Supplemental Material

Supplementary Table 1. Descriptions of Databases.

Supplementary Table 2. Full characteristics for SGLT2 inhibitors vs. DPP4 inhibitors.

Supplementary Table 3. Covariate Definition.

Supplementary Table 4. Breakdowns of baseline exposures.

Supplementary Table 5. Summary of Study End Points.

Supplementary Table 1. Descriptions of Databases.

Database	Description
Ontario Drug Benefit (ODB) database	This database contains records of all dispensed outpatient prescriptions covered by Ontario Drug Benefit in individuals mainly aged 65 years or older.
Ontario Diabetes Database (ODD)	This database contains individuals with diabetes identified by a validated algorithm and ascertains information on the age of diabetes diagnosis when available.
Continuing Care Reporting System (CCRS)	This database ascertains information on long-term care admission
Registered Persons Database (RPDB)	This database ascertains information on demographic characteristics and vital status
Ontario Health Insurance Plan (OHIP) physician billing database	This database ascertains records on physician claims and billings
National Ambulatory Care Reporting System (NACRS)	This database ascertains records on emergency visits.
Discharge Abstract Database (DAD)	This database ascertains records on hospitalizations.
ICES Physician Database (IPDB)	This database ascertains information on prescribing physicians

Supplementary Table 2. Full characteristics for SGLT2 inhibitors vs. DPP4 inhibitors.

Variables	Before Weighting			After Weighting		
	SGLT2 Inhibitors (n=36513)	DPP4 Inhibitors (n=70390)	SMD	SGLT2 Inhibitors (n=36513)	DPP4 Inhibitors (n=36545)	SMD
Age	72.4 (5.38)	74.26 (6.54)	-0.311	72.4 (5.38)	72.41 (3.89)	-0.002
66-69	36.92% (13482)	29.02% (20426)	0.169	36.92% (13482)	37.5% (13705)	-0.012
70-74	33.13% (12097)	29.27% (20604)	0.083	33.13% (12097)	33.03% (12073)	0.002
75-79	18.38% (6711)	20.14% (14174)	-0.045	18.38% (6711)	18.05% (6596)	0.008
80-84	8.34% (3045)	12.94% (9110)	-0.150	8.34% (3045)	8.21% (2999)	0.004
85-89	2.69% (981)	6.28% (4419)	-0.174	2.69% (981)	2.69% (982)	0.000
90+	0.54% (197)	2.35% (1657)	-0.152	0.54% (197)	0.52% (190)	0.002
Male	61.21% (22349)	52.95% (37270)	0.167	61.21% (22349)	61.04% (22308)	0.003
Rural	15.27% (5575)	11.2% (7883)	0.120	15.27% (5575)	15.53% (5677)	-0.008
Diabetes Duration, Years	12.03 (7.71)	11.19 (7.48)	0.111	12.03 (7.71)	12.03 (5.62)	0.000
Index Date Year						
2016	10.42% (3803)	15.11% (10634)	-0.141	10.42% (3803)	10.41% (3804)	0.000
2017	24.01% (8768)	30.33% (21351)	-0.142	24.01% (8768)	23.61% (8629)	0.009
2018	24.85% (9075)	27.58% (19411)	-0.062	24.85% (9075)	24.69% (9022)	0.004
2019	31.65% (11558)	22.8% (16049)	0.200	31.65% (11558)	32.1% (11732)	-0.010
2020	9.06% (3309)	4.18% (2945)	0.197	9.06% (3309)	9.19% (3358)	-0.005
Neighbourhood Income Quintiles						
1	20.93% (7643)	23.45% (16503)	-0.061	20.93% (7643)	21.03% (7685)	-0.002
2	21.8% (7959)	22.44% (15792)	-0.015	21.8% (7959)	21.93% (8016)	-0.003
3	20.6% (7520)	20.4% (14359)	0.005	20.6% (7520)	20.62% (7534)	-0.001
4	18.94% (6917)	17.79% (12520)	0.030	18.94% (6917)	18.93% (6918)	0.000
5	17.73% (6474)	15.93% (11216)	0.048	17.73% (6474)	17.49% (6392)	0.006
Neighbourhood Education Quintiles						
1	19.06% (6959)	20.36% (14334)	-0.033	19.06% (6959)	19.53% (7136)	-0.012
2	21.23% (7752)	21.24% (14949)	0.000	21.23% (7752)	20.97% (7662)	0.006
3	19.78% (7222)	18.56% (13067)	0.031	19.78% (7222)	19.86% (7258)	-0.002
4	20.61% (7526)	19.94% (14034)	0.017	20.61% (7526)	20.25% (7399)	0.009
5	19.32% (7054)	19.9% (14006)	-0.015	19.32% (7054)	19.4% (7091)	-0.002
Prescribing Physician Specialty						
Cardiology	5.38% (1965)	0.42% (295)	0.299	5.38% (1965)	5.29% (1934)	0.005
Endocrinology	12.34% (4505)	8.17% (5748)	0.138	12.34% (4505)	11.99% (4380)	0.012
General practitioner / Family physician	65.93% (24072)	76.45% (53813)	-0.234	65.93% (24072)	66.56% (24323)	-0.014

Internal Medicine	6.51% (2378)	4.6% (3237)	0.084	6.51% (2378)	6.31% (2305)	0.009
Nephrology	2.54% (926)	1.86% (1311)	0.046	2.54% (926)	2.46% (900)	0.005
Others	1.86% (678)	2.36% (1659)	-0.035	1.86% (678)	1.88% (687)	-0.002
Missing	5.45% (1989)	6.15% (4327)	-0.030	5.45% (1989)	5.52% (2016)	-0.003
Charlson Comorbidity Index						
0	82.58% (30154)	81.14% (57116)	0.037	82.58% (30154)	82.62% (30194)	-0.001
1	4.81% (1756)	5.31% (3741)	-0.023	4.81% (1756)	4.77% (1743)	0.002
2	5.35% (1955)	5.38% (3785)	-0.001	5.35% (1955)	5.27% (1927)	0.004
3+	7.25% (2648)	8.17% (5748)	-0.034	7.25% (2648)	7.33% (2680)	-0.003
Polypharmacy						
0	2.2% (805)	4.72% (3322)	-0.138	2.2% (805)	2.35% (857)	-0.008
1-5	28.67% (10469)	31.7% (22313)	-0.066	28.67% (10469)	29.04% (10613)	-0.008
6-10	45.31% (16544)	41.11% (28937)	0.085	45.31% (16544)	45.01% (16450)	0.006
10+	23.81% (8695)	22.47% (15818)	0.032	23.81% (8695)	23.6% (8625)	0.005
Comorbidities						
Chronic kidney disease	10.61% (3873)	15.49% (10901)	-0.145	10.61% (3873)	10.58% (3865)	0.001
Acute kidney injury	3.52% (1284)	5.92% (4170)	-0.114	3.52% (1284)	3.53% (1288)	0.000
Acute urinary retention	1.56% (570)	2.25% (1585)	-0.051	1.56% (570)	1.57% (574)	-0.001
Chronic lung disease	22.65% (8271)	21.96% (15457)	0.017	22.65% (8271)	22.85% (8351)	-0.005
Cancer	32.09% (11716)	32.64% (22976)	-0.012	32.09% (11716)	31.96% (11681)	0.003
Atrial fibrillation/Flutter	5.96% (2175)	5.45% (3839)	0.022	5.96% (2175)	5.9% (2156)	0.002
Coronary artery bypass graft surgery	3.65% (1331)	2.07% (1458)	0.095	3.65% (1331)	3.69% (1347)	-0.002
Percutaneous coronary intervention	7.11% (2596)	3.79% (2665)	0.147	7.11% (2596)	7.3% (2668)	-0.008
Pacemaker	9.24% (3372)	8.46% (5956)	0.027	9.24% (3372)	9.65% (3528)	-0.015
Congestive heart failure	13.78% (5033)	12.52% (8814)	0.037	13.78% (5033)	13.84% (5058)	-0.002
Chronic liver disease	4.84% (1768)	4.83% (3401)	0.000	4.84% (1768)	4.79% (1749)	0.003
Urinary tract infections	3.02% (1101)	4.98% (3507)	-0.101	3.02% (1101)	3.05% (1116)	-0.002
Asthma	14.84% (5418)	14.25% (10034)	0.017	14.84% (5418)	14.8% (5407)	0.001
Chronic obstructive pulmonary disease	21.94% (8010)	20.88% (14700)	0.026	21.94% (8010)	22.01% (8044)	-0.002
Obesity	9.01% (3291)	6.19% (4358)	0.107	9.01% (3291)	9.26% (3383)	-0.009
Hypertension	76.49% (27928)	71.07% (50028)	0.123	76.49% (27928)	75.9% (27738)	0.013
Stroke	2.48% (906)	3.19% (2243)	-0.043	2.48% (906)	2.5% (914)	-0.001
Diabetes Complications						
Diabetic retinopathy	0.8% (291)	0.7% (492)	0.011	0.8% (291)	0.78% (284)	0.002
Diabetic neuropathy	1.25% (456)	1.25% (882)	0.000	1.25% (456)	1.21% (443)	0.003
Peripheral vascular disease	1.41% (514)	1.33% (937)	0.007	1.41% (514)	1.37% (501)	0.003
Hypoglycemia	0.66% (242)	0.85% (596)	-0.021	0.66% (242)	0.7% (256)	-0.004

Hyperglycemic emergency	0.23% (84)	0.28% (198)	-0.010	0.23% (84)	0.23% (86)	-0.001
Medications						
ACE inhibitors	29.83% (10891)	27.71% (19505)	0.047	29.83% (10891)	29.55% (10799)	0.006
ARBs	22.61% (8254)	20.55% (14464)	0.050	22.61% (8254)	22.57% (8247)	0.001
Aspirin	0.77% (282)	1.15% (812)	-0.039	0.77% (282)	0.78% (285)	-0.001
Beta blockers	36.68% (13392)	30.97% (21802)	0.121	36.68% (13392)	35.93% (13130)	0.016
Calcium channel blockers	31.9% (11647)	31.73% (22338)	0.004	31.9% (11647)	31.48% (11505)	0.009
H2RAs	2.86% (1044)	3.3% (2324)	-0.026	2.86% (1044)	2.81% (1027)	0.003
NSAIDs (excluding aspirin)	8.98% (3278)	8.65% (6086)	0.012	8.98% (3278)	9.24% (3377)	-0.009
Statin	70.1% (25597)	64% (45048)	0.130	70.1% (25597)	69.59% (25432)	0.011
Proton pump inhibitors	20.67% (7549)	20.15% (14186)	0.013	20.67% (7549)	20.7% (7565)	-0.001
Loop diuretic	10.26% (3748)	10.39% (7315)	-0.004	10.26% (3748)	10.06% (3676)	0.007
Potassium sparing diuretics	4.87% (1778)	3.85% (2707)	0.050	4.87% (1778)	4.65% (1699)	0.011
Thiazide diuretics	16% (5841)	14.93% (10511)	0.029	16% (5841)	15.95% (5828)	0.001
Glucose-Lowering Medications						
Insulin	22.65% (8270)	12.19% (8581)	0.278	22.65% (8270)	22.68% (8288)	-0.001
Acarbose	0.48% (175)	0.41% (289)	0.010	0.48% (175)	0.49% (177)	-0.001
Metformin	68.58% (25041)	65.67% (46224)	0.062	68.58% (25041)	68.19% (24921)	0.008
Repaglinide	0.03% (10)	0.05% (33)	-0.010	0.03% (10)	0.03% (9)	0.001
Rosiglitazone	0.02% (8)	0.05% (33)	-0.013	0.02% (8)	0.02% (7)	0.001
Semaglutide	0.29% (106)	0.02% (15)	0.068	0.29% (106)	0.32% (116)	-0.007
Pioglitazone	0.29% (106)	0.37% (257)	-0.013	0.29% (106)	0.33% (120)	-0.006
Gliclazide	18.93% (6913)	18.25% (12845)	0.018	18.93% (6913)	19.41% (7094)	-0.012
Glyburide	2.47% (901)	3.55% (2500)	-0.063	2.47% (901)	2.71% (990)	-0.014

Proportions in % (counts) and mean (standard deviation) were reported for categorical and continuous variables, respectively. ACE = Angiotensin-converting enzyme; ARBs = Angiotensin II Receptor Blockers; H2RAs = Histamine-2 Receptor Antagonists; Non-steroidal anti-inflammatory drugs = NSAIDs; SMD = standardized mean difference.

Supplementary Table 3. Covariate Definition.

Variable	Code Set	Datasets Used	Details
Demographics			
Age	Categorized into 66-69, 70-74, 75-79, 80-84, 85-89, 90+	RPDB	Age was treated as a categorical variable when propensity score was calculated.
Sex - Male	Males, Females	RPDB	--
Rural	Yes/No	RPDB	Rural area is defined as population ≤10,000. People with missing rural indicator were excluded.
Duration of diabetes	Derived from age of diabetes diagnosis	ODD	People with missing data were excluded.
Neighbourhood Income Quintile	Coded as quintiles (1, 2, 3, 4, 5)	RPDB	Income quintiles used average neighbourhood income on index date as defined by Statistics Canada.

1 is lowest quintile (poorest) and 5 is highest quintile (richest). People with missing neighbourhood income quintiles were excluded. |
| Neighbourhood Post-Secondary Quintile | Coded as quintiles (1, 2, 3, 4, 5) | RPDB | Post-Secondary quintiles used average neighbourhood post-secondary completion rate on index date.

1 stands for the lowest and 5 stands for the highest. People with missing neighbourhood post-secondary quintiles were excluded. |
Prescriber Information			
Prescribing Physician	Coded as General Practitioner, Cardiologist, Endocrinologist, Internist, Nephrologist, Other, or Missing	ODB, IPDB	--
Comorbidities (5-year look-back window unless specified)			
Chronic kidney disease	Yes/No	DAD, OHIP	ICD-10: E102, E112, E132, E142, I12, I13, N00, N01, N02, N03, N04, N05, N06, N07, N08, N10, N11, N12, N13, N14, N15, N16, N17, N18, N19, N20, N21, N22, N23
OHIP diagnosis codes: 403, 585
Previous acute kidney injury	Yes/No	DAD	ICD-10: N17
Acute urinary retention (AUR)	Yes/No	DAD	ICD-10: R33

Chronic lung disease	Yes/No	OHIP, DAD, NACRS	ICD-10: I272, I278, I279, J40, J41, J42, J43, J44, J45, J47, J60, J61, J62, J63, J64, J65, J66, J67, J68, J701, J703, J704, J708, J709, J82, J84, J92, J941, J949, J953, J961, J969, J984, J988, J989, J99 OHIP dx: 491, 492, 493, 494, 496, 501, 502, 515, 518, 519 OHIP fee codes: J889, J689
Cancer	Yes/No	DAD, OHIP	ICD-10: C00, C01, C02, C03, C04, C05, C06, C07, C08, C09, C10, C11, C12, C13, C14, C15, C16, C17, C18, C19, C20, C21, C22, C23, C24, C25, C26, C30, C31, C32, C33, C34, C37, C38, C39, C40, C41, C43, C44, C45, C46, C47, C48, C49, C50, C51, C52, C53, C54, C55, C56, C57, C58, C60, C61, C62, C63, C64, C65, C66, C67, C68, C69, C70, C71, C72, C73, C74, C75, C76, C77, C78, C79, C80, C81, C82, C83, C84, C85, C86, C88, C90, C91, C92, C93, C94, C95, C96, C97, D00, D01, D02, D03, D04, D05, D06, D07, D09, Z85 OHIP diagnostic codes: 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 151, 152, 153, 154, 155, 156, 157, 158, 159, 160, 161, 162, 163, 164,165, 170, 171, 172, 173, 174, 175, 179, 180, 181, 182, 183, 184, 185, 186, 187, 188, 189, 190, 191, 192, 193, 194, 195, 196, 197, 198, 199, 200, 201, 202, 203, 204, 205, 206, 207, 208, 230, 231, 232, 233, 234
Stroke	Yes/No	DAD, NACRS	ICD-10: I60, I61, I63 (excluding I63.6), I64, H341, H340 Note: Transient ischemic attack was not included
Atrial Fibrillation/Flutter	Yes/No	DAD	ICD-10: I48
Coronary artery bypass graft surgery	Yes/No	DAD, OHIP	CCI (Canadian Classification of Health Interventions): 1IJ76 OHIP fee codes: R742, R743, E654, E645, E652, E646
Percutaneous coronary intervention	Yes/No	DAD	CCI: 1IJ50, 1IJ57GQ, 1IJ54GQAZ OHIP fee codes: Z434, G262, G298

Pacemaker	Yes/No	NACRS, DAD, OHIP	CCI: 1HZ37, 1HD53GRJA, 1HD54GRJA, 1HZ53GRNK, 1HZ53GRNL, 1HZ53GRNM, 1HZ54LANJ, 2HZ07NK 2HZ07NL, 2HZ07NM, 1HZ53GRFR, 1HZ53LAFR, 1HZ53SYFR, 1HD55, 1HZ09, 1HZ55, 2HZ24, 1Hz53GRNN OHIP fee codes: G303, Z433, Z435, Z443, Z444, Z445, R752, Z412, Z428, E628, G176, G177, G115
Congestive heart failure	Yes/No	DAD, OHIP	ICD-10: I500, I501, I509 OHIP diagnosis code: 428
Chronic Liver Disease	Yes/No	DAD, OHIP	ICD-10: B16, B17, B18, B19, I85, R17, R18, R160, R162, B942, Z225, E831, E830, K70, K713, K714, K715, K717, K721, K729, K73, K74, K753, K754, K758, K759, K76, K77 OHIP diagnosis codes: 571, 573, 070 OHIP fee codes: Z551, Z554
Hypertension	Yes/No	ODB	Any claim in the last 120 day for any hypertension medications: ACE inhibitors, ARBs, beta-blockers, calcium channel blockers, and thiazide diuretics
Previous urinary tract infections	Yes/No	DAD	ICD-10: N10, N11, N12, n136, N151, N159, N160, N300, N308, N309, N340, N390, N410, N411, N412, N413, N431, N45, T835
Chronic obstructive pulmonary disease	Yes/No	DAD, OHIP	ICD-10: J41, J42, J43, J44 OHIP diagnostic codes: 491, 492, 496
Asthma	Yes/No	DAD, OHIP	ICD-10: J45, J46 OHIP diagnostic code: 493
Obesity	Yes/No	NACRS, DAD, OHIP	ICD-10: E66.0, E66.1, E66.2, E66.8, E66.9 OHIP diagnostic code: 278
Diabetic retinopathy	Yes/No	DAD	ICD-10: E1030, E1031, E1032, E1033, E1130, E1131, E1132, E1133, E1330, E1331, E1332, E1333, E1430, E1431, E1432, E1433, H360
Diabetic neuropathy	Yes/No	DAD	ICD-10: E1040, E1041, E1042, E1048, E1049, E1440, E1441, E1442, E1448, E1140, E1141, E1142, E1148, E1340, E1341, E1342, E1348, E1349, G590, G632, G990
Peripheral Vascular Disease	Yes/No	DAD, OHIP	ICD-10: I700, I702, I708, I709, I731, I738, I739, K551

			CCP: 5125, 5129, 5014, 5016, 5018, 5028, 5038, 5126, 5159 CCI: 1KA76, 1KA50, 1KE76, 1KG50, 1KG57, 1KG76MI, 1KG87, 1IA87LA, 1IB87LA, 1IC87LA, 1ID87, 1KA87LA, 1KE57 OHIP fee codes: R787, R780, R797, R804, R809, R875, R815, R936, R783, R784, R785, E626, R814, R786, R937, R860, R861, R855, R856, R933, R934, R791, E672, R794, R813, R867, E649
Hypoglycemia	Yes/No	DAD	ICD-10: E15, E160, E161, E162, E1063, E1163, E1363, E1463
Hyperglycemic emergency	Yes/No	DAD	ICD-10: E1410, E1412, E1010, E1012, E1110, E1112, E1300, E140
Charlson comorbidity index	Categorized as 0 (or no hospitalization), 1, 2, and 3+	DAD	Identify all acute DAD records in **2 years prior** and then weight the records for index calculation
Prescribed Medication Use (120-day lookback window)			
Polypharmacy	Categorized as 0, 1-5, 6-10, and 10+	ODB	Identify the number of unique DINs (Drug Identification Numbers) in the past 120 days
Other Glucose-Lowering Medications	Yes/No	ODB	Insulin, metformin, acarbose, repaglinide, rosiglitazone, pioglitazone, semaglutide, gliclazide, glyburide
Medications for other indication	Yes/No	ODB	ACE inhibitors, ARBs, aspirin, beta-blockers, calcium channel blockers, H2RAs, NSAIDs (excluding aspirin), statin, proton pump inhibitors, loop diuretics, thiazide diuretics, potassium-sparing diuretics

Supplementary Table 4. Breakdowns of baseline exposures.

	Before Weighting		After Weighting	
	N	Proportion	N	Proportion
SGLT2 Inhibitors				
Canagliflozin	6293	17.23%	6293	17.23%
Dapagliflozin	5757	15.77%	5757	15.77%
Empagliflozin	24463	67.00%	24463	67.00%
DPP4 Inhibitors				
Linagliptin	17569	24.96%	8714	23.84%
Saxagliptin	1792	2.55%	798	2.18%
Sitagliptin	51029	72.49%	27032	73.97%

Wu et al. (2022)

Supplementary Table 5. Summary of Study End Points.

	Before Weighting		After Weighting	
	SGLT2 Inhibitors (n=36513)	DPP4 Inhibitors (n=70390)	SGLT2 Inhibitors (n=36513)	DPP4 Inhibitors (n=36545)
Intention-To-Treat Analysis				
Censoring due to death	1459 (4.0%)	5294 (7.5%)	1459 (4.0%)	2006 (5.5%)
Censoring due to end of eligibility or end of study period	34494 (94.5%)	62925 (89.4%)	34494 (94.5%)	33843 (92.6%)
Event	560 (1.5%)	2171 (3.1%)	560 (1.5%)	696 (1.90%)
As-Treated Analysis				
Censoring due to death	917 (2.5%)	3132 (4.5%)	917 (2.5%)	1193 (3.3%)
Censoring due to end of eligibility or end of study period	22953 (62.8%)	26505 (37.7%)	22953 (62.8%)	15819 (43.3%)
Censoring at 1 year after crossover	6288 (17.2%)	9880 (14.0%)	6288 (17.2%)	5642 (15.4%)
Censoring at 1 year after discontinuation	5992 (16.4%)	29540 (42.0%)	5992 (16.4%)	13465 (36.9%)
Event	363 (0.99%)	1333 (1.9%)	363 (0.99%)	426 (1.2%)