Electronic Supplementary Material 1

Does weight loss with GLP-1 receptor agonists weaken the pelvic floor? A mechanism-oriented disproportionality analysis of 336,826 reports in FAERS and Canada Vigilance

International Urology and Nephrology

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Part 1 (Tables S1 to S6 and the READUS-PV reporting items) accompanies the main analysis. Part 2 (Tables S7 to S15) accompanies the mechanism and sensitivity analyses in Sects. 2.8, 3.7 and 3.8.

Part 1. Main analysis

Table S1. Case definitions

Group	Definition
Semaglutide	semaglutide, Ozempic, Wegovy, Rybelsus
Tirzepatide	tirzepatide, Mounjaro, Zepbound
Liraglutide	liraglutide, Victoza, Saxenda
Dulaglutide	dulaglutide, Trulicity
Exenatide	exenatide, Byetta, Bydureon
SGLT2 inhibitors	empagliflozin, dapagliflozin, canagliflozin, ertugliflozin and brand names
DPP-4 inhibitors	sitagliptin, linagliptin, saxagliptin, alogliptin and brand names
Other comparators	metformin, insulin, glipizide, glimepiride, glyburide, gliclazide, pioglitazone, phentermine, orlistat, naltrexone with bupropion, setmelanotide
Incontinence	urinary incontinence, stress urinary incontinence, urge incontinence, mixed incontinence, overflow incontinence, incontinence, enuresis
Storage symptoms	nocturia, pollakiuria, micturition urgency
Voiding symptoms	urinary retention, urinary hesitation, urine flow decreased, residual urine volume increased, feeling of residual urine
LUT composite (primary)	any incontinence, storage or voiding term
Broader composite (sensitivity)	primary composite plus polyuria and dysuria
Urolithiasis	nephrolithiasis, calculus urinary, ureterolithiasis, renal colic, calculus bladder
Erectile dysfunction	erectile dysfunction, men only
Urinary tract infection (exploratory)	urinary tract infection, cystitis, pyelonephritis, urosepsis
Hematuria (exploratory)	haematuria, blood urine present

Drugs counted as exposure only when coded as primary or secondary suspect in FAERS, or as suspect in Canada Vigilance. Events are MedDRA preferred terms, shown in MedDRA spelling. Brand names are listed only because they were used as search terms. The mechanism and sensitivity analyses of Part 2 used the same definitions with a few additional brand synonyms (sotagliflozin, bexagliflozin, Inpefa, Brenzavvy, Xultophy, Galvus, Lomaira, Belviq), which enlarged the active comparator set from 684,794 to 686,363 reports.

Table S2. FAERS, crude and adjusted estimates with IC025 and false discovery rate

Drug group	Outcome	Cases	Crude ROR (95% CI)	IC025	Adjusted ROR (95% CI)	q
Semaglutide	LUT composite	468	0.74 (0.67 to 0.82)	-0.53	0.94 (0.85 to 1.04)	0.245
	Incontinence	130	1.03 (0.85 to 1.23)	-0.26	1.25 (1.03 to 1.51)	0.028
	Storage	263	0.61 (0.54 to 0.70)	-0.84	0.78 (0.68 to 0.88)	<0.001
	Voiding	100	0.93 (0.76 to 1.15)	-0.42	1.25 (1.01 to 1.56)	0.050
	Urolithiasis	325	1.57 (1.39 to 1.77)	0.37	1.64 (1.45 to 1.86)	<0.001
	Broader composite	593	0.73 (0.67 to 0.80)	-0.54	0.95 (0.87 to 1.03)	
Tirzepatide	LUT composite	311	0.22 (0.20 to 0.25)	-2.06	0.34 (0.30 to 0.38)	<0.001
	Incontinence	41	0.14 (0.10 to 0.19)	-3.04	0.19 (0.14 to 0.27)	<0.001

Drug group	Outcome	Cases	Crude ROR (95% CI)	IC025	Adjusted ROR (95% CI)	q
	Storage	228	0.25 (0.22 to 0.28)	-1.96	0.35 (0.30 to 0.41)	<0.001
	Voiding	49	0.20 (0.15 to 0.27)	-2.49	0.47 (0.34 to 0.64)	<0.001
	Urolithiasis	279	0.61 (0.54 to 0.70)	-0.77	0.66 (0.57 to 0.76)	<0.001
	Broader composite	371	0.21 (0.19 to 0.23)	-2.15	0.33 (0.30 to 0.37)	
Liraglutide	LUT composite	85	0.74 (0.60 to 0.92)	-0.77	0.70 (0.56 to 0.86)	0.001
	Incontinence	17	0.72 (0.44 to 1.15)	-1.28	0.63 (0.39 to 1.03)	0.074
	Storage	53	0.69 (0.53 to 0.91)	-0.97	0.66 (0.50 to 0.87)	0.004
	Voiding	18	0.91 (0.57 to 1.45)	-0.93	0.85 (0.53 to 1.36)	0.509
	Urolithiasis	61	1.50 (1.16 to 1.94)	0.14	1.35 (1.04 to 1.74)	0.030
	Broader composite	109	0.74 (0.61 to 0.90)	-0.73	0.68 (0.56 to 0.82)	
Dulaglutide	LUT composite	267	0.52 (0.46 to 0.59)	-1.08	0.54 (0.47 to 0.61)	<0.001
	Incontinence	41	0.38 (0.28 to 0.52)	-1.83	0.47 (0.34 to 0.64)	<0.001
	Storage	214	0.63 (0.55 to 0.72)	-0.84	0.56 (0.48 to 0.64)	<0.001
	Voiding	24	0.26 (0.17 to 0.39)	-2.50	0.49 (0.33 to 0.75)	0.001
	Urolithiasis	157	0.87 (0.74 to 1.02)	-0.45	1.14 (0.96 to 1.35)	0.156
	Broader composite	331	0.50 (0.45 to 0.56)	-1.11	0.55 (0.49 to 0.62)	
Exenatide	LUT composite	73	0.51 (0.41 to 0.64)	-1.33	0.33 (0.26 to 0.42)	<0.001
	Incontinence	11	0.37 (0.20 to 0.67)	-2.40	0.29 (0.16 to 0.53)	<0.001
	Storage	59	0.62 (0.48 to 0.80)	-1.10	0.34 (0.26 to 0.44)	<0.001
	Voiding	3	Not estimable		Not estimable	
	Urolithiasis	51	1.00 (0.76 to 1.32)	-0.47	1.15 (0.86 to 1.53)	0.372
	Broader composite	88	0.48 (0.39 to 0.59)	-1.39	0.32 (0.26 to 0.40)	
All GLP-1 RA	LUT composite	1,197	0.33 (0.30 to 0.35)	-1.14	0.43 (0.40 to 0.46)	<0.001
	Incontinence	238	0.31 (0.27 to 0.36)	-1.32	0.41 (0.35 to 0.49)	<0.001
	Storage	814	0.33 (0.31 to 0.36)	-1.13	0.40 (0.36 to 0.43)	<0.001
	Voiding	192	0.29 (0.25 to 0.34)	-1.40	0.63 (0.53 to 0.75)	<0.001
	Urolithiasis	860	0.92 (0.84 to 1.01)	-0.17	1.19 (1.07 to 1.32)	0.002
	Broader composite	1,481	0.31 (0.29 to 0.33)	-1.18	0.44 (0.41 to 0.46)	
SGLT2 inhibitors	LUT composite	2,284	5.58 (5.27 to 5.90)	1.72	5.03 (4.73 to 5.35)	
	Incontinence	379	3.74 (3.30 to 4.24)	1.29	2.98 (2.59 to 3.43)	
	Storage	1,711	6.88 (6.43 to 7.36)	1.87	7.17 (6.65 to 7.73)	
	Voiding	317	3.73 (3.25 to 4.28)	1.27	2.08 (1.79 to 2.42)	
	Urolithiasis	353	1.58 (1.41 to 1.78)	0.38	1.31 (1.15 to 1.48)	
	Broader composite	3,003	5.86 (5.58 to 6.15)	1.76	5.01 (4.74 to 5.29)	
DPP-4 inhibitors	LUT composite	259	1.48 (1.31 to 1.68)	0.33	0.93 (0.82 to 1.06)	
	Incontinence	75	2.10 (1.66 to 2.66)	0.62	1.22 (0.96 to 1.56)	
	Storage	149	1.26 (1.07 to 1.49)	0.05	0.92 (0.78 to 1.09)	
	Voiding	57	1.89 (1.45 to 2.47)	0.42	0.78 (0.59 to 1.02)	
	Urolithiasis	78	1.21 (0.97 to 1.52)	-0.11	0.86 (0.68 to 1.09)	
	Broader composite	378	1.70 (1.53 to 1.89)	0.55	1.00 (0.89 to 1.11)	

q values are Benjamini and Hochberg false discovery rate values across the GLP-1 receptor agonist estimates for the primary composite, its components and urolithiasis.

Table S3. Canada Vigilance, crude and adjusted estimates, women-only and indication analyses

Drug group	Outcome	Cases	Crude ROR (95% CI)	IC025	Adjusted ROR (95% CI)	q
Semaglutide	LUT composite	35	0.59 (0.41 to 0.85)	-1.16	0.62 (0.42 to 0.91)	0.043
	Incontinence	13	1.09 (0.58 to 2.05)	-0.84	1.37 (0.68 to 2.77)	0.457
	Storage	19	0.43 (0.27 to 0.69)	-1.75	0.41 (0.25 to 0.68)	0.002

Drug group	Outcome	Cases	Crude ROR (95% CI)	IC025	Adjusted ROR (95% CI)	q
	Urolithiasis	22	0.74 (0.47 to 1.18)	-1.04	0.76 (0.46 to 1.26)	0.445
	Broader composite	40	0.56 (0.40 to 0.79)	-1.19	0.60 (0.42 to 0.85)	
Liraglutide	LUT composite	7	0.37 (0.17 to 0.79)	-2.58	0.42 (0.19 to 0.90)	0.057
	Urolithiasis	8	0.85 (0.42 to 1.75)	-1.41	0.84 (0.40 to 1.78)	0.714
All GLP-1 RA	LUT composite	44	0.48 (0.34 to 0.67)	-1.27	0.50 (0.35 to 0.72)	0.001
	Incontinence	16	0.90 (0.50 to 1.62)	-0.95	1.07 (0.56 to 2.08)	0.830
	Storage	24	0.35 (0.22 to 0.53)	-1.84	0.33 (0.21 to 0.52)	<0.001
	Voiding	5	0.39 (0.15 to 1.01)	-2.53	0.63 (0.23 to 1.74)	0.457
	Urolithiasis	31	0.71 (0.47 to 1.07)	-0.94	0.70 (0.45 to 1.11)	0.236
	Broader composite	51	0.46 (0.34 to 0.63)	-1.28	0.48 (0.34 to 0.67)	
SGLT2 inhibitors	LUT composite	54	1.44 (1.06 to 1.96)	-0.05	1.64 (1.16 to 2.31)	
	Incontinence	11	1.24 (0.63 to 2.41)	-0.79	1.35 (0.65 to 2.81)	
	Storage	42	1.61 (1.13 to 2.29)	0.01	1.99 (1.34 to 2.97)	
	Voiding	5	0.89 (0.34 to 2.31)	-1.70	0.77 (0.28 to 2.14)	
	Urolithiasis	17	0.77 (0.46 to 1.28)	-1.13	0.89 (0.51 to 1.56)	
	Broader composite	84	2.09 (1.61 to 2.71)	0.42	2.52 (1.87 to 3.39)	
DPP-4 inhibitors	LUT composite	9	0.49 (0.25 to 0.95)	-2.06	0.43 (0.22 to 0.85)	
	Incontinence	6	1.57 (0.67 to 3.68)	-0.89	1.56 (0.64 to 3.76)	
Semaglutide, women	Incontinence	9	1.14 (0.53 to 2.45)	-1.01	1.53 (0.62 to 3.77)	
	LUT composite	22	0.56 (0.36 to 0.89)	-1.36	0.63 (0.39 to 1.04)	
All GLP-1 RA, women	Incontinence	12	0.95 (0.47 to 1.94)	-1.02	1.33 (0.58 to 3.06)	
	LUT composite	31	0.47 (0.31 to 0.70)	-1.35	0.55 (0.36 to 0.86)	
Semaglutide, obesity vs diabetes	LUT composite	14			OR 1.13 (0.31 to 4.16)	
	Urolithiasis	11			OR 0.91 (0.23 to 3.59)	
All GLP-1 RA, obesity vs diabetes	LUT composite	19			OR 0.69 (0.25 to 1.94)	
	Urolithiasis	19			OR 1.20 (0.37 to 3.85)	

Reports received from 2018 onward. Adjusted for age group, sex, reporter type and report year, with sex omitted in women-only models. Combinations not shown had fewer than five exposed cases. Cases in indication rows are cases among obesity users.

Table S4. FAERS sensitivity analyses, crude ROR (95% CI)

Drug group	Composite, health professionals	Incontinence, health professionals	Urolithiasis, health professionals	Composite, GI reports removed	Incontinence, GI reports removed	Urolithiasis, GI reports removed
Semaglutide	0.47 (0.40 to 0.56)	1.03 (0.76 to 1.38)	1.54 (1.25 to 1.90)	0.67 (0.59 to 0.75)	1.03 (0.81 to 1.31)	1.79 (1.55 to 2.06)
Tirzepatide	0.15 (0.09 to 0.24)	0.16 (0.05 to 0.50)	1.13 (0.79 to 1.62)	0.19 (0.16 to 0.21)	0.08 (0.05 to 0.14)	0.73 (0.63 to 0.84)
Liraglutide	0.37 (0.25 to 0.55)	0.27 (0.09 to 0.83)	1.38 (0.91 to 2.10)	0.62 (0.47 to 0.80)	0.75 (0.41 to 1.35)	1.84 (1.39 to 2.45)
Dulaglutide	0.38 (0.28 to 0.52)	0.29 (0.12 to 0.69)	1.17 (0.81 to 1.69)	0.55 (0.48 to 0.63)	0.46 (0.32 to 0.66)	0.94 (0.77 to 1.13)
Exenatide	0.23 (0.11 to 0.48)	Not estimable	0.78 (0.35 to 1.75)	0.42 (0.33 to 0.55)	0.27 (0.12 to 0.60)	1.04 (0.77 to 1.42)
All GLP-1 RA	0.33 (0.29 to 0.38)	0.56 (0.42 to 0.73)	1.43 (1.21 to 1.70)	0.29 (0.27 to 0.32)	0.29 (0.24 to 0.35)	1.12 (1.01 to 1.25)
SGLT2 inhibitors	3.13 (2.89 to 3.40)	2.16 (1.77 to 2.63)	1.33 (1.11 to 1.58)	7.39 (6.97 to 7.83)	4.86 (4.21 to 5.62)	1.82 (1.61 to 2.06)
DPP-4 inhibitors	1.35 (1.18 to 1.55)	1.67 (1.24 to 2.25)	0.88 (0.64 to 1.20)	1.75 (1.55 to 1.98)	2.47 (1.90 to 3.20)	1.24 (0.96 to 1.61)

The composite in this table is the broader definition that includes polyuria and dysuria. Health professionals means physician, pharmacist or other health professional reporter. GI reports removed means every report with a common gastrointestinal event was excluded from the whole set.

Table S5. FAERS exploratory outcomes, adjusted ROR (95% CI)

Drug group	Urinary tract infection	Hematuria
Semaglutide	0.83 (0.76 to 0.90)	0.98 (0.80 to 1.20)
Tirzepatide	0.26 (0.24 to 0.29)	0.59 (0.45 to 0.75)
Liraglutide	0.73 (0.61 to 0.87)	1.05 (0.73 to 1.50)
Dulaglutide	0.55 (0.49 to 0.63)	0.56 (0.41 to 0.76)
Exenatide	0.38 (0.31 to 0.46)	0.31 (0.17 to 0.55)
All GLP-1 RA	0.37 (0.35 to 0.40)	0.62 (0.53 to 0.72)
SGLT2 inhibitors	5.66 (5.37 to 5.96)	2.59 (2.28 to 2.94)
DPP-4 inhibitors	1.07 (0.97 to 1.18)	0.46 (0.34 to 0.62)

Adjusted for age group, sex, reporter type, report year and country. Hematuria includes haematuria and blood urine present.

Table S6. FAERS, tirzepatide versus semaglutide among reports naming only one of the two

Outcome	Tirzepatide, cases / reports	Semaglutide, cases / reports	ROR (95% CI)
Broader LUT composite	365 / 152,429	583 / 80,780	0.33 (0.29 to 0.38)
Incontinence	40 / 152,429	129 / 80,780	0.16 (0.12 to 0.23)
Urolithiasis	273 / 152,429	319 / 80,780	0.45 (0.38 to 0.53)
Erectile dysfunction	53 / 152,429	112 / 80,780	0.25 (0.18 to 0.35)

READUS-PV reporting items

Reporting domain	Where reported
Title and abstract identify a disproportionality analysis of spontaneous reports	Title, Abstract
Background, rationale and objectives	Introduction
Databases, versions and periods	Sect. 2.1
Deduplication	Sect. 2.2
Drug identification and suspect role	Sect. 2.3; Table S1
Event definitions with MedDRA preferred terms	Sect. 2.4; Table S1
Indication classification	Sect. 2.3; Table S13
Comparator and background set	Sect. 2.6; sensitivity without the positive control in Sect. 2.8 and Table 6
Disproportionality measures, thresholds and multiplicity	Sect. 2.6; q values in Tables S2, S3 and S14
Adjustment and missing data	Sect. 2.6; Table S13
Positive control	Sect. 2.5; Sect. 3.8
Preregistration and post hoc changes	Sect. 2.1 and 2.8 (mechanism tests written down before they were run, not preregistered)
Database overlap	Sect. 2.1; Sect. 4.1
External validation	Sect. 2.1; Sect. 3.2 and 3.3; Table 3; Table S3
Sensitivity and subgroup analyses	Sect. 2.7 and 2.8; Sect. 3.6 to 3.8; Tables 5 and 6; Tables S2 to S15
Time to onset and co-reporting	Sect. 2.8; Sect. 3.7; Tables S7 and S8
Flow of reports and descriptive characteristics	Sect. 3.1; Fig. 1; Table 1
Main estimates	Sect. 3.2 to 3.5; Tables 2 to 4; Figs. 2 and 3
Interpretation without incidence or causality	Sect. 4
Limitations	Sect. 4.1
Data and code availability	Declarations

Part 2. Mechanism and sensitivity analyses

Mechanism and sensitivity analyses in FAERS, first quarter of 2018 to second quarter of 2026, active comparator set of 686,363 reports (Sect. 2.8).

Table S7. Time to onset of selected events after the start of the suspect drug, FAERS

Drug and event	n	Median days (IQR)	Within 90 days, %	Weibull shape (95% CI)
Semaglutide, incontinence, all	23	2 (0 to 33)	87	0.48 (0.41 to 0.62)
Semaglutide, incontinence, women	18	2 (0 to 32)	89	0.52 (0.45 to 0.70)
Semaglutide, storage symptoms	68	0 (0 to 16)	91	0.44 (0.40 to 0.51)
Semaglutide, voiding symptoms	22	12 (0 to 85)	77	0.44 (0.38 to 0.60)
Semaglutide, urinary tract infection	124	16 (1 to 57)	82	0.51 (0.46 to 0.59)
Semaglutide, weight decreased	536	7 (0 to 68)	80	0.43 (0.41 to 0.45)
Semaglutide, all other events	16,687	14 (0 to 85)	76	0.45 (0.45 to 0.45)
Tirzepatide, storage symptoms	34	1 (0 to 43)	85	0.42 (0.37 to 0.52)
Tirzepatide, voiding symptoms	16	3 (0 to 14)	94	0.58 (0.46 to 0.89)
Tirzepatide, urinary tract infection	73	27 (1 to 102)	73	0.54 (0.47 to 0.65)
Tirzepatide, weight decreased	228	16 (0 to 77)	78	0.48 (0.45 to 0.53)
Tirzepatide, all other events	16,286	7 (0 to 62)	80	0.45 (0.45 to 0.46)
SGLT2 inhibitors, incontinence, all	83	14 (2 to 94)	75	0.48 (0.43 to 0.55)
SGLT2 inhibitors, storage symptoms	378	6 (0 to 49)	85	0.47 (0.45 to 0.49)
SGLT2 inhibitors, urinary tract infection	898	63 (12 to 242)	57	0.62 (0.60 to 0.65)
SGLT2 inhibitors, all other events	13,259	34 (4 to 205)	63	0.51 (0.51 to 0.51)

Time to onset is the interval from the recorded start date of the suspect drug to the event date, restricted to 0 to 1,095 days, among reports with both dates complete (semaglutide 16,919, tirzepatide 16,412, SGLT2 inhibitors 14,602). Weibull shape with bootstrap 95% confidence interval (300 resamples); a shape below 1 indicates risk concentrated early after exposure. Mann-Whitney test, incontinence versus all other events, p 0.16 for semaglutide and p 0.008 for SGLT2 inhibitors. Tirzepatide and liraglutide incontinence had fewer than 10 reports with dates and are not shown. IQR, interquartile range.

Table S8. Terms co-reported in incontinence reports compared with other reports of the same drug, FAERS

Drug	Term group	Incontinence reports with term, %	Other reports with term, %	OR (95% CI)	Fisher p
Semaglutide (130 incontinence reports)	Weight decreased	3.8	5.8	0.72 (0.31 to 1.69)	0.45
	Muscle weakness or atrophy	4.6	0.6	8.53 (3.86 to 18.9)	<0.001
	Hyperglycaemia, glycosuria, polyuria, dehydration	8.5	6.7	1.34 (0.73 to 2.45)	0.38
	Gastrointestinal events	37.7	26.1	1.72 (1.21 to 2.45)	0.004
	Pelvic organ prolapse	1.5	0.0	2 reports	<0.001
	Urinary tract infection	7.7	0.8	10.98 (5.82 to 20.7)	<0.001
	Storage symptoms	6.9	0.3	25.1 (12.8 to 49.2)	<0.001
	Voiding symptoms	5.4	0.1	53.2 (24.8 to 114)	<0.001
Tirzepatide (41 incontinence reports)	Weight decreased	4.9	1.4	4.42 (1.23 to 15.9)	0.11
	Muscle weakness or atrophy	2.4	0.3	12.2 (2.38 to 62.2)	0.12

Drug	Term group	Incontinence reports with term, %	Other reports with term, %	OR (95% CI)	Fisher p
	Hyperglycaemia, glycosuria, polyuria, dehydration	19.5	3.2	7.59 (3.57 to 16.1)	<0.001
	Gastrointestinal events	61.0	18.7	6.70 (3.61 to 12.4)	<0.001
	Urinary tract infection	7.3	0.2	38.1 (12.7 to 114)	<0.001
	Storage symptoms	9.8	0.1	82.1 (30.6 to 220)	<0.001
All GLP-1 receptor agonists	Weight decreased	5.5	3.4	1.70 (0.98 to 2.95)	0.10
	Muscle weakness or atrophy	3.4	0.4	10.1 (5.10 to 20.2)	<0.001
	Hyperglycaemia, glycosuria, polyuria, dehydration	16.0	6.7	2.65 (1.88 to 3.75)	<0.001
	Gastrointestinal events	36.6	19.4	2.39 (1.84 to 3.11)	<0.001
	Urinary tract infection	7.1	0.4	17.5 (10.7 to 28.5)	<0.001
	Storage symptoms	9.7	0.2	45.6 (29.6 to 70.1)	<0.001
	Voiding symptoms	3.8	0.1	74.7 (38.4 to 145)	<0.001

Crude odds ratios with Haldane correction. Term groups. Weight decreased includes weight decreased, abnormal loss of weight and cachexia. Muscle weakness or atrophy includes muscular weakness, muscle atrophy, sarcopenia and pelvic floor muscle weakness. Gastrointestinal events include nausea, vomiting, diarrhoea, constipation and faecal incontinence. Storage symptoms include nocturia, pollakiuria and micturition urgency. Voiding symptoms include urinary retention, urinary hesitation, urine flow decreased, residual urine volume increased and feeling of residual urine. Rows with no events in either group are omitted.

Table S9. Crude reporting odds ratio for semaglutide and incontinence by calendar year of FDA receipt, FAERS active comparator set

Year	Semaglutide reports	Incontinence reports	Crude ROR (95% CI)
2018	1,065	1	0.74 (0.15 to 3.73)
2019	1,409	3	1.53 (0.53 to 4.45)
2020	3,078	9	1.99 (1.01 to 3.88)
2021	4,135	17	2.05 (1.23 to 3.39)
2022	5,954	8	0.67 (0.33 to 1.35)
2023	8,670	18	1.15 (0.70 to 1.88)
2024	14,230	20	1.29 (0.80 to 2.07)
2025	22,667	34	1.28 (0.88 to 1.85)
2026 (first half)	20,904	20	0.78 (0.48 to 1.27)

Each year is analysed separately, comparing semaglutide reports with all other reports in the active comparator set received in that year. Wegovy was approved for obesity in June 2021 and use expanded widely from 2023. ROR, reporting odds ratio.

Table S10. Incontinence, lower urinary tract composite and urinary tract infection by recorded semaglutide dose, injectable and oral reports, FAERS

Injectable dose band, mg weekly	Reports	Incontinence, n (%)	LUT composite, n (%)	Urinary tract infection, n (%)
0.25 or less	8,425	34 (0.40)	73 (0.87)	66 (0.78)
>0.25 to 0.5	10,770	13 (0.12)	66 (0.61)	104 (0.97)
>0.5 to 1	9,706	19 (0.20)	61 (0.63)	95 (0.98)

Injectable dose band, mg weekly	Reports	Incontinence, n (%)	LUT composite, n (%)	Urinary tract infection, n (%)
>1 to 1.7	2,050	0 (0.00)	4 (0.20)	15 (0.73)
>1.7 to 2	4,307	8 (0.19)	19 (0.44)	39 (0.91)
>2 to 2.4	2,376	1 (0.04)	4 (0.17)	10 (0.42)
>2.4	673	1 (0.15)	2 (0.30)	2 (0.30)
Trend, Cochran-Armitage		z = -3.20, p = 0.001		

Oral dose band, mg daily	Reports	Incontinence, n (%)
3 or less	1,405	1 (0.07)
>3 to 7	1,416	3 (0.21)
>7 to 14	877	0 (0.00)
>14	1	0

Dose is the highest dose in milligrams recorded on a semaglutide line of the report among reports with a numeric dose and unit of milligrams (42,006 of 82,112 semaglutide reports). Injectable reports (38,307) are those naming Ozempic, Wegovy or no brand without an oral route; oral reports (3,699) name Rybelsus or an oral route. Values above 2.4 mg in injectable reports most often reflect cumulative amounts or data entry conventions. Among 2,241 reports recording the Wegovy maintenance dose of 2.4 mg there was 1 incontinence report (0.04%); among 23,024 Ozempic reports at 1 mg or less there were 35 (0.15%). The lowest bands include the dose escalation weeks, so dose and time since initiation are partly confounded. LUT, lower urinary tract.

Table S11. Heterogeneity of crude reporting odds ratios across the five GLP-1 receptor agonists, FAERS

Outcome	Agents, k	Cochran Q	p	I^2, %
Lower urinary tract composite	5	268.5	<0.001	99
Incontinence	5	127.4	<0.001	97
Storage symptoms	5	134.4	<0.001	97
Voiding symptoms	5	94.8	<0.001	96
Urinary tract infection	5	468.6	<0.001	99

Semaglutide, tirzepatide, liraglutide, dulaglutide and exenatide, each compared with all other reports in the active comparator set.

Table S12. Adjusted reporting odds ratios (95% CI) after removing SGLT2 inhibitor reports from the active comparator set, all GLP-1 receptor agonists, FAERS

Outcome	Semaglutide	Tirzepatide	Liraglutide	Dulaglutide	Exenatide	All GLP-1 RA	DPP-4 inhibitors
LUT composite	1.44 (1.29 to 1.60) [447]	0.47 (0.41 to 0.54) [304]	0.98 (0.79 to 1.22) [82]	0.83 (0.72 to 0.95) [236]	0.82 (0.62 to 1.09) [55]	0.79 (0.72 to 0.86) [1,117]	1.13 (0.99 to 1.30) [243]
Incontinence	1.77 (1.44 to 2.17) [124]	0.24 (0.17 to 0.34) [41]	0.75 (0.46 to 1.22) [17]	0.55 (0.40 to 0.77) [38]	0.57 (0.29 to 1.14) [9]	0.60 (0.50 to 0.72) [227]	1.60 (1.26 to 2.04) [85]
Storage symptoms	1.21 (1.05 to 1.39) [244]	0.51 (0.43 to 0.60) [221]	1.05 (0.79 to 1.40) [50]	1.01 (0.86 to 1.18) [190]	0.97 (0.70 to 1.35) [43]	0.80 (0.72 to 0.90) [745]	1.25 (1.04 to 1.51) [131]
Voiding symptoms	1.67 (1.32 to 2.12) [94]	0.60 (0.43 to 0.84) [49]	1.01 (0.63 to 1.62) [18]	0.49 (0.30 to 0.77) [19]	Not estimable	0.89 (0.72 to 1.09) [181]	0.76 (0.57 to 1.02) [53]
Urinary tract infection	1.49 (1.36 to 1.64) [602]	0.37 (0.32 to 0.41) [343]	1.04 (0.87 to 1.25) [120]	0.79 (0.69 to 0.90) [254]	1.07 (0.84 to 1.36) [80]	0.72 (0.66 to 0.78) [1,379]	1.76 (1.58 to 1.95) [469]

Comparator set of 596,859 reports. Adjusted for age group, sex, reporter type, report year and country. Numbers in brackets are exposed cases. With both SGLT2 and DPP-4 inhibitors removed (571,643 reports), semaglutide composite 1.37 (1.22 to 1.52), incontinence 1.43 (1.14 to 1.79); tirzepatide 0.47 (0.41 to 0.54) and 0.24 (0.17 to 0.34); class 0.76 (0.69 to 0.83) and 0.49 (0.41 to 0.59).

Table S13. Drug by sex interaction for incontinence, FAERS, reports with known sex

Drug	Adjusted ROR, men	Adjusted ROR, women	Interaction OR, women vs men (95% CI)	p
Semaglutide	0.79 (0.53 to 1.19) [26]	1.44 (1.15 to 1.82) [93]	1.71 (1.08 to 2.69)	0.022
All GLP-1 RA	0.32 (0.23 to 0.44) [47]	0.48 (0.39 to 0.59) [175]	1.57 (1.10 to 2.23)	0.013
SGLT2 inhibitors	2.69 (2.16 to 3.34) [159]	2.97 (2.46 to 3.59) [184]	1.10 (0.84 to 1.44)	0.48

Logistic models with frequency weights, adjusted for age group, reporter type, report year and country, with a drug by sex product term. The interaction odds ratio is the ratio of the women to men reporting odds ratios.

Table S14. Completeness of indication coding for GLP-1 receptor agonists, FAERS active comparator set

Drug	Reports	No indication, %	Obesity only, %	Diabetes only, %	Both, %	Other indication, %
Semaglutide	82,112	1.8	19.1	32.3	4.0	42.8
Tirzepatide	153,762	2.5	26.0	14.6	1.5	55.5
Liraglutide	15,255	2.5	17.0	38.2	2.0	40.2
Dulaglutide	65,978	0.7	0.7	40.5	0.8	57.3
Exenatide	18,912	29.9	0.6	62.7	0.5	6.4

Indication from the FAERS indication table linked to the suspect drug line. Other indication includes terms such as product used for unknown indication and off label use. Only reports coded obesity only or diabetes only entered the indication analyses.

Table S15. Mechanism tests with p values and Benjamini and Hochberg q values, FAERS

Test	Estimate	p	q
Obesity vs diabetes, women, incontinence	0.66	0.22	0.30
Obesity vs diabetes, women, composite	0.90	0.60	0.60
Obesity vs diabetes, women, storage symptoms	0.82	0.50	0.52
Obesity vs diabetes, women, urinary tract infection	0.57	<0.001	<0.001
Wegovy vs Ozempic, incontinence	0.64	0.14	0.22
Wegovy vs Ozempic, composite	0.77	0.063	0.10
Wegovy vs Ozempic, storage symptoms	0.68	0.056	0.099
Wegovy vs Ozempic, urinary tract infection	0.67	<0.001	0.002
Rybelsus vs Ozempic, incontinence	1.45	0.26	0.33
Rybelsus vs Ozempic, composite	1.42	0.033	0.064
Rybelsus vs Ozempic, storage symptoms	1.73	0.008	0.018
Rybelsus vs Ozempic, urinary tract infection	1.17	0.28	0.34
Zepbound vs Mounjaro, incontinence	0.55	0.16	0.23
Zepbound vs Mounjaro, composite	0.53	<0.001	<0.001
Zepbound vs Mounjaro, storage symptoms	0.52	<0.001	<0.001
Zepbound vs Mounjaro, urinary tract infection	0.53	<0.001	<0.001
Co-reporting, weight decreased	0.66	0.45	0.49
Co-reporting, muscle weakness or atrophy	7.92	<0.001	<0.001
Co-reporting, hyperglycaemia or dehydration	1.28	0.38	0.44
Co-reporting, gastrointestinal events	1.71	0.004	0.008
Co-reporting, urinary tract infection	10.5	<0.001	<0.001
Co-reporting, storage symptoms	23.9	<0.001	<0.001
Co-reporting, voiding symptoms	50.1	<0.001	<0.001

Indication and brand estimates are adjusted odds ratios from logistic models; co-reporting estimates are conditional maximum likelihood odds ratios from Fisher exact tests, which differ slightly from the Haldane-corrected values in Table S8. q values from the Benjamini and Hochberg procedure across the 23 tests.