

**Adverse events of oral GLP-1 receptor agonist (Semaglutide tablets):
a real-world study based on FAERS from 2019 to 2023**

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Additional MATERIALS

Supplementary Table 1 : Algorithms based on four grid table

	Drug-related ADEs	Non-drug-related ADEs	Total
Drug	a	b	a + b
Non-drug	c	d	c + d
Total	a + c	b + d	N = a + b + c + d

Supplementary Table 2 : Formulas and thresholds of proportional imbalance method

Method	Formula	Threshold
ROR	$ROR = \frac{a / c}{b / d}$	$a \geq 3$ $ROR \geq 3$ 95%CI (lower limit) > 1
	$SE(\ln ROR) = \sqrt{\frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}}$	
	$95\%CI = e^{\ln(ROR) \pm 1.96se}$	
PRR	$PRR = \frac{a / (a + b)}{c / (c + d)}$	$a \geq 3$ $PRR \geq 2$ 95%CI (lower limit) > 1
	$SE(\ln PRR) = \sqrt{\frac{1}{a} - \frac{1}{a + b} + \frac{1}{c} - \frac{1}{c + d}}$	
	$95\%CI = e^{\ln(PRR) \pm 1.96se}$	
BCPNN	$IC = \log_2 \frac{p(x, y)}{p(x)p(y)} = \log_2 \frac{a(a + b + c + d)}{(a + b)(a + c)}$	IC025>0
	$E(IC) = \log_2 \frac{(a + \gamma 11)(a + b + c + d + \alpha)(a + b + c + d + \beta)}{(a + b + c + d + \gamma)(a + b + \alpha 1)(a + c + \beta 1)}$	
	$V(IC) = \frac{1}{(\ln 2)^2} \left[\frac{(a + b + c + d) - a + \gamma - \gamma 11}{(a + \gamma 11)(1 + a + b + c + d + \gamma)} \right.$ $+ \frac{(a + b + c + d) - (a + b) + a - \alpha 1}{(a + b + \alpha 1)(1 + a + b + c + d + \alpha)}$ $\left. + \frac{(a + b + c + d + \alpha) - (a + c) + \beta - \beta 1}{(a + b + \beta 1)(1 + a + b + c + d + \beta)} \right]$	
	$\gamma = \gamma 11 \frac{(a + b + c + d + \alpha)(a + b + c + d + \beta)}{(a + b + \alpha 1)(a + c + \beta 1)}$	
	$IC - 2SD = E(IC) - 2\sqrt{V(IC)}$	
EBGM	$EBGM = \frac{a(a + b + c + d)}{(a + c)(a + b)}$	EBGM05>2
	$SE(\ln EBGM) = \sqrt{\frac{1}{a} + \frac{1}{b} + \frac{1}{c} + \frac{1}{d}}$	
	$95\%CI = e^{\ln(EBGM) \pm 1.96se}$	

Supplementary Table 3 : PTs induced by Semaglutide tablets as the PS (primary suspect)

soc	pt	Case Reports	ROR(95% CI)	PRR(95% CI)	chisq	IC(IC025)	EBGM (EBGM05)
endocrine disorders	thyroid cyst	3	70.04(22.31, 219.89)	70(22.46, 218.17)	199.74	6.1(4.67)	68.55(26.32)
hepatobiliary disorders	cholecystitis acute	18	50.41(31.62, 80.35)	50.24(31.39, 80.42)	855.54	5.63(4.97)	49.49(33.5)
metabolism and nutrition disorders	ketosis	4	46.87(17.46, 125.81)	46.84(17.58, 124.8)	176.88	5.53(4.25)	46.18(20.22)
nervous system disorders	vith nerve paralysis	3	40.91(13.1, 127.78)	40.88(13.12, 127.41)	115.27	5.34(3.91)	40.39(15.57)
neoplasms benign, malignant and unspecified (incl cysts and polyps)	adenocarcinoma pancreas	3	34.16(10.95, 106.58)	34.14(10.95, 106.41)	95.51	5.08(3.65)	33.8(13.04)
injury, poisoning and procedural complications	drug dose titration not performed	6	33.3(14.89, 74.46)	33.27(14.9, 74.31)	185.88	5.04(3.97)	32.94(16.8)
eye disorders	diabetic retinopathy	7	27.89(13.25, 58.72)	27.86(13.23, 58.67)	179.72	4.79(3.78)	27.63(14.82)
gastrointestinal disorders	eructation	35	26.43(18.93, 36.9)	26.27(18.83, 36.66)	844.02	4.7(4.23)	26.06(19.71)
musculoskeletal and connective tissue disorders	neck mass	7	26.28(12.49, 55.32)	26.25(12.46, 55.28)	168.65	4.7(3.7)	26.05(13.97)
general disorders and administration site conditions	early satiety	3	25.35(8.14, 78.98)	25.34(8.13, 78.98)	69.6	4.65(3.23)	25.15(9.72)
hepatobiliary disorders	bile duct stone	6	25.33(11.34, 56.59)	25.31(11.33, 56.53)	139	4.65(3.58)	25.12(12.82)
metabolism and nutrition disorders	weight loss poor	7	24.9(11.83, 52.4)	24.87(11.81, 52.38)	159.14	4.63(3.62)	24.69(13.24)
injury, poisoning and procedural complications	product package associated injury	5	23.32(9.67, 56.23)	23.3(9.65, 56.29)	105.96	4.53(3.37)	23.14(11.08)
metabolism and nutrition disorders	food craving	7	23.13(10.99, 48.66)	23.1(10.97, 48.65)	146.94	4.52(3.52)	22.94(12.31)
gastrointestinal disorders	pancreatitis	117	23.12(19.23, 27.78)	22.64(18.98, 27.01)	2405.99	4.49(4.23)	22.49(19.29)
metabolism and nutrition disorders	hyperglycaemia	3	22.43(7.2, 69.85)	22.42(7.19, 69.88)	60.97	4.48(3.06)	22.27(8.61)

	hyperosmolar nonketotic syndrome						
investigations	glycosylated haemoglobin increased	49	22.39(16.89, 29.69)	22.2(16.87, 29.21)	985.67	4.46(4.06)	22.06(17.4 2)
ear and labyrinth disorders	vertigo positional	3	21.73(6.98, 67.66)	21.72(6.97, 67.7)	58.9	4.43(3.01)	21.58(8.34)
neoplasms benign, malignant and unspecified (incl cysts and polyps)	pancreatic carcinoma metastatic	4	21.53(8.05, 57.57)	21.52(8.08, 57.34)	77.74	4.42(3.15)	21.38(9.39)
gastrointestinal disorders	impaired gastric emptying	15	21.22(12.76, 35.28)	21.16(12.71, 35.22)	286.31	4.39(3.68)	21.03(13.7 4)
eye disorders	vitreous haemorrhage	4	20.54(7.68, 54.92)	20.53(7.71, 54.7)	73.84	4.35(3.08)	20.41(8.96)
investigations	lipase increased	10	19.09(10.25, 35.56)	19.06(10.18, 35.69)	170.11	4.24(3.39)	18.95(11.2 6)
endocrine disorders	thyroid mass	6	14.26(6.39, 31.81)	14.25(6.38, 31.83)	73.58	3.83(2.75)	14.19(7.25)
investigations	blood glucose decreased	42	13.63(10.06, 18.48)	13.54(10.09, 18.17)	485.92	3.75(3.32)	13.49(10.4 5)
renal and urinary disorders	renal pain	12	13.15(7.46, 23.2)	13.13(7.44, 23.18)	133.92	3.71(2.92)	13.08(8.13)
metabolism and nutrition disorders	abnormal loss of weight	6	12.77(5.73, 28.49)	12.76(5.71, 28.5)	64.79	3.67(2.6)	12.72(6.5)
metabolism and nutrition disorders	diabetes mellitus inadequate control	19	12.67(8.07, 19.9)	12.63(8.05, 19.82)	202.76	3.65(3.02)	12.59(8.63)
investigations	amylase increased	4	12.56(4.7, 33.53)	12.55(4.71, 33.44)	42.35	3.64(2.38)	12.5(5.5)
gastrointestinal disorders	regurgitation	3	12.34(3.97, 38.35)	12.33(3.96, 38.43)	31.12	3.62(2.2)	12.29(4.76)
gastrointestinal disorders	oesophageal pain	3	11.69(3.76, 36.32)	11.68(3.75, 36.4)	29.2	3.54(2.12)	11.64(4.51)
general disorders and administration site conditions	hunger	10	11.6(6.23, 21.59)	11.58(6.18, 21.68)	96.33	3.53(2.67)	11.54(6.86)
hepatobiliary disorders	jaundice cholestatic	3	11.45(3.69, 35.59)	11.45(3.67, 35.69)	28.51	3.51(2.09)	11.41(4.42)
skin and	skin odour	3	11.19(3.6,	11.18(3.59,	27.73	3.48(2.06)	11.15(4.32

subcutaneous tissue disorders	abnormal		34.77)	34.85)			)
metabolism and nutrition disorders	euglycaemic diabetic ketoacidosis	7	11.14(5.3, 23.41)	11.13(5.28, 23.44)	64.32	3.47(2.47)	11.09(5.96)
hepatobiliary disorders	cholelithiasis	22	10.97(7.21, 16.69)	10.93(7.24, 16.5)	197.97	3.45(2.85)	10.9(7.67)
metabolism and nutrition disorders	diabetic ketoacidosis	21	10.86(7.07, 16.69)	10.83(7.04, 16.67)	186.72	3.43(2.83)	10.79(7.54)
investigations	glomerular filtration rate decreased	13	10.82(6.28, 18.67)	10.8(6.24, 18.7)	115.25	3.43(2.67)	10.77(6.82)
investigations	blood glucose increased	136	10.43(8.8, 12.37)	10.2(8.72, 11.93)	1127.48	3.35(3.1)	10.17(8.82)
injury, poisoning and procedural complications	drug titration error	3	10.32(3.32, 32.08)	10.32(3.31, 32.17)	25.17	3.36(1.95)	10.29(3.98)
endocrine disorders	goitre	3	10.24(3.29, 31.81)	10.23(3.28, 31.88)	24.91	3.35(1.93)	10.2(3.95)
respiratory, thoracic and mediastinal disorders	hiccups	6	9.81(4.4, 21.87)	9.8(4.39, 21.89)	47.27	3.29(2.22)	9.77(5)
hepatobiliary disorders	cholecystitis	7	9.4(4.48, 19.76)	9.39(4.46, 19.78)	52.36	3.23(2.23)	9.37(5.03)
hepatobiliary disorders	cholangitis	5	9.32(3.87, 22.42)	9.31(3.85, 22.49)	36.98	3.22(2.06)	9.29(4.45)
injury, poisoning and procedural complications	product label confusion	5	9.01(3.74, 21.69)	9(3.73, 21.74)	35.48	3.17(2.01)	8.98(4.31)
nervous system disorders	dysgeusia	48	8.98(6.76, 11.94)	8.91(6.77, 11.72)	336.51	3.15(2.75)	8.89(7.01)
gastrointestinal disorders	gastrointestinal sounds abnormal	4	8.9(3.34, 23.77)	8.9(3.34, 23.71)	27.97	3.15(1.88)	8.88(3.9)
gastrointestinal disorders	colitis ischaemic	4	8.31(3.11, 22.18)	8.31(3.12, 22.14)	25.64	3.05(1.78)	8.29(3.65)
hepatobiliary disorders	gallbladder disorder	8	7.83(3.91, 15.68)	7.82(3.94, 15.53)	47.48	2.96(2.02)	7.8(4.37)
gastrointestinal disorders	pancreatic disorder	3	7.7(2.48, 23.9)	7.69(2.47, 23.97)	17.43	2.94(1.52)	7.68(2.97)
gastrointestinal disorders	tongue discomfort	4	7.53(2.82, 20.09)	7.53(2.83, 20.06)	22.58	2.91(1.64)	7.51(3.3)
metabolism and	hypophagia	15	7.23(4.35, 12)	7.21(4.33, 12)	80.08	2.85(2.14)	7.2(4.71)

nutrition disorders							
metabolism and nutrition disorders	decreased appetite	146	7.14(6.05, 8.41)	6.97(5.96, 8.15)	748.21	2.8(2.56)	6.96(6.06)
metabolism and nutrition disorders	fluid intake reduced	3	6.97(2.24, 21.64)	6.97(2.24, 21.72)	15.29	2.8(1.38)	6.95(2.69)
gastrointestinal disorders	retching	11	6.97(3.85, 12.59)	6.95(3.86, 12.51)	55.97	2.8(1.98)	6.94(4.23)
metabolism and nutrition disorders	ketoacidosis	4	6.84(2.56, 18.25)	6.84(2.57, 18.22)	19.89	2.77(1.5)	6.82(3)
cardiac disorders	atrial flutter	4	6.76(2.53, 18.04)	6.76(2.54, 18.01)	19.58	2.75(1.49)	6.75(2.97)
gastrointestinal disorders	vomiting	237	6.69(5.87, 7.62)	6.44(5.73, 7.24)	1094.91	2.69(2.5)	6.43(5.77)
gastrointestinal disorders	flatulence	29	6.53(4.53, 9.4)	6.5(4.48, 9.43)	134.71	2.7(2.18)	6.49(4.78)
gastrointestinal disorders	nausea	394	6.52(5.89, 7.23)	6.12(5.55, 6.75)	1706.17	2.61(2.46)	6.11(5.61)
gastrointestinal disorders	gastrointestinal motility disorder	3	6.38(2.05, 19.8)	6.37(2.04, 19.85)	13.56	2.67(1.25)	6.36(2.47)
renal and urinary disorders	urine odour abnormal	3	6.34(2.04, 19.69)	6.34(2.03, 19.76)	13.47	2.66(1.25)	6.33(2.45)
gastrointestinal disorders	paraesthesia oral	7	5.94(2.83, 12.47)	5.93(2.82, 12.49)	28.64	2.57(1.56)	5.92(3.18)
respiratory, thoracic and mediastinal disorders	pharyngeal swelling	10	5.84(3.14, 10.86)	5.83(3.11, 10.92)	39.93	2.54(1.69)	5.82(3.46)
injury, poisoning and procedural complications	product communication issue	5	5.82(2.42, 14)	5.81(2.41, 14.04)	19.9	2.54(1.38)	5.81(2.79)
gastrointestinal disorders	gastrointestinal disorder	44	5.79(4.3, 7.79)	5.75(4.29, 7.72)	172.58	2.52(2.1)	5.74(4.48)
eye disorders	eye haemorrhage	6	5.73(2.57, 12.77)	5.73(2.57, 12.8)	23.36	2.52(1.44)	5.72(2.92)
gastrointestinal disorders	oral mucosal blistering	3	5.65(1.82, 17.54)	5.65(1.81, 17.61)	11.45	2.5(1.08)	5.64(2.19)
skin and subcutaneous tissue disorders	sensitive skin	7	5.57(2.65, 11.7)	5.57(2.64, 11.73)	26.18	2.47(1.47)	5.56(2.99)
injury, poisoning and procedural complications	foreign body in throat	3	5.56(1.79, 17.26)	5.56(1.78, 17.33)	11.19	2.47(1.06)	5.55(2.15)
eye disorders	vision blurred	56	5.42(4.17, 7.26)	5.38(4.17, 7.26)	199.5	2.42(2.05)	5.37(4.31)

			7.05)	6.94)			
gastrointestinal disorders	hypoaesthesia oral	6	5.28(2.37, 11.78)	5.28(2.36, 11.79)	20.78	2.4(1.33)	5.27(2.7)
metabolism and nutrition disorders	feeding disorder	11	5.24(2.9, 9.47)	5.23(2.9, 9.42)	37.62	2.39(1.57)	5.23(3.18)
gastrointestinal disorders	dyspepsia	40	5.19(3.8, 7.08)	5.16(3.77, 7.06)	134	2.36(1.92)	5.15(3.97)
gastrointestinal disorders	constipation	96	5.06(4.13, 6.19)	4.99(4.1, 6.07)	306.78	2.32(2.03)	4.98(4.21)
gastrointestinal disorders	ileus	4	4.97(1.86, 13.25)	4.97(1.87, 13.24)	12.65	2.31(1.04)	4.96(2.18)
gastrointestinal disorders	abdominal distension	41	4.97(3.65, 6.75)	4.94(3.61, 6.76)	128.66	2.3(1.86)	4.93(3.81)
gastrointestinal disorders	abdominal pain upper	84	4.94(3.98, 6.13)	4.88(3.93, 6.05)	259.64	2.29(1.98)	4.88(4.07)
metabolism and nutrition disorders	dehydration	47	4.87(3.65, 6.48)	4.83(3.6, 6.48)	142.87	2.27(1.86)	4.83(3.79)
investigations	weight decreased	111	4.4(3.65, 5.31)	4.33(3.63, 5.17)	285.57	2.11(1.84)	4.33(3.7)
gastrointestinal disorders	abdominal pain	82	4.35(3.5, 5.41)	4.3(3.47, 5.33)	208.04	2.1(1.79)	4.29(3.58)
investigations	blood glucose abnormal	7	4.32(2.06, 9.08)	4.32(2.05, 9.1)	17.84	2.11(1.11)	4.32(2.32)
general disorders and administration site conditions	feeling jittery	5	4.32(1.8, 10.39)	4.32(1.79, 10.44)	12.73	2.11(0.95)	4.31(2.07)
infections and infestations	gastroenteritis viral	6	4.15(1.86, 9.25)	4.15(1.86, 9.27)	14.32	2.05(0.98)	4.14(2.12)
gastrointestinal disorders	gastrooesophageal reflux disease	25	4.09(2.76, 6.06)	4.08(2.76, 6.04)	58.05	2.03(1.47)	4.07(2.93)
gastrointestinal disorders	abdominal discomfort	67	4.02(3.16, 5.12)	3.99(3.15, 5.05)	150.23	1.99(1.65)	3.98(3.26)
respiratory, thoracic and mediastinal disorders	throat tightness	8	3.89(1.94, 7.79)	3.89(1.96, 7.72)	17.14	1.96(1.01)	3.88(2.17)
nervous system disorders	taste disorder	13	3.75(2.17, 6.46)	3.74(2.16, 6.47)	26.07	1.9(1.14)	3.74(2.37)
renal and urinary disorders	pollakiuria	12	3.64(2.06, 6.41)	3.63(2.06, 6.41)	22.89	1.86(1.07)	3.63(2.26)
metabolism and nutrition disorders	hyperglycaemia	10	3.55(1.91, 6.61)	3.55(1.9, 6.65)	18.27	1.83(0.97)	3.54(2.11)
skin and	rash pruritic	15	3.42(2.06, 6.41)	3.42(2.05, 6.41)	25.63	1.77(1.06)	3.41(2.23)

subcutaneous tissue disorders			5.68)	5.69)			
gastrointestinal disorders	diarrhoea	186	3.19(2.75, 3.69)	3.11(2.71, 3.57)	269.4	1.64(1.43)	3.11(2.75)
gastrointestinal disorders	dry mouth	19	3.14(2, 4.93)	3.13(1.99, 4.91)	27.58	1.65(1.01)	3.13(2.15)
eye disorders	visual impairment	32	2.69(1.9, 3.8)	2.68(1.88, 3.81)	33.68	1.42(0.93)	2.68(2)