

Endoscopy International Open

GLP-1 Receptor Agonist Use Does Not Increase the Risk of Respiratory Complications Post-Endoscopy

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DOI: 10.1055/a-2487-2937

Please cite this article as: Velji-Ibrahim J, Nathani P, Patel H K et al. GLP-1 Receptor Agonist Use Does Not Increase the Risk of Respiratory Complications Post-Endoscopy. Endoscopy International Open 2024. doi: 10.1055/a-2487-2937

Conflict of Interest: The authors declare that they have no conflict of interest.

Abstract:

Background and study aims: Data on respiratory complications associated with GLP-1 receptor agonist (GLP-1 RA) use before endoscopic procedures is limited.

Methods: We conducted a retrospective cohort study using TriNetX in adults with diabetes or obesity on GLP-1 RAs within three months of endoscopy, comparing them to non-GLP-1 RA users. Propensity score matching and Cox proportional hazards models assessed outcomes.

Results: Among 46,948 patients, no significant differences in post-endoscopy aspiration pneumonitis (HR 0.92, 95% CI: 0.54-1.56) or pneumonia (HR 1.01, 95% CI: 0.83-1.24) were found between groups.

Conclusion: GLP-1 RA use before endoscopy does not increase respiratory complications, supporting continued preoperative medication use.

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Post-Endoscopy

INTRODUCTION

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are approved for diabetes treatment and recently, for weight loss, potentially addressing the global obesity epidemic, metabolic syndrome, and cardiovascular risk [1]. GLP-1 RAs are incretin mimics that prompt glucose-dependent insulin release from the pancreatic islets, reducing glucagon secretion, increasing satiety, and delaying gastric emptying [2].

In September 2023, the American Gastroenterological Association (AGA) addressed the management of patients taking GLP-1 RAs, finding no evidence to support all patients stopping GLP-1 RAs before elective endoscopy procedures [3]. This was in response to the American Society of Anesthesiologists' recommendation to discontinue GLP-1 RAs before elective procedures [4] due to reports suggesting an increased risk of aspiration and respiratory complications in patients who present for procedures requiring sedation [5, 6]. While preoperative medication guidelines can prevent complications, withholding medications can result in adverse effects and significant logistical burdens, including procedure cancellations, care delays, and financial losses [7, 8]. These issues are particularly significant for GLP-1 RAs, which require withholding periods of up to a week. Consequently, the ASA's preoperative suggestions may necessitate enhanced nursing resources, exacerbating barriers, and care delays for patients requiring endoscopic procedures [3]. Furthermore, it may not be appropriate to withhold these medications given the clear benefit of GLP-1 RAs in cardiovascular health and

glycemic control in diabetic patients, and it is unclear if withholding a single dose is sufficient for gastric motility to return to normal. We conducted a real-world analysis to determine the risk of respiratory complications in patients prescribed GLP-1 RAs within three months of an endoscopic procedure.

METHODS

We conducted a population-based retrospective cohort study using TriNetX, a global federated health research network with anonymized electronic medical records from 83 large healthcare organizations. We included all patients aged 18-70 years with type 2 diabetes mellitus or overweight/ obesity with active GLP-1 RA prescriptions within three months before undergoing endoscopic procedures defined by current procedural terminology codes. The age cutoff was set at 70 years to minimize confounding from age-related comorbidities and the higher baseline risk of pneumonia in older adults. The study period ranged from January 1, 2018, to December 31, 2022. For the GLP-1 procedure cohort, we selected patients who underwent endoscopic procedures during the study period and had an active GLP-1 RA prescription within 3 months before the procedure. For the control group, we selected patients who had endoscopic procedures between January 01, 2018, and June 30, 2022, and have never received a GLP-1 prescription in their entire lifetime. The control group enrollment period was shortened by 6 months to ensure that the sample size remained within the TriNetX processing capacity. Patients with a history of surgery, anesthesia, or mechanical ventilation within three months before the procedure were excluded.

The primary outcome was aspiration pneumonitis or pneumonia within 30 days of endoscopic procedures in patients taking preoperative GLP-1 RAs. Secondary outcomes included risk association of other outcomes, per procedure, and individual GLP-1 RA. The study was deemed exempt by the institutional review board and is reported in accordance with the STROBE guidelines [9].

We performed 1:1 propensity score matching using patient demographics, Charlson comorbidity index, aspiration risk factors, and frailty risk (**Supplemental Table 1**). We used Kaplan-Meier analysis and log-rank tests on the TriNetX platform to compare the time to event for all outcomes between cohorts. GLP-1RA users were 1:1 matched to non-users using the Greedy algorithm. A standardized mean difference below 0.1 between characteristics after matching was deemed appropriate. We calculated the association of aspiration using risk ratio (RR) and hazard ratio (HR), with 95% confidence intervals (CI) from a univariate Cox proportional hazards model. The proportionality of hazards was checked with scaled Schoenfeld residuals. For outcomes not meeting the proportional hazards assumption, we conducted a landmark analysis at three months. To explore potential unknown confounders, we performed an E-value sensitivity analysis for HR and CI using an online tool. Statistical significance was set at 0.05.

RESULTS

Of the 1,018,770 patients undergoing endoscopy, 29,094 were prescribed GLP-1 RAs and 989,676 were not. Of these, 46,948 patients met inclusion criteria, 23,474 in the GLP-1 RA cohort and 23,474 in the comparison group with baseline demographics shown in **Table 1**. As shown in **Figure 1A**, the overall incidence of post-endoscopy aspiration pneumonitis was 0.11%

for those with GLP-1 RA prescriptions and 0.12% for those without (hazard ratio [HR] 0.92; 95% CI: 0.54-1.56; p=0.752). Similarly, the incidence of pneumonia was not significantly different between those with GLP-1 RA prescription (0.81%) and those without (0.79%) (hazard ratio [HR] 1.01; 95% CI: 0.83-1.24; p=0.877). The risk of other adverse events post-endoscopy was also not significantly different between these two groups. On subgroup analysis, there was no significant difference between the incidence of aspiration pneumonitis or pneumonia for the type of endoscopic procedure or specific GLP-1 RA (**Figure 1B, 1C; Table 1**). Confidence intervals were wide for aspiration pneumonitis but narrow for pneumonia and subgroup analysis. There was no significant difference in the Charlson comorbidity index, risk factors for aspiration, and frailty between the groups.

DISCUSSION

GLP-1 RA use before endoscopy was not associated with a higher risk of post-procedure respiratory complications compared with patients not prescribed GLP-1 RAs. In our subgroup analysis by procedure, gender, and GLP-1 RA medication, this was also the case. Previous studies have indicated that the use of GLP-1 RAs is associated with retained gastric contents, which is a direct consequence of delayed gastric emptying [5]. The clinical impact of solid and liquid gastric emptying is different. Retained contents in the stomach may not pose a significant issue for patients undergoing combined EGD and colonoscopy, as they typically fast and consume only a liquid diet the day before the procedures and do not consume solids in that time. Given that our study included more participants undergoing colonoscopy than EGD, the duration of fasting may have contributed to our findings of no increased risk of respiratory complications.

While the nationwide rate of aspiration is reported to be around 1%, our findings indicated a lower rate. This may be due to the participants undergoing colonoscopy. The lower aspiration rate may also be attributed to differences in patient management practices across multiple hospitals and the lack of standardized protocols that exists in our population-based study that includes data from numerous healthcare organizations. Additionally, it is possible that not all aspirations may have been reported, as they may not have been clinically significant or accurately documented. This could lead to an underestimation of the true incidence of respiratory complications.

Our study has certain limitations. We were unable to measure the preoperative duration of GLP-1 RA therapy, duration of fasting, medication adherence, or cessation of medication before endoscopic procedures. Our selection of the 2018-2022 cohort was made before concerns arose regarding the risk of aspiration associated with GLP-1 RAs. Our study did not measure gastric contents, however, previous studies have addressed the association between GLP-1 RA use and retained gastric contents [5]. This retrospective study relies on accurate documentation of symptoms, disease, and treatments, rendering it susceptible to biases in charting, coding, and recall. Our study has wide confidence intervals which may be due to the low incidence of these events and a larger series is needed to further address the incidence and impact of GLP-1 RAs in this setting.

Our results align with those of Dixit et al., (2024) who found that the use of GLP-1 RAs before emergency surgery did not elevate the risk of respiratory complications [10]. However, Yeo et al. (2024) reported an increased risk of aspiration pneumonia associated with GLP-1 RAs following

endoscopy [6]. The discrepancy in results might stem from differences in the robustness of matching, as some covariates in their study exhibited residual imbalances.

Our study suggests a low incidence of respiratory complications including aspiration post-endoscopy in individuals prescribed a GLP-1 RA. Future large studies are needed to assess respiratory complications post-endoscopy including more complex procedures that require deep sedation such as endoscopic retrograde cholangiopancreatography or endoscopic ultrasound in which the risk of aspiration could be higher. An individualized approach based on GLP-1 RA indication and symptoms of nausea, vomiting, dyspepsia, or abdominal distention may be the best determination of those who can safely undergo upper and/or lower endoscopy procedures.

Figure 1. Incidence of aspiration pneumonitis and pneumonia among GLP-1 RA users and non-users post-endoscopy. 1A demonstrates the incidence of respiratory complications and other adverse events post-upper and/or lower endoscopy. 1B shows the results of subgroup analysis of the incidence of aspiration pneumonitis stratified by endoscopy type, sex, and GLP-1 RA. 1C illustrates subgroup analysis of the incidence of pneumonia stratified by endoscopy type, sex, and GLP-1 RA.

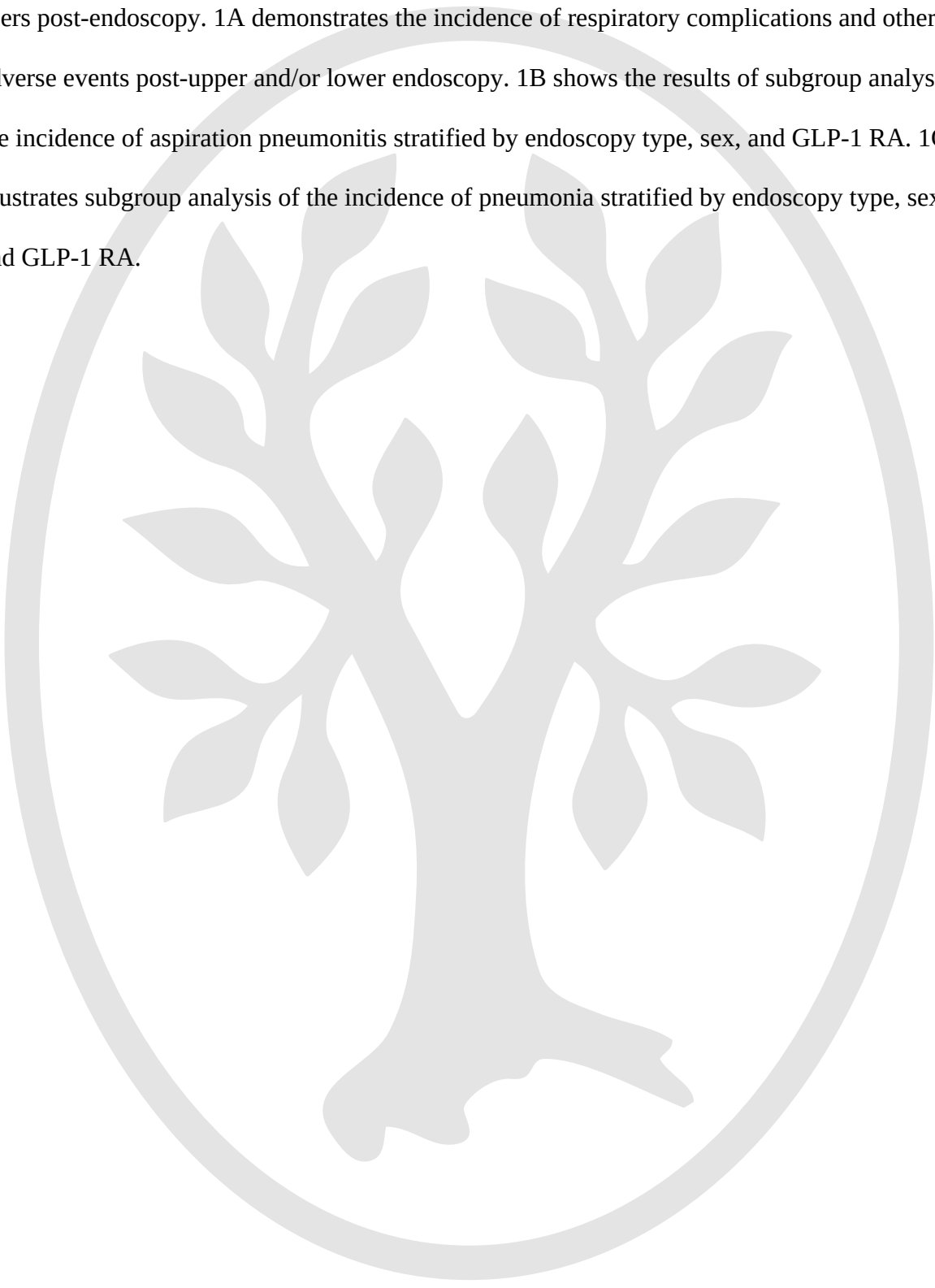


Table 1. Baseline characteristics and risk adverse events post-endoscopy in GLP-1 RA users and non-users. Subgroup analysis of aspiration pneumonitis and pneumonia risk by procedure type, sex, and GLP-1 RA.

Outcomes	GLP-1 Cohort	Control Cohort	Hazard Ratio [95% CI]	P-value
Sample Size Before Match	29,094	989,676	NA	NA
Sample Size After Match	23,474	23,474	NA	NA
Age	53.8 ± 9.3 years	54.2 ± 10.0 years	NA	NA
Females	58.7%	59.2%	NA	NA
Males	36.1%	35.5%	NA	NA
White	60.1%	59.3%	NA	NA
African American	19.3%	20.4%	NA	NA
Hispanic	10.6%	10.7%	NA	NA
Diabetes Mellitus	76.1%	78.7%	NA	NA
Overweight BMI and obesity	67.9%	72.3%	NA	NA
Hemoglobin A1c	7.3 ± 2.0	7.1 ± 2.0	NA	NA
BMI	36.1 ± 8.5	35.6 ± 8.9	NA	NA
Post-Endoscopy Adverse Events				
Aspiration Pneumonitis	0.11%	0.12%	0.92 [0.54, 1.57]	0.752
Pneumonia	0.81%	0.79%	1.01 [0.83, 1.24]	0.877
Cardiac adverse events	0.28%	0.28%	1.01 [0.71, 1.46]	0.941
Infectious adverse events	0.86%	0.76%	1.11 [0.91, 1.36]	0.313
Thoracic adverse events	0.14%	0.08%	1.65 [0.92, 0.96]	0.090
Genitourinary adverse events	1.44%	1.10%	1.30 [1.11, 1.53]	0.002
Other adverse events	0.19%	0.18%	1.05 [0.68, 1.64]	0.819
Deaths	0.20%	0.28%	0.71 [0.49, 1.04]	0.076
Subgroup Analysis of Aspiration Pneumonitis				
By Procedures				
EGD (n=11,477)	0.17%	0.19%	0.90 [0.49, 1.65]	0.732
Colonoscopy (n=15,910)	≤0.06%	≤0.06%	1.65 [0.60, 4.53]	0.328
By Sex				
Female (n=13,327)	0.13%	≤0.08%	2.10 [0.91, 4.87]	0.076
Male (n=7,893)	≤0.13%	0.20%	0.43 [0.18, 1.05]	0.056
By GLP Medication				
Semaglutide (n=10,717)	≤0.09%	0.11%	0.82 [0.36, 1.91]	0.650
Dulaglutide (n=9,366)	0.14%	0.14%	0.99 [0.46, 2.13]	0.976
Liraglutide (n=6,928)	0.16%	≤0.14%	1.82 [0.67, 4.92]	0.232
Subgroup Analysis of Pneumonia				
By Procedures				
EGD (n=11,477)	1.09%	1.04%	1.04 [0.81, 1.34]	0.757

Colonoscopy (n= 15,910)	0.78%	0.61%	1.27 [0.97, 1.65]	0.081
By Sex				
Female (13,327)	0.94%	0.71%	1.32 [1.00, 1.72]	0.050
Male (7,893)	0.79%	0.71%	1.09 [0.76, 1.57]	0.625
By GLP-1 Medication				
Semaglutide (10,717)	0.88%	0.77%	1.12 [0.83, 1.50]	0.452
Dulaglutide (n=9,366)	0.89%	1.01%	0.86 [0.64, 1.16]	0.323
Liraglutide (n=6,928)	0.97%	1.03%	0.94 [0.97, 1.31]	0.697

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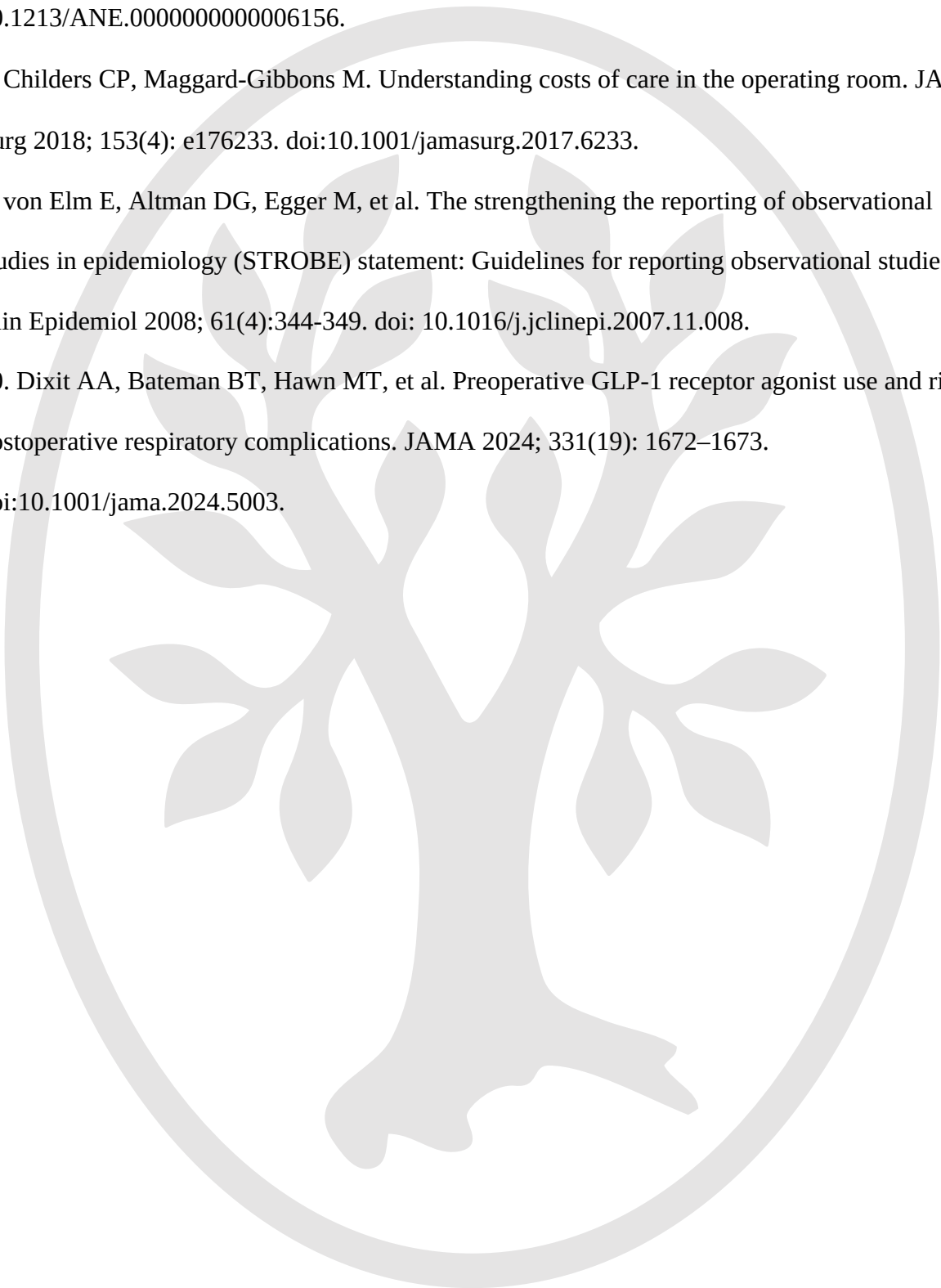
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Supplemental Table 1: Demographic and clinical characteristics of GLP-1 RA users and non-users before and after propensity matching results. Propensity matching was done for the 59 characteristics.

Cohort patient count before and after propensity score matching								
Cohort			Patient count before matching			Patient count after matching		
Cohort 1: GLP-1 procedures			29,094			23,474		
Cohort 2: Control procedures			989,676			23,474		
Propensity score density function - Before and after matching (GLP1 - purple, control - green)								
PLEASE INSERT SUPPL FIG 1 HERE				PLEASE INSERT SUPPL FIG 2 HERE				
GLP 1 (N = 23,474) and control (N = 23,474) characteristics before and after propensity score matching								
Age								
			Before Matching			After Matching		
Cohort	Code	Characteristic	Patients	Mean ± SD	Std diff.	Patients	Mean ± SD	Std diff.
1	AI	Age at Index	29,094	54.1 +/- 9.1	0.381	23,474	53.8 +/- 9.3	0.040
2			989,676	49.8 +/- 13.0		23,474	54.2 +/- 10.0	
Demographics								
			Before Matching			After Matching		
Cohort	Code	Characteristic	Patients	% of Cohort	Std diff.	Patients	% of Cohort	Std diff.
1	2106-3	White	17,665	60.7%	0.074	14,112	60.1%	0.017
2			636,551	64.3%		13,912	59.3%	
1	UNK	Unknown Race	3,765	12.9%	0.074	3,071	13.1%	0.004
2			153,737	15.5%		3,042	13.0%	
1	F	Female	17,383	59.7%	0.172	13,786	58.7%	0.010
2			507,003	51.2%		13,905	59.2%	
1	2135-2	Hispanic or Latino	3,095	10.6%	0.048	2,486	10.6%	0.003
2			91,088	9.2%		2,508	10.7%	
1	2186-5	Not Hispanic or Latino	20,983	72.1%	0.109	16,795	71.5%	0.002
2			664,244	67.1%		16,821	71.7%	
1	2054-5	Black or African American	5,596	19.2%	0.211	4,534	19.3%	0.028
2			115,406	11.7%		4,797	20.4%	
1	M	Male	10,266	35.3%	0.138	8,481	36.1%	0.012
2			415,677	42.0%		8,344	35.5%	
1	2131-1	Other Race	1,133	3.9%	0.012	939	4.0%	0.008
2			36,325	3.7%		904	3.9%	
Diagnosis								
			Before Matching			After Matching		
Cohort	Code	Characteristic	Patients	% of Cohort	Std diff.	Patients	% of Cohort	Std diff.
1	E08-E13	Diabetes mellitus	23,477	80.7%	1.999	17,865	76.1%	0.062
2			101,789	10.3%		18,476	78.7%	
1	E65-E68	Overweight, obesity and other hyperalimentionation	21,131	72.6%	1.303	15,929	67.9%	0.096
2			180,910	18.3%		16,964	72.3%	
1	K21	Gastro-esophageal reflux disease	15,468	53.2%	0.556	11,686	49.8%	0.016
2			266,456	26.9%		11,870	50.6%	
1	K25	Gastric ulcer	1,054	3.6%	0.160	717	3.1%	<0.001
2			11,694	1.2%		717	3.1%	
1	K26	Duodenal ulcer	358	1.2%	0.072	259	1.1%	0.002
2			5,510	0.6%		253	1.1%	
1	K44	Diaphragmatic hernia	3,180	10.9%	0.245	2,319	9.9%	0.010
2			43,977	4.4%		2,391	10.2%	

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1	2	K74	Fibrosis and cirrhosis of liver	2,135	7.3%	0.261	1,490	6.3%	0.003
				18,816	1.9%		1,507	6.4%	
1	2	K22.4	Dyskinesia of esophagus	538	1.8%	0.100	381	1.6%	0.004
				7,189	0.7%		393	1.7%	
1	2	R13	Aphagia and dysphagia	5,566	19.1%	0.290	3,964	16.9%	0.003
				90,472	9.1%		3,934	16.8%	
1	2	I20-I25	Ischemic heart diseases	7,299	25.1%	0.528	5,224	22.3%	0.001
				64,127	6.5%		5,238	22.3%	
1	2	I60-I69	Cerebrovascular diseases	4,122	14.2%	0.359	2,914	12.4%	0.005
				39,685	4.0%		2,954	12.6%	
1	2	I50	Heart failure	3,738	12.8%	0.404	2,607	11.1%	0.006
				23,381	2.4%		2,655	11.3%	
1	2	I73	Other peripheral vascular diseases	2,886	9.9%	0.318	1,929	8.2%	0.004
				23,577	2.4%		1,906	8.1%	
1	2	M30-M36	Systemic connective tissue disorders	2,042	7.0%	0.221	1,379	5.9%	0.001
				23,424	2.4%		1,382	5.9%	
1	2	J45	Asthma	7,530	25.9%	0.430	5,411	23.1%	0.008
				96,899	9.8%		5,488	23.4%	
1	2	J44	Other chronic obstructive pulmonary disease	3,281	11.3%	0.309	2,355	10.0%	0.002
				32,908	3.3%		2,370	10.1%	
1	2	J43	Emphysema	823	2.8%	0.115	613	2.6%	0.002
				12,002	1.2%		619	2.6%	
1	2	C00-D49	Neoplasms	14,548	50.0%	0.449	10,900	46.4%	0.003
				283,249	28.6%		10,931	46.6%	
1	2	B20-B20	Human immunodeficiency virus [HIV] disease (B20)	723	2.5%	0.127	486	2.1%	0.006
				8,497	0.9%		465	2.0%	
1	2	F17	Nicotine dependence	6,474	22.3%	0.283	4,896	20.9%	0.002
				115,939	11.7%		4,874	20.8%	
1	2	F10	Alcohol related disorders	2,382	8.2%	0.151	1,793	7.6%	0.006
				44,766	4.5%		1,756	7.5%	
1	2	F11	Opioid related disorders	780	2.7%	0.114	569	2.4%	0.005
				11,132	1.1%		550	2.3%	
1	2	G30-G32	Other degenerative diseases of the nervous system	449	1.5%	0.106	308	1.3%	<0.001
				4,819	0.5%		309	1.3%	
1	2	G47.3	Sleep apnea	12,483	42.9%	0.835	8,962	38.2%	0.014
				90,199	9.1%		9,121	38.9%	
1	2	I38	Endocarditis, valve unspecified	319	1.1%	0.099	221	0.9%	0.005
				2,778	0.3%		210	0.9%	
1	2	I35	Nonrheumatic aortic valve disorders	1,093	3.8%	0.179	765	3.3%	0.008
				10,153	1.0%		734	3.1%	
1	2	I34	Nonrheumatic mitral valve disorders	1,902	6.5%	0.204	1,368	5.8%	0.004
				23,292	2.4%		1,390	5.9%	
1	2	I48	Atrial fibrillation and flutter	1,878	6.5%	0.216	1,400	6.0%	0.010
				20,795	2.1%		1,456	6.2%	
1	2	I21	Acute myocardial infarction	1,994	6.9%	0.262	1,391	5.9%	0.005
				15,997	1.6%		1,420	6.0%	
1	2	I22	Subsequent ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction	12	0.0%	0.014	10	0.0%	0.011
				170	0.0%		16	0.1%	
1	2	I46	Cardiac arrest	189	0.6%	0.075	129	0.5%	0.002
				1,687	0.2%		126	0.5%	
1	2	E78	Disorders of lipoprotein metabolism and other lipidemias	22,096	75.9%	1.126	16,798	71.6%	0.030
				266,185	26.9%		17,113	72.9%	
1	2	N17	Acute kidney failure	3,501	12.0%	0.370	2,552	10.9%	0.001
				25,484	2.6%		2,560	10.9%	
1	2	I05-I09	Chronic rheumatic heart diseases	1,172	4.0%	0.174	848	3.6%	0.007
				12,384	1.3%		817	3.5%	
1		N18	Chronic kidney disease	4,996	17.2%	0.434	3,609	15.4%	0.003

	2		(CKD)	40,618	4.1%		3,631	15.5%	
	1	N28	Other disorders of kidney and ureter, not elsewhere classified	4,208	14.5%	0.361	2,946	12.6%	0.006
	2			41,028	4.1%		2,896	12.3%	
	1	N20-N23	Urolithiasis	3,455	11.9%	0.274	2,502	10.7%	0.009
	2			44,061	4.5%		2,438	10.4%	
	1	N10-N16	Renal tubulo-interstitial diseases	2,778	9.5%	0.272	1,949	8.3%	0.015
	2			29,752	3.0%		1,851	7.9%	
	1	F01	Vascular dementia	42	0.1%	0.031	34	0.1%	0.001
	2			467	0.0%		35	0.1%	
	1	F02	Dementia in other diseases classified elsewhere	44	0.2%	0.023	39	0.2%	0.001
	2			737	0.1%		38	0.2%	
	1	F03	Unspecified dementia	183	0.6%	0.070	142	0.6%	0.005
	2			1,812	0.2%		133	0.6%	
	1	F04	Amnestic disorder due to known physiological condition	16	0.1%	0.023	13	0.1%	0.006
	2			126	0.0%		10	0.0%	
	1	M62.84	Sarcopenia	12	0.0%	0.015	10	0.0%	<0.001
	2			155	0.0%		10	0.0%	
	1	R54	Age-related physical debility	46	0.2%	0.037	32	0.1%	0.003
	2			411	0.0%		35	0.1%	
Procedure									
Cohort	Code	Characteristic		Patients	% of Cohort	Std diff.	Patients	% of Cohort	Std diff.
	1	1006964	Surgical Procedures on the Digestive System	11,679	40.1%	0.494	8,523	36.3%	0.001
	2			181,446	18.3%		8,513	36.3%	
Medication									
Cohort	Code	Characteristic		Patients	% of Cohort	Std diff.	Patients	% of Cohort	Std diff.
	1	CN101	OPIOID ANALGESICS	21,314	73.3%	0.729	16,403	69.9%	0.046
	2			388,931	39.3%		16,894	72.0%	
	1	M05BA	Bisphosphonates	507	1.7%	0.064	370	1.6%	0.008
	2			9,846	1.0%		393	1.7%	
	1	24947	ferrous sulfate	4,130	14.2%	0.353	2,963	12.6%	0.011
	2			41,105	4.2%		3,052	13.0%	
	1	3640	doxycycline	7,265	25.0%	0.478	5,021	21.4%	<0.001
	2			77,020	7.8%		5,018	21.4%	
	1	CN104	NON-STEROIDAL ANTI-INFLAMMATORY ANALGESICS	11,960	41.1%	0.493	8,853	37.7%	0.001
	2			189,372	19.1%		8,859	37.7%	
	1	DX100	RADIOLOGICAL/ CONTRAST MEDIA	293	1.0%	0.064	198	0.8%	0.010
	2			4,566	0.5%		178	0.8%	
	1	CV800	ACE INHIBITORS	13,970	48.0%	0.898	10,247	43.7%	0.011
	2			106,052	10.7%		10,377	44.2%	
	1	6809	metformin	21,164	72.7%	1.940	15,643	66.6%	0.006
	2			48,297	4.9%		15,714	66.9%	
	1	26225	ondansetron	17,132	58.9%	0.620	12,996	55.4%	0.035
	2			291,814	29.5%		13,403	57.1%	
	1	CN302	BENZODIAZEPINE DERIVATIVE SEDATIVES/HYPNOTICS	16,649	57.2%	0.601	12,595	53.7%	0.026
	2			284,175	28.7%		12,897	54.9%	
	1	N05CD	Benzodiazepine derivatives	12,745	43.8%	0.537	9,451	40.3%	0.010
	2			194,651	19.7%		9,564	40.7%	
	1	4821	glipizide	5,528	19.0%	0.639	3,544	15.1%	0.017
	2			7,976	0.8%		3,400	14.5%	
	1	3498	diphenhydramine	9,243	31.8%	0.452	6,829	29.1%	0.013
	2			131,994	13.3%		6,968	29.7%	
	1	8745	promethazine	8,028	27.6%	0.416	5,958	25.4%	0.017
	2			113,210	11.4%		6,137	26.1%	
	1	3444	dimenhydrinate	516	1.8%	0.115	362	1.5%	0.001
	2			5,386	0.5%		366	1.6%	

1	2	A10BB	Sulfonylureas	9,314 13,493	32.0% 1.4%	0.902	6,004 5,606	25.6% 23.9%	0.039
1	2	A10BK	Sodium-glucose co-transporter 2 (SGLT2) inhibitors	8,017 5,142	27.6% 0.5%	0.845	4,106 3,337	17.5% 14.2%	0.090
1	2	6676	meclizine	2,616 26,812	9.0% 2.7%	0.270	1,817 1,780	7.7% 7.6%	0.006
1	2	CN601	TRICYCLIC ANTIDEPRESSANTS	4,062 41,599	14.0% 4.2%	0.345	2,811 2,792	12.0% 11.9%	0.002
1	2	9601	scopolamine	2,273 27,322	7.8% 2.8%	0.227	1,628 1,755	6.9% 7.5%	0.021
1	2	A10BH	Dipeptidyl peptidase 4 (DPP-4) inhibitors	5,970 7,984	20.5% 0.8%	0.674	3,750 3,448	16.0% 14.7%	0.036
1	2	8704	prochlorperazine	3,421 38,556	11.8% 3.9%	0.296	2,431 2,447	10.4% 10.4%	0.002
1	2	A10BG	Thiazolidinediones	2,569 2,608	8.8% 0.3%	0.420	1,444 1,264	6.2% 5.4%	0.033
1	2	HS501	INSULIN	16,090 49,516	55.3% 5.0%	1.310	11,223 11,076	47.8% 47.2%	0.013
1	2	A10A	INSULINS AND ANALOGUES	15,995 48,821	55.0% 4.9%	1.304	11,146 11,001	47.5% 46.9%	0.012
1	2	8782	propofol	11,774 161,924	40.5% 16.4%	0.555	8,520 8,619	36.3% 36.7%	0.009
1	2	6915	metoclopramide	5,105 61,338	17.5% 6.2%	0.356	3,693 3,754	15.7% 16.0%	0.007
1	2	N05A	ANTIPSYCHOTICS	6,684 88,147	23.0% 8.9%	0.392	4,942 5,036	21.1% 21.5%	0.010
1	2	A10BF	Alpha glucosidase inhibitors	158 259	0.5% 0.0%	0.097	84 78	0.4% 0.3%	0.004
1	2	A04AA	Serotonin (5HT3) antagonists	17,144 292,071	58.9% 29.5%	0.620	13,007 13,409	55.4% 57.1%	0.035
1	2	2403	chlorpromazine	115 1,578	0.4% 0.2%	0.045	88 90	0.4% 0.4%	0.001
1	2	2356	chlordiazepoxide	144 4,123	0.5% 0.4%	0.012	117 121	0.5% 0.5%	0.002
1	2	173107	fosaprepitant	141 1,806	0.5% 0.2%	0.052	107 98	0.5% 0.4%	0.006
Laboratory									
Cohort	Code	Characteristic	Patients	Mean ± SD	Std diff	Patients	Mean ± SD	Std diff	
1	2	4548-4	Hemoglobin A1c (Hb A1c) %	22,690 248,694	7.5 +/- 2.0 6.1 +/- 1.8	0.776	17,427 17,174	7.3 +/- 2.0 7.1 +/- 2.0	0.100
1	2	9083	BMI	22,948 649,696	36.4 +/- 8.5 29.4 +/- 20.6	0.443	18,247 18,414	36.1 +/- 8.5 35.6 +/- 8.9	0.057
Cohort	Code	Characteristic	Patients	% of Cohort	Std diff.	Patients	% of Cohort	Std diff.	
1	2	4548-4	HbA1c: 0 - 6.50 %	14,313 223,213	49.2% 22.6%	0.578	11,287 12,099	48.1% 51.5%	0.069
1	2	4548-4	HbA1c: 6.50 - 9 %	15,936 38,212	54.8% 3.9%	1.349	11,145 10,823	47.5% 46.1%	0.027
1	2	4548-4	HbA1c: 9 - 0 %	10,873 23,261	37.4% 2.4%	0.977	6,900 6,255	29.4% 26.6%	0.061
1	2	9083	BMI: 0 - 25 kg/m2	3,629 264,421	12.5% 26.7%	0.365	3,069 2,810	13.1% 12.0%	0.033
1	2	9083	BMI: 25 - 40 kg/m2	18,586 472,858	63.9% 47.8%	0.329	14,779 15,231	63.0% 64.9%	0.040
1	2	9083	BMI: > 40 kg/m2	10,478 80,942	36.0% 8.2%	0.712	7,663 8,017	32.6% 34.2%	0.032

