

Online Supplementary Material regarding the review manuscript

The science of safety: Adverse effects of GLP-1 based glucose-lowering and obesity medications

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Supplemental Table 1. A score summarizing gastrointestinal symptoms and their potential role in discontinuing treatment because of adverse events for people with type 2 diabetes or clinical obesity treated with GLP-1 receptor agonists, the dual GIP/GLP-1 receptor co-agonist tirzepatide, and next-generation incretin-based medications.

Grade	Severity determining score				Discontinuation of treatment due to adverse events
	Non-disturbing	mild	intermediate	severe	
Score	0	1	2	3	5
Symptom					
Gastro-esophageal acid reflux	Occasional symptoms, rapid and spontaneous recovery	Occasional symptoms, sometimes prolonged episodes, spontaneous recovery	Repeated symptoms occasionally needing symptomatic treatment	Persistent symptoms needing continuous proton pump inhibitor	unlikely
Nausea	Occasional mild, short-lasting symptoms, immediate and spontaneous recovery	Occasional symptoms, sometimes prolonged episodes, spontaneous recovery	Repeated symptoms occasionally needing symptomatic treatment (anti-emetics)	Persistent symptoms repeatedly needing treatment (anti-emetics)	expected
Vomiting	No meaningful category	Occasional regurgitation of gastric content into the oesophagus, but not into the throat or oral cavity or expelled	More than 1 episode of vomiting, leading to rapid symptomatic relief (with or without medication)	More than 1 episode of vomiting, accompanied by feeling ill, requiring treatment (anti-emetics)	expected
Diarrhea	Minor change in stool consistency (softer) not accompanied by other symptoms	Slightly more frequent bowel movements (≤ 2 times daily) and/or softer stool consistency, not accompanied by other symptoms	Moderately more frequent bowel movements (≥ 2 times daily) and/or softer stool consistency, accompanied by other symptoms (e.g., urgency)	Substantially more frequent bowel movements (≥ 3 times daily) and/or softer/watery stool consistency, accompanied by other symptoms (e.g., urgency, abdominal pain)	expected
Constipation	Minor change in the frequency of bowel movements, without noticeable changes in stool consistency (harder), not accompanied by other symptoms	Slightly reduced frequency of bowel movements (≤ 1 times daily) and/or harder stool consistency, not accompanied by other symptoms	Moderately reduced bowel movements (≤ 1 times daily, but ≥ 3 times weekly) and/or harder stool consistency, accompanied by other symptoms (strain, abdominal discomfort or pain)	Substantially reduced bowel movements (≤ 3 times weekly) and/or harder stool consistency, accompanied by other symptoms (strain, abdominal discomfort or pain)	expected
Abdominal discomfort/pain (should only be scored if not associated with any of the above symptoms)	Occasional abdominal discomfort or pain, rapid and spontaneous recovery	Occasional abdominal discomfort or pain, sometimes prolonged episodes, spontaneous recovery	Repeated symptoms occasionally needing symptomatic treatment (e.g., anti-cholinergic medications)	Persistent symptoms repeatedly needing treatment (e.g., anti-cholinergic medications)	unlikely

Supplemental Table 2. Studies assessing the risk for residual gastric content (RGC; a) and aspiration (A; b) in the settings “upper gastrointestinal endoscopy” (UGE) and “general anaesthesia/surgery” (GA/S) in association with GLP-1RA therapy

Setting	Reference	Participants (n)		% DM		N (%) with RGC		Difference	Commentary
(a) RGC	First author, year	GLP-1 RA +	GLP-1 RA -	GLP-1 RA +	GLP-1 RA -	GLP-1 RA +	GLP-1 RA -	RR, OR, PR	
UGE	Silveira 2023 (1)	33	371	n.a.	n.a.	8 (24.2)	19 (5.1)	PR 5.2	Risk ↑ with diabetes, CKD, cerebrovascular disease
UGE	Garza 2024 (2)	306	306	87.9	87.6	39 (14.4)	11 (4.1)	OR 4.4	Risi ↑ only with insulin-dependent diabetes
UGE	Robalino Gonzaga 2024 (3)	73	973	72.6	13.5	10 (13.7)	15 (1.5)	OR 10.1	Risiko ↑ with diabetes, CKD (stage 3-4)
UGE	Nasser 2024 (4)	70	129	82.9	32.6	4 (8.5)	0 (0.0)	P = 0.01	Risk ↓ with same-day colonoscopy
UGE	Nadeem 2024 (5)	922	34261	82.0	15.5	125 (13.6)	788 (2.3)	OR 4.1	Risk ↑ for discontinuation of endoscopy/scheduling of another attempt
UGE	Wu 2024 (6)	90	102	68.9	24.5	19 (18.6)	5 (5.6)	OR 4.8	-
UGE	Chapman 2024 (7)	84	84	86.9	84.5	11 (13.1)	4 (4.8)	aOR 4.6	-
UGE	Quinn 2025 (8)	470	470	74.5	20.6	59 (12.6)	26 (5.5)	OR 1.0	-
GA/S	Sherwin 2023 (9)	10	10	10.0	0.0	9 (90.0)	1 (10.0)	P = 0.005	Diagnosis with ultrasound in lateral position
GA/S	Nersessian 2024 (10)	107	113	0.0	0.0	43 (40.2)	3 (2.7)	OR 24.6	No reduction in risk with durations between 1 and 10 days since last administration of long-acting GLP-1 RA
GA/S	Sen 2024 (11)	62	62	71.0	24.2	35 (56.5)	12 (19.4)	PR 2.9	No reduction in risk with durations between 1 and 17 days since last administration of long-acting GLP-1 RA
All		2227	36881	74.8	16.4	362 (16.3)	884 (2.4)	Risk ↑ with GLP-1RAs	Risk ↑ by approximately 7-fold
(b) Aspiration		GLP-1 RA +	GLP-1 RA -	GLP-1 RA +	GLP-1 RA -	N (%) mit aspiration/pneumonia		Difference	Commentary
		GLP-1 RA +	GLP-1 RA -	GLP-1 RA +	GLP-1 RA -	GLP-1 RA +	GLP-1 RA -	RR, OR, PR	
UGE	Peng 2024 (12)	29320	52184	78.4	69.2	160 (0.5)	143 (0.3)	RR 1.1	-
UGE	Yeo 2024 (13)	15908	15908	71.5	72.7	132 (0.8)	100 (0.6)	HR 1.3, p = 0,036	Risk ↓ with same-day colonoscopy
UGE	Alkabbani 2024 (14)	24317	18537	100.0	100.0	103 (0.4)	79 (0.4)	RR 1.0	Comparison to SGLT-2 inhibitor therapy
UGE	Velji-Ibrahim 2025 (15)	11477	11477	76.1	78.7	20 (0.1)	22 (0.1)	HR 0.9	-
GA/S	Welk 2024 (16)	3833	14072	100.1	100.1	10 (0.3)	49 (0.3)	RR 0.7	General and spinal anaesthesia without difference
GA/S	Klonoff 2024 (17)	2256	11405	98.4	97.8	9 (0.4)	70 (0.6)	OR 0.8	-
GA/S	Buddhiraju 2024 (18) a (THA)	1044	1044	69.3	68.3	0 (0.0)	0 (0.0)	-	No difference regarding other post-anaesthesia/post-surgery complications
GA/S	Buddhiraju 2024 (18) b (TKA)	2095	2095	68.9	68.4	10 (0.5)	10 (0.5)	RR 1.0	No difference regarding other post-anaesthesia/post-surgery complications
GA/S	Chen 2025 (19)	5931	360545	84.3	17.1	42 (0.7)	2335 (0.6)	HR 0.8	Risk ↑ with higher age, diabetes, obesity, CKD, and cerebrovascular disease
GA/S	Poeran 2025 (20)	17665	17665	13.2	13.2	14 (0.1)	12 (0.1)	OR 0.8	-
GA/S	Wright 2025 (21)	31488	31488	68.3	69.0	252 (0.8)	110 (0.7)	OR 1.1	-
All		145334	536420	65.1	35.1	752 (0.5)	2930 (0.5)	Risk unchanged	Overall low risk (approximately 0.5 %)

A: Aspiration; GA/S: general anaesthesia/surgery; aOR: adjusted odds ratio; DM: Diabetes mellitus; UGE: Endoscopy of the upper gastrointestinal tract; GLP-1 RAs: GLP-1 receptor agonists; HR: Hazard ratio; OR: Odds ratio; PR: Prevalence ratio; PSM: Propensity score matching; RGC: Residual gastric content; RR: Relative risk; T2D: Type 2 Diabetes; THA: Total hip arthroplasty; TKA: total knee arthroplasty

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