were treated with semaglutide than those treated with bupropion-naltrexone (aHR 2.46; 95% CI 1.32, 4.55) and those who had an SG (aHR 4.36; 95% CI 2.02, 9.43) (see online supplemental eTable 4).

DISCUSSION

This real-world data study found that individuals with obesity without T2D who were treated with semaglutide were substantially more likely to be diagnosed with gastroparesis than individuals treated with bupropion-naltrexone or those who had an SG. Baseline prevalence of gastroparesis in the individuals who were excluded from the study is shown for frame of reference in online supplemental eTable 2, and there, it appears that the cohort receiving semaglutide had the highest prevalence compared with those who received SG or bupropion-naltrexone. The results were consistent even after restricting incident gastroparesis cases to only those who are diagnosed and are being treated for gastroparesis. Our exploratory analysis showed that MAFLD and GERD were associated with incident gastroparesis cases, though this is likely identifying a group of individuals with more severe metabolic dysfunction who may be more likely to have gastroparesis. It is noteworthy that our cohort included those with pre-diabetes, though the prevalence was overall low across all study groups.

Interestingly, there were significant differences between the cohorts who received bupropion-naltrexone or SG as compared with those who received semaglutide. Individuals who received SG had higher baseline BMI and higher amounts of obesity-related comorbidities, which align with current guideline indications for surgical treatment. It is unclear why the baseline characteristics of individuals treated with bupropion-naltrexone and those treated with semaglutide are not more alike, given the indications for prescribing these antiobesity medications are generally similar. Given the vastly different side effect profile and the highest total body weight loss achievable between the two medications, it is possible that the treatment plan is somewhat influenced by patient preference.

Our findings indicating an increased risk of gastroparesis among individuals treated with semaglutide, as compared with individuals treated with bupropion-naltrexone, align with findings from a recent study.[4] In their analysis, which included both semaglutide and liraglutide in comparison to bupropion-naltrexone, Sodhi *et al* reported a greater incidence of gastroparesis in users of semaglutide vs liraglutide versus bupropion-naltrexone, respectively. Our findings expanded on this study to focus on semaglutide with a larger cohort sample size as well as comparison with a group that received a surgical weight loss modality.

The downstream implications of this increased risk of gastroparesis among individuals treated with semaglutide and other GLP-1 agonists remain to be studied. Though prior clinical trials have reported the significant benefits of GLP-1 agonists in weight loss[23] and reducing detrimental effects on the cardiovascular system,[24] one real-world study found a 12-month and 24-month discontinuation of 45.2% and 64.7%, respectively, among individuals with T2D.[25] The STEP 8 randomised clinical trial comparing the efficacy and side effect profiles of semaglutide and liraglutide in individuals with obesity without T2D reported a discontinuation of 13.5% with semaglutide and 27.6% with liraglutide.[23] It is generally recognised that the efficacy of medications noted in clinical trials often exceeds their effectiveness in real-world applications, which could be due to a number of factors including lower adherence to therapy, discontinuation of therapy or lack of representativeness among clinical trial participants—who tend to have the resources, support and motivation to comply with the therapy regimens

Table 3 Predictors of gastroparesis among individuals treated with semaglutide

Baseline demographic and health characteristics	Gastroparesis rate per 1000 PY	Unadjusted		Adjusted*	
		Estimate	P value	Estimate	P value
Age					
18–24	9.69	1.23 (0.59, 2.57)	0.59	1.39 (0.66, 2.94)	0.39
25–34	6.47	0.82 (0.52, 1.29)	0.38	0.93 (0.58, 1.48)	0.75
35–44	7.18	0.91 (0.65, 1.29)	0.60	0.99 (0.70, 1.41)	0.95
45–54	5.08	0.65 (0.46, 0.92)	0.01	0.68 (0.48, 0.97)	0.03
55–64	7.85	Reference			
Sex					
Female	7.29	1.56 (1.14, 2.13)	<0.01	1.56 (1.14, 2.13)	<0.01
Male	4.65	Reference		Reference	
Baseline BMI					
30–34	10.14	1.95 (1.41, 2.70)	<0.01	1.93 (1.42, 2.62)	<0.01
35–39	5.21	0.96 (0.69, 1.34)	0.82	0.98 (0.70, 1.36)	0.89
40+	5.43	Reference			
Obesity-related comorbidities					
Hypertension					
Yes	7.20	1.16 (0.89, 1.52)	0.28	1.14 (0.81, 1.59)	0.45
No	6.20	Reference			
Dyslipidaemia					
Yes	7.65	1.21 (0.85, 1.72)	0.29	1.10 (0.72, 1.69)	0.65
No	6.33	Reference			
GERD					
Yes	13.2	2.11 (1.32, 3.37)	<0.01	1.80 (1.09, 2.97)	0.02
No	6.2	Reference			
MAFLD					
Yes	14.0	2.29 (1.52, 3.45)	<0.01	2.11 (1.39, 3.21)	<0.01
No	6.1	Reference			
Pre-diabetes					
Yes	5.36	0.81 (0.46, 1.46)	0.049	0.69 (0.38, 1.28)	0.24
No	6.59	Reference			

*Adjusted for age, sex, baseline BMI, baseline comorbidities (hypertension, dyslipidaemia, GERD, MAFLD, pre-diabetes).
BMI, body mass index; GERD, gastro-oesophageal reflux disease; MAFLD, metabolic dysfunction-associated fatty liver disease.

under investigation.[26 27] Whether discontinuation is directly related to the high frequency of gastrointestinal adverse events, reported to be 84.1% with semaglutide and 82.7% with liraglutide,[23] requires further study. A more recent investigation broadly aimed at characterising GLP-1 agonist discontinuation noted that in addition to several socioeconomic factors, the diagnosis of obesity only (as opposed to T2D only or obesity and T2D) and new gastrointestinal adverse effects at follow-up were associated with significantly higher odds of discontinuation at 12 months; however, the researchers cited as a limitation the inability to decipher whether achieving transiently satisfactory weight reduction as opposed to adverse effects could have explained the higher prevalence of discontinuation among individuals with obesity.[28] Taken together, the findings of these studies seem to suggest a relationship between gastrointestinal adverse effects of GLP-1 agonists and their discontinuation in individuals with obesity without T2D; how this specifically ties to gastroparesis requires further investigation.

In addition to the potential associations of gastroparesis and other gastrointestinal side effects of GLP-1 agonists and decreased therapy adherence or discontinuation, these effects also have implications in the periprocedural period. Studies on this topic have emerged since the American Society of Anesthesiologists (ASA) noted concerns about the potential association between GLP-1 agonist use with residual gastric contents and risk of periprocedural aspiration, thus suggesting holding GLP-1 agonists before endoscopic or surgical procedures.[29] Studies

highlight an association between use of GLP-1 agonists and risk of retained gastric contents,[30–35] and the findings of one recent study at a single large tertiary university-affiliated hospital also suggested that the preprocedural GLP-1 agonist interruption duration in current guidelines may not be adequate for this group of individuals.[36] In contrast, a recent systematic review and meta-analysis suggested that although there is a detectable delay in gastric emptying for individuals taking GLP-1 agonists, it is of limited magnitude relative to standard periprocedural fasting periods and thus of low clinical significance with respect to sedation risks.[37] Another retrospective cohort study found that the increase in retained gastric contents in individuals undergoing esophagogastroduodenoscopy was not statistically significant, despite GLP-1 agonist use.[38] In sum, an association between the use of GLP-1 agonists and gastroparesis is described, but its clinical significance in the context of preprocedural interruption of GLP-1 agonists and fasting regimens requires further investigation. As some have noted, there may be other drawbacks to interrupting GLP-1 agonist use in the periprocedure period given its beneficial effects on glycaemic control.[39–43]

With respect specifically to the risk of aspiration in the setting of gastroparesis, this has been a subject of recent studies given the previously mentioned ASA guidance.[38 44] Many of these studies have been case reports describing instances of aspiration in individuals receiving GLP-1 agonists,[35 45 46] and it should be noted that while the patients in these reports underwent preoperative fasting; they did not undergo cessation of GLP-1 agonist in the preprocedure period. In a retrospective cohort study that does not distinguish between individuals who did or did not hold GLP-1 agonists in the preprocedure period, it was noted that the incidence of aspiration pneumonia after endoscopic procedures was higher in individuals who use GLP-1 agonists compared with those who did not (HR 1.33; 95% CI 1.02, 1.74; p=0.036).[47] In contrast, another retrospective cohort study found that the use of GLP-1 agonists within 1 month before endoscopy was not associated with a statistically significant increased risk of aspiration pneumonia.[48] In a separate cohort study focused on individuals on GLP-1 agonists for T2D, researchers found no increase in risk of pneumonia or outcomes more specific to aspiration, such as need for bronchoscopy, in individuals undergoing elective surgery while on GLP-1 agonists.[49] In a study that complements these findings, researchers used a population-based sample of individuals with T2D presenting for emergency surgery and found that individuals using GLP-1 agonists did not have an increased risk of a composite outcome of aspiration pneumonitis, postoperative respiratory failure, or intensive care admission compared with matched non-users (adjusted OR 1.03; 95% CI 0.82, 1.29).[50]

After the publication of the consensus-based ASA guidance around periprocedure cessation of GLP-1 agonists, the American Gastroenterological Association (AGA) published a clinical practice update acknowledging the current lack of data to make a rigorous evidence-based recommendation about GLP-1 agonist use and the relative risk of complications from aspiration during sedation for endoscopy.[51] A separate multisociety statement by the AGA, along with the American Association for the Study of Liver Disease, American College of Gastroenterology, American Society for Gastrointestinal Endoscopy and North American Society for Pediatric Gastroenterology, Hepatology and Nutrition, makes a similar claim.[52] These publications highlight the need for additional prospective research studies in this domain,[38 53] and as most prior studies have examined individuals with T2D, there is also a gap in the literature to describe whether individuals on GLP-1 agonists without T2D have a similar periprocedure risk profile.

Limitations

This study has significant strengths, including a large sample size, a focus on a single GLP-1 agonist (semaglutide), comparison with a surgical treatment modality, as well as sensitivity analysis using a more stringent criterion for the identification of gastroparesis cases. However, the findings of this study should be interpreted with several limitations in mind. First, ensuring that we had sufficient baseline data to assess comorbidities also decreased the sample size, thus impacting the generalisability of these results. Second, the dataset allows for the identification of individuals who were prescribed semaglutide or other medications, and whether claims were filed; however, it is unknown whether or how patients took the medications after the prescriptions were filled. Third, only individuals who were diagnosed with gastroparesis by ICD10 codes were identified—this diagnosis was not verified by measurements from a gastric emptying study and does not capture individuals who may have gastroparesis but did not have a formal diagnosis. Nonetheless, the findings of higher risk of gastroparesis remained true even after restricting the analysis to include only those who were diagnosed with gastroparesis and were being treated for it. The differences in follow-up time between groups also present a limitation, although more incident cases of gastroparesis were identified in the semaglutide group, despite a shorter follow-up time. Fourth, the follow-up time is shorter in our study as compared with previous studies examining the gastrointestinal side effects of GLP-1 agonists. Given that the dataset used claims data, the follow-up time was limited as individuals switch between commercial insurers every few years. Relatedly, as this study uses commercial claims data, this excludes individuals whose healthcare is delivered through other plans, thus limiting generalisability. Fifth, there are factors that could impact the risk of gastroparesis among individuals without T2D that are not captured or accounted for in the data. Sixth, given physician knowledge of gastroparesis as a side effect of semaglutide, the data from this cohort could have been subject to selective reporting bias. Lastly, we are unable to distinguish whether the gastroparesis is permanent or transient, though this is a rich

area for future research given the increasing prevalence of semaglutide use for the management of obesity.

CONCLUSIONS

Overall, this study builds on previous findings of an increased incidence of gastroparesis among individuals without T2D who use semaglutide as compared with bupropion-naltrexone and newly describes an increased incidence of gastroparesis as compared with individuals who underwent SG. Understanding these potential side effects, rare as they may be, may help guide individuals and their care teams on how best to weigh each treatment's risks and benefits and personalise a regimen for patients with obesity.

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Patient consent for publication Not applicable.

Ethics approval As this was an observational study of deidentified patients in the Merative database, Institutional Review Board approval and consent were exempt (in accordance with the Health Insurance Portability and Accountability Act Privacy Rule).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data may be obtained from a third party and are not publicly available. This study is a retrospective analysis of insurance claims data which was purchased from Merative MarketScan; primary data were not collected for the purposes of this study.

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