Supplemental Online Content

Supplemental References

eTable 1. STROBE checklist for cohort studies

	Item No.	Recommendation	Page No.
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Abstract, *Design*
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	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	Abstract & Introduction
Methods			
Study design	4	Present key elements of study design early in the paper	Methods, *Design & Setting*
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Methods, *Design & Setting* and *Patient Population*
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	Methods, *Patient Population, eFigure 1*
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Methods, *Study outcomes, Table 2, eTable 4*
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	*eTable 2a-c*
Bias	9	Describe any efforts to address potential sources of bias	Methods, *Statistical analysis*
Study size	10	Explain how the study size was arrived at	Methods, eFigure 1, population based study
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Methods eTable 5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Methods, *Statistical analysis*
		(*b*) Describe any methods used to examine subgroups and interactions	Methods, *Statistical analysis*
		(*c*) Explain how missing data were addressed	Methods, *Data sources*
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed	Methods, *Patient Population*
		(*e*) Describe any sensitivity analyses	Methods, *Statistical analysis*
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	*eFigure 1*
		(b) Give reasons for non-participation at each stage	NA
		(c) Consider use of a flow diagram	*eFigure 1*
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	*eTable 5*
		(b) Indicate number of participants with missing data for each variable of interest	Methods, *Data sources*
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	NA.
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	Table 1
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 1, Table 2

		(*b*) Report category boundaries when continuous variables were categorized	Results Interquartile range
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Results Table 1, Table 2
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Table 2, eTable 7

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	Discussion
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Discussion
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	Acknowledgements

eTable 2a. Administrative data definitions used to define medical comorbidities.

Variable	Database	Codes
Acute kidney injury	CIHI-DAD	ICD-9 584 ICD-10 N17
Alcoholism	CIHI-DAD	ICD-9 303, 3050 ICD-10 E244, E512, F10, G312, G621, G721, I426, K292, K70, K860, T510, X45, X65, Y15, Y573, Z502, Z714, Z721
Atrial fibrillation/flutter	CIHI-DAD	ICD-9 4273 ICD-10 I48
Cancer	CIHI-DAD	ICD-9 150, 154, 155, 157, 162, 174, 175, 185, 203, 204, 205, 206, 207, 208, 230 ICD-10 971, 980, 982, 984, 985, 986, 987, 988, 989, 990, 991, 993, C15, C18, C19, C20, C22, C25, C34, C50, C56, C61, C82, C83, C85, C91, C92, C93, C94, C95, C00, D00, D01 D02, D05, D07
	OHIP	ICD-9 203, 204, 205, 206, 207, 208, 150, 154, 155, 157, 162, 174, 175, 183, 185
Cataract	CIHI-DAD	ICD-9 366 ICD-10 H25, H26, H27, H28
	OHIP	Fee code E214, E140, E141
Chronic kidney disease	CIHI-DAD	ICD-9 4030, 4031, 4039, 4040, 4041, 4049, 582, 583, 580, 581, 584, 585, 586, 587, 5880, 5888, 5889, 5937 ICD-10 E102, E112, E132, E142, I12, I13, N08, N18, N19
	OHIP	ICD-9 403, 585
Chronic liver disease	CIHI-DAD	ICD-9 4561, 4562, 070, 5722, 5723, 5724, 5728, 573, 7824, V026, 2750, 2751, 7891, 7895, 571 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	ICD-9 571, 573, 070, Fee code Z551, Z554
Chronic lung disease	CIHI-DAD	ICD-9 491, 492, 493, 494, 495, 496, 500, 501, 502, 503, 504, 505, 5064, 5069, 5081, 515, 516, 517, 5185, 5188, 5198, 5199, 4168, 4169 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	ICD-9 491, 492, 493, 494, 496, 501, 502, 515, 518, 519, Fee code J689, J889
Congestive heart failure	CIHI-DAD	ICD-9 425, 5184, 514, 428 ICD-10 I500, I501, I509, I255, J81 CCP 4961, 4962, 4963, 4964 CCI 1HP53, 1HP55, 1HZ53GRFR, 1HZ53LAFR, 1HZ53SYFR
	OHIP	ICD-9 428, Fee code R701, R702, Z429
Coronary artery disease or angina	CIHI-DAD	ICD-9 410 412, 414, 4292, 4295, 4296, 4297, 413 ICD-10 I21, I22, I23, I24, I25, Z955, Z958, Z959, R931, T822, I20 CCP 4801, 4802, 4803, 4804, 4805, 481, 482, 483 CCI 1IJ26, 1IJ27, 1IJ54, 1IJ57, 1IJ50, 1IJ76
	OHIP	ICD-9 410, 412, 413, Fee code R741, R742, R743, G298, E646, E651, E652, E654, E655, G262, Z434, Z448
Dementia	CIHI-DAD	ICD-9 2900, 2901, 2903, 2904, 2908, 2909, 2948, 2949, 3310, 3311, 3312, 2941, 797 ICD-10 F065, F066, F068, F069, F09, F00, F01, F02, F03, F051, G30, G31, R54
	OHIP	ICD-9 290, 331, 797
Diabetes mellitus	ODB	Insulin (Isophane) Beef & Pork, Insulin (Isophane) Human Biosynthetic, Insulin (Isophane) Human Semi-synthetic, Insulin (Isophane) Pork, Insulin (Neutral) Human Semi-synthetic, Insulin (Neutral) Pork, Insulin, (Protamine Zinc) Beef & Pork, Insulin (Sulfated) Beef, Insulin (Zinc) Beef, Insulin (Zinc) Beef & Pork, Insulin (Zinc) Human Biosynthetic, Insulin (Zinc) Human Semi-synthetic, Insulin (Zinc) Pork, Insulin Aspart, Insulin Aspart & Insulin Aspart Protamine, Insulin Detemir, Insulin Glargine, Insulin Glulisine, Insulin Human Bio-synthetic, Insulin Human Semi-synthetic, Insulin Injection Pork, Insulin Isophane Injection Pork, Insulin Lispro, Acarbose, Acetohexamide, Chlorpropamide, Gliclazide, Glimepir, Glyburide, Metformin HCL, Nateglinide, Pioglitazone HCL, Repaglinide, Rosiglitazone Male, Sitagliptin Phosphate Monohydrate, Tolbutamide
Glaucoma	CIHI-DAD	ICD-9 365 ICD-10 H25, H40, H42
	OHIP	Fee code E132, E133
Hypertension	ODB	Acebutolol HCL, Aliskiren Fumarate, Amlodipine Besylate, Amlodipine Besylate & Atrovastatin, Atenolol, Atenolol & Chlorthalidone, Benazepril HCL, Bisoprolol Fumurate, Brimonidine Tartrate & Timolol Maleate, Brizolamide Tartrate & Timolol Maleate, Bumetanide, Candesartan Cilexetil, Candesartan Cilexetil & Hydrochlorothizide, Captopril, Carvedilol, Chlorthalidone, Cilazapril, Cilazapril &

Hydrochlorothizide, Diltiazem HCL, Enalapril Sodium, Enalapril Maleate, Eprosartan Mesylate, Eprosartan Mesylate & Hydrochlorothizide, Erythrityl Tetranitrate, Felodipine, Flunarizine HCL, Fosinopril Sodium, Hydralazine HCL, Hydrochlorothizide, Indapamide, Irbesartan, Irbesartan & Hydrochlorothiazide, Hydrochlorothiazide , Hydrochlorothiazide, Labetalol HCL, Lisinopril, Lisinopril & Hydrochlorothiazide, Losartan Potassium, Losartan Potassium & Hydrochlorothiazide, Methyldopa & Hydrochlorothiazide, Metoprolol Tartrate, Minoxidil, Nadolol, Nicardipine HCL, Nifedipine, Nimodipine, Olmesartan Medoxomil, Olmesartan Medoxomil & Hydrochlorothiazide, Oxprenolol HCL, Perindopril Erbamine, Perindopril Erbamine & Indapamine, Phenoxybenzamine, Pindolol, Pindolol & Hydrochlorothiazide, Propanolol HCL, Quinapril HCL & Hydrochlorothiazide, Ramipril, Ramipril & Hydrochlorothiazide, Spironolactone, Spironolactone & Hydrochlorothiazide, Telmisartan, Telmisartan & Hydrochlorothiazide, Timolol Maleate, Timolol Maleate & Hydrochlorothiazide, Timolol Maleat Hydrochlorothiazide e & Travoprost, Trandolapril, Triamterene, Triamterene & Hydrochlorothiazide, Valsartan, Valsartan & Hydrochlorothiazide, Verapamil HCL.

Hypotension	CIHI-DAD	ICD-9 458
		ICD-10 I95
Macular degeneration	CIHI-DAD	ICD-9 362
		ICD-10 H35
	OHIP	Fee code E154, E125, E126, E147
Obesity	CIHI-DAD	ICD-9 278
		ICD-10 E66
	OHIP	ICD-9 278
Osteoporosis	CIHI-DAD	ICD-9 733
		ICD-10 M80, M81
	OHIP	ICD-9 733
Parkinson's disease	CIHI-DAD	ICD-9 332
		ICD-10 G20, F023
Peripheral vascular disease	CIHI-DAD	ICD-9 4402, 4408, 4409, 5571, 4439, 444
		ICD-10 I700, I702, I708, I709, I731, I738, I739, K551
		CCP 5125, 5126, 5129, 5159, 5014, 5016, 5018, 5028, 5038
		CCI 1KA76, 1KA50, 1KE76, 1KG50, 1KG57, 1KG76MI, 1KG87, 1IA87, 1IB87, 1IC87, 1ID87, 1KA87, 1KE57
	OHIP	Fee code 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
Prostate Cancer	OHIP	Feecode A355, A356, A353, A935, A354, C355, C356, C353, C935, C354 A345, A745, A346, A343, A340, A341, A348 C345, C745, C346, C343, C340, C341, C348 A445, A845, A446, A443, A444, A441, A448, C445, C845, C446, C443, C444, C441, C448 with ICD-9 185
Rheumatoid arthritis	CIHI-DAD	ICD-9 714
		ICD-10 M05, M06
	OHIP	ICD-9 714
Seizure	CIHI-DAD	ICD-9 345, 7803
		ICD-10 G40, G41
Stroke or TIA	CIHI-DAD	ICD-9 430, 431, 436, 432, 4340, 4341, 4349, 3623, 435
		ICD-10 I600, I601, I602, I603, I604, I605, I606, I607, I609, I61, I630, I631, I632, I633, I634, I635, I638, I639, I64, I92, H341, G450, G451, G452, G453, G458, G459, H340

Data sources included CIHI-DAD (inpatient discharge abstracts), OHIP (physician billings) and ODB (universal medication coverage). CIHI-DAD used ICD-10 (for diagnostic coding) and CCI coding (for interventions) after April 1, 2002, and ICD-9/CCP coding prior to this. Specific ICD 9/10 and CCP/CCI codes, and medication classes used to define hypertension and diabetes are defined above. The presence of any data element was considered evidence of the comorbidity. A look-back window of 5 years prior to index date was used for all conditions, aside from prior falls and fractures (1 year look-back), and hypertension and diabetes (6 month look-back).

eTable 2b. Specific drugs included within each medication class. Approximately 7,400 individual Drug Identification Numbers (DINs) were used to identify relevant brands and doses.

Medication class	Medications
5 alpha reductase inhibitor	Finasteride, Dutasteride
ACE inhibitors or ARBs	Ramipril, Ramipril & Hydrochlorothiazide, Trandolapril, Candesartan Cilexetil, Candesartan Cilexetil & Hydrochlorothiazide, Eprosartan Mesylate, Eprosartan Mesylate & Hydrochlorothiazide, Irbesartan, Irbesartan & Hydrochlorothiazide, Losartan potassium, Losartan potassium & Hydrochlorothiazide, Olmesartan Medoxomil, Olmesartan Medoxomil & Hydrochlorothiazide, Telmisartan , Telmisartan & Hydrochlorothiazide, Valsartan, Valsartan & Hydrochlorothiazide
Androgen deprivation therapy	Buserelin Acetate, Goserelin Acetate, Leuprolide, Leuprolide Acetate
Anti-inflammatory	Cannabidiol & Dronabinol, Celecoxib, Diclofenac sodium, Diclofenac sodium & Misoprostol, Diflunisal, Etodolac, Fenoprofen calcium, Floctafenine, Flurbiprofen, Glucosamine & Chondroitin, Ibuprofen, Indomethacin, Ketoprofen, Ketoralac Tromethamine, Mefenamic Acid, Meloxicam, Nabumetone, Naproxen, Naproxen sodium, Oxaprpozin, Phenylbutazone, Piroxicam, Rofecoxib, Sulindac, Tenoxicam, Tiaprofenic acid, Tolmetin sodium, Valdecoxib
Antiandrogens	Bicalutamide, Cyproterone, Cyproterone Acetate, Flutamide, Nilutamide
Antibiotic	Amikacin Sulphate, Amoxicillin, Amoxicillin & Clavulanic Acid Potassium, Amoxicillin Trihydrate, Amoxicillin Trihydrate & Clavulanic Acid Potassium, Ampicillin, Ampicillin Sodium, Ampicillin Trihydrate, Azithromycin, Azithromycin Dihydrate, Bacampicillin HCL, Bacitracin, Bacitracin Zinc & Cysteine & Glycine & Neomycin Sulphate & Threonine, Bacitracin Zinc & Neomycin Sulphate & Polymyxin B Sulphate, Bacitracin Zinc & Polymyxin B Sulphate, Carbenicillin, Carbenicillin Disodium, Cefaclor, Cefadroxil, Cefadroxil Monohydrate, Cefazolin Sodium, Cefepime HCL, Cefixime, Cefoperazone Sodium, Cefotaxime Sodium, Cefoxitin Sodium, Cefprozil, Ceftazidime Sodium, Ceftazidme Hydrate, Ceftriaxone Sodium, Cefuroxime Axetil, Cephalexin, Cephalexin Monohydrate, Cephradine, Ciprofloxacin, Ciprofloxacin HCL, Ciprofloxacin HCL & Dexamethasone, Clindamycin, Clindamycin Phosphate, Clindamycin Phosphate & Glycolic Acid, Cloxacillin, Cloxacillin Sodium, Colistin Sodium Methanesulfonate, Daptomycin, Dicloxacillin Sodium, Erythromycin, Erythromycin Estolate, Erythromycin Ethyl Succinate, Erythromycin Ethyl Succinate & Sulfixoxazole, Erythromycin Gluceptate, Erythromycin Lactobionate, Erythromycin Stearate, Flucloxacillin Sodium, Fluocinolone Acetonide & Neomycin Sulphate & Polymyxin B Sulphate, Framycetin Sulphate, Fusidic Acid, Fusidic Acid Sodium, Gatifloxacin, Gentamicin, Gentamicin & Colistin, Gentamicin Sulphate, Garamicidin & Neomycin & Polymyxin B Sulphate, Garamicidin & Polymyxin B Sulphate, Grepafloxacin HCL, Levofloxacin, Linezolid, Moxifloxicin HCL, Mupirocin, Neomycin Sulphate, Neomycin Sulphate & Polymyxin B Sulphate, Netilmicin Sulphate, Norfloxacin, Ofloxacin, Paromomycin, Penicillin G Benzathine, Penicillin G Potassium, Penicillin G Procain Salt, Penicillin G Sodium, Penicillin V, Penicillin V Benzathine, Penicillin V Potassium, Piperacillin, Piperacillin Sodium & Tazobactam Sodium, Pivampicillin, Pivmecillinam, Polymyxin B Sulphate & Trimethoprim, Spectinomycin HCL, Spiramycin, Streptomycin, Streptomycin Sulphate, Sulfabenzamide & Sulfacetamide & Sulfathiazole, Sulfacetamide Sodium, Sulfadiazine, Sulfadiazine & Trimethoprim, Sulfamethoxazole, Sulfamethoxazole & Trimethoprim, Sulfapyridine, Sulfisoxazole, Telithromycin, Tobramycin, Tobramycin Sulphate, Trimethoprim, Azithromycin, Azithromycin Dihydrate, Clarithromycin
Anticoagulant	Enoxaparin, Dalteparin Sodium, Tinzaparin Sodium, Nadroparin Calc, Enoxaparin Sodium, Dabigatran Etexilate, Rivaroxaban, Fondaparinux Sodium, Lepirudin, Heparin Sodium, Coumadin, Heparin, Heparin Calcium, Danaparoid Sodium
Anticonvulsants	Carbamazepine, Clobazam, Clonazepam, Divalproex sodium, Ethosuximide, Fosphenytoin, Gabapentin, Lacosamide, Lamotrigine, Levetiracetam, Magnesium pyrogluconate, Magnesium sulphate, Mephenytoin, Mephobarbital, Methsuximide, Oxcarbazepine, Phenobarbital, Phensuximide, Phenytoin, Phenytoin sodium, Pregabalin, Primidone, Secobarbital sodium, Topiramate, Valproate sodium, Valproic acid, Vigabatrin
Antidepressants	Amitriptyline, Amitriptyline HCL, Amitriptyline HCL & Baclofen, Amitriptyline HCL & Perphenazine, Amoxapine, Bupropion HCL, Clomipramine HCL, Desipramine HCL, Doxepine HCL, Duloxetine, Imipramine, Imipramine HCL, Isocarboxazid, Maprotiline HCL, Mirtazapine, Moclobemide, Nortriptyline, Nortiptyline HCL, Phenelzine sulphate, Protriptyline HCL, Selegiline HCL, Tranylcypromine sulphate, Trazadone HCL, Trimipramine, Trimipramine maleate
Antineoplastic	Abatacept, Aldesleukin, Alemtuzumab, Altretamine, Aminoglutethimide,

	Anastrozole, Aspariginase, Azathioprine, Bicalutamide, Bleomycin Sulphate, Buserelin Acetate, Busulfan, Capecitabine, Carmustine, Chlorambucil, Cladribine, Cyclophosphamide, Cyproterone Acetate, Cytarabine, Decarbazine, Dasatinib Monohydrate, Daunorubicin, Degarelix Acetate, Diethylstilbestrol, Diethylstilbestrol Diphosphate Sodium, Doxorubicin HCL, Efalizumab, Epirubicin HCL, Erlotinib HCL, Estramustine Phosphate Disodium, Etoposide, Everolimus, Exemestane, Fludarabine Phosphate Sodium, Fluorouracil, Flutamide, Formestane, Goserelin Acetate, Hydroxyurea, Imatinib Mesylate, Interferon, Interferon Alfa-2B, Irinotecan HCL, Lanreotide, Lenalidomide, Letrozole, Leuprolide Acetate, Levamisole HCL, Lomustine, Mechlorethamine HCL, Megestrol Acetate, Melphalan, Mercaptopurine, Methotrexate Sodium, Mitomycin, Mitotane, Nilotinib HCL Monohydrate, Nilutamide, Profimer Sodium, Procarbazine HCL, Rituximab, Sirolimus, Sorafenib, Sunitinib Malate, Tacrolimus, Tamoxifen Citrate, Temozolomide, Thioguanine, Thiotepa, Tretinoin, Triptorelin, Triptorelin Pamoate, Vaccine- B.C.G, Vinblastine Sulphate, Vincristine Sulphate
Antiparkinson drugs	Benserazide HCL & Levodopa, Benztropine Mesylate, Biperiden HCL, Bromocriptine Mesylate, Carbidopa & Entacapone & Levodopa, Carbidopa & Levodopa, Entacapone, Pergolide Mesylate, Pramipexole HCL, Procyclidine HCL, Profenamine HCL, Rasagiline Mesylate, Ropinirole HCL, Selegiline HCL, Trihexyphenidyl HCL
Antiplatelet	Ticlopidine HCl, Ticlopidine, Clopidogrel, Clopidogrel Bisulphate, Prasugrel HCL, Dipyridamole, Acetylsalicylic Acid & Dipyridamole
Antipsychotic (atypical)	Risperidone, Quetiapine fumarate, Olanzapine
Antipsychotic (other)	Chlorpromazine HCL, Clozapine, Flupenthixol decanoate, Flupenthixol HCL, Fluphenazine decanoate, Fluphenazine HCL, Haloperidol, Haloperidol decanoate, Loxapine HCL, Loxapine succinate, Mesoridazine besylate, Methotrimeprazine, Olanzapine tartrate, Paliperidone, Pericyazine, Perphenazine, Pimozide, Pipotiazine palmitate, Prochlorperazine maleate, Prochlorperazine mesylate, Risperidone, Thioridazine HCL, Thiothixene, Trifluoperazine HCL, Ziprasidone HCL, Zuclopenthixol acetate, Zuclopenthixol decanoate, Zuclopenthixol dihyrochloride
Benzodiazepine	Alprazolam, Bromazepam, Chlordiazepoxide HCL, Chlordiazepoxide HCL & Clidinium Bromide, Clobazam, Clonazepam, Clorazepate Dipotassium, Diazepam, Diazepam & Methycellulose, Estazolam, Flumazenil, Flurazepam HCL, Ketazolam, Lorazepam, Midazolam HCL, Nitrazepam, Oxazepam, Temazepam, Triazolam, Zaleplon, Zopiclone
Beta blockers	Acebutolol HCL, Atenolol, Atenolol & Chlorthalidone, Betaxolol HCL, Bisoprolol fumurate, Brimonidine tartrate & Timolol maleate, Carvedilol, Brinzolamide & Timolol maleate, Labetalol HCL, Metoprolol tartrate, Nadolol, Oxprenolol HCL, Pindolol, Pindolol & Hydrochlorothiazide, Propanolol HCL, Propanolol HCL & Hydrochlorothiazide, Sotalol HCL, Timolol maleate, Timolol maleate & Travoprost
Bisphosphonate	Alendronate, Alendronate Sodium, Alendronate Sodium & Cholecalciferol, Calcium Carbonate & Etidronic Acid, Calcium Carbonate & Etidronic Acid Sodium, Calcium Carbonate & Risedronate Sodium, Clodronate Disodium, Clodronate Acid Disodium, Etidronate & Calcium Carbonate, Etidronate Disodium, Etidronic Acid Disodium, Ibandronate, Pamidronate Disodium, Pamidronic Acid Disodium, Risedronate Sodium & Calcium, Risedronate Sodium & Calcium & Vitamin D3, Zoledronic Acid
Calcium channel blockers	Amlodipine besylate, Amlodipine besylate & Atorvastatin, Diltiazem HCL, Erythrityl Tetranitrate, Felodipine, Flunarizine HCL, Nifedipine, Nicardipine HCL, Nimodipine, Verapamil HCL
Cholinesterase inhibitors	Aricept, Mylan-Galantamine ER, Pat-Galantamine ER, Sandoz-Rivastigmine, Ratio-Rivastigmine, PMS-Rivastigmine, Teva-Rivastigmine, APO-Rivastigmine, Mylan-Rivastigmine, Exelon, Reminyl ER
Denosumab	Denosumab, Denosumab Recombinant, Pamidronic Acid Disodium, Tiludronate Disodium
Digoxin	Digoxin
Glucocorticoids	Budenoside, Methylprednisone, Hydrocortisone, Dexamethasone, Betamethasone, Triamcin, Cortisone, Fludrocortisone,
Glucose test strip	Diagnostic Agent- Diabetes, Glucose, Blood Tests, Glucose, Urine Tests, Non Pharmaceutical Ingredient
Inhaled acetylcholine	Ipratropium Bromide, Tiotropium Bromide
Inhaled beta-agonist	Methaproterenol Sulfate, Albuterol, Albuterol & Albuterol Sulfate, Albuterol Sulfate, Fenoterol HBR, Zenhale, Foradil, Oxeze, Pirbuterol Acetate, Procaterol HCL, Salmeterol Xinafoate, Formoterol & Mometasone, Formoterol Fumarate, Terbutaline Sulfate, Fluticasone Propionate & Salmeterol Xinafoate, Budesonide & Formoterol Fumarate, Albuterol Sulfate & Ipratropium Bromide
Inhaled corticosteroid	Beclomethasone Dipropionate, Budesonide, Ciclesonide, Flunisolide, Fluticasone Propionate, Triamcinolone Acetonide

Narcotics	Acetaminophen & Caffeine & Codeine, Acetaminophen & Caffeine & Codeine Phosphate, Acetaminophen & Caffeine Citrate & Codeine Phosphate, Acetaminophen & Chlorzoxazone & Codeine, Acetaminophen & Chlorzoxazone & Codeine Phosphate, Acetaminophen & Codeine & Doxylamine, Acetaminophen & Codeine Phosphate, Acetaminophen & Dextromethorphan Hbr & Doxylamine & Pseudoephedrine Hcl, Acetaminophen & Dextromethorphan Hbr & Doxylamine Succinate & Pseudoephedrine Hcl, Acetaminophen & Oxycodone Hcl, Acetaminophen & Pseudoephedrine Hcl, Acetylsalicylic Acid & Caffeine & Codeine Phosphate, Acetylsalicylic Acid & Caffeine & Dextropropoxyphene Hcl, Acetylsalicylic Acid & Caffeine & Propoxyphene Hcl, Acetylsalicylic Acid & Codeine Phosphate, Acetylsalicylic Acid & Oxycodone Hcl, Alfentanil Hcl, Ammonium Chloride & Codeine Phosphate & Guaifenesin, Analgesics, Anileridine Hcl, Atropine Sulfate & Attapulgite & Hyoscyamine Sulfate & Opium Powder & Pectin & Scopolamine Hbr, Belladona & Opium, Belladona Extract For Oral Use & Opium Powder, Codeine, Codeine Phosphate, Dextromethorphan Hbr & Guaifenesin & Menthol, Dextropropoxyphene Hcl, Dextropropoxyphene Napsylate, Diamorphine Hcl, Fentanyl, Fentanyl & Baclofen, Fentanyl & Bupivacaine, Fentanyl & Bupivacaine & Baclofen, Fentanyl & Bupivacaine & Clonidine, Fentanyl & Bupivicaine & Clonidin & Baclofen, Fentanyl & Clonidine Hcl, Fentanyl Citrate, Hydrocodone Bitartrate & Ibuprofen, Hydromorphone, Hydromorphone & Baclofen, Hydromorphone & Bupivacaine & Baclofen, Hydromorphone & Bupivicaine, Hydromorphone & Bupivicaine & Baclofen, Hydromorphone & Bupivicaine & Baclofen & Clonidine, Hydromorphone & Bupivicaine & Clonidine, Hydromorphone Hbr, Hydromorphone Hcl, Ibuprofen & Diphenhydramine Hcl, Levorphanol Tartrate, Meperidine Hcl, Meperidine Hcl & Promethazine Hcl, Morphine, Morphine & Baclofen, Morphine & Bupivicaine, Morphine & Bupivicaine & Baclofen, Morphine & Lioresal, Morphine Hcl, Morphine Succinate, Morphine Sulfate, Naloxone Hcl & Oxycodone Hcl, Opium, Narcotic Compound, Opium & Belladonna, Opium & Camphor, Opium Tincture, Oxycodone Hcl, Oxymorphone Hcl, Propoxyphene Hcl, Remifentanil Hcl, Sufentanil Citrate, Tapentadol Hcl, Tramadol, Tramadol Hcl, Bupivacaine & Fentanyl, Fentanyl & Baclofen & Clonidine, Fentanyl & Bupivacaine, Fentanyl & Bupivicaine & Clonidine, Fentanyl & Bupivicaine & Clonidine & Baclofen, Hydromorphine & Bupivicaine & Clonidine, Morphine & Bupivicaine, Acetylsalicylic Acid & Caffeine & Pentazocine Hcl, Butorphanol Tartrate, Nalbuphine Hcl, Pentazocine Lactate, Pentazocine Hcl
Non-potassium sparing diuretics	Bumetanide, Ethacrynic Acid, Furosemide, Chlorthalidone, Hydrochlorothiazide, Indapamide, Methyldopa & Hydrochlorothiazide, Metolazone, Timolol Maleate & Hydrochlorothiazide
Overactive bladder medication	Darifenacin, Flavoxate HCL, Oxybutynin, Oxybutynin Chloride, Solifenacin Succinate, Tolterodine Tartrate, Trospium Chloride, Trospium Hydroxide Chloride
Potassium sparing diuretics	Amiloride HCL, Amiloride HCL & Hydrochlorothiazide, Epleronone, Spironolactone, Spironolactone & Hydrochlorothiazide, Triamterene, Triamterene & Hydrochlorothiazide,
Proton Pump inhibitors	Amoxicillin Trihydrate & Clarithromycin & Lansoprazole, Dexlansoprazole, Esomeprazole Magnesium, Lansoprazole, Lansoprazole Sodium, Omeprazole, Omeprazole Magnesium, Pantoprazole, Pantoprazole Magnesium, Pantoprazole Sodium, Rabeprazole Sodium
Selective Serotonin Reuptake Inhibitors	Fluoxetine HCL, Fluvoxamine Maleate, Paroxetine HCL, Sertraline HCL, Fluoxetine, Sertraline, Citalopram HBR, Escitalopram Oxalate, Citalopram Hydrobromide, Nefazodone HCL,
Smoking cessation aid	Varenicline Tartrate, Bupropion HCL, Nicotine
Statins	Atorvastatin, Cerivastatin Sodium, Fluvastatin Sodium, Lovastatin, Provastatin Sodium, Rosuvastatin Calcium, Simvastatin
Testosterone replacement	Androderm, Testosterone Cipionate, Androgel, Testim, Testosterone Enanthate, Testosterone Propionate, Testosterone Cypionate, Testosterone, Methyltestosterone, Testosterone Powder, Testosterone Decanoate

Data source was the ODB, which provides universal medication coverage to all people over 65 years of age. Each medication is identified with a unique and permanent DIN. The presence of any medication within the medication class in the 6 months prior to the index date was considered evidence of recent or current medication usage.

eTable 2c. Administrative data definitions used to define medical investigations and procedures.

Variable	Database	Codes
Bone mineral density test	OHIP	Fee code J654, J688, J854, J888, X149, X152, X153, X155, Y654, Y688, Y854, Y888
Bone scan	OHIP	Fee code J850, J650, J852, J862
Cardiac catheterization	CIHI-DAD/SDS	CCP 4995, 4996, 4997
		CCI 3IJ30GP, 3HZ30GP, 2HZ24GPKJ, 2HZ24GPKL, 2HZ24GPKM, 2HZ24GPXJ, 2HZ28GPPL, 2HZ71GP
	OHIP	Fee code G296, G297, G299, G300, G301, G304, G305, G306
Cardiac stress test	CIHI-DAD/SDS	CCP 0341, 0342, 0343, 0344, 0605
		CCI 2HZ08, 3IP70
	OHIP	Fee code G315, G174, G111, G112, G319, G582, G583, G584, J604, J606, J607, J608, J611, J612, J613, J667, J807, J808, J809, J804, J811, J812, J813, J866, J867, J609, J666, J814, J614, J810, J610
Carotid endarterectomy	OHIP	Fee code N220, R792
Carotid ultrasound	CIHI-DAD/SDS	CCP 0281
		CCI 3JE30, 3JG30
	OHIP	Fee code J201, J501, J190, J191, J490, J491, J492
Chest x-ray	OHIP	Fee code X090, X091, X092, X195
CT head	OHIP	Fee code X188, X400, X401, X402, X405, X408
CT spine	OHIP	Fee code X128, X415, X416
Echocardiography	CIHI-DAD/SDS	CCP 0282
		CCI 3IP30
	OHIP	Fee code G560, G561, G562, G566, G567, G568, G570, G571, G572, G574, G575, G576, G577, G578, G581
EEG	OHIP	Fee code G414, G415, G416, G417, G418, G540, G542, G544, G545, G546, G554, G555
Heart valve replacement	OHIP	Fee code R728, R735, R738, R772
Holter monitoring	CIHI-DAD/SDS	CCP 0354
		CCI 2HZ24JAKH
	OHIP	Fee code G311, G320, G647, G648, G649, G650, G651, G652, G653, G654, G655, G656, G657, G658, G659, G660, G661, G682, G683, G684, G685, G686, G687, G688, G689, G690, G692, G693
Prostate-specific antigen (PSA) test	OHIP	Fee code L354, L358
Pulmonary function test	OHIP	Fee code J301, J303, J304, J305, J306, J307, J308, J309, J310, J311, J313, J315, J316, J317, J318, J319, J320, J322, J323, J324, J327, J328, J330, J331, J332, J333, J334, J335, J340, J341, E450, E451
Postvoid urine measurement	OHIP	Fee code G900
TRUS biopsy	OHIP	Fee code Z712
Urodynamic study	OHIP	Fee code G192, G193, G447
Urine culture	OHIP	Fee code L633, L634, L641
Noninvasive uroflowmetry	OHIP	Fee code G475

Data sources included CIHI-DAD (inpatient discharge abstracts) and OHIP (physician billings). CIHI-DAD used ICD-10 (for diagnostic coding) and CCI coding (for interventions) after April 1, 2002, and ICD-9/CCP coding prior to this. Specific ICD 9/10 and CCP/CCI codes are defined above. The presence of any data element within the year prior to the index date was considered evidence of the medical test or intervention.

eTable 3. Variables included in the propensity score.

Demographics

Year of cohort entry (based on 2 year increments)
Region of residence (Using 1 of 14 Local Health Integration Networks (LHINs))
Rural location

Comorbid medical conditions

Cancer
Chronic lung disease
Dementia
Diabetes
Hypertension
Osteoporosis
Prior fall
Prostate Cancer

Comorbidity Index

John Hopkins ACG count

Medication use

ACE inhibitor or ARB
Androgen deprivation therapy
Antiandrogen therapy
Antibiotic
Benzodiazepine
Bisphosphonates
Denosumab
Glucocorticoids
Narcotics
Overactive bladder medication
Proton Pump Inhibitors
Statin
Total medication count

Hospital and physician utilization

Number of hospital admissions
Number of emergency room visits
Number of family physician visits
Number of geriatric medicine visits
Number of neurology visits
Number of cardiology visits
Number of urologist visits

Medical investigations and procedures

Echocardiography
Bone mineral density test
Bone scan
Cardiac stress test
Chest X-ray
CT head
Prostate specific antigen test
Transrectal ultrasound guided prostate biopsy
Urine culture
Urodynamic test or post void residual measurement

Selected based on review of standardized differences between exposed and unexposed men prior to matching, and known association with falls or fractures.

eTable 4. Coding definition for primary and secondary outcomes

	Data sources	Codes
Fall*	NACRS or CIHI-DAD	ICD 10 W00-W19
Any Fracture**	NACRS or CIHI-DAD or OHIP	*Hip* (ICD 10 S720, S721; CCI 1VA73, 1VC73, 1VA74, 1VA53, 1VC74, 1VA80)
		Forearm (ICD 10 S52; CCI 1TV73, 1TV74, 1TV03; OHIP F014, F022, F023, F025, F026, F028, F030, F032, F033, F046, F024, F027, F031, Z203)
		Humerus (ICD 10 S422, S423, S424)
		Vertebral (S220, S221, S320, T080, T081)
		Femur (ICD 10 S723; CCI 1VC73, 1VC74, 1VC03, 1VC80; OHIP F095, F096, F097, Z211)
		Pelvis (ICD 10 S321, S322, S324, S323, S325, S327, S328)
		Ankle (ICD 10 S825, S826, S827, S828, S829)
		Patella (ICD 10 S820)
		Tibia/Fibula (ICD 10 S821, S822, S823, S824)
		Ribs/sternum (ICD 10 S222, S223, S224)
		Trunk (ICD 10 S228, S29)
		Scapula (ICD 10 S421, S29)
		Clavicle (ICD 10 S420)
		Other (ICD 10 M844, M843)
Major Osteoporotic fracture**	NACRS or CIHI-DAD or OHIP	*Hip* (ICD 10 S720, S721; CCI 1VA73, 1VC73, 1VA74, 1VA53, 1VC74, 1VA80)
		Forearm (ICD 10 S52; CCI 1TV73, 1TV74, 1TV03; OHIP F014, F022, F023, F025, F026, F028, F030, F032, F033, F046, F024, F027, F031, Z203)
		Humerus (ICD 10 S422, S423, S424)
		Pelvis (ICD 10 S321, S322, S324, S323, S325, S327, S328)
Hip fracture**	NACRS or CIHI-DAD	ICD 10 S720, S721; CCI 1VA73, 1VC73, 1VA74, 1VA53, 1VC74, 1VA80
Hypotension***	CIHI-DAD or NACRS	ICD 10 I95
Head injury***	CIHI-DAD or NACRS	ICD 10 S00-S09

CIHI DAD (hospital discharge abstracts) and NACRS (all emergency room visits) data is extracted from medical records by trained abstractors, and data quality is maintained though audit-feedback systems. Data on diagnoses are coded using ICD 10, and data for interventions are coded using Canadian Classification of Health Intervention (CCI). Up to 25 diagnoses and 25 interventions can be coded per patient. Data elements have shown >80% agreement with medical records during reabstraction studies[1].

*Using medical chart abstraction as the reference standard, PPV for ICD 10 codes for falls in NACRS is 91.4% (email communication, Dr Lisa-Ann Fraser, June 2015).

**PPV for the coding combinations for fractures ranges between 0.81-0.96 depending on fracture site. Hip/femur fracture has an estimated PPV of 0.83[2].

***Using reabstracted information written in a patient's chart as the reference standard, the codes for hypotension (I95) and head injury (S06) have a sensitivity of 72% and 77% respectively, and a positive predictive value of 39% and 79% respectively[3].

eTable 5. Complete baselines for unmatched and matched cohorts.

		Unmatched Cohort			SD*	Matched Cohort			SD
		Unexposed n=426,106		Exposed n=186,004		Unexposed n=147,084		Exposed n=147,084	
Demographics									
Age	*Median (IQR)*	73 (69-79)		74 (69-80)		75 (70-80)		75 (70-80)	
	66-69.9	118718	27.9%	47798	25.7%	5%	35520	24.1%	35800	24.3%	0%
	70-74.9	116482	27.3%	46751	25.1%	5%	36549	24.8%	36306	24.7%	0%
	75-79.9	89097	20.9%	41518	22.3%	3%	33075	22.5%	33130	22.5%	0%
	80-84.9	60538	14.2%	29281	15.7%	4%	24412	16.6%	24329	16.5%	0%
	85-89.9	29644	7.0%	15171	8.2%	5%	12843	8.7%	12824	8.7%	0%
	≥90	11627	2.7%	5485	2.9%	1%	4685	3.2%	4695	3.2%	0%
Fiscal year of cohort entry (index date)	*2003-2004*	35310	8.3%	18969	10.2%	7%	14002	9.5%	14598	9.9%	1%
	2005-2006	59789	14.0%	30036	16.1%	6%	22316	15.2%	23616	16.1%	2%
	2007-2008	72225	17.0%	34202	18.4%	4%	25289	17.2%	27490	18.7%	4%
	2009-2010	72156	16.9%	31478	16.9%	0%	24377	16.6%	24927	16.9%	1%
	2011-2012	125153	29.4%	49057	26.4%	7%	41603	28.3%	38526	26.2%	5%
	2013	61473	14.4%	22262	12.0%	7%	19497	13.3%	17927	12.2%	3%
Rural Residence		66897	15.7%	23937	12.9%	8%	20064	13.6%	19968	13.6%	0%
Socioeconomic Status	*1-Lowest*	76410	17.9%	32566	17.5%	1%	26256	17.9%	25871	17.6%	1%
	2	86180	20.2%	37196	20.0%	0%	29685	20.2%	29543	20.1%	0%
	3	84010	19.7%	36322	19.5%	1%	28675	19.5%	28804	19.6%	0%
	4	87012	20.4%	38332	20.6%	0%	30106	20.5%	30205	20.5%	0%
	5-Highest	91099	21.4%	41056	22.1%	2%	31924	21.7%	32244	21.9%	0%
	Missing	1395	0.3%	532	0.3%	0%	438	0.3%	417	0.3%	0%
Resides in long term care		13565	3.2%	4799	2.6%	4%	4068	2.8%	4068	2.8%	0%
Local Health Integration Network (LHIN)	*1*	23315	5.5%	11464	6.2%	3%	8940	6.1%	8941	6.1%	0%
	2	36753	8.6%	12419	6.7%	7%	10854	7.4%	10585	7.2%	1%
	3	22425	5.3%	7668	4.1%	6%	6474	4.4%	6390	4.3%	0%
	4	54938	12.9%	21993	11.8%	3%	18107	12.3%	18226	12.4%	0%
	5	19085	4.5%	9652	5.2%	3%	6992	4.8%	7282	5.0%	1%
	6	27924	6.6%	14313	7.7%	4%	11082	7.5%	10999	7.5%	0%
	7	30823	7.2%	16495	8.9%	6%	12191	8.3%	12286	8.4%	0%
	8	47803	11.2%	24870	13.4%	7%	18494	12.6%	18417	12.5%	0%
	9	52636	12.4%	20688	11.1%	4%	16832	11.4%	16596	11.3%	0%
	10	21035	4.9%	8542	4.6%	1%	6964	4.7%	6982	4.7%	0%
	11	39183	9.2%	17725	9.5%	1%	13964	9.5%	14016	9.5%	0%
	12	17218	4.0%	7696	4.1%	1%	6053	4.1%	6179	4.2%	1%
	13	23854	5.6%	9878	5.3%	1%	8000	5.4%	8035	5.5%	0%
	14	9114	2.1%	2601	1.4%	5%	2137	1.5%	2150	1.5%	0%
Comorbid medical conditions									
Acute Kidney injury		8913	2.1%	5611	3.0%	6%	4351	3.0%	4393	3.0%	0%
Alcoholism		4661	1.1%	2022	1.1%	0%	1702	1.2%	1616	1.1%	1%

		N	%	N	%	SMD	N	%	N	%	SMD
Atrial fibrillation/flutter		27665	6.5%	13945	7.5%	4%	12034	8.2%	11391	7.7%	2%
Cancer		69442	16.3%	38230	20.6%	11%	32379	22.0%	30194	20.5%	4%
Cataract		74269	17.4%	34179	18.4%	3%	28455	19.3%	27981	19.0%	1%
Chronic kidney disease		32710	7.7%	16670	9.0%	5%	14429	9.8%	13425	9.1%	2%
Chronic liver disease		14329	3.4%	7092	3.8%	2%	5853	4.0%	5516	3.8%	1%
Chronic lung disease		103516	24.3%	51517	27.7%	8%	41298	28.1%	41344	28.1%	0%
Congestive heart failure		49675	11.7%	23908	12.9%	4%	20714	14.1%	19577	13.3%	2%
Coronary artery disease or angina		166116	39.0%	76510	41.1%	4%	63040	42.9%	62404	42.4%	1%
Dementia		38377	9.0%	18690	10.0%	3%	14590	9.9%	15461	10.5%	2%
Diabetes mellitus		92023	21.6%	36461	19.6%	5%	30307	20.6%	30784	20.9%	1%
Number of previous falls	*0*	422786	99.2%	183224	98.5%	7%	145058	98.6%	145036	98.6%	0%
	1	2986	0.7%	2460	1.3%	6%	1794	1.2%	1817	1.2%	0%
	2	274	0.1%	268	0.1%	0%	187	0.1%	188	0.1%	0%
	≥3	60	0.0%	52	0.0%	0%	45	0.0%	43	0.0%	0%
Prior Fracture		2256	0.5%	1838	1.0%	6%	1294	0.9%	1294	0.9%	0%
Glaucoma		27244	6.4%	11507	6.2%	1%	9956	6.8%	9556	6.5%	1%
Hypertension		304887	71.6%	120457	64.8%	15%	102623	69.8%	102036	69.4%	1%
Hypotension		6068	1.4%	3310	1.8%	3%	2796	1.9%	2615	1.8%	1%
Macular degeneration		12028	2.8%	5097	2.7%	1%	4428	3.0%	4144	2.8%	1%
Obesity (BMI >40)		18567	4.4%	8740	4.7%	1%	6854	4.7%	6835	4.6%	0%
Osteoporosis		21179	5.0%	11257	6.1%	5%	9010	6.1%	8795	6.0%	0%
Parkinson's disease		2251	0.5%	1477	0.8%	4%	1113	0.8%	1169	0.8%	0%
Peripheral vascular disease		9107	2.1%	4017	2.2%	1%	3691	2.5%	3331	2.3%	1%
Prostate cancer		39758	9.3%	21332	11.5%	7%	19112	13.0%	17173	11.7%	4%
Rheumatoid arthritis		15407	3.6%	7734	4.2%	3%	6248	4.2%	6216	4.2%	0%
Seizure		2599	0.6%	1306	0.7%	1%	1090	0.7%	1040	0.7%	0%
Stroke or TIA		12592	3.0%	6687	3.6%	3%	5195	3.5%	5368	3.6%	1%
Comorbidity Index (based on 3 year lookback window)											
Charlson comorbidity index	*Median (IQR)*	0	(0-2)	0	(0-2)		0	(0-2)	0	(0-2)	
	0	325765	76.5%	134274	72.2%	10%	102838	69.9%	105567	71.8%	4%
	1	38987	9.1%	18379	9.9%	3%	15051	10.2%	14841	10.1%	0%
	2	31279	7.3%	16564	8.9%	6%	14598	9.9%	13138	8.9%	3%
	≥3	30075	7.1%	16787	9.0%	7%	14597	9.9%	13538	9.2%	2%
Number of Johns Hopkins ACG Aggregated Diagnosis Groups	*Median (IQR)*	7 (5-10)		9 (6-11)					8 (6-11)		
	0-4	103199	24.2%	25020	13.5%	28%	19630	13.3%	19152	13.0%	1%
	5-9	97005	22.8%	61420	33.0%	7%	68262	46.4%	70116.00	47.7%	2%
	10-14	14866	3.5%	13165.00	7.1%	23%	48762	33.2%	47961.00	32.6%	1%
	15-19	424	0.1%	565	0.3%	16%	10085	6.9%	9482	6.4%	2%
	≥20	210612	49.4%	85834	46.1%	4%	345	0.2%	373	0.3%	2%
Medication use (in the 180 days prior to the index date)											
5 alpha reductase inhibitor		10838	2.5%	20474	11.0%	34%	10826	7.4%	10826	7.4%	0%
ACE inhibitors or ARBs		218787	51.3%	85697	46.1%	10%	72764	49.5%	72529	49.3%	0%
Androgen deprivation therapy		6728	1.6%	5120	2.8%	8%	4051	2.8%	3974	2.7%	1%

Anti-inflammatory		61927	14.5%	29786	16.0%	4%	23196	15.8%	24681	16.8%	3%
Antiandrogens		4479	1.1%	3676	2.0%	7%	2736	1.9%	2743	1.9%	0%
Antibiotic		118029	27.7%	71863	38.6%	23%	54917	37.3%	56281	38.3%	2%
Anticoagulant		5411	1.3%	2526	1.4%	1%	2372	1.6%	2047	1.4%	2%
Anticonvulsants		18254	4.3%	9170	4.9%	3%	7411	5.0%	7429	5.1%	0%
Antidepressants		25650	6.0%	13242	7.1%	4%	10568	7.2%	10846	7.4%	1%
Antineoplastic		15852	3.7%	9293	5.0%	6%	8139	5.5%	7419	5.0%	2%
Antiparkinson drug		8326	2.0%	4813	2.6%	4%	3552	2.4%	3970	2.7%	2%
Antiplatelet		27649	6.5%	12724	6.8%	1%	10700	7.3%	10561	7.2%	0%
Antipsychotic (atypical)		12243	2.9%	4917	2.6%	2%	4572	3.1%	4153	2.8%	2%
Antipsychotic (other)		3644	0.9%	1854	1.0%	1%	1663	1.1%	1497	1.0%	1%
Benzodiazepine		49030	11.5%	25979	14.0%	8%	20868	14.2%	21220	14.4%	1%
Beta blockers		135582	31.8%	53959	29.0%	6%	47435	32.3%	45448	30.9%	3%
Bisphosphonate		22573	5.3%	12004	6.5%	5%	10024	6.8%	9590	6.5%	1%
Calcium channel blockers		111886	26.3%	47549	25.6%	2%	39507	26.9%	40141	27.3%	1%
Cholinesterase inhibitors		13344	3.1%	5727	3.1%	0%	5169	3.5%	4893	3.3%	1%
Denosumab		93	0.0%	41	0.0%	5%	41	0.0%	34	0.0%	1%
Digoxin		14499	3.4%	6405	3.4%	0%	6062	4.1%	5378	3.7%	2%
Glucocorticoids		32037	7.5%	17262	9.3%	6%	14149	9.6%	14000	9.5%	0%
Glucose test strip		4736	1.1%	1939	1.0%	0%	1626	1.1%	1604	1.1%	0%
Inhaled acetylcholine		26936	6.3%	13319	7.2%	4%	10994	7.5%	11138	7.6%	0%
Inhaled beta-agonist		47862	11.2%	22750	12.2%	3%	19544	13.3%	18805	12.8%	1%
Inhaled corticosteroid		21522	5.1%	10007	5.4%	1%	8764	6.0%	8145	5.5%	2%
Narcotics		63767	15.0%	35285	19.0%	11%	28254	19.2%	28523	19.4%	1%
Non-potassium sparing diuretics		107470	25.2%	41600	22.4%	7%	38851	26.4%	35062	23.8%	6%
Overactive bladder medication		5342	1.3%	6439	3.5%	14%	4057	2.8%	4411	3.0%	1%
Potassium sparing diuretics		16418	3.9%	6306	3.4%	3%	6224	4.2%	5321	3.6%	3%
Proton Pump inhibitors		91823	21.5%	45558	24.5%	7%	38025	25.9%	37415	25.4%	1%
Selective Serotonin Reuptake Inhibitors		25783	6.1%	12471	6.7%	2%	10368	7.0%	10315	7.0%	0%
Smoking cessation aid		501	0.1%	200	0.1%	0%	151	0.1%	158	0.1%	0%
Statins		211307	49.6%	85185	45.8%	8%	71769	48.8%	71449	48.6%	0%
Testosterone replacement		2401	0.6%	1326	0.7%	1%	996	0.7%	1064	0.7%	0%
Number of unique medications	Median (IQR)	6 (3-9)		6 (3-10)			7 (4-10)		7 (4-10)	
	0	0	0.0%	10793	35%	35%	0	0.0%	0	0.0%	0%
	1-4	163603	38.4%	53418	21%	21%	45795	31.1%	47086	32.0%	2%
	5-8	147738	34.7%	58162.00	7%	7%	50084	34.1%	49144.00	33.4%	1%
	9-12	71489	16.8%	35343.00	6%	6%	29317	19.9%	28799.00	19.6%	1%
	13-16	27772	6.5%	16619	9%	9%	13350	9.1%	13150	8.9%	1%
	≥17	15504	3.6%	11669	12%	12%	8538	5.8%	8905	6.1%	1%

Hospital and Physician Utilisation

Number of hospital admissions	Median (IQR)	0 (0-1)		0 (0-1)					0 (0-1)	
	0	304363	71.4%	109456	58.8%	27%	89192	60.6%	88795	60.4%	0%
	1	74362	17.5%	43584	23.4%	15%	32978	22.4%	33218	22.6%	0%

	2	28981	6.8%	18345	9.9%	11%	14010	9.5%	14120	9.6%	0%
	≥3	18400	4.3%	14619	7.9%	15%	10904	7.4%	10951	7.4%	0%
Number of Emergency Room visits	*Median (IQR)*	0 (0-1)		0 (0-1)					0 (0-1)		
	0	306292	71.9%	115537	62.1%	21%	92414	62.8%	91941	62.5%	1%
	1	70553	16.6%	36929	19.9%	9%	29150	19.8%	29305	19.9%	0%
	2	25618	6.0%	16289	8.8%	11%	12612	8.6%	12679	8.6%	0%
	≥3	23643	5.5%	17249	9.3%	15%	12908	8.8%	13159	8.9%	0%
Number of family physician visits	*Median (IQR)*	6 (3-11)		7 (4-13)					7 (4-13)		
	0	17514	4.1%	5791	3.1%	5%	3918	2.7%	3967	2.7%	0%
	1-2	54261	12.7%	17635	9.5%	10%	12899	8.8%	12995	8.8%	0%
	3-4	79480	18.7%	27662	14.9%	10%	22140	15.1%	21980	14.9%	1%
	5-6	75196	17.6%	30102	16.2%	4%	24651	16.8%	24344	16.6%	1%
	7-8	54448	12.8%	24611	13.2%	1%	20198	13.7%	19881	13.5%	1%
	9-10	36712	8.6%	18061	9.7%	4%	14772	10.0%	14506	9.9%	0%
	≥11	108495	25.5%	62142	33.4%	17%	48506	33.0%	49411	33.6%	1%
Number of Geriatrician visits	*Median (IQR)*	0 (0-0)		0 (0-0)					0 (0-0)		
	0	415069	97.4%	177844	95.6%	10%	141198	96.0%	140922	95.8%	1%
	1	5097	1.2%	3352	1.8%	5%	2503	1.7%	2594	1.8%	1%
	2	2418	0.6%	1671	0.9%	3%	1234	0.8%	1257	0.9%	1%
	≥3	3522	0.8%	3137	1.7%	8%	2149	1.5%	2311	1.6%	1%
Number of Neurologist visits	*Median (IQR)*	0 (0-0)		0 (0-0)					0 (0-0)		
	0	401060	94.1%	169928	91.4%	10%	135241	91.9%	134846	91.7%	1%
	1	13397	3.1%	7847	4.2%	6%	5974	4.1%	6104	4.2%	1%
	2	6448	1.5%	4112	2.2%	5%	3053	2.1%	3127	2.1%	0%
	≥3	5201	1.2%	4117	2.2%	8%	2816	1.9%	3007	2.0%	1%
Number of Cardiologist visits	*Median (IQR)*	0 (0-1)		0 (0-1)					0 (0-2)		
	0	265403	62.3%	103906	55.9%	13%	81840	55.6%	82042	55.8%	0%
	1	74142	17.4%	35826	19.3%	5%	28238	19.2%	28237	19.2%	0%
	2	33092	7.8%	16785	9.0%	4%	13555	9.2%	13379	9.1%	0%
	≥3	53469	12.5%	29487	15.9%	10%	23451	15.9%	23426	15.9%	0%
Number of Urologist visits	*Median (IQR)*	0 (0-0)		0 (0-2)					0 (0-1)		
	0	357268	83.8%	100518	54.0%	68%	89489	60.8%	90134	61.3%	1%
	1	27955	6.6%	32619	17.5%	34%	23241	15.8%	22430	15.2%	2%
	2	17502	4.1%	21662	11.6%	28%	14517	9.9%	14257	9.7%	1%
	≥3	23381	5.5%	31205	16.8%	36%	19837	13.5%	20263	13.8%	1%
Number of Ophthalmolo-gist visits	*Median (IQR)*	2 (1-4)		2 (1-4)					2 (1-4)		
	0	306825	72.0%	129425	69.6%	5%	100668	68.4%	101731	69.2%	2%
	1	47864	11.2%	23761	12.8%	5%	18585	12.6%	18854	12.8%	1%
	2	25373	6.0%	12011	6.5%	2%	9928	6.7%	9573	6.5%	1%
	≥3	46044	10.8%	20807	11.2%	1%	17903	12.2%	16926	11.5%	2%
Medical investigations and procedures											
Bone mineral density test		15490	3.6%	8704	4.7%	6%	6842	4.7%	6636	4.5%	1%
Bone scan		9798	2.3%	9465	5.1%	15%	6446	4.4%	6668	4.5%	0%

Cardiac catheterization	8512	2.0%	4377	2.4%	3%	3373	2.3%	3565	2.4%	1%
Cardiac stress test	51037	12.0%	26955	14.5%	7%	21126	14.4%	21066	14.3%	0%
Carotid endarterectomy	402	0.1%	241	0.1%	0%	176	0.1%	191	0.1%	0%
Carotid ultrasound	20098	4.7%	10647	5.7%	5%	8495	5.8%	8466	5.8%	0%
Chest x-ray	128826	30.2%	71018	38.2%	17%	55893	38.0%	55992	38.1%	0%
CT head	29622	7.0%	18993	10.2%	11%	14361	9.8%	14752	10.0%	1%
CT spine	5304	1.2%	3833	2.1%	7%	2638	1.8%	2930	2.0%	1%
Echocardiography	73390	17.2%	37689	20.3%	8%	30330	20.6%	29944	20.4%	0%
EEG	2075	0.5%	1322	0.7%	3%	1042	0.7%	980	0.7%	0%
Heart valve replacement	622	0.1%	408	0.2%	3%	253	0.2%	329	0.2%	0%
Holter monitoring	24508	5.8%	13320	7.2%	6%	10305	7.0%	10578	7.2%	1%
Prostate-specific antigen test	39022	9.2%	28331	15.2%	18%	22420	15.2%	20168	13.7%	4%
Pulmonary function test	35519	8.3%	18704	10.1%	6%	15006	10.2%	14784	10.1%	0%
Postvoid urine measurement	4606	1.1%	8964	4.8%	22%	4490	3.1%	4689	3.2%	1%
TRUS biopsy	4116	1.0%	8570	4.6%	22%	4026	2.7%	4710	3.2%	3%
Urodynamic study	462	0.1%	1087	0.6%	8%	451	0.3%	569	0.4%	2%
Urine culture	56320	13.2%	58941	31.7%	45%	39070	26.6%	40731	27.7%	2%
Noninvasive uroflowmetry	9192	2.2%	19372	10.4%	34%	8960	6.1%	9968	6.8%	3%

*Standardized differences (SD) describe differences in between group means relative to a pooled standard deviation, and better demonstrate significant differences in large samples.
A SD > 10% is considered a meaningfully difference between groups.

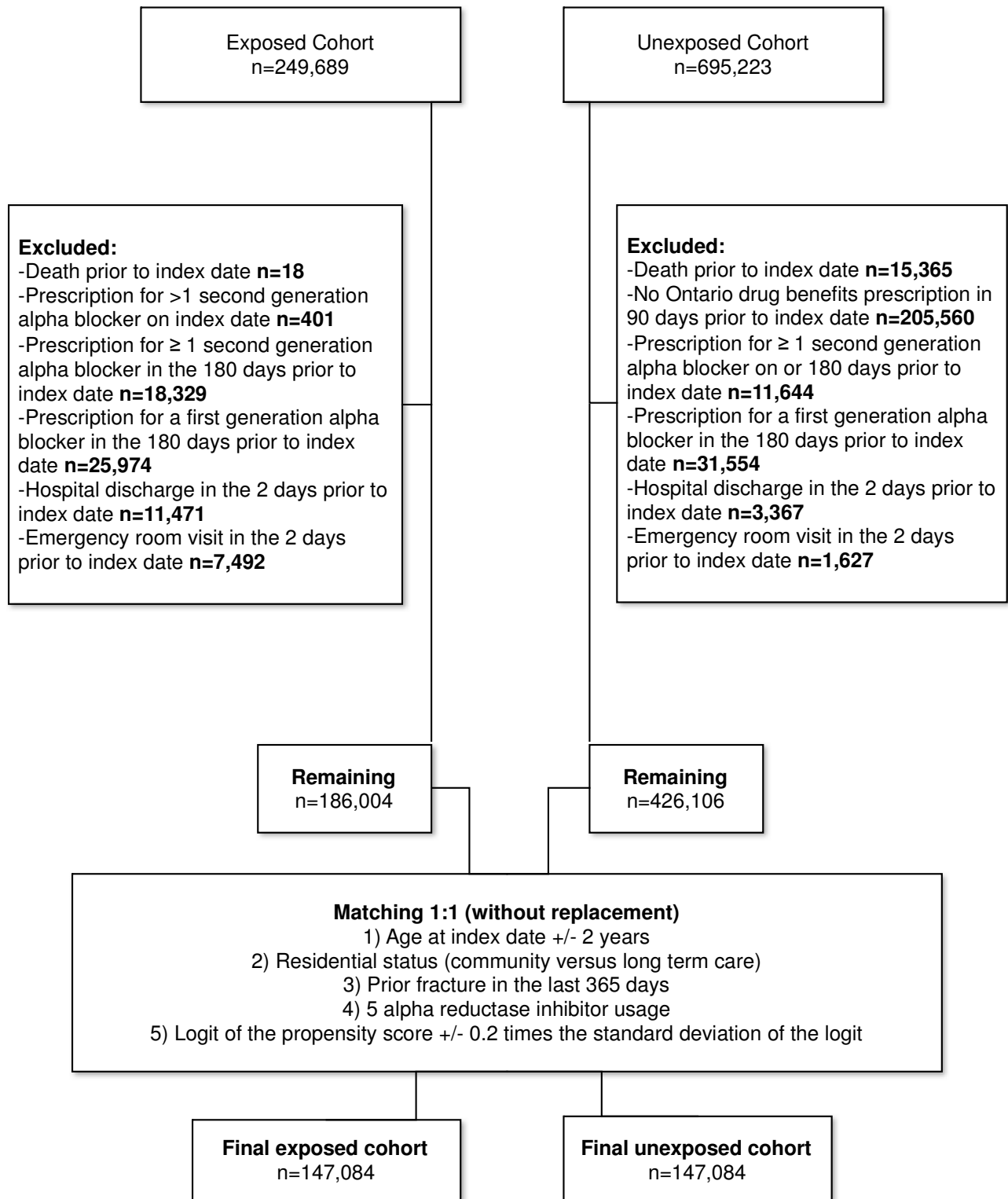**eTable 6.** Study alpha antagonists and their doses and prescription details for the 147,084 exposed men.

	Tamsulosin	Silodosin	Alfuzosin
Number (%)	123537 (84.0%)	2720 (1.8%)	20827 (14.2%)
Median Dose (IQR)	0.4mg (0.4-0.4)	8mg (8-8)	10mg (10-10)
	0.4mg: 114509 (92.7%)	4mg: 354 (13.0%)	10mg: 20418 (98.0%)
	0.8mg: 6802 (5.5%)	8mg: 2324 (85.4%)	20mg: 135 (0.6%)
	Other: 2226 (1.8%)	Other: 42 (1.5%)	Other: 274 (1.3%)
Labelled dose	0.4mg	4mg or 8mg	10mg
Included formulations	Tamsulosin (generic), Flomax™, and Flomax CR™	Rapaflo™	Alfuzosin (generic), and Xatral™
Median Prescription length, days (IQR)	30 (30-60)	30 (30-30)	30 (30-30)
Number (%) of men that refill a prescription within 7 days of predicted end-date of initial prescription	59558 (48.2%)	1465 (53.9%)	10174 (48.9%)

eTable 7. Primary outcomes among exposed and unexposed patients in the 180 days prior to alpha antagonist initiation or index date.

	Events n (%)		Odds Ratio (95% CI)	Change in Percent Absolute Risk (95% CI)
	Future alpha antagonist users (Exposed cohort)	*Future non-alpha antagonist users (Unexposed cohort)*		
	n=119,831	*n=119,831*		
Primary outcome				
Fall	1469 (1.23%)	1595 (1.33%)	0.92 (0.86-0.99)	-0.11 (-0.20 to -0.02)
Fracture	495 (0.41%)	577 (0.48%)	0.86 (0.76-0.97)	-0.07 (-0.12 to -0.01)

Exclusion criteria were reapplied to the study cohort based on a new index date 180 days prior to primary study index date (initiation of alpha antagonist). All eligible matched pairs who were not excluded were retained. The primary outcomes of 90-day risk of fall and fracture were then determined to assess for a potential baseline increased risk of fall and fracture due to lower urinary tract symptoms among men who go on to initiate alpha antagonist therapy in the future.

eFigure 1. Flow diagram of cohort selection.

| Exposed Cohort
n=249,689 | | Unexposed Cohort
n=695,223 |

Excluded:
-Death prior to index date **n=18**
-Prescription for >1 second generation alpha blocker on index date **n=401**
-Prescription for ≥ 1 second generation alpha blocker in the 180 days prior to index date **n=18,329**
-Prescription for a first generation alpha blocker in the 180 days prior to index date **n=25,974**
-Hospital discharge in the 2 days prior to index date **n=11,471**
-Emergency room visit in the 2 days prior to index date **n=7,492**

Excluded:
-Death prior to index date **n=15,365**
-No Ontario drug benefits prescription in 90 days prior to index date **n=205,560**
-Prescription for ≥ 1 second generation alpha blocker on or 180 days prior to index date **n=11,644**
-Prescription for a first generation alpha blocker in the 180 days prior to index date **n=31,554**
-Hospital discharge in the 2 days prior to index date **n=3,367**
-Emergency room visit in the 2 days prior to index date **n=1,627**

Remaining
n=186,004

Remaining
n=426,106

Matching 1:1 (without replacement)
1) Age at index date +/- 2 years
2) Residential status (community versus long term care)
3) Prior fracture in the last 365 days
4) 5 alpha reductase inhibitor usage
5) Logit of the propensity score +/- 0.2 times the standard deviation of the logit

Final exposed cohort
n=147,084

Final unexposed cohort
n=147,084

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