

Supplemental Material

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Supplemental Appendix A- RECORD PE Statement

Item No	STROBE items	RECORD items	RECORD-PE items	Reported
Title and abstract				
1	(a) Indicate the study's design with a commonly used term in the title or the abstract. (b) Provide in the abstract an informative and balanced summary of what was done and what was found.	1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. 1.2: If applicable, the geographical region and timeframe within which the study took place should be reported in the title or abstract. 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	—	Abstract
Introduction				
Background rationale				
2	Explain the scientific background and rationale for the investigation being reported.	—	—	Introduction
Objectives				
3	State specific objectives, including any prespecified hypotheses.	—	—	Introduction
Methods				
Study design				
4	Present key elements of study design early in the paper.	—	4.a: Include details of the specific study design (and its features) and report the use of multiple designs if used. 4.b: The use of a diagram(s) is	Methods: Study Design and Setting

			recommended to illustrate key aspects of the study design(s), including exposure, washout, lag and observation periods, and covariate definitions as relevant.	
Setting				
5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection.	—	—	Methods: Study Design and Setting
Participants				
6	(a) Cohort study—give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up. Case-control study—give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls. Cross sectional study—give the eligibility criteria, and the sources and methods of selection of participants.	6.1: The methods of study population selection (such as codes or algorithms used to identify participants) should be listed in detail. If this is not possible, an explanation should be provided. 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was conducted for this study and not published elsewhere, detailed methods and results should be provided. 6.3: If the study involved linkage of databases, consider use of a flow diagram or other graphical display to demonstrate the data linkage process, including the number of individuals with linked data at each stage.	6.1.a: Describe the study entry criteria and the order in which these criteria were applied to identify the study population. Specify whether only users with a specific indication were included and whether patients were allowed to enter the study population once or if multiple entries were permitted. See explanatory document for guidance related to matched designs.	Methods: Population Supplemental Appendix D and G

	(b) Cohort study—for matched studies, give matching criteria and number of exposed and unexposed. Case-control study—for matched studies, give matching criteria and the number of controls per case.			
Variables				
7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	7.1.a: Describe how the drug exposure definition was developed. 7.1.b: Specify the data sources from which drug exposure information for individuals was obtained. 7.1.c: Describe the time window(s) during which an individual is considered exposed to the drug(s). The rationale for\ selecting a particular time window should be provided. The extent of potential left truncation or left censoring should be specified. 7.1.d: Justify how events are attributed to current, prior, ever, or cumulative drug exposure. 7.1.e: When examining drug dose and risk attribution, describe how current, historical	Methods: Population, Patient Characteristics, and Outcomes Supplemental Appendices: C, D, and E

			<p>or time on therapy are considered.</p> <p>7.1.f: Use of any comparator groups should be outlined and justified.</p> <p>7.1.g: Outline the approach used to handle individuals with more than one relevant drug exposure during the study period.</p>	
Data sources/measurement				
8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group.		8.a: Describe the healthcare system and mechanisms for generating the drug exposure records. Specify the care setting in which the drug(s) of interest was prescribed.	<p>Methods: Data Sources, Population, Patient Characteristics, and Outcomes</p> <p>Supplemental Appendices: B, C, D, and E</p>
Bias				
9	Describe any efforts to address potential sources of bias.	—	—	<p>Methods: Statistical Analysis</p>
Study size				
10	Explain how the study size was arrived at.	—	—	<p>Results</p> <p>Supplemental Appendix G</p>
Quantitative variables				
11	Explain how quantitative variables were handled in the analyses. If applicable,	—	—	<p>Methods: Statistical Analysis</p>

	describe which groupings were chosen, and why.			
Statistical methods				
	<p>(a) Describe all statistical methods, including those used to control for confounding.</p> <p>(b) Describe any methods used to examine subgroups and interactions.</p> <p>(c) Explain how missing data were addressed.</p> <p>(d) Cohort study—if applicable, explain how loss to follow-up was addressed.</p> <p>Case-control study—if applicable, explain how matching of cases and controls was addressed.</p> <p>Cross sectional study—if applicable, describe analytical methods taking account of sampling strategy.</p> <p>(e) Describe any sensitivity analyses.</p>	—	<p>12.1.a: Describe the methods used to evaluate whether the assumptions have been met.</p> <p>12.1.b: Describe and justify the use of multiple designs, design features, or analytical approaches.</p>	Methods: Statistical Analysis
Data access and cleaning methods				
12	—	<p>12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population.</p> <p>12.2: Authors should provide information on the data cleaning methods used in the study.</p>	—	<p>Methods: Population, and Data Sources</p> <p>Data access/access to data analysis protocol</p>
Linkage				

12	—	12.3: State whether the study included person level, institutional level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.	—	Methods: Data Sources
Results				
Participants				
13	(a) Report the numbers of individuals at each stage of the study (e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed). (b) Give reasons for non-participation at each stage. (c) Consider use of a flow diagram.	13.1: Describe in detail the selection of the individuals included in the study (that is, study population selection) including filtering based on data quality, data availability, and linkage. The selection of included individuals can be described in the text or by means of the study flow diagram.	—	Results Supplemental Appendix G
Descriptive data				
14	(a) Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders. (b) Indicate the number of participants with missing data for each variable of interest. (c) Cohort study—summarise follow-up time	—	—	Results Table 1 Supplemental Appendices: H and I

	(e.g., average and total amount).			
Outcome data				
15	Cohort study—report numbers of outcome events or summary measures over time. Case-control study—report numbers in each exposure category, or summary measures of exposure. Cross sectional study—report numbers of outcome events or summary measures.	—	—	Results Table 3
Main results				
16	(a) Give unadjusted estimates and, if applicable, confounder adjusted estimates and their precision (e.g., 95% confidence intervals). Make clear which confounders were adjusted for and why they were included. (b) Report category boundaries when continuous variables are categorised. (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period.	—	—	Results Table 3 Supplemental Appendix F

Other analyses				
17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses.	—	—	Results Table 4
Discussion				
Key results				
18	Summarise key results with reference to study objectives.	—	—	Discussion
Limitations				
19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias.	19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	19.1.a: Describe the degree to which the chosen database(s) adequately captures the drug exposure(s) of interest.	Discussion
Interpretation				
20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence.	—	20.a: Discuss the potential for confounding by indication, contraindication or disease severity or selection bias (healthy adherer/sick stopper) as alternative explanations for the study findings when relevant.	Conclusion
Generalisability				
21	Discuss the generalisability (external validity) of the study results.	—	—	Discussion
Other information				
Funding				

22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based.	—	—	Funding
Accessibility of protocol, raw data, and programming code				
22	—	22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	—	Data access/access to data analysis protocol

*REFERENCE: Langan SM, Schmidt S, Wing K, Ehrenstein V, Nicholls S, Filion K, Klungel O, Petersen I, Sorensen H, Guttmann A, Harron K, Hemkens L, Moher D, Schneeweiss S, Smeeth L, Sturkenboom M, von Elm E, Wang S, Benchimol EI. The REporting of studies Conducted using Observational

Database	Description
Canadian Institute for Health Information Discharge Abstract Database/ Same Day Surgery (CIHI-DAD/SDS)	Diagnostic and procedural information for all hospitalizations and same day surgeries.
Ontario Lab Information System (OLIS)	Laboratory test orders and results from hospitals, community labs, and public health labs.
ICES-derived Physician Database (IPDB)	Physician related information such as birth date, sex, education, and specializations.
Canadian Institute for Health Information National Ambulatory Care Reporting System (NACRS)	Information on emergency department visits.
Ontario Drug Benefit (ODB)	Highly accurate records of all dispensed outpatient prescriptions covered through the Ontario Drug Benefit program, including domperidone and metoclopramide.
Ontario Health Insurance Plan (OHIP)	Diagnostic information and health claims for inpatient and outpatient physician services.
Office of the Registrar General- Deaths (ORDG)	Cause of death information extracted from death certificates
Registered Persons Database (RPDB)	Information on vital patient statistics including sex, birth and death dates for all residents who have been issued a health card

Supplemental Appendix B- Descriptions of databases used to obtain demographic, comorbid condition and outcome data

Variable	Database	Codes Used
Age	RPDB	
Sex	RPDB	
Location of residence- rural status	RPDB	RURAL
Socioeconomic statusas (neighbourhood income quintiles)	RPDB	INCQUINT
Index Year	ODB	
Residential Status- Long term care	ODB	LTC=1
Prescribing physician	IPDB	MAINSPECIALTY
Duration of Diabetes	CIHI-DAD OHIP	OHIP Feecode: K045, K046, K029 K030, Q040 OHIP Diagnostic Code: 250 ICD10: E10, E11, E13, E14 ODD: Diagdate-index date
Fragility Fracture	CIHI DAD NACRS OHIP	ICD10: S720, S721, S722, S220, S221, S320, S327, S328, S422, S520-S529, S321, S323-S328 OHIP Diagnostic code: 805, 808, 812, 813
Previous fall	CIHI-DAD NACRS	S220, S221, S320, S327, S328 OHIP Diagnostic code: 805
Major cancer	CIHI-DAD OHIP	ICD10: S422 OHIP Diagnostic Code: 812
Dementia	CIHI-DAD OHIP	ICD10: S520-S529 OHIP Diagnostic Code: 813
Rheumatoid arthritis	CIHI-DAD OHIP	S321, S323-S328 OHIP Diagnostic Code: 808
Osteoporosis	CIHI-DAD OHIP	OHIP Diagnostic Code: 733 ICD10 M80-M82
Hypertension	CIHI-DAD OHIP	OHIP Diagnostic Code: 401-405 ICD10: I10-13, I15 HYPERTENSION: DIAGATE
Hypotension	CIHI-DAD	ICD10: I95
Coronary artery disease (excluding angina)	CIHI-DAD OHIP	OHIP Feecode: R741-743, G298, E646, E651, E652, E654, E655, Z434, Z448 OHIP Diagnostic Coe: 410, 412 ICD10: I21, I22, Z955, T822 CCI: 1IJ50, 1IJ76
Arrhythmia	CIHI-DAD OHIP	OHIP Feecode: G178, G179, G249, G259, G261, Z431, Z437, Z443

		ICD10: I44, I45, I47, I48, I4900, I4901, I491-I494, !498, !499, R000, R001
Diabetic retinopathy	CIHI-DAD	ICD10: E1030-E1033, E1130-E1133, E1330-E1333, E1430-E1433, H360
Diabetic neuropathy	CIHI-DAD	ICD10: E1040-1042, E1048, E1049, E1440-E1442, E1448, E1140-E1242, E1148, E1340-E1342, E1348, G590, G632, G990
Hypoglycemia	CIHI-DAD NACRS	ICD10: E15, E160-E162, E1063, E1163, E1363, E1463
Peripheral vascular disease	CIHI-DAD OHIP	OHIP Feecode: R787, R780, R797, R804, R809, R875, R815, R936, R783-R785, E626, R814, R786, R937, R860, R861, R855, R856, R933, R934, R791, E672, R794, R813, R867, E649 ICD10: I700, I702, I708, !709, !731, 1738, I739, K551 CCI: 1KA76, 1KA50, 1KE76, 1KG50, 1KG57, 1KG76MI, 1KG87, 1IA87LA, 1IB87LA, 1IC87LA, 1ID87LA, 1KA87LA, 1KE57
Liver disease	CIHI-DAD OHIP	OHIP Feecode: Z551, Z554 OHIP Dx Code: 571, 573, 070 ICD10: B16-19, I85, R17, R18, R160, R162, B942, Z225, E831, E830, K70, K713-K715, K717, K721, K729, K73, K74, K753, K754, K758, K759, K76, K77
COPD	CIHI-DAD COPD	ICD10: J41, J43, J44 COPD DIAGDATE
CHF	CIHI-DAD OHIP CHF	OHIP Diagnostic Code: 428 ICD10: I500, I501, I509 DIAGDATE
Hypothyroidism	CIHI-DAD	ICD10: E00, E01, E02, E03, E890
Disorder of calcium metabolism/dietary calcium deficiency	CIHI-DAD	ICD10: E58, E835
Stroke/TIA	CIHI-DAD OHIP NACRS	OHIP diagnostic Code: 436, 432, 435 ICD10: I60, I61, I600-I619, I630-I635, I638, I639, I64, H342, G450-G453, G459, H340
Syncope	CIHI-DAD	ICD10: R55
Alcohol misuse	CIHI-DAD	ICD10: E244, E512, E52, F10, G312, G621, G721, I426, K292, K70, K860, T51, X45, X65, Y15, Y573, Z502, Z714, Z721
Medication Use	ODB	
Hemoglobin A1C	OLIS	OBSERVATIONCODE: 4548-4, 71875-9, 59261-8, 17855-8, 17856-6, 41995-2
ACR (mg/mmol)	OLIS	OBSERVATIONCODE: 14959-1, 30000-1, 32294-1, XON10383-8, XON12394-3
Diabetes management	OLIS OHIP	OHIP Feecode: K030, Q040, K045, K046 OHIP Diagnostic code: K046
GP/FP visits	IPDB	Mainspeciality = "GP/FP" or "F.P./EMERGENCY MEDICINE"
Nephrologist visit	IPDB OHIP	Mainspecialty = "NEPHROLOGY" OR OHIP Feecode: A160, A161, A163-A166, A168, A865, C160-C167, C169, C865, W165, W160-W166, W168, W865, W862, W864, W867, W869,

Orthopedist visit	IPDB	Mainspecialty= "ORTHOPEDIC SURGERY"
Endocrinologist visit	IPDB	Mainspecialty = "ENDOCRINOLOGY"
Internist visit	IPDB	Mainspecialty = "INTERNAL MEDICINE"
Geriatrician visit	IPDB	Mainspecialty = "GERIATRIC MEDICINE"
Ophthalmologist visit	IPDB	Mainspecialty= "OTHALMOLOGY"
episodes of care	CIHI-DAD	ADMDATE, DDATE, EPI, EPIFLAG, EPIVISIT
ER visits	NACRS	"regdate"
Laboratory calcium test	OLIS OHIP	OHIP FEECODE: L045, L046 OBSERVATIONCODE: 29265-6, 1995-0, 19072-8, 1994-3, 47598-8, 34581-9, 59473-9, 41645-3, 12180-6, 13959-2, 47596-2, 53140-0, 41644-6, 53139-2, 3000-9
Laboratory serum creatinine tests	OHIP	OHIP feecode: L065, L067, L068
CT scan	OHIP	OHIP Feecode: X126, X188, X400-X410, X124, X231-X233, X128, X415, X416
Carotid ultrasound	OHIP CIHI-DAD	OHIP Feecode: J201, J501, J190, J490 CCI: 3JE30, 3JG30
Echocardiography	OHIP CIHI-DAD	OHIP Feecode: G560-G562, G566-G568, G570-G572, G574-G578, G581 CCI: 3IP30
Cardiac stress test	OHIP CIHI DAD	OHIP Feecode: G315, G174, G112, G112, G319, G582, G583, G584, J604, J606-J609, J611-J613, J667, J807- J809, J804, J811-J813, J867, J666, J866 CCI: 2HZ08, 3IP70
Bone mineral density test	OHIP	OHIP Feecode: J654, J688, J854, J888, X149, X152, X153, X155, Y654, Y688, Y854, Y888
Chest x-ray	OHIP	OHIP Feecode: X090, X091, X092, X195
Pulmonary function test	OHIP	OHIP Feecode: J301, J303-J311, J313, J315-J320, J322-J324, J327, J328, J330-J335, J340, J341, E450, E451

Supplemental Appendix C- Codes used to obtain information about baseline measures and the databases used to obtain the information

RPDB: Registered Persons Database, ODB: Ontario Drug Benefit, IPDB: ICES Physician Database, CIHI-DAD: Canadian Institute of Health Information Discharge Abstract Database, OHIP: Ontario Health Insurance Plan, NACRS: National Ambulatory Care Reporting System, OLIS: Ontario Lab Information Services,

Medication	Drug Identification Numbers included
Canagliflozin	2425483, 2425491
Dapagliflozin	2435462, 2435470 With Metformin: 2449935, 2449943
Empagliflozin	2443937, 2443945 With Metformin: 2456575, 2456583, 2456591, 2456605, 2456613, 2456621
Linagliptin	2370921 With Metformin: 2403250, 2403269, 2403277
Sitagliptin	2388839, 2388847, 2303922 With Metformin: 2333856, 2333864, 2333872
Saxagliptin	2403250, 2403269, 2403277 With Metformin: 2389169, 2389177, 2389185

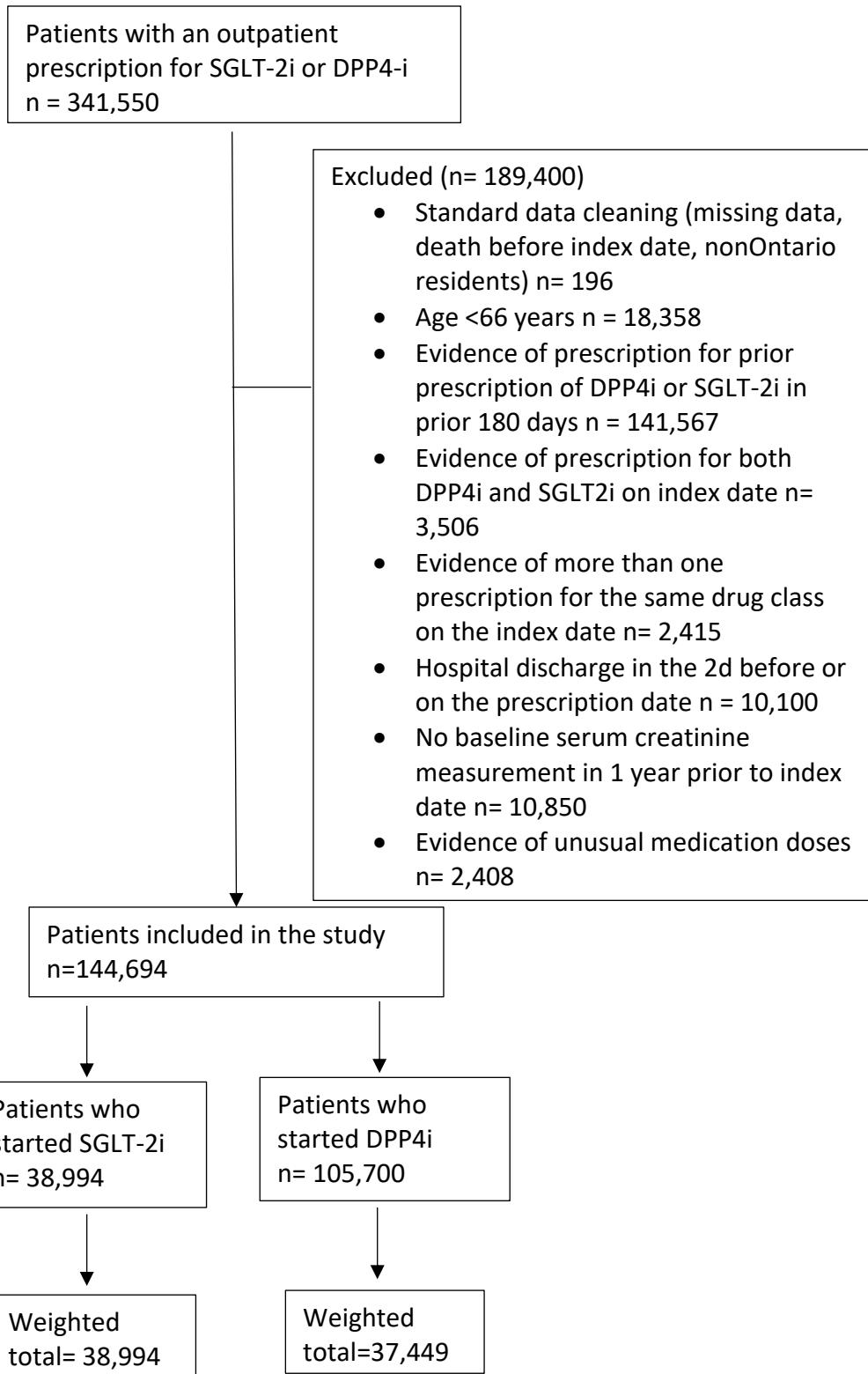
Supplemental Appendix D- Drug Identification Numbers used to identify study drugs

Outcome		Database Used	Codes Used
Fracture	Hip	CIHI DAD	ICD10: S720, S721, S722
	Spine	CIHI DAD CIHI NACRS OHIP	S220, S221, S320, S327, S328 OHIP Diagnostic code: 805
	Shoulder and Upper Arm	CIHI DAD, NACRS OHIP	ICD10: S422 OHIP Diagnostic Code: 812
	Wrist and Forearm	CIHI DAD NACRS OHIP	ICD10: S520-S529 OHIP Diagnostic Code: 813
	Pelvic	CIHI DAD NACRS OHIP	S321, S323-S328 OHIP Diagnostic Code: 808
Hypoglycemia		CIHI- DAD NACRS	ICD10: E15, E160, E161, E162, E1063, E1163, E1363, E1463
Falls		CIHI-DAD	ICD10: W00-W19
Hypotension		CIHI-DAD	ICD10: I95

Supplemental Appendix E- Codes used to define study outcomes

Demographics	Age, Sex, Income quintile, Rurality, Residential status – Long-term care, Prescriber
Comorbidities	Charlson comorbidity index, duration of diabetes, fragility fracture, previous fall, major cancer, dementia, rheumatoid arthritis, osteoporosis, hypertension, hypotension, coronary artery disease, arrhythmia, diabetic retinopathy, diabetic neuropathy, hypoglycemia, peripheral vascular disease, liver disease, COPD CHF, hypothyroidism, disorder of calcium metabolism/dietary calcium deficiency, stroke/TIA, syncope, alcohol misuse
Medication Use	Number of unique drug names, bisphosphonates, denosumab, oral steroid, estrogen, proton pump inhibitors, loop diuretics, potassium-sparing diuretics, thiazide diuretics, beta blockers, opiates, antidepressants, antipsychotics, testosterone, number of unique oral hypoglycemic agents used, Acarbose, gliclazide, glyburide, metformin, thiazolidinedione
Health Care Utilization	Diabetes management, GP/FP visits, nephrologist visit, orthopedist visit, endocrinologist visit, internist visit, geriatrician visit, ophthalmologist visit, number of episodes of care, number of ER visits
Investigations	Hemoglobin A1C, ACR, laboratory calcium testing, laboratory serum creatinine testing, CT scan, carotid ultrasound, echocardiography, cardiac stress test, bone mineral density test, chest x-ray, pulmonary function test

Supplemental Appendix F- Covariates used to create the propensity score



Supplemental Appendix G- Study flow diagram of older adults with a new prescription for SGLT-2i or DPP-4i

Mean Charlson comorbidity index (SD)	0.5 (1.2)	0.4 (1.1)	0.05	0.4 (0.7)	0.4 (1.1)	0.02
Mean duration of diabetes, y (SD)	11.5 (7.4)	12.4 (7.6)	0.11	12.2 (4.4)	12.4 (7.6)	0.03
Fragility fracture	4,012 (4)	1,204 (3)	0.04	1,197 (3)	1,204 (3)	0.01
Previous fall	17,225 (16)	5,572 (14)	0.06	5,439 (15)	5,572 (14)	0.01
Major cancer	13,220 (13)	4,290 (11)	0.05	4,153 (11)	4,290 (11)	0.00
Dementia	7,636 (7)	1,094 (3)	0.20	1,111 (3)	1,094 (3)	0.01
Rheumatoid arthritis	2,398 (2)	848 (2)	0.01	815 (2)	848 (2)	0.00
Osteoporosis	7,839 (7)	1,969 (5)	0.10	1,926 (5)	1,969 (5)	0.00
Hypertension	85,593 (81)	31,941 (82)	0.02	30,500 (81)	31,941 (82)	0.01
Hypotension	1,802 (2)	497 (1)	0.03	472 (1)	497 (1)	0.00
Coronary artery disease (excluding angina)	24,571 (23)	12,258 (31)	0.18	10,961 (29)	12,258 (31)	0.05
Arrhythmia	8,612 (8)	3,355 (9)	0.02	3,047 (8)	3,355 (9)	0.02
Diabetic retinopathy	750 (1)	338 (1)	0.02	314 (1)	338 (1)	0.01
Diabetic neuropathy	1,431 (1)	604 (2)	0.01	577 (2)	604 (2)	0.00
Hypoglycemia	2,387 (2)	805 (2)	0.01	756 (2)	805 (2)	0.01
Peripheral vascular disease	1,196 (1)	487 (1)	0.01	436 (1)	487 (1)	0.00
Liver disease	5,014 (5)	1,940 (5)	0.01	1,862 (5)	1,940 (5)	0.00
Coronary obstructive pulmonary disease	21,795 (21)	8,718 (22)	0.04	8,386 (22)	8,718 (22)	0.00
Congestive heart failure	12,300 (12)	5,093 (13)	0.05	4,607 (12)	5,093 (13)	0.02
Hypothyroidism	1,265 (1)	338 (1)	0.03	330 (1)	338 (1)	0.00
Disorder of calcium metabolism/dietary calcium deficiency	379 (0)	65 (0)	0.04	67 (0)	65 (0)	0.00
Stroke/TIA	10,153 (10)	3,089 (8)	0.06	2,935 (8)	3,089 (8)	0.00
Syncope	1,324 (1)	383 (1)	0.03	377 (1)	383 (1)	0.00
Alcohol misuse	624 (1)	234 (1)	0.00	223 (1)	234 (1)	0.00
Medication Use, No. (%)						
Mean number of Unique Drug Names (SD)	6.9 (4.5)	7.6 (4.2)	0.18	7.6 (2.7)	7.6 (4.2)	0.02
Bisphosphonates	9,199 (9)	1,952 (5)	0.15	1,939 (5)	1,952 (5)	0.01

Denosumab	2,053 (2)	486 (1)	0.06	479 (1)	486 (1)	0.01
Oral steroid	8,038 (8)	2,732 (7)	0.02	2,641 (7)	2,732 (7)	0.00
Estrogen	2,099 (2)	802 (2)	0.01	814 (2)	802 (2)	0.01
Thiazolidinedione	466 (0)	144 (0)	0.00	146 (0)	144 (0)	0.00
Proton pump inhibitors	28,426 (27)	11,396 (29)	0.05	10,895 (29)	11,396 (29)	0.00
Loop diuretics	9,830 (9)	4,049 (10)	0.04	3,701 (10)	4,049 (10)	0.02
Potassium-sparing diuretics	3,673 (4)	1,872 (5)	0.07	1671 (5)	1,872 (5)	0.01
Thiazide diuretics	13,960 (13)	6,183 (16)	0.08	5,935 (16)	6,183 (16)	0.00
Beta blockers	28,903 (27)	13,662 (35)	0.17	12,554 (34)	13,662 (35)	0.03
Opiates	11,846 (11)	4,571 (12)	0.02	4,434 (12)	4,571 (12)	0.00
Antidepressants	17,489 (17)	6,965 (18)	0.04	6,758 (18)	6,965 (18)	0.00
Antipsychotics	3,285 (3)	874 (2)	0.06	890 (2)	874 (2)	0.01
Testosterone	352 (0)	216 (1)	0.04	204 (1)	216 (1)	0.01
Number of unique oral hypoglycemic agents used						
0	37,006 (35)	10,916 (28)	0.15	10,454 (28)	10,916 (28)	0.00
1	51,484 (49)	20,902 (54)	0.10	19,976 (53)	20,902 (54)	0.01
2+	17,210 (16)	7,176 (18)	0.06	7,019 (19)	7,176 (18)	0.01
Acarbose	502 (1)	218 (1)	0.01	210 (1)	218 (1)	0.00
Gliclazide	20,070 (19)	8,082 (21)	0.04	7,927 (21)	8,082 (21)	0.01
Glyburide	3,905 (4)	1,105 (3)	0.05	1,115 (3)	1,105 (3)	0.01
Metformin	61,485 (58)	25,896 (66)	0.17	24,803 (66)	25,896 (66)	0.00
Health care utilization, No. (%)						
General practitioner visits	103,120 (98)	37,951 (97)	0.02	36,397 (97)	37,951 (97)	0.01
Mean number of visits (SD)	14.2 (19.2)	12.4 (15.0)	0.11	12.4 (8.2)	12.4 (15.0)	0.01
Nephrologist visit	7,743 (7)	2,426 (6)	0.04	2,216 (6)	2,426 (6)	0.01
Mean number of visits (SD)	0.18 (1.2)	0.13 (0.7)	0.05	0.13 (0.52)	0.13 (0.7)	0.00
Orthopedist visit	10,378 (10)	4,060 (10)	0.02	3,944 (11)	4,060 (10)	0.00

Mean number of visits (SD)	0.5 (3.1)	0.5 (2.5)	0.01	0.5 (1.8)	0.5 (2.5)	0.01
Endocrinologist visit	12,998 (12)	7,112 (18)	0.16	6,499 (17)	7,112 (18)	0.02
Mean number of visits (SD)	0.5 (2.0)	0.8 (2.2)	0.13	0.7 (1.2)	0.8 (2.2)	0.06
Internist visit	31,277 (30)	11,993 (31)	0.03	11,386 (30)	11,993 (31)	0.01
Mean number of visits (SD)	2.3 (8.02)	1.9 (5.5)	0.05	2.0 (3.74)	1.9 (5.5)	0.02
Geriatrician visit	3,980 (4)	759 (2)	0.11	732 (2)	759 (2)	0.01
Mean number of visits (SD)	0.2 (2.4)	0.1 (1.1)	0.08	0.1 (0.8)	0.1 (1.1)	0.01
Ophthalmologist visit	32,083 (30)	12,550 (32)	0.04	11,957 (32)	12,550 (32)	0.01
Mean number of visits (SD)	2.2 (5.9)	2.53 (6.6)	0.05	2.46 (3.8)	2.53 (6.6)	0.01
Episodes of care	15,087 (14)	4,770 (12)	0.06	4,455 (12)	4,770 (12)	0.01
Mean number of visits (SD)	0.2 (0.58)	0.16 (0.49)	0.07	0.16 (0.3)	0.16 (0.49)	0.00
Emergency Room visits	35,140 (33)	12,514 (32)	0.02	11,961 (32)	12,514 (32)	0.00
Mean number of visits (SD)	0.7 (1.4)	0.6 (1.3)	0.04	0.6 (0.8)	0.6 (1.3)	0.02
Laboratory Testing No. (%)						
Diabetes management	54,022 (51)	22,108 (57)	0.11	21,383 (57)	22,108 (57)	0.01
Mean Hemoglobin A1c (SD)	8.1 (1.6)	8.0 (1.5)	0.03	8.1 (0.9)	8.0 (1.5)	0.02
Missing Hemoglobin A1c	3,097 (3)	702 (2)	0.07	844 (2)	702 (2)	0.04
Mean Urine Albumin to Creatinine ratio (SD)	11.6 (42.2)	11.8 (41.4)	0.01	11.3 (25.8)	11.8 (41.4)	0.02
Missing Urine Albumin to Creatinine ratio	31,502 (30)	9,683 (25)	0.11	9,370 (25)	9,683 (25)	0.00
Mean number of laboratory serum creatinine tests (SD)	4.1 (5.6)	3.8 (4.0)	0.06	3.8 (2.5)	3.8 (4.0)	0.01
Mean eGFR (SD)	69 (19)	73 (17)	0.23	73 (10)	73 (17)	0.01
eGFR						
≥90	14,853 (14)	6,485 (17)	0.07	6,319 (17)	6,485 (17)	0.01
60-<90	55,500 (53)	23,520 (60)	0.16	22,547 (60)	23,520 (60)	0.00
45-<60	20,617 (20)	6,577 (17)	0.07	6,250 (17)	6,577 (17)	0.01
30-<45	14,730 (14)	2,412 (6)	0.26	2,332 (6)	2,412 (6)	0.00
Laboratory calcium test	26,012 (25)	7,798 (20)	0.11	7,414 (20)	7,798 (20)	0.01

Mean number of tests (SD)	0.6 (1.9)	0.4 (1.4)	0.11	0.4 (0.9)	0.4 (1.4)	0.03
Diagnostic Imaging No. (%)						
CT scan	22,582 (21)	7,271 (19)	0.07	6,952 (19)	7,271 (19)	0.00
Carotid ultrasound	4,598 (4)	1,789 (5)	0.01	1,656 (4)	1,789 (5)	0.01
Echocardiography	21,789 (21)	9,545 (25)	0.09	8,573 (23)	9,545 (25)	0.04
Cardiac stress test	12,626 (12)	6,419 (17)	0.13	5,753 (15)	6,419 (17)	0.03
Bone mineral density test	6,743 (6)	2,109 (5)	0.04	2,062 (6)	2,109 (5)	0.00
Chest x-ray	32,516 (31)	11,218 (29)	0.04	10,593 (28)	11,218 (29)	0.01
Pulmonary function test	7,451 (7)	3,504 (9)	0.07	3,221 (9)	3,504 (9)	0.01

Supplemental Appendix H- Full baseline characteristics for the weighted and unweighted cohorts

Abbreviations: DPP-4i- Dipeptidyl peptidase 4 inhibitor, SGLT-2i- Sodium glucose 2 transporter inhibitor, SD: standard deviation, TIA- Transient ischemic attack, Charlson comorbidity score was calculated using five years of hospitalization data. “No hospitalizations” received a score of 0.

	eGFR ≥90 (N=12,814)			eGFR 60 - <90 (N=46,145)			eGFR 45 - <60 (N=12,777)			eGFR 30 - <45 (N=4,617)		
	DPP4i users (N=6,329)	SGLT2i users (N=6,485)	Std Diff	DPP4i users (N=22,625)	SGLT2i users (N=23,520)	Std Diff	DPP4i users (N=6,200)	SGLT2i users (N=6,577)	Std Diff	DPP4i users (N=2,205)	SGLT2i users (N=2,412)	Std Diff
Demographics												
Age, mean, y (SD)	69 (2)	69 (3)	0.00	72 (3)	72 (5)	0.01	74 (3)	74 (6)	0.00	76 (3)	76 (6)	0.02
Female No. (%)	2,744 (43)	2,745 (42)	0.02	8,878 (39)	8,964 (38)	0.02	2,594 (42)	2,659 (40)	0.03	1,020 (46)	1,089 (45)	0.02
Income quintile No. (%)												
1	1,413 (22)	1,410 (22)	0.01	4,799 (21)	4,926 (21)	0.01	1,329 (21)	1,372 (21)	0.01	511 (23)	549 (23)	0.01
2	1,381 (22)	1,417 (22)	0.00	4,818 (21)	5,024 (21)	0.00	1,335 (22)	1,414 (22)	0.00	485 (22)	528 (22)	0.00
3	1,295 (21)	1,336 (21)	0.00	4,790 (21)	4,947 (21)	0.00	1,264 (20)	1,341 (20)	0.00	450 (20)	485 (20)	0.01
4	1,185 (19)	1,224 (19)	0.01	4,225 (19)	4,441 (19)	0.01	1,184 (19)	1,275 (19)	0.01	408 (19)	465 (19)	0.02
5	1,057 (17)	1,098 (17)	0.01	3,992 (18)	4,182 (18)	0.01	1,086 (18)	1,175 (18)	0.01	352 (16)	385 (16)	0.00
Rurality No. (%)	1,136 (18)	1,177 (18)	0.01	3,545 (16)	3,655 (16)	0.01	925 (15)	975 (15)	0.00	331 (15)	360 (15)	0.00
Index year No. (%)												
2015	753 (12)	785 (12)	0.01	2,266 (10)	2,300 (10)	0.01	545 (9)	543 (8)	0.02	144 (7)	142 (6)	0.02
2016	1,437 (23)	1,457 (23)	0.00	4,101 (18)	4,157 (18)	0.01	913 (15)	934 (14)	0.01	254 (12)	256 (11)	0.03
2017	1,366 (22)	1,396 (22)	0.00	5,456 (24)	5,712 (24)	0.00	1,389 (22)	1,468 (22)	0.00	404 (18)	420 (17)	0.02
2018	1,434 (23)	1,482 (23)	0.00	5,737 (25)	6,003 (26)	0.00	1,667 (27)	1,783 (27)	0.00	579 (26)	618 (26)	0.02
2019	1,339 (21)	1,365 (21)	0.00	5,065 (22)	5,348 (23)	0.01	1,684 (27)	1,849 (28)	0.02	824 (37)	976 (41)	0.07
Long-term care status No. (%)	42 (1)	37 (1)	0.01	167 (1)	154 (1)	0.00	64 (1)	60 (1)	0.01	33 (2)	32 (1)	0.02
Prescriber No. (%)												
Cardiology	79 (1)	140 (2)	0.07	366 (2)	931 (4)	0.15	128 (2%)	362 (6)	0.18	55 (3)	147 (6)	0.18
Endocrinology	831 (13)	893 (14)	0.02	3,074 (14)	3,333 (14)	0.02	902 (15)	957 (15)	0.00	282 (13)	297 (12)	0.02
General Practitioner	4,603 (73)	4,597 (71)	0.04	16,323 (72)	16,216 (69)	0.07	4,136 (67)	4,097 (62)	0.09	1,295 (59)	1,280 (53)	0.11
Internal Medicine	337 (5)	361 (6)	0.01	1342 (6)	1476 (6)	0.02	514 (8)	576 (9)	0.02	218 (10)	239 (10)	0.00

Nephrology	25 (%)	38 (1)	0.03	127 (1)	168 (1)	0.01	173 (3)	235 (4)	0.05	226 (10)	317 (13)	0.09
Other	455 (7)	456 (7)	0.01	1394 (6)	1,396 (6)	0.01	344 (6)	350 (5)	0.01	130 (6)	132 (6)	0.02
Comorbidities No. (%)												
Mean Charlson comorbidity index (SD)	0.3 (0.7)	0.4 (1.0)	0.01	0.4 (0.7)	0.4 (1.0)	0.02	0.6 (0.7)	0.6 (1.2)	0.02	0.8 (0.6)	0.8 (1.4)	0.00
Mean duration of diabetes, y (SD)	11.2 (4.6)	11.4 (7.2)	0.02	11.9 (4.7)	12.1 (7.5)	0.03	13.4 (4.2)	13.5 (7.9)	0.02	15.1 (3.0)	15.3 (7.9)	0.03
Fragility fracture	207 (3)	206 (3)	0.01	672 (3)	678 (3)	0.01	228 (4)	228 (4)	0.01	85 (4)	92 (4)	0.01
Previous fall	885 (14)	907 (14)	0.00	3,139 (14)	3,207 (14)	0.01	1,000 (16)	1,029 (16)	0.01	397 (18)	429 (18)	0.01
Major cancer	619 (10)	642 (10)	0.00	2,520 (11)	2584 (11)	0.00	714 (12)	744 (11)	0.01	296 (13)	320 (13)	0.00
Dementia	94 (2)	90 (1)	0.01	653 (3)	635 (3)	0.01	258 (4)	255 (4)	0.02	108 (5)	114 (5)	0.01
Rheumatoid arthritis	145 (2)	150 (2)	0.00	469 (2)	489 (2)	0.00	147 (2)	151 (2)	0.01	52 (2)	58 (2)	0.00
Osteoporosis	334 (5)	338 (5)	0.00	1,178 (5)	1,189 (5)	0.00	307 (5)	321 (5)	0.00	112 (5)	121 (5)	0.00
Hypertension	4,728 (75)	4,859 (75)	0.00	18,237 (81)	19,058 (81)	0.01	5,422 (88)	5,783 (88)	0.01	2,035 (92)	2,241 (93)	0.03
Hypotension	47 (1)	50 (1)	0.01	233 (1)	236 (1)	0.00	122 (2)	144 (2)	0.01	66 (3)	67 (3)	0.01
Coronary artery disease (excluding angina)	1,376 (22)	1,512 (23)	0.04	6,543 (29)	7,317 (31)	0.05	2,151 (35)	2,445 (37)	0.05	853 (39)	984 (41)	0.04
Arrhythmia	292 (5)	310 (5)	0.01	1,664 (7)	1,831 (8)	0.02	736 (12)	829 (13)	0.02	334 (15)	385 (16)	0.02
Diabetic retinopathy	34 (1)	36 (1)	0.01	174 (1)	181 (1)	0.00	67 (1)	77 (1)	0.01	37 (2)	44 (2)	0.01
Diabetic neuropathy	79 (1)	82 (1)	0.01	310 (1)	325 (1)	0.00	125 (2)	141 (2)	0.01	55 (3)	56 (2)	0.01
Hypoglycemia	89 (1)	90 (1)	0.00	367 (2)	392 (2)	0.01	197 (3)	213 (3)	0.00	104 (5)	110 (5)	0.00
Peripheral vascular disease	57 (1)	66 (1)	0.01	243 (1)	279 (1)	0.01	87 (1)	96 (2)	0.01	45 (2)	46 (2)	0.01
Liver disease	386 (6)	391 (6)	0.00	1,069 (5)	1113 (5)	0.00	276 (4)	300 (5)	0.01	120 (5)	136 (6)	0.01
Coronary Obstructive Pulmonary Disease	1,358 (21)	1,373 (21)	0.00	4,908 (22)	5,081 (22)	0.00	1,539 (25)	1,633 (25)	0.00	577 (26)	631 (26)	0.00

0	1,622 (26)	1,661 (26)	0.00	6,199 (27)	6,472 (28)	0.00	1,785 (29)	1,909 (29)	0.00	790 (36)	874 (36)	0.01
1	3,407 (54)	3,528 (54)	0.01	12,187 (54)	12,729 (54)	0.00	3,281 (53)	3,490 (53)	0.00	1,058 (48)	1,155 (48)	0.00
2+	1,301 (21)	1,296 (20)	0.01	4,239 (19)	4,319 (18)	0.01	1,132 (18)	1,178 (18)	0.01	358 (16)	383 (16)	0.01
Acarbose	31 (1)	29 (0)	0.01	131 (1)	138 (1)	0.00	35 (1)	36 (1)	0.01	15 (1)	15 (1)	0.01
Gliclazide	1,377 (22)	1,383 (21)	0.01	4,771 (21)	4,837 (21)	0.01	1,340 (22)	1,373 (21)	0.02	458 (21)	489 (20)	0.01
Glyburide	202 (3)	198 (3)	0.01	652 (3)	641 (3)	0.01	207 (3)	207 (3)	0.01	59 (3)	59 (2)	0.02
Metformin	4,406 (70)	4,516 (70)	0.00	15,143 (67)	15,783 (67)	0.00	3,963 (64)	4,233 (64)	0.01	1,248 (57)	1,364 (57)	0.00
Health Care Utilization, No. (%)												
General Practitioner visits	6,129 (97)	6,297 (97)	0.02	21,997 (97)	22,883 (97)	0.01	6,034 (97)	6,429 (98)	0.02	2,151 (98)	2,342 (97)	0.02
Mean number of visits (SD)	11.9 (8.4)	11.6 (15.7)	0.02	12.1 (8.5)	12.1 (14.3)	0.01	13.4 (8.4)	13.4 (15.9)	0.00	14.5 (6.2)	14.4 (15.9)	0.01
Nephrologist visit	154 (2)	178 (3)	0.02	703 (3)	759 (3)	0.01	662 (11)	738 (11)	0.02	637 (29)	751 (31)	0.05
Mean number of visits (SD)	0.0 (0.3)	0.1 (0.4)	0.03	0.1 (0.4)	0.1 (0.5)	0.00	0.2 (0.7)	0.2 (0.9)	0.03	0.7 (0.9)	0.7 (1.5)	0.03
Orthopedist visit	689 (11)	689 (11)	0.01	2,332 (10)	2,392 (10)	0.00	669 (11)	711 (11)	0.00	238 (11)	268 (11)	0.01
Mean number of visits (SD)	0.6 (2.3)	0.5 (2.3)	0.03	0.5 (1.6)	0.5 (2.6)	0.01	0.5 (2.2)	0.5 (2.3)	0.01	0.6 (1.0)	0.5 (2.1)	0.03
Endocrinologist visit	1,035 (16)	1,117 (17)	0.02	3,844 (17)	4,201 (18)	0.02	1,206 (20)	1,317 (20)	0.01	419 (19)	477 (20)	0.02
Mean number of visits (SD)	0.6 (1.2)	0.8 (2.2)	0.07	0.7 (1.3)	0.8 (2.1)	0.05	0.8 (1.2)	0.9 (2.4)	0.04	0.8 (1.0)	1.0 (2.5)	0.08
Internist visit	1,698 (27)	1,760 (27)	0.01	6,640 (29)	6,962 (30)	0.01	2,155 (35)	2,329 (35)	0.01	866 (39)	942 (39)	0.00
Mean number of visits (SD)	1.6 (4.0)	1.5 (4.3)	0.02	1.9 (3.8)	1.7 (5.4)	0.03	2.5 (4.4)	2.4 (6.2)	0.02	3.3 (3.7)	2.9 (6.8)	0.08
Geriatrician visit	78 (1)	79 (1)	0.00	424 (2)	437 (2)	0.00	157 (3)	166 (3)	0.00	71 (3)	77 (3)	0.00
Mean number of visits (SD)	0.1 (0.6)	0.1 (1.0)	0.00	0.1 (0.9)	0.1 (1.0)	0.01	0.1 (0.8)	0.1 (1.1)	0.02	0.2 (0.7)	0.2 (1.7)	0.01
Ophthalmologist visit	1,755 (28)	1,811 (28)	0.00	7,154 (32)	7,500 (32)	0.01	2,133 (34)	2,284 (35)	0.01	864 (39)	955 (40)	0.01
Mean number of visits (SD)	2.0 (3.6)	2.0 (5.7)	0.00	2.4 (4.1)	2.5 (6.4)	0.01	2.7 (3.7)	2.9 (7.2)	0.04	3.3 (2.8)	3.6 (8.6)	0.05
Episodes of care	689 (11)	716 (11)	0.00	2462 (11)	2629 (11)	0.01	883 (14)	977 (15)	0.02	415 (19)	448 (19)	0.01

Mean number of visits (SD)	0.1 (0.3)	0.1 (0.4)	0.00	0.1 (0.3)	0.1 (0.5)	0.00	0.2 (0.3)	0.2 (0.6)	0.02	0.3 (0.3)	0.3 (0.7)	0.02
Emergency room visits	1,911 (30)	1,979 (31)	0.01	6,907 (31)	7,201 (31)	0.00	2,199 (36)	2,341 (36)	0.00	920 (42)	993 (41)	0.01
Mean number of visits (SD)	0.6 (0.92)	0.56 (1.18)	0.04	0.59 (0.88)	0.57 (1.27)	0.02	0.74 (0.83)	0.71 (1.39)	0.03	0.89 (0.61)	0.86 (1.63)	0.02
Laboratory Testing No. (%)												
Diabetes management	3,594 (57)	3,645 (56)	0.01	13,056 (58)	13,480 (57)	0.01	3,505 (57)	3,699 (56)	0.01	1,192 (54)	1,284 (53)	0.02
Mean Hemoglobin A1C (SD)	8.3 (1.1)	8.3 (1.6)	0.01	8.0 (0.9)	8.0 (1.4)	0.02	8.0 (0.8)	7.9 (1.4)	0.04	8.0 (0.6)	7.9 (1.5)	0.05
Missing Hemoglobin A1C	158 (3)	111 (2)	0.06	492 (2)	386 (2)	0.04	137 (2)	133 (2)	0.01	52 (2)	72 (3)	0.04
Mean Urine albumin to creatinine ratio (SD)	7.5 (19.4)	7.8 (26.4)	0.01	8.3 (20.5)	8.7 (32.5)	0.02	16.5 (30.4)	17.9 (53.1)	0.04	33.5 (34.8)	35.4 (82.6)	0.04
Missing Urine albumin to creatinine ratio	1,620 (26)	1,633 (25)	0.01	5,669 (25)	5,879 (25)	0.00	1,545 (25)	1,633 (25)	0.00	516 (23)	538 (22)	0.03
Laboratory calcium test	1,013 (16)	1,019 (16)	0.01	3,928 (17)	4,107 (18)	0.00	1,548 (25)	1,680 (26)	0.01	873 (40)	992 (41)	0.03
Mean number of calcium tests (SD)	0.3 (1.1)	0.3 (1.4)	0.04	0.4 (1.0)	0.3 (1.2)	0.04	0.6 (1.0)	0.5 (1.8)	0.04	0.9 (0.8)	0.9 (1.7)	0.02
Mean number of laboratory serum creatinine tests (SD)	3.3 (2.8)	3.3 (3.5)	0.01	3.6 (2.6)	3.56 (3.47)	0.00	4.5 (3.0)	4.5 (5.0)	0.01	5.9 (2.7)	5.7 (5.7)	0.05
Mean eGFR (SD)	94 (3)	94 (4)	0.00	76 (6)	76 (9)	0.01	53 (2)	53 (4)	0.00	39 (2)	39 (4)	0.01
Diagnostic Testing No. (%)												
CT scan	1,046 (17)	1,076 (17)	0.00	4,021 (18)	4,186 (18)	0.00	1,336 (22)	1,433 (22)	0.00	534 (24)	576 (24)	0.01
Carotid ultrasound	222 (4)	232 (4)	0.01	983 (4)	1,062 (5)	0.01	317 (5)	352 (5)	0.01	136 (6)	143 (6)	0.01
Echocardiogram	1,153 (18)	1,250 (19)	0.03	4,908 (22)	5,462 (23)	0.04	1,755 (28)	1,999 (30)	0.05	708 (32)	834 (35)	0.05
Cardiac stress test	869 (14)	944 (15)	0.03	3,459 (15)	3,846 (16)	0.03	1,052 (17)	1,200 (18)	0.03	352 (16)	429 (18)	0.05

Bone mineral density test	366 (6)	370 (6)	0.00	1,251 (6)	1262 (5)	0.00	334 (5)	357 (5)	0.00	113 (5)	120 (5)	0.00
Chest x-ray	1,598 (25)	1,656 (26)	0.00	6,165 (27)	6,498 (28)	0.01	1,986 (32)	2,153 (33)	0.01	827 (38)	911 (38)	0.01
Pulmonary function test	467 (7)	488 (8)	0.00	1900 (8)	2050 (9)	0.01	644 (10)	715 (11)	0.02	212 (10)	251 (10)	0.03

Supplemental Appendix I – Full baseline characteristics, stratified by eGFR category, after weighting

Abbreviations: DPP-4i- Dipeptidyl peptidase 4 inhibitor, SGLT-2i- Sodium glucose 2 transporter inhibitor, Std Diff- standardized difference, SD: standard deviation, TIA- Transient ischemic attack, Charlson comorbidity score was calculated using five years of hospitalization data. “No hospitalizations” received a score of 0.

Site of Fracture	DPP-4i Users N=37,449 n (%)	SGLT-2i Users N=3,8994 n (%)	HR (95% CI)
Hip	36 (0.1%)	30 (0.08%)	0.81 (0.52-1.24)
Spine	13 (0.03%)	11 (0.03%)	0.83 (0.39-1.78)
Shoulder and Upper Arm	47 (0.12%)	56 (0.14%)	1.15 (0.82-1.63)
Wrist and Forearm	59 (0.16%)	57 (0.15%)	0.92 (0.67-1.27)
Pelvis	32 (0.09%)	24 (0.06%)	0.72 (0.44-1.17)

Supplemental Appendix J- Fracture at 180 days by fracture site