

Supplementary Online Content

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Figure S1. Development of study population for SGLT2i vs. GLP1-RA comparison.

SGLT2i, sodium glucose cotransporter-2 inhibitors; GLP1-RA, glucagon-like peptide-1 receptor agonists.

Figure S2. Development of study population for SGLT2i vs. DPP-4i comparison.

SGLT2i, sodium glucose cotransporter-2 inhibitors; DPP-4i, dipeptidyl peptidase 4 inhibitors.

Table S1. Emulated target trial framework for nephrolithiasis recurrence among nephrolithiasis patients

Protocol Component	Target Trial	Emulated Trial
Aim	To compare the risk of recurrent nephrolithiasis events among nephrolithiasis patients with type 2 diabetes initiating SGLT2i versus GLP1-RA	Same as for the target trial.
Eligibility Criteria	<ul style="list-style-type: none"> • Aged ≥ 18 years at cohort entry • Type 2 diabetes • Prior nephrolithiasis diagnosis • No prior SGLT2i or GLP1-RA use 	Same as for the target trial
Treatment Strategies	<p>(1) Initiate SGLT2i and continue to use through the follow-up period (defined below), unless otherwise clinically indicated.</p> <p>(2) Initiate GLP1-RA and continue through the follow-up period (defined below), unless otherwise clinically indicated.</p>	Same as for the target trial.
Treatment Assignment	Individuals are randomly assigned to initiate one medication and are aware of the treatment to which they have been assigned.	Individuals were non-randomly assigned to SGLT2i or GLP1-RA based on a new prescription for the respective medication. Randomization was emulated by inverse probability of treatment weighting, adjusting for pre-exposure prognostic patient characteristics, including nephrolithiasis duration, frequency of nephrolithiasis events during the year prior, obesity, gout, and thiazide diuretic use.
Follow-up	Starts at the time of initiation of a treatment strategy and ends on the day of the outcome of interest (except for recurrent nephrolithiasis counts), death, loss of follow-up, or the end of the study period (June 30, 2022).	Same as for the target trial, except that follow-up would also end upon discontinuation of index medication.
Outcomes	<ul style="list-style-type: none"> • Primary outcome <ul style="list-style-type: none"> ○ Counts of recurrent nephrolithiasis • Secondary outcomes <ul style="list-style-type: none"> ○ Counts of recurrent nephrolithiasis events requiring ED visit or hospitalization ○ Counts of recurrent nephrolithiasis events requiring procedure ○ First recurrent nephrolithiasis event 	Same as for the target trial, plus control outcomes of genital infection, osteoarthritis encounter, and appendicitis, defined by ICD-9/10 codes (Table S5).
Causal Contrasts	<p>Intention-to-treat effect.</p> <p>Per-protocol effect.</p>	<p>On-treatment effect (observational analogue of the per-protocol effect) with continuous treatment status assessed using days of supply in each prescription dispensing, allowing a 60 days of grace period between prescription refills.</p> <p>Intention-to-treat effect (secondary analysis) limited to 1 year, given the substantial percentage of subjects known to discontinue the index medications during the follow up of typical epidemiologic studies (Table S8).</p>
Statistical Analysis	<p>Comparison of the rates and adjusted rate ratios or hazard ratios, and rate differences, among individuals assigned to each treatment strategy.</p> <p>Subgroup analyses by baseline age, sex, thiazide diuretic use, and recently active nephrolithiasis.</p>	Same as for the target trial.

SGLT2i, sodium glucose cotransporter-2 inhibitors; GLP1-RA, glucagon-like peptide-1 receptor agonists; ED, emergency department

Table S2. Emulated target trial framework for nephrolithiasis recurrence among nephrolithiasis patients with concurrent gout

Protocol Component	Target Trial	Emulated Trial
Aim	To compare the risk of recurrent nephrolithiasis events among nephrolithiasis patients with type 2 diabetes and gout initiating SGLT2i versus GLP1-RA	Same as for the target trial.
Eligibility Criteria	<ul style="list-style-type: none"> • Aged ≥ 18 years at cohort entry • Type 2 diabetes • Prior nephrolithiasis diagnosis • Prior gout diagnosis • No prior SGLT2i or GLP1-RA use 	Same as for the target trial
Treatment Strategies	<p>(1) Initiate SGLT2i and continue to use through the follow-up period (defined below), unless otherwise clinically indicated.</p> <p>(2) Initiate GLP1-RA and continue through the follow-up period (defined below), unless otherwise clinically indicated.</p>	Same as for the target trial.
Treatment Assignment	Individuals are randomly assigned to initiate one medication and are aware of the treatment to which they have been assigned.	Individuals were non-randomly assigned to SGLT2i or GLP1-RA based on a new prescription for the respective medication. Randomization was emulated by inverse probability of treatment weighting, adjusting for pre-exposure prognostic patient characteristics including nephrolithiasis duration, frequency of nephrolithiasis events during the year prior, obesity, gout duration, use of urate-lowering therapy and thiazide diuretics, and number of gout flares within the past year.
Follow-up	Starts at the time of initiation of a treatment strategy and ends on the day of death, loss of follow-up, or the end of the study period (June 30, 2022).	Same as for the target trial, except that follow-up would also end upon discontinuation of index medication.
Outcomes	<ul style="list-style-type: none"> • Primary outcome <ul style="list-style-type: none"> ◦ Counts of recurrent nephrolithiasis • Secondary outcome <ul style="list-style-type: none"> ◦ Counts of recurrent gout flare 	Same as for the target trial (Table S5)
Causal Contrasts	<p>Intention-to-treat effect.</p> <p>Per-protocol effect.</p>	On-treatment effect (observational analogue of the per-protocol effect) with continuous treatment status assessed using days of supply in each prescription dispensing, allowing a 60 days of grace period between prescription refills.
Statistical Analysis	Comparison of the rates and adjusted rate ratios and rate differences, among individuals assigned to each treatment strategy.	Same as for the target trial.

SGLT2i, sodium glucose cotransporter-2 inhibitors; GLP1-RA, glucagon-like peptide-1 receptor agonists; ED, emergency department

Table S3. Emulated target trial framework for nephrolithiasis recurrence among nephrolithiasis patients without concurrent gout

Protocol Component	Target Trial	Emulated Trial
Aim	To compare the risk of recurrent nephrolithiasis events among nephrolithiasis patients with type 2 diabetes and no history of gout initiating SGLT2i versus GLP1-RA	Same as for the target trial.
Eligibility Criteria	<ul style="list-style-type: none"> • Aged ≥ 18 years at cohort entry • Type 2 diabetes • Prior nephrolithiasis diagnosis • No prior gout diagnosis • No prior SGLT2i or GLP1-RA use 	Same as for the target trial
Treatment Strategies	<p>(1) Initiate SGLT2i and continue to use through the follow-up period (defined below), unless otherwise clinically indicated.</p> <p>(2) Initiate GLP1-RA and continue through the follow-up period (defined below), unless otherwise clinically indicated.</p>	Same as for the target trial.
Treatment Assignment	Individuals are randomly assigned to initiate one medication and are aware of the treatment to which they have been assigned.	Individuals were non-randomly assigned to SGLT2i or GLP1-RA based on a new prescription for the respective medication. Randomization was emulated by inverse probability of treatment weighting, adjusting for pre-exposure prognostic patient characteristics including nephrolithiasis duration, frequency of nephrolithiasis events during the year prior, obesity, and thiazide diuretic use.
Follow-up	Starts at the time of initiation of a treatment strategy and ends on the day of death, loss of follow-up, or the end of the study period (June 30, 2022).	Same as for the target trial, except that follow-up would also end upon discontinuation of index medication.
Outcomes	<ul style="list-style-type: none"> • Counts of recurrent nephrolithiasis 	Same as for the target trial (Table S5)
Causal Contrasts	<p>Intention-to-treat effect.</p> <p>Per-protocol effect.</p>	On-treatment effect (observational analogue of the per-protocol effect) with continuous treatment status assessed using days of supply in each prescription dispensing, allowing a 60 days of grace period between prescription refills.
Statistical Analysis	Comparison of the rates and adjusted rate ratios and rate differences, among individuals assigned to each treatment strategy.	Same as for the target trial.

SGLT2i, sodium glucose cotransporter-2 inhibitors; GLP1-RA, glucagon-like peptide-1 receptor agonists; ED, emergency department

Table S4. Emulated target trial framework for incident nephrolithiasis among patients without nephrolithiasis at baseline

Protocol Component	Target Trial	Emulated Trial
Aim	To compare the risk of new nephrolithiasis events among patients with type 2 diabetes initiating SGLT2i versus GLP1-RA	Same as for the target trial.
Eligibility Criteria	<ul style="list-style-type: none"> Aged ≥ 18 years at cohort entry Type 2 diabetes No prior nephrolithiasis diagnosis No prior SGLT2i or GLP1-RA use 	Same as for the target trial
Treatment Strategies	(1) Initiate SGLT2i and continue to use through the follow-up period (defined below), unless otherwise clinically indicated. (2) Initiate GLP1-RA and continue through the follow-up period (defined below), unless otherwise clinically indicated.	Same as for the target trial.
Treatment Assignment	Individuals are randomly assigned to initiate one medication and are aware of the treatment to which they have been assigned.	Individuals were non-randomly assigned to SGLT2i or GLP1-RA based on a new prescription for the respective medication. Randomization was emulated by inverse probability of treatment weighting, adjusting for pre-exposure prognostic patient characteristics including obesity, gout, and thiazide diuretic use.
Follow-up	Starts at the time of initiation of a treatment strategy and ends on the day of death, loss of follow-up, or the end of the study period (June 30, 2022).	Same as for the target trial, except that follow-up would also end upon discontinuation of index medication.
Outcomes	<ul style="list-style-type: none"> Counts of new nephrolithiasis 	Same as for the target trial (Table S5)
Causal Contrasts	Intention-to-treat effect. Per-protocol effect.	On-treatment effect (observational analogue of the per-protocol effect) with continuous treatment status assessed using days of supply in each prescription dispensing, allowing a 60 days of grace period between prescription refills.
Statistical Analysis	Comparison of the rates and adjusted rate ratios and rate differences, among individuals assigned to each treatment strategy.	Same as for the target trial.

SGLT2i, sodium glucose cotransporter-2 inhibitors; GLP1-RA, glucagon-like peptide-1 receptor agonists; ED, emergency department

Table S5. Exposure and outcome definitions

Item	Codes
Gout	<u>ICD-9</u> : 274.xx <u>ICD-10</u> : M10.xx, M1.xxx
Type 2 diabetes	<u>ICD-9</u> : 250.xx <u>ICD-10</u> : E11.xx-E14.xx
Kidney stone	<u>ICD-9</u> : 592, 592.0, 592.1 or 592.9 <u>ICD-10</u> : N20.xx, N13.2 <u>Fee item (procedure) codes</u> : 978, 979, 989, 8102, 8123, 8117, 8118, 8119, 8149, 8150, 8168
Genital infection	<u>ICD-9</u> : 112.1, 112.2, 605, 607.0, 607.1, 616.1* <u>ICD-10</u> : B37.3, B37.42, B37.49, N47.1, N47.2, N47.6, N48.0, N48.1, N76.0, N76.1, N76.2, N76.3, N77.1
Osteoarthritis	<u>ICD-9</u> : 715.xx <u>ICD-10</u> : M15.xx-M19.xx
Appendicitis	<u>ICD-9</u> : 540.x, 541.x, 542.x, 543.x <u>ICD-10</u> : K35.x, K36.x, K37.x, K38.x

All were primary-position diagnoses ascertained from inpatient and outpatient data.

Table S6. Baseline characteristics among nephrolithiasis patients with type 2 diabetes initiating SGLT2i versus GLP1-RA, before and after inverse probability of treatment weighting

Variable list	Before weighting			After weighting		
	SGLT2i (n=14,400)	GLP1-RA (n=5746)	Standardized difference*	SGLT2i (n=14,456)	GLP1-RA (n=5877)	Standardized difference*
Demographics						
Age, mean (SD), y	63.70 (11.02)	59.83 (11.40)	0.35	62.53 (11.45)	63.03 (11.06)	0.04
Male (%)	9846 (68.4)	2655 (46.2)	0.46	8988 (62.2)	3741 (63.7)	0.03
Neighbourhood Income Quintile			0.09			0.02
1=Lowest	2943 (20.4)	1102 (19.2)		2888 (20.0)	1161 (19.7)	
2	3301 (22.9)	1187 (20.7)		3217 (22.3)	1317 (22.4)	
3	2992 (20.8)	1196 (20.8)		3083 (21.3)	1246 (21.2)	
4	2758 (19.2)	1153 (20.1)		2781 (19.2)	1098 (18.7)	
5=Highest	2256 (15.7)	1048 (18.2)		2335 (16.2)	992 (16.9)	
Health Region			0.10			0.05
Interior	2068 (14.4)	721 (12.5)		2018 (14.0)	907 (15.4)	
Fraser	6797 (47.2)	2911 (50.7)		6905 (47.8)	2797 (47.6)	
Vancouver Coastal	2889 (20.1)	986 (17.2)		2833 (19.6)	1067 (18.2)	
Vancouver Island	1842 (12.8)	800 (13.9)		1888 (13.1)	776 (13.2)	
Northern	787 (5.5)	318 (5.5)		791 (5.5)	320 (5.4)	
Type 2 diabetes duration, mean (SD), y	13.96 (7.19)	13.01 (7.92)	0.13	13.73 (7.36)	13.95 (7.60)	0.03
Gout prevalence, anytime (%)	3159 (22.0)	1250 (21.8)	< 0.01	3155 (21.8)	1293 (22.0)	< 0.01
Nephrolithiasis duration, mean (SD), y	13.39 (8.77)	12.96 (8.80)	0.05	13.15 (8.78)	13.16 (8.85)	< 0.01
Nephrolithiasis events, mean (SD)	0.30 (1.13)	0.37 (1.27)	0.06	0.33 (1.33)	0.31 (1.13)	0.02
Comorbidity (%)						
Obesity	1507 (10.5)	1591 (27.7)	0.45	2135 (14.8)	883 (15.0)	< 0.01
Hypertension	9246 (64.2)	3722 (64.8)	0.01	9344 (64.6)	3809 (64.8)	< 0.01
Myocardial infarction	2020 (14.0)	580 (10.1)	0.12	1881 (13.0)	754 (12.8)	< 0.01
Stroke	1871 (13.0)	768 (13.4)	0.01	1900.7 (13.1)	801 (13.6)	0.01
Heart failure	2237 (15.5)	749 (13.0)	0.07	2189 (15.1)	935 (15.9)	0.02
Ischaemic heart disease	6411 (44.5)	2538 (44.2)	< 0.01	6379.6 (44.1)	2641 (44.9)	0.02

Variable list	Before weighting			After weighting		
	SGLT2i (n=14,400)	GLP1-RA (n=5746)	Standardized difference*	SGLT2i (n=14,456)	GLP1-RA (n=5877)	Standardized difference*
Atrial fibrillation	800 (5.6)	243 (4.2)	0.06	773 (5.3)	347 (5.9)	0.02
Varicose veins	823 (5.7)	457 (8.0)	0.09	909 (6.3)	373 (6.3)	< 0.01
Venous thromboembolism	354 (2.5)	181 (3.2)	0.04	388 (2.7)	189 (3.2)	0.03
Peripheral vascular disease	1752 (12.2)	671 (11.7)	0.02	1716 (11.9)	699 (11.9)	< 0.01
Chronic kidney disease	2330 (16.2)	1026 (17.9)	0.05	2455 (17.0)	1043 (17.7)	0.02
Acute kidney injury	471 (3.3)	213 (3.7)	0.02	575 (4.0)	216 (3.7)	0.02
Urinary tract infection	360 (2.5)	243 (4.2)	0.10	414 (2.9)	204 (3.5)	0.03
Diabetes complications (%)						
Nephropathy	1313 (9.1)	631 (11.0)	0.06	1447 (10.0)	616 (10.5)	0.02
Retinopathy	3226 (22.4)	1074 (18.7)	0.09	3135 (21.7)	1355 (23.1)	0.03
Neuropathy	2842 (19.7)	1500 (26.1)	0.15	3241 (22.4)	1340 (22.8)	< 0.01
Medication‡ (%)						
Other diabetes medication						
Metformin	12065 (83.8)	3681 (64.1)	0.46	11308 (78.2)	4665 (79.4)	0.03
Sulfonylureas	7067 (49.1)	1955 (34.0)	0.31	6583 (45.5)	2749 (46.8)	0.03
DPP-4i	4065 (28.2)	1112 (19.4)	0.21	3739 (25.9)	1560 (26.5)	0.02
Insulin	3449 (24.0)	1737 (30.2)	0.14	3980 (27.5)	1600 (27.2)	< 0.01
Gout medication						
Urate-lowering therapy (<i>allopurinol, febuxostat, or probenecid</i>)	1318 (9.2)	539 (9.4)	0.01	1332 (9.2)	536 (9.1)	< 0.01
Colchicine	435 (3.0)	174 (3.0)	< 0.01	445 (3.1)	183 (3.1)	< 0.01
Corticosteroid	802 (5.6)	439 (7.6)	0.08	857 (5.9)	345 (5.9)	< 0.01
NSAIDs	1100 (7.6)	588 (10.2)	0.09	1164 (8.1)	477 (8.1)	< 0.01
Aspirin	318 (2.2)	104 (1.8)	0.03	313 (2.2)	131 (2.2)	0.01
PPIs	4325 (30.0)	2071 (36.0)	0.13	4696 (32.5)	1893 (32.2)	0.01
Statins	922 (6.4)	292 (5.1)	0.06	868 (6.0)	381 (6.5)	0.02
Nitrates	946 (6.6)	290 (5.0)	0.07	911 (6.3)	391 (6.6)	0.01
Fibrates	149 (1.0)	48 (0.8)	0.02	149 (1.0)	83 (1.4)	0.04
Other cardiovascular medication	4412 (30.6)	1715 (29.8)	0.02	4504 (31.2)	1832 (31.2)	< 0.01

Variable list	Before weighting			After weighting		
	SGLT2i (n=14,400)	GLP1-RA (n=5746)	Standardized difference*	SGLT2i (n=14,456)	GLP1-RA (n=5877)	Standardized difference*
Thiazide diuretics	3133 (21.8)	1320 (23.0)	0.03	3186 (22.0)	1316 (22.4)	0.01
Opioids	4126 (28.7)	1955 (34.0)	0.12	4375 (30.3)	1773 (30.2)	< 0.01
Loop diuretics	1310 (9.1)	626 (10.9)	0.06	1427 (9.9)	591 (10.1)	< 0.01
Potassium-sparing diuretics	840 (5.8)	317 (5.5)	0.01	879 (6.1)	389 (6.6)	0.02
Oral immunosuppressants	383 (2.7)	238 (4.1)	0.08	440 (3.0)	170 (2.9)	< 0.01
Biologics	123 (0.9)	74 (1.3)	0.04	144 (1.0)	61 (1.0)	< 0.01
Healthcare utilization, mean (SD)‡						
Hospitalizations	0.53 (1.10)	0.57 (1.04)	0.04	0.57 (1.23)	0.58 (1.04)	< 0.01
Emergency department (ED) visits	0.68 (1.60)	0.85 (2.37)	0.09	0.77 (1.73)	0.74 (1.99)	0.02
Hospitalizations and ED visits for diabetes						
Total outpatient encounters	24.16 (17.21)	27.78 (19.11)	0.20	26.15 (20.27)	25.67 (16.69)	0.03
Endocrinology encounters	0.57 (1.61)	0.87 (2.11)	0.16	1.02 (4.08)	0.72 (1.65)	0.01
Urology encounters	0.51 (1.52)	0.61 (1.73)	0.06	0.52 (1.60)	0.59 (1.66)	0.04
Nephrology encounters	0.17 (1.06)	0.55 (6.12)	0.09	0.23 (1.49)	0.36 (4.07)	0.04
Internal medicine encounters	0.98 (2.49)	1.38 (3.17)	0.14	1.22 (3.57)	1.11 (2.51)	0.04

*difference < 0.1 indicates negligible differences. ‡Frequency during the past 1 year. n, number; y, years; SD, standard deviation; SGLT2i, sodium glucose cotransporter-2 inhibitors; GLP1-RA, glucagon-like peptide-1 receptor agonists, DPP-4i, dipeptidyl peptidase 4 inhibitors; NSAIDs, non-steroidal anti-inflammatory drugs; PPIs, proton pump inhibitors.

Table S7. Individual SGLT2i and active comparators included in the study population

Individual glucose-lowering medication	Frequency (% in class)	Weighted Frequency (% in class)
SGLT2i vs. GLP1-RA		
SGLT2i		
Empagliflozin	9776 (67.9)	9903 (68.5)
Canagliflozin	2987 (20.7)	2962 (20.5)
Dapagliflozin	1637 (11.4)	1591 (11.0)
GLP1-RA		
Semaglutide	3387 (58.9)	3018 (51.4)
Liraglutide	1982 (34.5)	2373 (40.4)
Dulaglutide	344 (6.0)	452 (7.7)
Exenatide	33 (0.6)	34 (0.6)
SGLT2i vs. DPP-4i		
SGLT2i		
Empagliflozin	8364 (69.0)	7520 (63.6)
Canagliflozin	2429 (20.1)	2987 (25.1)
Dapagliflozin	1323 (10.9)	1344 (11.3)
DPP-4i		
Linagliptin	5494 (64.4)	5794 (65.5)
Sitagliptin	2023 (23.7)	2018 (22.8)
Saxagliptin	1006 (11.8)	1028 (11.6)
Alogliptin	3 (0.0)	3 (0.0)

SGLT2i, sodium glucose cotransporter-2; DPP-4i, dipeptidyl peptidase 4 inhibitors; GLP1-RA, glucagon-like peptide-1 receptor agonists

Table S8. Reasons for censoring among the unweighted study population

	Whole Follow-Up Period		Truncation After 1 Year		Truncation After 1 Year, Intention-to-Treat Analysis	
	SGLT2i (n=14,456)	GLP1-RA (n=5877)	SGLT2i (n=14,456)	GLP1-RA (n=5877)	SGLT2i (n=14,456)	GLP1-RA (n=5877)
Death	198 (1.4)	86 (1.5)	115 (0.8)	54 (0.9)	170 (1.2)	88 (1.5)
End of index medication	8945 (61.9)	3994 (68.0)	5947 (41.1)	3028 (51.5)	0	0
End of study/analysis period (i.e., June 30, 2022 or 1-year follow-up)	4822 (33.4)	1716 (29.2)	8141 (56.3)	2742 (46.7)	13929 (96.4)	5699 (97.0)
Deregistration from medical plan	490 (3.4)	81 (1.4)	252 (1.7)	53 (0.9)	357 (2.5)	90 (1.5)

SGLT2i, sodium glucose cotransporter-2; GLP1-RA, glucagon-like peptide-1 receptor agonists

Table S9: Baseline characteristics among nephrolithiasis patients with type 2 diabetes initiating SGLT2i versus GLP1-RA, before and after propensity score overlap weighting

Variable list	Before overlap weighting			After overlap weighting		
	SGLT2i	GLP1-RA	Standardized difference*	SGLT2i	GLP1-RA	Standardized difference*
Demographics						
Age, mean (SD), y	63.70 (11.02)	59.83 (11.40)	0.35	61.52 (11.23)	61.52 (10.99)	< 0.001
Male (%)	68.4	46.2	0.46	55.4	55.4	< 0.001
Neighbourhood Income Quintile			0.09			< 0.001
1=Lowest	20.4	19.2		19.9	19.9	
2	22.9	20.7		21.4	21.4	
3	20.8	20.8		20.9	20.9	
4	19.2	20.1		19.5	19.5	
5=Highest	15.7	18.2		17.3	17.3	
Health Region			0.10			< 0.001
Interior	14.4	12.5		13.8	13.8	
Fraser	47.2	50.7		49.1	49.1	
Vancouver Coastal	20.1	17.2		17.7	17.7	
Vancouver Island	12.8	13.9		13.7	13.7	
Northern	5.5	5.5		5.5	5.5	
Type 2 diabetes duration, mean (SD), y	13.96 (7.19)	13.01 (7.92)	0.13	13.51 (7.48)	13.51 (7.75)	< 0.001
Gout prevalence, anytime (%)	22.0	21.8	< 0.01	22.3	22.3	< 0.001
Nephrolithiasis duration, mean (SD), y	13.39 (8.77)	12.96 (8.80)	0.05	13.07 (8.73)	13.07 (8.85)	< 0.001
Nephrolithiasis events, mean (SD)	0.30 (1.13)	0.37 (1.27)	0.06	0.34 (1.34)	0.34 (1.21)	< 0.001
Comorbidity (%)						
Obesity	10.5	27.7	0.45	18.7	18.7	< 0.001
Hypertension	64.2	64.8	0.01	64.7	64.7	< 0.001
Myocardial infarction	14.0	10.1	0.12	11.4	11.4	< 0.001
Stroke	13.0	13.4	0.01	13.2	13.2	< 0.001
Heart failure	15.5	13.0	0.07	14.2	14.2	< 0.001
Ischaemic heart disease	44.5	44.2	< 0.01	44.2	44.2	< 0.001
Atrial fibrillation	5.6	4.2	0.06	4.9	4.9	< 0.001
Varicose veins	5.7	8.0	0.09	7.0	7.0	< 0.001

Variable list	Before overlap weighting			After overlap weighting		
	SGLT2i	GLP1-RA	Standardized difference*	SGLT2i	GLP1-RA	Standardized difference*
Venous thromboembolism	2.5	3.2	0.04	2.9	2.9	< 0.001
Peripheral vascular disease	12.2	11.7	0.02	11.6	11.6	< 0.001
Chronic kidney disease	16.2	17.9	0.05	18.0	18.0	< 0.001
Acute kidney injury	4.7	4.7	< 0.01	3.7	3.7	< 0.001
Urinary tract infection	3.7	3.4	0.02	3.4	3.4	< 0.001
Diabetes complications (%)						
Nephropathy	9.1	11.0	0.06	10.7	10.7	< 0.001
Retinopathy	22.4	18.7	0.09	20.8	20.8	< 0.001
Neuropathy	19.7	26.1	0.15	24.3	24.3	< 0.001
Medication‡ (%)						
Other diabetes medication						
Metformin	83.8	64.1	0.46	73.6	73.6	< 0.001
Sulfonylureas	49.1	34.0	0.31	40.2	40.2	< 0.001
DPP-4i	28.2	19.4	0.21	23.0	23.0	< 0.001
Insulin	24.0	30.2	0.14	30.3	30.3	< 0.001
Gout medication						
Urate-lowering therapy (<i>allopurinol, febuxostat, or probenecid</i>)	9.2	9.4	0.01	9.6	9.6	< 0.001
Colchicine	3.0	3.0	< 0.01	3.1	3.1	< 0.001
Corticosteroid	5.6	7.6	0.08	6.6	6.6	< 0.001
NSAIDs	7.6	10.2	0.09	8.7	8.7	< 0.001
Aspirin	2.2	1.8	0.03	2.1	2.1	< 0.001
PPIs	30.0	36.0	0.13	33.9	33.9	< 0.001
Statins	6.4	5.1	0.06	5.7	5.7	< 0.001
Nitrates	6.6	5.0	0.07	5.7	5.7	< 0.001
Fibrates	1.0	0.8	0.02	1.0	1.0	< 0.001
Other cardiovascular medication	30.6	29.8	0.02	30.1	30.1	< 0.001
Thiazide diuretics	21.8	23.0	0.03	23.0	23.0	< 0.001
Opioids	28.7	34.0	0.12	31.9	31.9	< 0.001
Loop diuretics	9.1	10.9	0.06	10.4	10.4	< 0.001

Variable list	Before overlap weighting			After overlap weighting		
	SGLT2i	GLP1-RA	Standardized difference*	SGLT2i	GLP1-RA	Standardized difference*
Potassium-sparing diuretics	5.8	5.5	0.01	5.9	5.9	< 0.001
Oral immunosuppressants	2.7	4.1	0.08	3.4	3.4	< 0.001
Biologics	0.9	1.3	0.04	1.2	1.2	< 0.001
Healthcare utilization, mean (SD)‡						
Hospitalizations	0.53 (1.10)	0.57 (1.04)	0.04	0.56 (1.17)	0.56 (1.02)	< 0.001
Emergency department (ED) visits	0.68 (1.60)	0.85 (2.37)	0.09	0.78 (1.77)	0.78 (2.10)	< 0.001
Hospitalizations and ED visits for diabetes						
Total outpatient encounters	24.16 (17.21)	27.78 (19.11)	0.20	26.29 (19.63)	26.29 (17.06)	< 0.001
Endocrinology encounters	0.57 (1.61)	0.87 (2.11)	0.16	0.77 (2.26)	0.77 (1.68)	< 0.001
Urology encounters	0.51 (1.52)	0.61 (1.73)	0.06	0.57 (1.72)	0.57 (1.60)	< 0.001
Nephrology encounters	0.17 (1.06)	0.55 (6.12)	0.09	0.26 (1.59)	0.26 (1.94)	< 0.001
Internal medicine encounters	0.98 (2.49)	1.38 (3.17)	0.14	1.18 (3.20)	1.18 (2.49)	< 0.001

*difference < 0.1 indicates negligible differences. ‡Frequency during the past 1 year. n, number; y, years; SD, standard deviation; SGLT2i, sodium glucose cotransporter-2 inhibitors; GLP1-RA, glucagon-like peptide-1 receptor agonists, DPP-4i, dipeptidyl peptidase 4 inhibitors; NSAIDs, non-steroidal anti-inflammatory drugs; PPIs, proton pump inhibitors.

Table S10: Baseline characteristics among nephrolithiasis patients with type 2 diabetes initiating SGLT2i versus DPP-4i, before and after inverse probability of treatment weighting

Variable list	Before weighting			After weighting		
	SGLT2i (n=12,116)	DPP-4i (n=8,526)	Standardized difference*	SGLT2i (n=11,911)	DPP-4i (n=8,843)	Standardized difference*
Demographics						
Age, mean (SD), y	63.10 (11.07)	65.97 (11.79)	0.25	63.99 (11.05)	63.89 (11.80)	< 0.01
Male (%)	8120 (67.0)	5584 (65.5)	0.03	7906 (66.4)	5824 (65.9)	0.01
Neighbourhood Income Quintile (%)			0.1			0.02
1=Lowest	2364 (19.5)	1972 (23.1)		2488 (20.9)	1867 (21.1)	
2	2753 (22.7)	1956 (22.9)		2729 (22.9)	1949 (22.0)	
3	2506 (20.7)	1744 (20.5)		2484 (20.9)	1897 (21.5)	
4	2382 (19.7)	1527 (17.9)		2226 (18.7)	1647 (18.6)	
5=Highest	1984 (16.4)	1250 (14.7)		1867 (15.7)	1400 (15.8)	
Health Region (%)			0.10			0.03
Interior	1754 (14.5)	1126 (13.2)		1688 (14.2)	1269 (14.4)	
Fraser	5733 (47.3)	4110 (48.2)		5662 (47.5)	4167 (47.1)	
Vancouver Coastal	2275 (18.8)	1830 (21.5)		2347 (19.7)	1680 (19.0)	
Vancouver Island	1651 (13.6)	966 (11.3)		1517 (12.7)	1166 (13.2)	
Northern	690 (5.7)	490 (5.7)		686 (5.8)	553 (6.3)	
Type 2 diabetes duration, mean (SD), y	13.77 (7.33)	13.99 (7.02)	0.03	13.83 (7.20)	13.91 (7.19)	0.01
Gout prevalence, anytime (%)	2735 (22.6)	1907 (22.4)	< 0.01	2649 (22.2)	2007 (22.7)	0.01
Nephrolithiasis duration, mean (SD), y	13.40 (8.75)	13.11 (8.65)	0.03	13.31 (8.66)	13.24 (8.74)	< 0.01
Nephrolithiasis events, mean (SD)	0.30 (1.16)	0.34 (1.39)	0.03	0.31 (1.18)	0.31 (1.23)	< 0.01
Comorbidity (%)						
Obesity	1604 (13.2)	787 (9.2)	0.13	1393 (11.7)	1087 (12.3)	0.02
Hypertension	8024 (66.2)	5171 (60.6)	0.12	7578 (63.6)	5657 (64.0)	< 0.01
Myocardial infarction	1725 (14.2)	1082 (12.7)	0.05	1573 (13.2)	1139 (12.9)	0.01
Stroke	1617 (13.3)	1261 (14.8)	0.04	1613 (13.5)	1182 (13.4)	< 0.01
Heart failure	1972 (16.3)	1330 (15.6)	0.02	1810 (15.2)	1268 (14.3)	0.02
Ischaemic heart disease	5589 (46.1)	3506 (41.1)	0.10	5178 (43.5)	3750 (42.4)	0.02
Atrial fibrillation	696 (5.7)	457 (5.4)	0.02	641 (5.4)	464 (5.2)	< 0.01

Variable list	Before weighting			After weighting		
	SGLT2i (n=12,116)	DPP-4i (n=8,526)	Standardized difference*	SGLT2i (n=11,911)	DPP-4i (n=8,843)	Standardized difference*
Varicose veins	725 (6.0)	478 (5.6)	0.02	680 (5.7)	542 (6.1)	0.02
Venous thromboembolism	49 (0.4)	59 (0.7)	0.04	57 (0.5)	43 (0.5)	< 0.01
Peripheral vascular disease	1547 (12.8)	1082 (12.7)	< 0.01	1490 (12.5)	1031 (11.7)	0.03
Chronic kidney disease	2022 (16.7)	1753 (20.6)	0.10	2073 (17.4)	1518 (17.2)	< 0.01
Acute kidney injury	400 (3.3)	580 (6.8)	0.16	560 (4.7)	418 (4.7)	< 0.01
Urinary tract infection	309 (2.6)	404 (4.7)	0.12	442 (3.7)	298 (3.4)	0.02
Diabetes complications (%)						
Nephropathy	1123 (9.3)	1350 (15.8)	0.20	1354 (11.4)	1016 (11.5)	< 0.01
Retinopathy	6941 (57.3)	5028 (59.0)	0.03	6861 (57.6)	5084 (57.5)	< 0.01
Neuropathy	2494 (20.6)	1590 (18.6)	0.05	2353 (19.8)	1812 (20.5)	0.02
Medication‡ (%)						
Other diabetes medication						
Metformin	9877 (81.5)	6888 (80.8)	0.02	9704 (81.5)	7253 (82.0)	0.01
Sulfonylureas	5372 (44.3)	4486 (52.6)	0.17	5656 (47.5)	4227 (47.8)	< 0.01
GLP1-RA	1724 (14.2)	283 (3.3)	0.39	1194 (10.0)	1071 (12.1)	0.07
Insulin	3360 (27.7)	1603 (18.8)	0.21	2896 (24.3)	2259 (25.5)	0.03
Gout medication						
Urate-lowering therapy (<i>allopurinol, febuxostat, or probenecid</i>)	1131 (9.3)	830 (9.7)	0.01	1091 (9.2)	806 (9.1)	< 0.01
Colchicine	371 (3.1)	275 (3.2)	< 0.01	360 (3.0)	266 (3.0)	< 0.01
Corticosteroid	691 (5.7)	576 (6.8)	0.04	709 (5.9)	529 (6.0)	< 0.01
NSAIDs	967 (8.0)	654 (7.7)	0.01	955 (8.0)	737 (8.3)	0.01
Aspirin	261 (2.2)	297 (3.5)	0.08	312 (2.6)	217 (2.5)	0.01
PPIs	3628 (29.9)	2534 (29.7)	< 0.01	3525 (29.6)	2662 (30.1)	0.01
Statins	749 (6.2)	534 (6.3)	< 0.01	711 (6.0)	506 (5.7)	0.01
Nitrates	768 (6.3)	541 (6.3)	< 0.01	728 (6.1)	490 (5.5)	0.02
Fibrates	119 (1.0)	85 (1.0)	< 0.01	113 (1.0)	81 (0.9)	< 0.01
Other cardiovascular medication	3809 (31.4)	2638 (30.9)	0.01	3685 (30.9)	2753 (31.1)	< 0.01
Thiazide diuretics	2656 (21.9)	1900 (22.3)	< 0.01	2622 (22.0)	1997 (22.6)	0.01
Opioids	3559 (29.4)	2615 (30.7)	0.03	3541 (29.7)	2659 (30.1)	< 0.01

Variable list	Before weighting			After weighting		
	SGLT2i (n=12,116)	DPP-4i (n=8,526)	Standardized difference*	SGLT2i (n=11,911)	DPP-4i (n=8,843)	Standardized difference*
Loop diuretics	1151 (9.5)	891 (10.5)	0.03	1125 (9.4)	788 (8.9)	0.02
Potassium-sparing diuretics	755 (6.2)	355 (4.2)	0.09	630 (5.3)	436 (4.9)	0.02
Oral immunosuppressants	310 (2.6)	293 (3.4)	0.05	349 (2.9)	281 (3.2)	0.01
Biologics	108 (0.9)	49 (0.6)	0.04	91 (0.8)	77 (0.9)	0.01
Healthcare utilization, mean (SD)‡						
Hospitalizations	0.54 (1.12)	0.65 (1.22)	0.09	0.57 (1.16)	0.57 (1.14)	< 0.01
Emergency department (ED) visits	0.70 (1.63)	0.85 (1.87)	0.08	0.76 (1.75)	0.77 (1.75)	0.01
Hospitalizations and ED visits for diabetes						
Total outpatient encounters	24.26 (17.02)	26.80 (22.64)	0.13	24.85 (18.07)	24.88 (20.40)	< 0.01
Endocrinology encounters	0.65 (1.80)	0.52 (1.76)	0.07	0.59 (1.66)	0.59 (2.16)	< 0.01
Urology encounters	0.50 (1.48)	0.61 (1.79)	0.06	0.57 (1.62)	0.54 (1.61)	0.01
Nephrology encounters	0.17 (1.03)	1.00 (8.53)	0.14	0.28 (2.16)	0.50 (5.44)	0.05
Internal medicine encounters	1.00 (2.40)	1.28 (3.89)	0.09	1.05 (2.59)	1.04 (3.13)	< 0.01

*difference < 0.1 indicates negligible differences. ‡Frequency during the past 1 year. n, number; y, years; SD, standard deviation; SGLT2i, sodium glucose cotransporter-2 inhibitors; GLP1-RA, glucagon-like peptide-1 receptor agonists, DPP-4i, dipeptidyl peptidase 4 inhibitors; NSAIDs, non-steroidal anti-inflammatory drugs; PPIs, proton pump inhibitors.

Table S11. Risk of the first recurrent nephrolithiasis event among nephrolithiasis patients with type 2 diabetes initiating SGLT2i versus GLP1-RA, after inverse probability of treatment weighting

	SGLT2i	GLP1-RA
First Recurrent Nephrolithiasis Event During the Study Period		
Patients, number	14,456	5877
Event, number	927	450
Mean follow-up (years)	1.18	0.85
IR, per 1000 person-years	54.2	90.3
HR (95% CI)	0.68 (0.58 to 0.79)	1.0 (ref)
RD (95% CI)	-36 (-45 to -27)	Reference
NNT (95% CI)	28 (22 to 37)	Reference
First Recurrent Nephrolithiasis Event Requiring ED Visit or Hospitalization		
Patients, number	14,456	5877
Event, number	254	137
Mean follow-up (years)	1.24	0.90
IR, per 1000 person-years	14.2	25.8
HR (95% CI)	0.59 (0.45 to 0.78)	1.0 (ref)
RD (95% CI)	-12 (-16 to -7)	Reference
NNT (95% CI)	83 (63 to 143)	Reference

SGLT2i, sodium glucose cotransporter-2 inhibitors; GLP1-RA, glucagon-like peptide-1 receptor agonists; IR, incidence rate; HR, hazard ratio; NNT, number needed to treat; RD, rate difference; 95% CI, 95% confidence interval

Table S12. Baseline characteristics among nephrolithiasis patients with type 2 diabetes and gout initiating SGLT2i versus GLP1-RA, before and after inverse probability of treatment weighting

Variable list	Before weighting			After weighting		
	SGLT2i (n=3159)	GLP1-RA (n=1250)	Standardized difference*	SGLT2i (n=3159)	GLP1-RA (n=1272)	Standardized difference*
Demographics						
Age, mean (SD), y	66.01 (10.62)	62.78 (10.37)	0.31	65.10 (10.82)	65.26 (10.19)	0.02
Male (%)	2444 (77.4)	754 (60.3)	0.37	2306 (73.0)	942 (74.1)	0.03
Neighbourhood Income Quintile (%)			0.07			0.06
1=Lowest	638 (20.2)	238 (19.0)		618 (19.6)	249 (19.6)	
2	712 (22.5)	262 (21.0)		703 (22.2)	267 (21.0)	
3	655 (20.7)	256 (20.5)		653 (20.7)	264 (20.8)	
4	630 (19.9)	264 (21.1)		645 (20.4)	267 (21.0)	
5=Highest	496 (15.7)	216 (17.3)		511 (16.2)	206 (16.2)	
Health Region (%)			0.17			0.03
Interior	489 (15.5)	166 (13.3)		477 (15.1)	207 (16.2)	
Fraser	1409 (44.6)	646 (51.7)		1462 (46.3)	579 (45.5)	
Vancouver Coastal	680 (21.5)	206 (16.5)		634 (20.1)	253 (19.9)	
Vancouver Island	398 (12.6)	154 (12.3)		393 (12.5)	159 (12.5)	
Northern	182 (5.8)	77 (6.2)		191 (6.1)	75 (5.9)	
Type 2 diabetes duration, mean (SD), y	14.49 (7.23)	13.88 (7.77)	0.08	14.35 (7.31)	14.50 (7.59)	0.02
Gout duration, mean (SD), y	12.16 (8.21)	11.50 (8.17)	0.08	11.98 (8.16)	12.12 (8.42)	0.02
Gout flares, mean (SD)	0.12 (0.47)	0.13 (0.59)	0.03	0.12 (0.47)	0.11 (0.49)	0.03
Nephrolithiasis duration, mean (SD), y	13.93 (8.80)	13.65 (8.65)	0.03	13.86 (8.82)	13.90 (8.93)	< 0.01
Nephrolithiasis events, mean (SD)	0.34 (1.38)	0.44 (1.43)	0.07	0.39 (1.52)	0.37 (1.30)	0.01
Comorbidity (%)						
Obesity	406 (12.9)	371 (29.7)	0.42	546 (17.3)	217 (17.1)	< 0.01
Hypertension	2261 (71.6)	886 (70.9)	0.02	2254 (71.4)	931 (73.2)	0.04
Myocardial infarction	559 (17.7)	156 (12.5)	0.15	523 (16.5)	228 (17.9)	0.04
Stroke	516 (16.3)	204 (16.3)	< 0.01	526 (16.6)	226 (17.8)	0.03
Heart failure	700 (22.2)	233 (18.6)	0.09	679 (21.5)	282 (22.2)	0.02
Ischaemic heart disease	1639 (51.9)	660 (52.8)	0.02	1649 (52.2)	681 (53.5)	0.03

Variable list	Before weighting			After weighting		
	SGLT2i (n=3159)	GLP1-RA (n=1250)	Standardized difference*	SGLT2i (n=3159)	GLP1-RA (n=1272)	Standardized difference*
Atrial fibrillation	255 (8.1)	86 (6.9)	0.05	249 (7.9)	107 (8.4)	0.02
Varicose veins	227 (7.2)	125 (10.0)	0.10	257 (8.1)	106 (8.3)	< 0.01
Venous thromboembolism	101 (3.2)	46 (3.7)	0.03	113 (3.6)	45 (3.5)	< 0.01
Peripheral vascular disease	488 (15.4)	177 (14.2)	0.04	472 (14.9)	208 (16.3)	0.04
Chronic kidney disease	829 (26.2)	340 (27.2)	0.02	848 (26.8)	370 (29.1)	0.05
Acute kidney injury	154 (4.9)	74 (5.9)	0.05	173 (5.5)	67 (5.2)	0.01
Urinary tract infection	77 (2.4)	72 (5.8)	0.17	84 (2.7)	57 (4.5)	0.098
Diabetes complications (%)						
Nephropathy	439 (13.9)	221 (17.7)	0.10	476 (15.1)	185 (14.5)	0.02
Retinopathy	771 (24.4)	279 (22.3)	0.05	770 (24.4)	301 (23.6)	0.02
Neuropathy	723 (22.9)	391 (31.3)	0.19	809 (25.6)	328 (25.8)	< 0.01
Medication‡ (%)						
Other diabetes medication						
Metformin	2624 (83.1)	824 (65.9)	0.40	2472 (78.3)	1004 (78.9)	0.02
Sulfonylureas	1540 (48.7)	446 (35.7)	0.27	1433 (45.4)	588 (46.2)	0.02
DPP-4i	862 (27.3)	259 (20.7)	0.15	816 (25.8)	366 (28.8)	0.07
Insulin	751 (23.8)	447 (35.8)	0.26	898 (28.4)	355 (27.9)	0.01
Gout medication						
Urate-lowering therapy (<i>allopurinol, febuxostat, or probenecid</i>)	1065 (33.7)	436 (34.9)	0.03	1075 (34.0)	439 (34.5)	0.01
Colchicine	382 (12.1)	147 (11.8)	0.01	388 (12.3)	156 (12.3)	< 0.01
Corticosteroid	244 (7.7)	136 (10.9)	0.11	273 (8.7)	107 (8.4)	< 0.01
NSAIDs	314 (9.9)	148 (11.8)	0.06	322 (10.2)	129 (10.1)	< 0.01
Aspirin	78 (2.5)	24 (1.9)	0.04	77 (2.4)	36 (2.8)	0.02
PPIs	1053 (33.3)	483 (38.6)	0.11	1115 (35.3)	456 (35.9)	0.01
Statins	221 (7.0)	89 (7.1)	< 0.01	218 (6.9)	91 (7.2)	0.01
Nitrates	258 (8.2)	73 (5.8)	0.09	245 (7.8)	101 (7.9)	< 0.01
Fibrates	46 (1.5)	13 (1.0)	0.04	45 (1.4)	24 (1.9)	0.04
Other cardiovascular medication	1163 (36.8)	481 (38.5)	0.03	1171 (37.1)	464 (36.5)	0.01
Thiazide diuretics	757 (24.0)	307 (24.6)	0.01	760 (24.1)	298 (23.4)	0.02

Variable list	Before weighting			After weighting		
	SGLT2i (n=3159)	GLP1-RA (n=1250)	Standardized difference*	SGLT2i (n=3159)	GLP1-RA (n=1272)	Standardized difference*
Opioids	958 (30.3)	465 (37.2)	0.15	1028 (32.5)	415 (32.6)	< 0.01
Loop diuretics	440 (13.9)	215 (17.2)	0.09	466 (14.7)	178 (14.0)	0.02
Potassium-sparing diuretics	251 (7.9)	94 (7.5)	0.02	253 (8.0)	102 (8.0)	< 0.01
Oral immunosuppressants	107 (3.4)	76 (6.1)	0.13	129 (4.1)	46 (3.6)	0.02
Biologics	32 (1.0)	18 (1.4)	0.04	35.0 (1.1)	12.3 (1.0)	0.01
Healthcare utilization, mean (SD)‡						
Hospitalizations	0.61 (1.06)	0.71 (1.16)	0.08	0.66 (1.13)	0.65 (1.11)	< 0.01
Emergency department (ED) visits	0.75 (1.66)	0.92 (1.98)	0.09	0.82 (1.70)	0.76 (1.68)	0.04
Hospitalizations and ED visits for diabetes						
Total outpatient encounters	27.17 (17.72)	31.27 (20.29)	0.22	28.56 (19.29)	28.27 (17.80)	0.02
Rheumatology encounters	0.16 (0.78)	0.27 (1.08)	0.12	0.18 (0.84)	0.18 (0.83)	< 0.01
Endocrinology encounters	0.58 (1.70)	1.02 (2.12)	0.23	0.77 (2.25)	0.75 (1.71)	< 0.01
Urology encounters	0.60 (1.63)	0.82 (1.98)	0.12	0.63 (1.71)	0.73 (1.73)	0.06
Nephrology encounters	0.33 (1.51)	0.92 (6.54)	0.13	0.43 (1.97)	0.67 (4.77)	0.07
Internal medicine encounters	1.14 (2.46)	1.47 (2.77)	0.13	1.24 (2.62)	1.24 (2.38)	< 0.01

*difference < 0.1 indicates negligible differences. ‡Frequency during the past 1 year. n, number; y, years; SD, standard deviation; SGLT2i, sodium glucose cotransporter-2 inhibitors; GLP1-RA, glucagon-like peptide-1 receptor agonists, DPP-4i, dipeptidyl peptidase 4 inhibitors; NSAIDs, non-steroidal anti-inflammatory drugs; PPIs, proton pump inhibitors.

Table S13. Recurrent nephrolithiasis event count among nephrolithiasis patients with type 2 diabetes initiating SGLT2i versus GLP1-RA or DPP-4i, after inverse probability of treatment weighting, among patients with and without concomitant gout

	SGLT2i	GLP1-RA
Gout		
Patients, number	3159	1272
Event, number	479	218
Mean follow-up (years)	1.24	0.98
IR, per 1000 person-years	122.4	174.1
RR (95% CI)	0.67 (0.57 to 0.79)	1.0 (ref)
RD (95% CI)	-53 (-78 to -27)	Reference
NNT (95% CI)	19 (13 to 37)	Reference
Non-Gout		
Patients, number	11,256	4205
Event, number	1434	624
Mean follow-up (years)	1.27	0.97
IR, per 1000 person-years	100.5	148.4
RR (95% CI)	0.68 (0.62 to 0.75)	1.0 (ref)
RD (95% CI)	-48 (-61 to -35)	Reference
NNT (95% CI)	21 (16 to 29)	Reference
	SGLT2i	DPP-4i
Gout		
Patients, number	2668	2028
Event, number	418	439
Mean follow-up (years)	1.38	1.24
IR, per 1000 person-years	113.5	175.0
RR (95% CI)	0.63 (0.55 to 0.72)	1.0 (ref)
RD (95% CI)	-62 (-81 to -42)	Reference
NNT (95% CI)	16 (12 to 24)	Reference
Non-Gout		
Patients, number	9239	6801
Event, number	1423	1199
Mean follow-up (years)	1.43	1.27
IR, per 1000 person-years	107.9	138.4
RR (95% CI)	0.77 (0.72 to 0.83)	1.0 (ref)
RD (95% CI)	-31 (-40 to -21)	Reference
NNT (95% CI)	32 (25 to 48)	Reference

SGLT2i, sodium glucose cotransporter-2 inhibitors; GLP1-RA, glucagon-like peptide-1 receptor agonists; DPP-4i, dipeptidyl peptidase 4 inhibitors; IR, incidence rate; NNT, number needed to treat; RR, rate ratio; RD, rate difference; 95% CI, 95% confidence interval

Table S14. Baseline characteristics among patients with type 2 diabetes and no history of nephrolithiasis initiating SGLT2i versus GLP1-RA, before and after inverse probability of treatment weighting

Variable list	Before weighting			After weighting		
	SGLT2i (n=112,771)	GLP1-RA (n=40,674)	Standardized difference*	SGLT2i (n=112,728)	GLP1-RA (n=41,623)	Standardized difference*
Demographics						
Age, mean (SD), y	61.49 (12.05)	56.76 (12.65)	0.38	60.30 (12.54)	60.68 (12.17)	0.03
Male (%)	67667 (60.0)	15543 (38.2)	0.45	61476 (54.5)	23686 (56.9)	0.05
Neighbourhood Income Quintile			0.17			0.01
1=Lowest	25510 (22.6)	7506 (18.5)		24321 (21.6)	8922 (21.4)	
2	25697 (22.8)	8004 (19.7)		24829 (22.0)	9075 (21.8)	
3	22832 (20.2)	8388 (20.6)		22886 (20.3)	8371 (20.1)	
4	20881 (18.5)	8694 (21.4)		21679 (19.2)	8118 (19.5)	
5=Highest	16610 (14.7)	7658 (18.8)		17775 (15.8)	6683 (16.1)	
Health Region			0.08			0.04
Interior	14252 (12.6)	5059 (12.4)		14361 (12.7)	5724 (13.8)	
Fraser	52467 (46.5)	18915 (46.5)		52110 (46.2)	18932 (45.5)	
Vancouver Coastal	26256 (23.3)	8672 (21.3)		25689 (22.8)	9191 (22.1)	
Vancouver Island	14048 (12.5)	5978 (14.7)		14859 (13.2)	5540 (13.3)	
Northern	5546 (4.9)	1995 (4.9)		5517 (4.9)	2162 (5.2)	
Type 2 diabetes duration, mean (SD), y	12.49 (7.51)	11.49 (8.10)	0.13	12.41 (7.63)	12.25 (7.79)	0.02
Gout prevalence, anytime (%)	14969 (13.3)	4994 (12.3)	0.03	14654 (13.0)	5856 (14.1)	0.03
Comorbidity (%)						
Obesity	9093 (8.1)	10404 (25.6)	0.48	13990 (12.4)	5122 (12.3)	< 0.01
Hypertension	65929 (58.5)	23188 (57.0)	0.03	66254 (58.8)	24063 (57.8)	0.02
Myocardial infarction	11890 (10.5)	2764 (6.8)	0.13	10942 (9.7)	4390 (10.5)	0.03
Stroke	11107 (9.8)	3688 (9.1)	0.03	11285 (10.0)	4039 (9.7)	0.01
Heart failure	13399 (11.9)	3917 (9.6)	0.07	13008 (11.5)	5266 (12.7)	0.03
Ischaemic heart disease	39960 (35.4)	13781 (33.9)	0.03	39571 (35.1)	15335 (36.8)	0.04
Atrial fibrillation	4318 (3.8)	1301 (3.2)	0.03	4332 (3.8)	1636 (3.9)	< 0.01
Varicose veins	5396 (4.8)	3005 (7.4)	0.11	6067 (5.4)	2253 (5.4)	< 0.01
Venous thromboembolism	2070 (1.8)	1032 (2.5)	0.05	2365 (2.1)	910 (2.2)	< 0.01

Variable list	Before weighting			After weighting		
	SGLT2i (n=112,771)	GLP1-RA (n=40,674)	Standardized difference*	SGLT2i (n=112,728)	GLP1-RA (n=41,623)	Standardized difference*
Peripheral vascular disease	10151 (9.0)	3471 (8.5)	0.02	10211 (9.1)	3954 (9.5)	0.02
Chronic kidney disease	11448 (10.2)	4320 (10.6)	0.02	11965 (10.6)	4899 (11.8)	0.04
Acute kidney injury	2338 (2.1)	792 (1.9)	0.01	2722 (2.4)	782 (1.9)	0.04
Urinary tract infection	1472 (1.3)	801 (2.0)	0.05	1744 (1.5)	747 (1.8)	0.02
Diabetes complications (%)						
Nephropathy	5684 (5.0)	2486 (6.1)	0.05	6344 (5.6)	2573 (6.2)	0.02
Retinopathy	24540 (21.8)	6628 (16.3)	0.14	24284 (21.5)	8151 (19.6)	0.05
Neuropathy	16779 (14.9)	7793 (19.2)	0.11	17855 (15.8)	7371 (17.7)	0.05
Medication‡ (%)						
Other diabetes medication						
Metformin	93703 (83.1)	24842 (61.1)	0.51	87684 (77.8)	32580 (78.3)	0.01
Sulfonylureas	55102 (48.9)	11411 (28.1)	0.44	49223 (43.7)	18489 (44.4)	0.02
DPP-4i	30919 (27.4)	6460 (15.9)	0.28	27901 (24.8)	10719 (25.8)	0.02
Insulin	24753 (21.9)	10797 (26.5)	0.11	27764 (24.6)	10743 (25.8)	0.03
Gout medication						
Urate-lowering therapy (<i>allopurinol</i> , <i>febuxostat</i> , or <i>probenecid</i>)	4962 (4.4)	1757 (4.3)	< 0.01	4807 (4.3)	2248 (5.4)	0.05
Colchicine	2151 (1.9)	761 (1.9)	< 0.01	2209 (2.0)	890 (2.1)	0.01
Corticosteroid	4862 (4.3)	2476 (6.1)	0.08	5349 (4.7)	1979 (4.8)	< 0.01
NSAIDs	6720 (6.0)	2924 (7.2)	0.05	7143 (6.3)	2390 (5.7)	0.03
Aspirin	2327 (2.1)	525 (1.3)	0.06	2215 (2.0)	694 (1.7)	0.02
PPIs	27489 (24.4)	12175 (29.9)	0.13	29331 (26.0)	10873 (26.1)	< 0.01
Statins	6325 (5.6)	1824 (4.5)	0.05	6059 (5.4)	2438 (5.9)	0.02
Nitrates	5466 (4.8)	1319 (3.2)	0.08	5105 (4.5)	2122 (5.1)	0.03
Fibrates	876 (0.8)	270 (0.7)	0.01	905 (0.8)	350 (0.8)	< 0.01
Other cardiovascular medication	29659 (26.3)	9654 (23.7)	0.06	29547 (26.2)	11022 (26.5)	< 0.01
Thiazide diuretics	23694 (21.0)	8587 (21.1)	< 0.01	23961 (21.3)	8999 (21.6)	< 0.01
Opioids	24086 (21.4)	10034 (24.7)	0.08	25384 (22.5)	9206 (22.1)	0.01
Loop diuretics	8291 (7.4)	3314 (8.1)	0.03	8785 (7.8)	3718 (8.9)	0.04
Potassium-sparing diuretics	5482 (4.9)	1905 (4.7)	< 0.01	5917 (5.2)	1993 (4.8)	0.02

Variable list	Before weighting			After weighting		
	SGLT2i (n=112,771)	GLP1-RA (n=40,674)	Standardized difference*	SGLT2i (n=112,728)	GLP1-RA (n=41,623)	Standardized difference*
Oral immunosuppressants	2366 (2.1)	1378 (3.4)	0.08	2600 (2.3)	1279 (3.1)	0.05
Biologics	586 (0.5)	418 (1.0)	0.06	714 (0.6)	355 (0.9)	0.03
Healthcare utilization, mean (SD)‡						
Hospitalizations	0.36 (0.87)	0.37 (0.96)	< 0.01	0.38 (0.92)	0.51 (2.36)	0.07
Emergency department (ED) visits	0.45 (1.36)	0.52 (1.51)	0.05	0.51 (1.64)	0.46 (1.27)	0.03
Hospitalizations and ED visits for diabetes						
Total outpatient encounters	20.35 (15.18)	22.90 (17.18)	0.16	21.58 (18.00)	21.57 (15.52)	< 0.01
Endocrinology encounters	0.57 (1.64)	0.82 (2.16)	0.13	0.82 (3.20)	0.74 (1.82)	0.03
Urology encounters	0.14 (0.76)	0.15 (0.81)	0.02	0.13 (0.74)	0.21 (1.03)	0.09
Nephrology encounters	0.10 (0.94)	0.35 (4.78)	0.07	0.14 (1.35)	0.24 (3.34)	0.04
Internal medicine encounters	0.81 (2.39)	1.18 (2.70)	0.15	0.99 (3.33)	0.96 (2.23)	0.01

*difference < 0.1 indicates negligible differences. ‡Frequency during the past 1 year. n, number; y, years; SD, standard deviation; SGLT2i, sodium glucose cotransporter-2 inhibitors; GLP1-RA, glucagon-like peptide-1 receptor agonists, DPP-4i, dipeptidyl peptidase 4 inhibitors; NSAIDs, non-steroidal anti-inflammatory drugs; PPIs, proton pump inhibitors.

Table S15. Recurrent nephrolithiasis event count among patients with type 2 diabetes and no history of nephrolithiasis initiating SGLT2i versus GLP1-RA, after inverse probability of treatment weighting or overlap weighting of the propensity score

	SGLT2i	GLP1-RA
Inverse Probability of Treatment Weighting		
Patients, number	112,728	41,623
Event, number	1072	499
Mean follow-up (years)	1.28	0.94
IR, per 1000 person-years	7.4	12.8
RR (95% CI)	0.58 (0.52 to 0.64)	1.0 (ref)
RD (95% CI)	-5 (-7 to -4)	Reference
NNT (95% CI)	200 (143 to 250)	Reference
Overlap Weighting of the Propensity Score		
Patients, number	112,771	40,674
Event, number	1081	427
Mean follow-up (years)	1.18	0.88
IR, per 1000 person-years	7.3	13.0
RR (95% CI)	0.56 (0.49 to 0.68)	1.0 (ref)
RD (95% CI)	-6 (-8 to -4)	Reference
NNT (95% CI)	167 (125 to 250)	Reference

SGLT2i, sodium glucose cotransporter-2 inhibitors; GLP1-RA, glucagon-like peptide-1 receptor agonists; IR, incidence rate; NNT, number needed to treat; RR, rate ratio; RD, rate difference; 95% CI, 95% confidence interval

Table S16. Control outcomes among nephrolithiasis patients with type 2 diabetes initiating SGLT2i versus GLP1-RA, propensity score overlap weighting analysis

	SGLT2i	GLP1-RA
<i>Genital Infection (POSITIVE CONTROL OUTCOME)</i>		
Patients, number	14,400	5746
Event, number	395	68
Mean follow-up (years)	1.17	0.88
IR, per 1000 person-years	28.6	12.7
HR (95% CI)	2.31 (1.59 to 3.35)	1.0 (ref)
RD (95% CI)	16 (9 to 23)	Reference
<i>Any Osteoarthritis Encounter (NEGATIVE CONTROL OUTCOME)</i>		
Patients, number	14,400	5746
Event, number	227	70
Mean follow-up (years)	1.17	0.88
IR, per 1000 person-years	13.5	14.1
HR (95% CI)	0.97 (0.64 to 1.46)	1.0 (ref)
RD (95% CI)	-1 (-6 to 5)	Reference
<i>Appendicitis (NEGATIVE CONTROL OUTCOME)</i>		
Patients, number	14,400	5746
Event, number	83	35
Mean follow-up (years)	1.17	0.88
IR, per 1000 person-years	5.9	6.9
HR (95% CI)	0.84 (0.45 to 1.52)	1.0 (ref)
RD (95% CI)	-1 (-5 to 3)	Reference

SGLT2i, sodium glucose cotransporter-2 inhibitors; GLP1-RA, glucagon-like peptide-1 receptor agonists; IR, incidence rate; HR, hazard ratio; RD, rate difference; 95% CI, 95% confidence interval

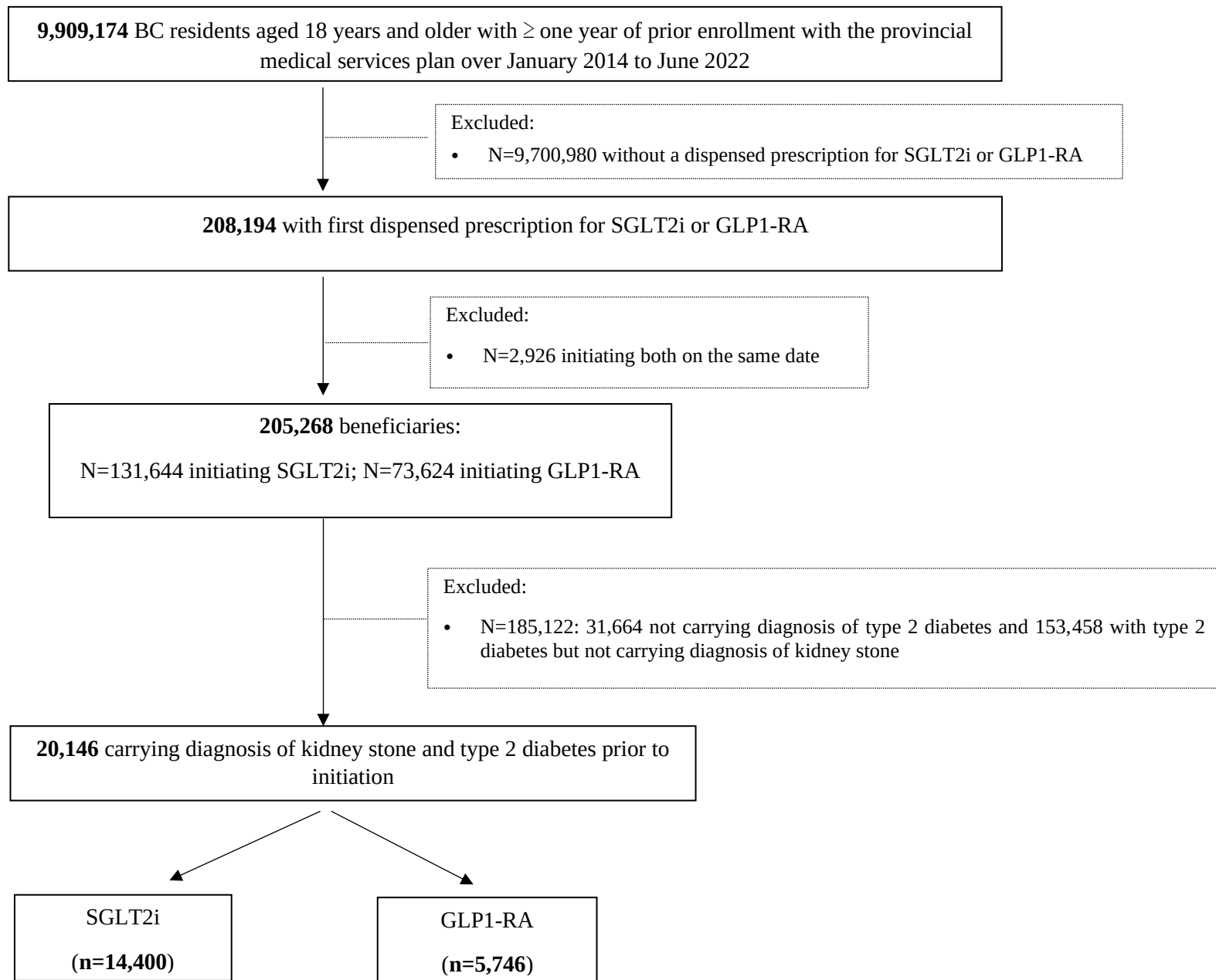


Figure S1. Development of study population for SGLT2i vs. GLP1-RA comparison. SGLT2i, sodium glucose cotransporter-2 inhibitors; GLP1-RA, glucagon-like peptide-1 receptor agonists.

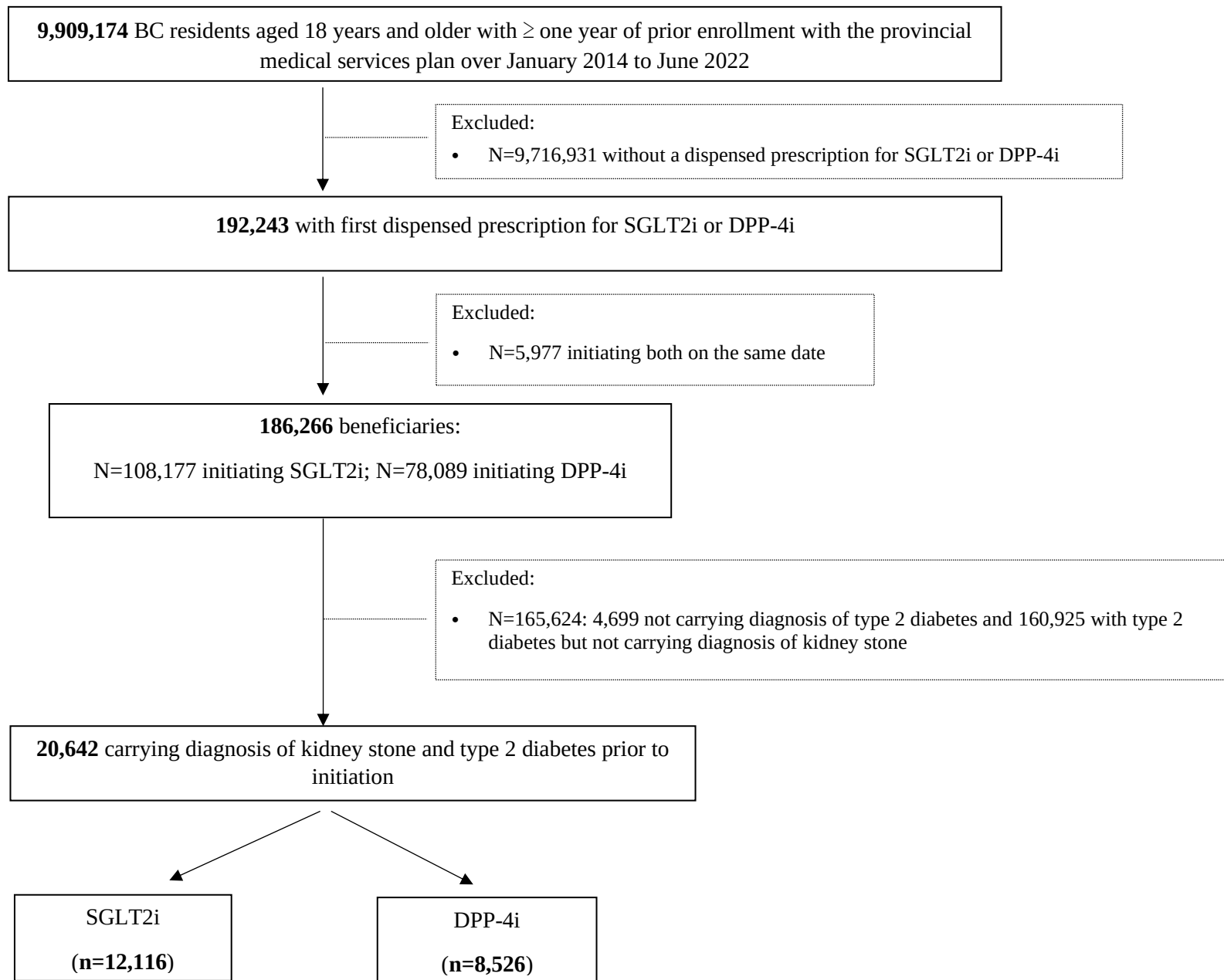


Figure S2. Development of study population for SGLT2i vs. DPP-4i comparison. SGLT2i, sodium glucose cotransporter-2 inhibitors; DPP-4i, dipeptidyl peptidase 4 inhibitors.