

**sSupplementary Appendix:** Efficacy and safety of sodium glucose co-transporter 2 inhibitors with and without glucagon-like peptide-1 receptor agonists: A SMART-C collaborative meta-analysis of randomized controlled trials

**Table of Contents:**

	<b>Page</b>
<b>Table S1.</b> Details of included trials.	2
<b>Table S2.</b> Effects of SGLT2 inhibitors on major adverse cardiovascular events by baseline use of GLP-1RA in individual trials.	3
<b>Table S3.</b> Effects of SGLT2 inhibitors on (A) heart failure hospitalisation or cardiovascular death and (B) hospitalisation for heart failure by baseline use of GLP-1RA in individual trials.	4
<b>Table S4.</b> Effects of SGLT2 inhibitors on CKD progression by baseline use of GLP-1RA in individual trials.	6
<b>Table S5.</b> Effects of SGLT2 inhibitors on chronic and total eGFR slope by baseline use of GLP-1RA in individual trials.	7
<b>Table S6.</b> Number of participants experiencing (A) serious adverse events; (B) hypoglycaemia (C) volume depletion by baseline GLP-1RA in individual trials.	9

**Table S1. Details of included trials.**

Study	Population	Year	NCT ID	Participants, n	Diabetes, n (%)	GLP-1RA, n (%)	SGLT2i, dose	Median F/U (years)
EMPA-REG OUTCOME	Diabetes at high ASCVD risk	2015	NCT01131676	7020	7020 (100.0)	196 (2.8)	Empaglifozin, 10/25mg	3.1
CANVAS Program	Diabetes at high ASCVD risk	2017	NCT01032629	10142	10142 (100.0)	407 (4.0)	Canaglifozin 100mg	3.6
DECLARE-TIMI 58	Diabetes at high ASCVD risk	2019	NCT01730534	17160	17160 (100.0)	750 (4.4)	Capaglifozin 10mg	4.2
VERTIS CV	Diabetes at high ASCVD risk	2020	NCT01986881	8238	8238 (100.0)	277 (3.4)	Ertuglifozin 5/15mg	3.5
CREDENCE	CKD	2019	NCT02065791	4401	4401 (100.0)	183 (4.2)	Canaglifozin 100mg	2.6
DAPA-CKD	CKD	2020	NCT03036150	4304	2906 (67.5)	122 (4.2)	Dapaglifozin 10mg	2.4
SCORED	CKD	2021	NCT03315143	10584	10584 (100.0)	633 (6.0)	Sotaglifozin 400mg	1.3
EMPA-KIDNEY	CKD	2023	NCT03594110	6609	2936 (44.4)	337 (5.1)	Empaglifozin 10mg	2.0
DAPA-HF	HF	2019	NCT03036124	4744	1983 (41.8)	21 (1.1)	Dapaglifozin 10mg	1.5
EMPEROR-REDUCED	HF	2020	NCT03057977	3730	1856 (49.8)	19 (1.0)	Empaglifozin 10mg	1.3
EMPEROR-PRESERVED	HF	2021	NCT03057951	5988	2938 (49.1)	59 (2.0)	Empaglifozin 10mg	2.2
DELIVER	HF	2022	NCT03619213	6263	2806 (44.8)	61 (2.2)	Dapaglifozin 10mg	2.3
<b>Total</b>				<b>89183</b>	<b>72970 (81.8)</b>	<b>3065 (4.2)</b>		

SGLT2i: sodium glucose co-transporter 2 inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; ASCVD: atherosclerotic cardiovascular disease; CKD: chronic kidney disease; HF: heart failure; NCT ID: national clinical trial identification number; F/U: follow-up.

**Table S2. Effects of SGLT2 inhibitors on major adverse cardiovascular events by baseline use of GLP-1 in individual trials.**

	Events/patients (%)		Event rate /100 patient years		HR (95% CI)
	SGLT2i	Placebo	SGLT2i	Placebo	
<b>Baseline use of GLP-1 RA</b>					
EMPA-REG OUTCOME	15/126 (11.9)	10/70 (14.3)	4.32	5.42	0.83 (0.37 to 1.84)
CANVAS Program	18/222 (8.1)	15/185 (8.1)	2.64	3.1	0.73 (0.36 to 1.46)
DECLARE-TIMI 58	31/397 (7.8)	32/353 (9.1)	1.9	2.3	0.84 (0.51 to 1.38)
VERTIS CV	21/192 (10.9)	9/85 (10.6)	3.54	3.79	0.94 (0.43 to 2.05)
CREDENCE	11/89 (12.4)	11/94 (11.7)	4.65	4.23	1.13 (0.49 to 2.64)
DAPA-CKD	8/63 (12.7)	6/59 (10.2)	5.91	4.78	1.31 (0.42 to 4.09)
SCORED	17/310 (5.5)	18/323 (5.6)	3.9	4.2	0.90 (0.46 to 1.74)
EMPA-KIDNEY	6/173 (3.5)	11/164 (6.7)	1.8	3.6	0.46 (0.17 to 1.26)
DAPA-HF	1/11 (9.1)	3/10 (30)	6.1	33.3	0.23 (0.02 to 2.92)
EMPEROR-REDUCED	2/13 (15.4)	1/6 (16.7)	12.19	11.54	1.12 (0.1 to 12.36)
EMPEROR-PRESERVED	5/30 (16.7)	5/29 (17.2)	7.59	9.03	0.85 (0.24 to 2.93)
DELIVER	4/34 (11.8)	8/27 (29.6)	5.5	17.1	0.32 (0.1 to 1.08)
<b>No baseline use of GLP1-RA</b>					
EMPA-REG OUTCOME	475/4561 (10.4)	272/2263 (12)	3.72	4.36	0.86 (0.74 to 1.00)
CANVAS Program	567/5573 (10.2)	411/4162 (9.9)	2.69	3.15	0.86 (0.76 to 0.98)
DECLARE-TIMI 58	734/8185 (9)	788/8225 (9.6)	2.3	2.5	0.93 (0.84 to 1.03)
VERTIS CV	632/5301 (11.9)	318/2660 (12)	3.91	4.02	0.97 (0.85 to 1.11)
CREDENCE	206/2113 (9.7)	258/2105 (12.3)	3.84	4.9	0.78 (0.65 to 0.94)
DAPA-CKD	105/1392 (7.5)	112/1392 (8)	3.49	3.75	0.93 (0.71 to 1.21)
SCORED	269/4982 (5.4)	316/4969 (6.4)	4.1	4.9	0.84 (0.72 to 0.99)
EMPA-KIDNEY	85/1352 (6.3)	96/1351 (7.1)	3.2	3.6	0.89 (0.66 to 1.19)
DAPA-HF	156/1064 (14.7)	173/1054 (16.4)	10.3	11.7	0.88 (0.71 to 1.1)
EMPEROR-REDUCED	124/914 (13.6)	126/923 (13.7)	10.4	10.35	1.01 (0.78 to 1.29)
EMPEROR-PRESERVED	166/1436 (11.6)	171/1443 (11.9)	5.71	5.79	0.98 (0.79 to 1.21)
DELIVER	168/1367 (12.3)	191/1378 (13.9)	5.7	6.4	0.88 (0.72 to 1.08)

SGLT2i: sodium glucose co-transporter 2 inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; HR: hazard ratio; CI: confidence interval. Major adverse cardiovascular events was defined as cardiovascular death, nonfatal myocardial infarction or nonfatal stroke.

**Table S3. Effects of SGLT2 inhibitors on (A) heart failure hospitalisation or cardiovascular death and (B) hospitalisation for heart failure by baseline use of GLP-1RA in individual trials.**

A.	Events/patients (%)		Event rate per 100 patient years		
	SGLT2i	Placebo	SGLT2i	Placebo	HR (95% CI)
<b>Baseline use of GLP-1 RA</b>					
EMPA-REG OUTCOME	5/126 (4.0)	3/70 (4.3)	1.39	1.59	0.85 (0.2 to 3.56)
CANVAS Program	13/222 (5.9)	5/185 (2.7)	1.89	1.01	1.85 (0.65 to 5.27)
DECLARE-TIMI 58	4/397 (1.0)	18/353 (5.1)	0.2	1.3	0.2 (0.07 to 0.6)
VERTIS CV	9/192 (4.7)	3/85 (3.5)	1.32	1.01	1.30 (0.35 to 4.80)
CREDENCE	4/89 (4.5)	8/94 (8.5)	1.67	3.1	0.54 (0.16 to 1.08)
DAPA-CKD	2/63 (3.2)	5/59 (8.5)	1.39	3.98	0.29 (0.05 to 1.54)
SCORED	9/310 (2.9)	14/323 (4.3)	2	3.3	0.58 (0.25 to 1.35)
EMPA-KIDNEY	5/173 (2.9)	5/164 (3)	1.5	1.6	0.79 (0.23 to 2.72)
DAPA-HF	5/11 (45.5)	1/10 (10)	41.3	10.2	4.39 (0.45 to 43.19)
EMPEROR-REDUCED	4/13 (30.8)	1/6 (16.7)	29.15	13.07	1.81 (0.2 to 16.24)
EMPEROR-PRESERVED	4/30 (13.3)	2/29 (6.9)	6.29	3.71	1.59 (0.29 to 8.68)
DELIVER	5/34 (14.7)	5/27 (18.5)	7.1	11.7	0.58 (0.17 to 2.01)
<b>No baseline use of GLP1-RA</b>					
EMPA-REG OUTCOME	121/4561 (2.7)	92/2263 (4.1)	0.92	1.44	0.65 (0.49 to 0.85)
CANVAS Program	110/5573 (2)	115/4162 (2.8)	0.51	0.86	0.62 (0.48 to 0.81)
DECLARE-TIMI 58	208/8185 (2.5)	268/8225 (3.3)	0.6	0.8	0.77 (0.64 to 0.92)
VERTIS CV	130/5307 (2.4)	96/2662 (3.6)	0.71	1.05	0.68 (0.52 to 0.88)
CREDENCE	85/2113 (4.0)	133/2105 (6.3)	1.56	2.51	0.62 (0.47 to 0.81)
DAPA-CKD	29/1392 (2.1)	59/1392 (4.2)	0.95	1.97	0.48 (0.31 to 0.75)
SCORED	149/4982 (3.0)	211/4969 (4.2)	2.3	3.3	0.70 (0.57 to 0.86)
EMPA-KIDNEY	60/1352 (4.4)	75/1351 (5.6)	2.2	2.8	0.78 (0.55 to 1.09)
DAPA-HF	133/1064 (12.5)	171/1054 (16.2)	9.1	12.3	0.74 (0.59 to 0.93)
EMPEROR-REDUCED	136/914 (14.9)	200/923 (21.7)	12.15	18.66	0.66 (0.53 to 0.82)
EMPEROR-PRESERVED	151/1436 (10.5)	213/1443 (14.8)	5.36	7.65	0.68 (0.55 to 0.84)
DELIVER	172/1367 (12.6)	210/1378 (15.2)	6	7.5	0.80 (0.66 to 0.98)

SGLT2i: sodium glucose co-transporter 2 inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; HR: hazard ratio; CI: confidence interval.

B.	Events/patients (%)		Event rate per 100 patient years		
	SGLT2i	Placebo	SGLT2i	Placebo	HR (95% CI)
<b>Baseline use of GLP-1 RA</b>					
EMPA-REG OUTCOME	11/126 (8.7)	6/70 (8.6)	3.06	3.18	0.96 (0.36 to 2.61)
CANVAS Program	17/222 (7.7)	8/185 (4.3)	2.47	1.61	1.38 (0.59 to 3.23)
DECLARE-TIMI 58	10/397 (2.5)	24/353 (6.8)	0.6	1.7	0.37 (0.18 to 0.78)
VERTIS CV	14/192 (7.3)	4/85 (4.7)	2.05	1.35	1.51 (0.50 to 4.60)
CREDENCE	9/89 (10.1)	11/94 (11.7)	3.76	4.26	0.96 (0.39 to 2.35)
DAPA-CKD	3/63 (4.8)	6/59 (10.2)	2.09	4.78	0.4 (0.1 to 1.67)
SCORED	13/310 (4.2)	18/323 (5.6)	2.9	4.2	0.65 (0.32 to 1.34)
EMPA-KIDNEY	7/173 (4)	9/164 (5.5)	2.1	2.9	0.63 (0.24 to 1.7)
DAPA-HF	5/11 (45.5)	3/10 (30)	41.3	30.7	1.62 (0.33 to 7.85)
EMPEROR-REDUCED	5/13 (38.5)	1/6 (16.7)	36.44	13.07	2.46 (0.29 to 21.07)
EMPEROR-PRESERVED	6/30 (20)	5/29 (17.2)	9.43	9.27	0.94 (0.29 to 3.1)
DELIVER	7/34 (20.6)	9/27 (33.3)	9.9	21.1	0.47 (0.17 to 1.26)
<b>No baseline use of GLP1-RA</b>					
EMPA-REG OUTCOME	269/4561 (5.9)	203/2263 (9)	2.05	3.18	0.65 (0.54 to 0.78)
CANVAS Program	347/5573 (6.2)	280/4162 (6.7)	1.6	2.1	0.76 (0.65 to 0.9)
DECLARE-TIMI 58	407/8185 (5)	472/8225 (5.7)	1.2	1.5	0.86 (0.75 to 0.98)
VERTIS CV	430/5307 (8.1)	246/2662 (9.2)	2.35	2.7	0.87 (0.75 to 1.02)
CREDENCE	170/2113 (8)	242/2105 (11.5)	3.12	4.56	0.68 (0.56 to 0.83)
DAPA-CKD	82/1392 (5.9)	113/1392 (8.1)	2.68	3.78	0.71 (0.53 to 0.94)
SCORED	270/4982 (5.4)	339/4969 (6.8)	4.1	5.2	0.78 (0.67 to 0.92)
EMPA-KIDNEY	89/1352 (6.6)	109/1351 (8.1)	3.3	4.1	0.8 (0.61 to 1.07)
DAPA-HF	208/1064 (19.5)	265/1054 (25.1)	14.2	19	0.74 (0.62 to 0.89)
EMPEROR-REDUCED	195/914 (21.3)	264/923 (28.6)	17.43	24.63	0.72 (0.59 to 0.86)
EMPEROR-PRESERVED	233/1436 (16.2)	286/1443 (19.8)	8.27	10.27	0.79 (0.66 to 0.94)
DELIVER	241/1367 (17.6)	289/1378 (21)	8.5	10.4	0.82 (0.69 to 0.97)

SGLT2i: sodium glucose co-transporter 2 inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; HR: hazard ratio; CI: confidence interval.

**Table S4. Effects of SGLT2 inhibitors on CKD progression by baseline use of GLP-1RA in individual trials.**

	Events/patients (%)		Event rate per 100 patient years		
	SGLT2i	Placebo	SGLT2i	Placebo	HR (95% CI)
<b>Baseline use of GLP-1 RA</b>					
EMPA-REG OUTCOME	4/125 (3.2)	2/70 (2.9)	1.21	1.13	1.19 (0.22 to 6.51)
CANVAS Program	1/222 (0.5)	3/185 (1.6)	0.14	0.6	0.37 (0.04 to 3.56)
DECLARE-TIMI 58	4/397 (1)	10/353 (2.8)	0.2	0.7	0.36 (0.11 to 1.15)
VERTIS CV	5/192 (2.6)	2/85 (2.4)	0.74	0.67	1.10 (0.21 to 5.67)
CREDENCE	12/89 (13.5)	11/94 (11.7)	5.18	4.17	1.21 (0.53 to 2.76)
DAPA-CKD	2/63 (3.2)	9/59 (15.3)	1.52	7.58	0.21 (0.04 to 0.97)
SCORED	8/310 (2.6)	9/323 (2.8)	1.8	2.1	0.82 (0.32 to 2.14)
EMPA-KIDNEY	18/173 (10.4)	24/164 (14.6)	5.4	8	0.53 (0.29 to 0.98)
DAPA-HF	0/11 (0)	2/10 (20)	N/A	20.7	N/A
EMPEROR-REDUCED	1/13 (7.7)	1/6 (16.7)	7.93	15.46	0.45 (0.03 to 7.36)
EMPEROR-PRESERVED	0/30 (0)	2/29 (6.9)	N/A	4.58	N/A
DELIVER	2/34 (5.9)	2/27 (7.4)	2.8	4.0	0.76 (0.11 to 5.37)
<b>No baseline use of GLP1-RA</b>					
EMPA-REG OUTCOME	104/4520 (2.3)	85/2253 (3.8)	0.84	1.43	0.57 (0.43 to 0.76)
CANVAS Program	123/5573 (2.2)	122/4162 (2.9)	0.57	0.91	0.61 (0.47 to 0.78)
DECLARE-TIMI 58	128/8185 (1.6)	232/8225 (2.8)	0.4	0.7	0.55 (0.44 to 0.68)
VERTIS CV	114/5307 (2.1)	87/2662 (3.3)	0.63	0.95	0.66 (0.5 to 0.87)
CREDENCE	237/2113 (11.2)	361/2105 (17.1)	4.48	7.11	0.62 (0.53 to 0.73)
DAPA-CKD	101/1392 (7.3)	164/1392 (11.8)	3.59	5.96	0.59 (0.46 to 0.75)
SCORED	186/4982 (3.7)	254/4969 (5.1)	2.8	3.9	0.72 (0.60 to 0.87)
EMPA-KIDNEY	164/1352 (12.1)	236/1351 (17.5)	6.2	9.1	0.63 (0.52 to 0.77)
DAPA-HF	32/1064 (3)	37/1054 (3.5)	2.2	2.6	0.84 (0.52 to 1.34)
EMPEROR-REDUCED	21/914 (2.3)	38/923 (4.1)	2.22	4.09	0.52 (0.30 to 0.88)
EMPEROR-PRESERVED	75/1436 (5.2)	72/1443 (5)	3.16	3.01	1.03 (0.74 to 1.42)
DELIVER	107/1367 (7.8)	84/1378 (6.1)	3.7	2.8	1.30 (0.98 to 1.73)

SGLT2i: sodium glucose co-transporter 2 inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; HR: hazard ratio; CI: confidence interval. N/A: Not applicable. CKD progression defined as  $\geq 40\%$  decline in eGFR, kidney failure or death due to kidney failure.

**Table S5. Effects of SGLT2 inhibitors on chronic and total eGFR slope by baseline use of GLP-1RA in individual trials.**

A. Chronic slope	eGFR slope (mL/min/1.73m <sup>2</sup> /year)			
	SGLT2i (95% CI)	Placebo (95% CI)	Mean Difference (95% CI)	SE
<b>Baseline use of GLP-1 RA</b>				
EMPA-REG OUTCOME	0.78 (-0.34 to 1.91)	-2.7 (-4.39 to -1)	3.48 (1.45 to 5.51)	1.04
CANVAS Program	0.11 (-0.51 to 0.73)	-1.13 (-1.98 to -0.29)	1.24 (0.2 to 2.29)	0.53
DECLARE-TIMI 58	-1.29 (-1.64 to -0.94)	-2.34 (-2.74 to -1.94)	1.05 (0.51 to 1.58)	0.27
VERTIS CV	-0.6 (-1.05 to -0.14)	-1.58 (-2.32 to -0.85)	0.99 (0.12 to 1.85)	0.44
CREDENCE	-1.86 (-2.88 to -0.85)	-4.05 (-5.07 to -3.04)	2.19 (0.75 to 3.62)	0.72
DAPA-CKD	-1.21 (-2.57 to 0.15)	-3.98 (-5.39 to -2.57)	2.77 (0.81 to 4.73)	0.08
SCORED	-0.23 (-1.01 to 0.56)	-0.64 (-1.46 to 0.17)	0.42 (-0.71 to 1.55)	0.05
EMPA-KIDNEY	-1.13 (-1.86 to -0.40)	-2.56 (-3.32 to -1.80)	1.42 (0.37 to 2.47)	0.54
DAPA-HF	-2.26 (-7.1 to 2.59)	-3.72 (-9.78 to 2.35)	1.46 (-6.31 to 9.23)	3.96
EMPEROR-REDUCED	-1.87 (-7.58 to 3.85)	-0.98 (-9.03 to 7.07)	-0.89 (-10.76 to 8.98)	5.04
EMPEROR-PRESERVED	0.08 (-2.2 to 2.36)	-6.91 (-9.39 to -4.43)	6.99 (3.62 to 10.37)	1.72
DELIVER	1.5 (-0.7 to 3.7)	-4.3 (-8.1 to -0.6)	6 (1.7 to 10.3)	2.20
<b>No baseline use of GLP1-RA</b>				
EMPA-REG OUTCOME	-0.39 (-0.48 to -0.17)	-1.72 (-1.97 to -1.46)	1.39 (1.09 to 1.68)	0.15
CANVAS Program	0.35 (0.25 to 0.45)	-0.73 (-0.87 to -0.6)	1.09 (0.92 to 1.26)	0.09
DECLARE-TIMI 58	-1.52 (-1.6 to -1.44)	-2.51 (-2.59 to -2.43)	0.99 (0.87 to 1.1)	0.06
VERTIS CV	-0.87 (-0.96 to -0.79)	-1.79 (-1.91 to -1.67)	0.91 (0.77 to 1.06)	0.07
CREDENCE	-1.91 (-2.17 to -1.65)	-4.61 (-4.88 to -4.35)	2.7 (2.33 to 3.07)	0.19
DAPA-CKD	-1.6 (-1.89 to -1.31)	-3.83 (-4.12 to -3.54)	2.23 (1.82 to 2.64)	0.02
SCORED	-0.06 (-0.32 to 0.2)	-2.17 (-2.43 to -1.9)	2.11 (1.73 to 2.48)	0.02
EMPA-KIDNEY	-1.23 (-1.48 to -0.98)	-2.84 (-3.09 to -2.59)	1.61 (1.25 to 1.97)	0.18
DAPA-HF	-1.5 (-1.99 to -1)	-3.73 (-4.24 to -3.22)	2.23 (1.52 to 2.95)	0.36
EMPEROR-REDUCED	-0.7 (-1.4 to 0)	-3.01 (-3.71 to -2.3)	2.3 (1.31 to 3.3)	0.51
EMPEROR-PRESERVED	-1.3 (-1.63 to -0.96)	-3.02 (-3.35 to -2.69)	1.72 (1.25 to 2.19)	0.24
DELIVER	0.1 (-0.4 to 0.5)	-1.9 (-2.3 to -1.4)	1.9 (1.3 to 2.6)	0.3

SGLT2i: sodium glucose co-transporter 2 inhibitors; GLP-1RA: glucagon-like peptide-1 receptor agonists; CI: confidence interval; SE: standard error.

B. Total Slope	eGFR slope (mL/min/1.73m <sup>2</sup> /year)			
	SGLT2i (95% CI)	Placebo (95% CI)	Mean Difference (95% CI)	SE
<b>Baseline use of GLP-1 RA</b>				
EMPA-REG OUTCOME	-0.39 (-1.47 to -0.68)	-2.63 (-4.24 to -1.02)	2.24 (0.3 to 4.17)	0.99
CANVAS Program	-0.06 (-0.63 to 0.5)	-0.97 (-1.73 to -0.2)	0.9 (-0.05 to 1.85)	0.48
DECLARE-TIMI 58	-1.55 (-1.76 to -1.33)	-2.22 (-2.47 to -1.97)	0.67 (0.34 to 1.01)	0.17
VERTIS CV	-0.63 (-1.03 to -0.22)	-1.65 (-2.31 to -0.99)	1.02 (0.25 to 1.8)	0.39
CREDENCE	-1.36 (-7.81 to 5.09)	-4.85 (-12.54 to 2.84)	3.49 (-6.54 to 13.53)	5.11
DAPA-CKD	-2.87 (-4.24 to -1.49)	-4.14 (-5.56 to -2.71)	1.27 (-0.71 to 3.25)	0.08
SCORED	-3.02 (-3.82 to -2.23)	-1.32 (-2.13 to -0.51)	-1.7 (-2.83 to -0.57)	0.05
EMPA-KIDNEY	-2.09 (-2.78 to -1.40)	-2.83 (-3.56 to -2.10)	0.73 (-0.27 to 1.73)	0.51
DAPA-HF	-3.23 (-7.93 to 1.48)	-4.19 (-10.01 to 1.63)	0.96 (-6.53 to 8.45)	3.82
EMPEROR-REDUCED	-3.87 (-9.22 to 1.47)	-2 (-9.62 to 5.61)	-1.87 (-11.16 to 7.43)	4.74
EMPEROR-PRESERVED	-2.71 (-4.98 to -0.44)	-5.53 (-7.94 to -3.13)	2.83 (-0.48 to 6.14)	1.69
DELIVER	0.1 (-1.9 to 2.1)	-4.1 (-7.3 to -0.9)	4.2 (0.3 to 8)	2.00
<b>No baseline use of GLP1-RA</b>				
EMPA-REG OUTCOME	-1.12 (-1.27 to -0.97)	-1.74 (-1.98 to -1.49)	0.62 (0.33 to 0.91)	0.15
CANVAS Program	-0.19 (-0.28 to -0.09)	-0.83 (-0.96 to -0.7)	0.64 (0.48 to 0.8)	0.08
DECLARE-TIMI 58	-1.78 (-1.83 to -1.73)	-2.41 (-2.46 to -2.36)	0.63 (0.57 to 0.7)	0.03
VERTIS CV	-0.87 (-0.94 to -0.8)	-1.71 (-1.81 to -1.6)	0.84 (0.71 to 0.97)	0.07
CREDENCE	0.77 (-1.19 to 2.73)	-5.05 (-6.82 to -3.28)	5.82 (3.18 to 8.46)	1.35
DAPA-CKD	-2.83 (-3.12 to -2.54)	-4 (-4.3 to -3.71)	1.17 (0.76 to 1.59)	0.02
SCORED	-1.86 (-2.12 to -1.61)	-1.9 (2.16 to -1.64)	0.04 (-0.33 to 0.4)	0.02
EMPA-KIDNEY	-2.12 (-2.36 to -1.88)	-2.87 (-3.12 to -2.62)	0.75 (0.4 to 1.09)	0.18
DAPA-HF	-3.04 (-3.52 to -2.54)	-3.95 (-4.44 to -3.46)	0.91 (0.22 to 1.61)	0.35
EMPEROR-REDUCED	-2 (-2.66 to -1.34)	-3.38 (-4.04 to -2.71)	1.38 (0.44 to 2.31)	0.48
EMPEROR-PRESERVED	-2.72 (-3.05 to -2.39)	-3.1 (-3.43 to -2.78)	0.38 (-0.08 to 0.84)	0.24
DELIVER	-1.2 (-1.6 to -0.8)	-2.1 (-2.5 to -1.7)	0.9 (0.3 to 1.5)	0.30



**Table S5. Number of participants experiencing (A) serious adverse events; (B) hypoglycaemia (C) volume depletion by baseline GLP-1RA in individual trials.**

A. Serious adverse events	Events/Participants (%)	
	SGLT2i	Placebo
<b>Baseline use of GLP-1RA</b>		
EMPA-REG OUTCOME	60/126 (47.6)	40/70 (57.1)
CANVAS Program	79/222 (35.6)	67/185 (36.2)
DECLARE-TIMI 58	145/397 (36.5)	134/352 (38.1)
VERTIS CV	70/192 (36.5)	38/85 (44.7)
CREDENCE	34/89 (38.2)	39/94 (41.5)
DAPA-CKD	18/63 (28.6)	27/59 (45.8)
SCORED	86/310 (27.7)	89/323 (27.6)
EMPA-KIDNEY	70/173 (40.5)	79/164 (48.2)
DAPA-HF	7/10 (70)	5/10 (50)
EMPEROR-REDUCED	7/13 (53.8)	6/6 (100)
EMPEROR-PRESERVED	21/29 (72.4)	16/29 (55.2)
DELIVER	23/34 (67.6)	17/27 (63)
<b>No baseline use of GLP-1RA</b>		
EMPA-REG OUTCOME	1729/4561 (37.9)	948/2263 (41.9)
CANVAS Program	1842/5568 (33.1)	1289/4159 (31)
DECLARE-TIMI 58	2780/8177 (34)	2966/8217 (36.1)
VERTIS CV	1825/5301 (34.4)	952/2660 (35.8)
CREDENCE	703/2111 (33.3)	767/2103 (36.5)
DAPA-CKD	435/1390 (31.3)	494/1391 (35.5)
SCORED	1150/4981 (23.1)	1242/4963 (25)
EMPA-KIDNEY	577/1352 (42.7)	626/1351 (46.3)
DAPA-HF	440/1063 (41.4)	508/1053 (48.2)
EMPEROR-REDUCED	390/914 (42.7)	451/920 (49)
EMPEROR-PRESERVED	711/1436 (49.5)	782/1442 (54.2)
DELIVER	637/1367 (46.6)	684/1378 (49.6)

SGLT2i: sodium glucose cotransporter-2 inhibitor. GLP-1RA: glucagon-like peptide-1 receptor agonist.

<b>B. Hypoglycaemia</b>	<b>Events/Participants (%)</b>	
	<b>SGLT2i</b>	<b>Placebo</b>
<b>Baseline use of GLP-1 RA</b>		
EMPA-REG OUTCOME	0/126 (0)	1/70 (1.4)
CANVAS Program	7/156 (4.5)	5/155 (3.2)
DECLARE-TIMI 58	3/397 (0.8)	5/352 (1.4)
VERTIS CV	0/192 (0)	0/85 (0)
CREDENCE	11/89 (12.4)	7/94 (7.4)
DAPA-CKD	0/63 (0)	0/59 (0)
SCORED	28/310 (9)	15/323 (4.6)
EMPA-KIDNEY	13/173 (7.5)	10/164 (6.1)
DAPA-HF	0/10 (0)	0/10 (0)
EMPEROR-REDUCED	0/13 (0)	0/6 (0)
EMPEROR-PRESERVED	0/29 (0)	1/29 (3.4)
DELIVER	0/34	0/27
<b>No baseline use of GLP-1 RA</b>		
EMPA-REG OUTCOME	63/4561 (1.4)	35/2263 (1.5)
CANVAS Program	376/2820 (13.3)	163/1411 (11.6)
DECLARE-TIMI 58	55/8177 (0.7)	78/8217 (0.9)
VERTIS CV	21/5301 (0.4)	14/2660 (0.5)
CREDENCE	214/2111 (10.1)	233/2103 (11.1)
DAPA-CKD	14/1390 (1)	28/1391 (2)
SCORED	378/4981 (7.6)	401/4963 (8.1)
EMPA-KIDNEY	60/1352 (4.4)	67/1351 (5)
DAPA-HF	4/1062 (0.4)	4/1053 (0.4)
EMPEROR-REDUCED	6/914 (0.7)	7/920 (0.8)
EMPEROR-PRESERVED	22/1436 (1.5)	17/1442 (1.2)
DELIVER	4/1367 (0.3)	1/1378 (0.1)

SGLT2i: sodium glucose cotransporter-2 inhibitor. GLP-1RA: glucagon-like peptide-1 receptor agonist.

C. Volume depletion	Events/Participants (%)	
	SGLT2i	Placebo
<b>Baseline use of GLP-1 RA</b>		
EMPA-REG OUTCOME	0/126 (0)	1/70 (1.4)
CANVAS Program	8/156 (5.1)	5/155 (3.2)
DECLARE-TIMI 58	15/397 (3.8)	13/352 (3.7)
VERTIS CV	1/192 (0.5)	1/85 (1.2)
CREDENCE	10/89 (11.2)	10/94 (10.6)
DAPA-CKD	6/63 (9.5)	1/59 (1.7)
SCORED	25/310 (8.1)	15/323 (4.6)
EMPA-KIDNEY	10/173 (5.8)	6/164 (3.7)
DAPA-HF	1/10 (10)	1/10 (10)
EMPEROR-REDUCED	0/13 (0)	0/6 (0)
EMPEROR-PRESERVED	3/29 (10.3)	1/29 (3.4)
DELIVER	3/35 (8.6)	0/27 (0)
<b>No baseline use of GLP-1 RA</b>		
EMPA-REG OUTCOME	38/4561 (0.8)	15/2263 (0.7)
CANVAS Program	191/2820 (6.8)	62/1411 (4.4)
DECLARE-TIMI 58	198/8177 (2.4)	194/8217 (2.4)
VERTIS CV	50/5301 (0.9)	27/2660 (1)
CREDENCE	134/2111 (6.3)	105/2103 (5)
DAPA-CKD	86/1390 (6.2)	70/1391 (5)
SCORED	253/4981 (5.1)	198/4963 (4)
EMPA-KIDNEY	43/1352 (3.2)	30/1351 (2.2)
DAPA-HF	83/1063 (7.8)	82/1053 (7.8)
EMPEROR-REDUCED	14/914 (1.5)	13/920 (1.4)
EMPEROR-PRESERVED	28/1436 (1.9)	28/1442 (1.9)
DELIVER	14/1367 (1)	12/1378 (0.9)

SGLT2i: sodium glucose cotransporter-2 inhibitor. GLP-1RA: glucagon-like peptide-1 receptor agonist.