Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

Supplemental Material

eTable 1. STROBE/RECORD checklist.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are 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	*Title, Abstract (Design)* *Abstract*	RECORD 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. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	*Abstract (Design, Setting). Note: due to numerous data sources they are only fully listed in Methods (Data Sources)* *Abstract (Setting)* *Abstract (Design)*
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	*Objective: Introduction (last paragraph), Hypothesis: Methods (study outcomes)*		
Methods					
Study Design	4	Present key elements of study design early in the paper	*Methods (design and setting)*		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	*Methods (design and setting, data sources, 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 *(b) Cohort study* - For matched studies, give matching criteria and number of exposed and unexposed	*Methods (patient population)* *Methods (patient population), eFigure 1*	RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not possible, an explanation should be provided. RECORD 6.2: Any validation studies of the codes or algorithms used to select the population should be referenced. If validation was	*Methods (patient population)* *Reference: Levy AR, O'Brien BJ, Sellors C, et al. Coding accuracy of administrative drug*

				conducted for this study and not published elsewhere, detailed methods and results should be provided. RECORD 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.	*claims in the Ontario Drug Benefit database. Can J Clin Pharmacol 2003;**10**:67–71.* *Methods (design and setting). All individuals were successfully linked in this study.*
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	*Methods (patient population, study outcomes)*	RECORD 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.	*Covariates/ confounders: eTable 2* *Outcomes/effect modifiers: 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	*Covariates/ confounders: eTable 2,* *Outcomes/ effect modifiers: eTable 4*		
Bias	9	Describe any efforts to address potential sources of bias	*Methods (patient population)*		
Study size	10	Explain how the study size was arrived at	*NA*		
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	*Methods (patient population)*		
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) *Cohort study* - If applicable, explain how loss to follow-up was addressed (e) Describe any sensitivity analyses	*Methods (statistical analysis)* *Methods (statistical analysis)* *Methods (data sources)* *Methods (statistical analysis)* *Methods (statistical analysis*)		
Data access and cleaning methods				RECORD 12.1: Authors should describe the extent to which	*Acknowledgements: Contributors*

				the investigators had access to the database population used to create the study population. RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.	*eFigure 1*
Linkage				RECORD 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 (design and setting)*
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	*eFigure 1* *eFigure 1* *eFigure 1*	RECORD 13.1: Describe in detail the selection of the persons included in the study (*i.e.,* study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.	*eFigure 1*
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 (*e.g.*, average and total amount)	*Table 1, eTable 5* *Methods (data sources)* *Table 2*		
Outcome data	15	*Cohort study* - Report numbers of outcome events or summary measures over time	*Table 2*		
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included	*Table 2*		

		(b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	*NA* *Table 2*		
Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	*Results, Table 3*		
Discussion					
Key results	18	Summarise key results with reference to study objectives	*Discussion (principle findings)*		
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 (strengths and limitations)*	RECORD 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.	*Discussion (strengths and limitations)*
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	*Discussion (practise implications)*		
Generalisability	21	Discuss the generalisability (external validity) of the study results	*Discussion (practise implications)*		
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*		
Accessibility of protocol, raw data, and programming code		..		RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, or programming code.	*eResults, Acknowledgements*

eTable 2a. Administrative data definitions used to define medical comorbidities. A 5 year lookback window relative to the index date was used.

Variable	Database	Codes
1. Acute Urinary Retention	CIHI-DAD CIHI-SDS NACRS	ICD-9: 7882 ICD-10: R33, R3912
2. Acute kidney injury	CIHI-DAD	ICD-9: 584 ICD-10: N17
3. Alcoholism	CIHI-DAD OHIP	ICD-9: 3030, 3039, 3050 ICD-10: K70, G721, I426, K292, F10, G621, G312, Z714, K860, T510, E244, T519, E512, X45, X65, Y15, Y573, Z502, Z721
4. Anxiety	CIHI-DAD CIHI-SDS	ICD-9: 30000, 30001, 30002, 30009, 30020, 30022, 30023, 30029, 3004, 3083, 3089, 3090, 30981, 30989 ICD-10: F400, F401, F402, F408, F409, F410, F411, F412, F413, F418, F419, F430, F431, F432, F438, F439
5. Atrial fibrillation/flutter	CIHI-DAD	ICD-9: 4273 ICD-10: I48
6. Benign Prostatic Hyperplasia	CIHI-DAD CIHI-SDS OHIP	ICD-9: 600 ICD-10: N40 OHIP Diagnostic Code: 600
7. Bipolar disorder	CIHI-DAD CIHI-SDS	ICD-9: 29600, 29640, 29651, 29653, 29660, 2967, 29689 ICD-10: F300, F301, F302, F308, F309, F310, F311, F312, F313, F314, F315, F316, F317, F318, F319
8. Bowel Cancer	CIHI-DAD OHIP	ICD-9: 154, 2303, 2304, 2307 ICD-10: C18, C19, C20, D010, D011, D012 OHIP Diagnostic Code: 154
9. Brain tumor	CIHI-DAD CIHI-SDS	ICD-9: 1910, 1911, 1912, 1913, 1914, 1915, 1916, 1917, 1918, 1919, 1920, 1921, 1922, 1923, 1928, 1929, 2375, 2376, 2379, 2370, 2371, 23712, 2373, 2374, 1983, 1984 ICD-10: C70, C71, C72, D42, D43, D479, C793, C794
10. Breast Cancer	CIHI-DAD OHIP	ICD-9: 174, 175, 2330 ICD-10: C50, D05 OHIP Diagnostic Code: 174, 175
11. Chronic kidney disease	CIHI-DAD OHIP	ICD-9: 4030, 4031, 4039, 4040, 4041, 4049, 585, 586, 5888, 5889, 2504 ICD-10: E102, E112, E132, E142, I12, I13, N08, N18, N19 OHIP Diagnostic Code: 403, 585
12. Chronic liver disease	CIHI-DAD OHIP	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 Diagnostic Code: 571, 573, 070, OHIP Fee Code: Z551, Z554
13. Chronic lung disease	CIHI-DAD OHIP	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 Diagnostic Code: 491, 492, 493, 494, 496, 501, 502, 515, 518, 519, OHIP Fee Code: J689, J889
14. Congestive heart failure	CIHI-DAD OHIP 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 Diagnostic Code: 428, OHIP Fee Code: R701, R702, Z429 ICD-9: 410, 411, 412, 413, 414, 4292, 4296, 4297

15. Coronary artery disease or angina	OHIP	ICD-10: I20, I21, I22, I23, I24, I25, Z955, Z958, Z959, R931, T822 CCP: 4801, 4802, 4803, 4804, 4805, 481, 482, 483 CCI: 1IJ26, 1IJ27, 1IJ54, 1IJ57, 1IJ50, 1IJ76 OHIP Diagnostic Code: 410, 412, 413, OHIP Fee Code: R741, R742, R743, G298, E646, E651, E652, E654, E655, G262, Z434, Z448
16. Cranial head trauma	CIHI-DAD CIHI-SDS NACRS	ICD-9: 509, 9510, 9511, 9512, 9513, 9514, 9515, 9516, 9518, 9519, 850, 8500, 8510, 8511, 85181, 85191, 8520, 85201, 8521, 85221, 85241, 8530, 85301, 8531, 85311, 8540, 85401, 8541, 85411, 80300, 9251, 8730, 87200, 8738, 85400, 85409, 87261, 90089, 95909 ICD-10: S04, S06, S07, S08, S09
17. Dementia	CIHI-DAD OHIP	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 Diagnostic Code: 290, 331, 797
18. Depression		See primary outcome tables
19. 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 Human Biosynthetic, Insulin Human Semi-Synthetic, Insulin Injection Pork, Insulin Isophane Injection Pork, Insulin Lispro, Acarbose, Acetohexamide, Chlorpropamide, Gliclazide, Glimepiride, Glyburide, Metformin HCL, Nateglinide, Pioglitazone HCL, Repaglinide, Rosiglitazone Male, Sitagliptin Phosphate Monohydrate, Tolbutamide
20. Encephalitis/atypical CNS disorders/Multi-system atrophy/Progressive supranuclear palsy/Primary lateral sclerosis	CIHI-DAD CIHI-SDS	ICD-9: 0620, 0621, 0622, 0623, 0624, 0625, 0628, 0629, 0461, 0462, 0463, 0468, 0469, 0630, 0632, 0638, 0639, 0499, 0498, 064, 0470, 0471, 0478, 0479, 048, 0490, 0491, 0498, 0499 ICD-10: A81, A83, A84, A85, A86, A87, A88, A89
21. Hypertension	ODB	Acebutolol HCL, Aliskiren Fumarate, Amlodipine Besylate, Amlodipine Besylate & Atorvastatin, Atenolol, Atenolol & Chlorthalidone, Betaxolol HCL, Bisoprolol Fumarate, Brimonidine Tartrate & Timolol Maleate, Brinzolamide & Timolol Maleate, Bumetanide, Candesartan Cilexetil, Candesartan Cilexetil & Hydrochlorothiazide, Captopril, Carvedilol, Chlorthalidone, Diltiazem HCL, Enalapril Sodium, Eprosartan Mesylate, Eprosartan Mesylate & Hydrochlorothiazide, Erythrityl Tetranitrate, Felodipine, Flunarizine HCL, Hydralazine HCL, Hydrochlorothiazide, Indapamide, Irbesartan, Irbesartan & Hydrochlorothiazide, Labetalol HCL, Lisinopril, Losartan Potassium, Losartan Potassium & Hydrochlorothiazide, Metolazone, Metoprolol Tartrate, Minoxidil, Nadolol, Nicardipine HCL, Nifedipine, Nimodipine, Olmesartan Medoxomil, Olmesartan Medoxomil & Hydrochlorothiazide, Oxprenolol HCL, Phenoxybenzamine, Pindolol, Pindolol & Hydrochlorothiazide, Propranolol HCL, Propranolol HCL & Hydrochlorothiazide, Spironolactone, Spironolactone & Hydrochlorothiazide, Telmisartan, Telmisartan & Hydrochlorothiazide, Timolol Maleate, Timolol Maleate & Hydrochlorothiazide, Timolol Maleate & Travoprost, Triamterene, Triamterene & Hydrochlorothiazide, Valsartan, Valsartan & Hydrochlorothiazide, Verapamil HCL
22. Lung cancer	CIHI-DAD OHIP	ICD9: 162, 2312 ICD-10: C34, D022 OHIP Diagnostic Code: 162
23. Melanoma	CIHI-DAD OHIP	ICD-9: 172 ICD-10: C43 OHIP Diagnostic Code: 172
24. Migraine	CIHI-DAD	ICD-9: 3460, 3461, 3462, 3468, 3469, 30781, 34620, 7840

	CIHI-SDS	
	NACRS	ICD-10: G43, G44
25. Multiple sclerosis	CIHI-DAD	ICD-9: 340
	CIHI-SDS	ICD-10: G35
	OHIP	OHIP Diagnostic Code: 340 [≥7 contacts for code 340]
26. Obesity	CIHI-DAD	ICD-9: 2780
	OHIP	ICD-10: E660, E661, E662, E668, E669
		OHIP Diagnostic Code: 278
27. Osteoporosis	CIHI-DAD	ICD-9: 733
	CIHI-SDS	ICD-10: M80, M81
	OHIP	OHIP Diagnostic Code: 733
28. Peripheral vascular disease	CIHI-DAD	ICD-9: 4402, 4408, 4409, 5571, 4439, 444
	OHIP	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, 1IA87LA, 1IB87LA, 1IC87LA, 1ID87, 1KA87LA, 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
29. Personality disorder	CIHI-DAD CIHI-SDS	ICD-9: 30016, 3010, 30120, 3013, 3014, 30150, 30151, 3016, 3017, 30182, 30189, 3019, 3022, 3023, 3023, 3024, 30250, 3026, 30281, 30282, 30284, 30289, 3029, 31230, 31231, 31232, 31233, 31234, 31239 ICD-10: F600, F601, F602, F603, F604, F605, F606, F607, F608, F609, F61, F620, F621, F628, F629, F630, F631, F632, F633, F638, F639, F640, F641, F642, F648, F649, F650, F651, F652, F653, F654, F655, F656, F658, F659, F660, F661, F662, F668, F669, F680, F681, F688, F69
30. Prostate Cancer	OHIP	ICD-9: 185, 2334 ICD-10: C61, D075 OHIP Diagnostic Code: 185
31. Renal cancer	CIHI-DAD	ICD-9: 189
	OHIP	ICD-10: C64
		OHIP Diagnostic Code: 189
32. Rheumatoid arthritis	CIHI-DAD	ICD-9: 714
	OHIP	ICD-10: M05, M06
		OHIP Diagnostic Code: 714
33. Schizophrenia/delusional disorders	CIHI-DAD CIHI-SDS	ICD-9: 29500, 29510, 29520, 29530, 29540, 29550, 29560, 29570, 29580, 29590, 2971, 2973, 2978, 2979, 2983, 2984, 2988, 2989 ICD-10: F200, F201, F202, F203, F204, F205, F206, F208, F209, F21, F220, F228, F229, F230, F231, F232, F233, F238, F239, F24, F250, F251, F252, F258, F259, F28, F29
34. Seizure	CIHI-DAD	ICD-9: 345, 7803 ICD-10: G40, G41, R560, R568
35. Self-harm	CIHI-DAD NACRS OMHRS	See Table 2c (primary outcomes)
36. Stroke or TIA	CIHI-DAD	ICD-9: 430, 431, 432, 434, 435, 436, 3623 ICD-10: I62, I630, I631, I632, I633, I634, I635, I638, I639, I64, H341, I600, I601, I602, I603, I604, I605, I606, I607, I609, I61, G450, G451, G452, G453, G458, G459, H340
37. Substance abuse (excluding alcohol)	CIHI-DAD CIHI-SDS NACRS	ICD-9: 2920, 29211, 2922, 29283, 29289, 2929, 30400, 30410, 30420, 30430, 30440, 30453, 30460, 30490, 30520, 30530, 30540, 30550, 30560, 30570, 30590 ICD-10: F110, F111, F112, F113, F114, F115, F116, F117, F118, F119, F120, F121, F122, F123, F124, F125, F126, F127, F128, F129, F130, F131, F132, F133, F134, F135, F136, F137, F138, F139, F140, F141, F142, F143, F144, F145, F146, F147, F148, F149, F150, F151, F152, F153, F154, F155, F156, F157, F158, F159, F160, F161, F162, F163, F164, F165, F166, F167, F168,

		F169, F180, F181, F182, F183, F184, F185, F186, F187, F188, F189, F190, F191, F192, F193, F194, F195, F196, F197, F198
38. Superficial head trauma	CIHI-DAD CIHI-SDS NACRS	ICD-9: 9180, 9108, 9109, 8700, 87200, 87210, 8730, 8731, 87320, 87330, 87341, 87343, 87351, 87353, 8738, 8739, 80001, 80051, 80101, 80151, 8020, 8021, 80220, 80224, 80228, 80229, 80230, 80234, 80238, 80239, 8024, 8025, 8026, 8027, 8028, 8029, 80300, 80350, 8736, 87363, 8737, 80401, 80451, 8300, 83961, 83969, 8481, 8488, 87363, 8703, 8710, 8711, 8713, 8715, 8717, 9212, 9213, 9219 ICD-10: S00, S01, S02, S03, S05
39. Urinary tract infection	CIHI-DAD CIHI-SDS OHIP NACRS	GP visit code: OHIP Fee Code: A001, A003, A004, A007, A008, A263, A264, A888, A900, A901 K004, K005, 006, K007, K013, K022, K023, K032, K033, K037, K623 With OHIP Diagnostic Code: 599 OR Urology Visit in the past year With OHIP Diagnostic Code: 599 OR Evidence of any UTI code below: ICD-9: 58381, 58390, 59001, 59020, 59080, 59081, 59090, 59500, 59540, 59581, 59589, 59590, 59700, 59780, 59900, 59910, 59911, 99664, 99665 ICD-10: N10, N110, N111, N118, N119, N12, N136, N151, N159, N160, N300, N308, N309, N340, N390, T835

Data sources included CIHI-DAD (inpatient discharge abstracts), CIHI-SDS (same day surgeries), NACRS (National Ambulatory Care Reporting System), OHIP (physician billings and diagnosis descriptions), ODB (universal medication coverage), and OMHRS (Ontario Mental Health Reporting System). 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 hypertension and diabetes (which used a 6 month look-back period due to the use of medications to define these conditions).

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. A 6 month lookback window relative to the index date was used.

Medication class	Medications
1. Alpha antagonist (prostate specific)	Alfuzosin, Apo-Alfuzosin, Auro-Alfuzosin, Flomax, Flomax CR, Rapaflo, Sandoz Alfuzosin, Tamsulosin, Tamsulosin CR, Teva-Alfuzosin PR, Teva-Tamsulosin CR, Xatral
2. Alpha antagonist (non-specific)	Doxazosin Mesylate, Prazosin HCL, Terazosin HCL
3. ACE inhibitors or ARBs	Benazepril HCL, Candesartan Cilexetil, Candesartan Cilexetil & Hydrochlorothiazide, Captopril, Cilazapril, Cilazapril & Hydrochlorothiazide, Enalapril Maleate, Enalapril Sodium, Eprosartan Mesylate, Eprosartan Mesylate & Hydrochlorothiazide, Fosinopril Sodium, Irbesartan, Irbesartan & Hydrochlorothiazide, Lisinopril, Lisinopril & Hydrochlorothiazide, Losartan Potassium, Losartan Potassium & Hydrochlorothiazide, Olmesartan Medoxomil, Olmesartan Medoxomil & Hydrochlorothiazide, Perindopril Erbumine, Perindopril Erbumine & Indapamide, Quinapril HCL, Quinapril HCL & Hydrochlorothiazide, Ramipril, Ramipril & Hydrochlorothiazide, Telmisartan, Telmisartan & Hydrochlorothiazide, Trandolapril, Valsartan, Valsartan & Hydrochlorothiazide
4. Androgen deprivation therapy	Buserelin Acetate, Leuprolide Acetate, Goserelin Acetate
5. Antibiotic	Amikacin, Amikacin Sulfate, 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 Sulfate & Threonine, Bacitracin Zinc & Neomycin Sulfate & Polymyxin B Sulfate, Bacitracin Zinc & Polymyxin B Sulfate, Carbenicillin, Carbenicillin Disodium, Cefaclor, Cefadroxil, Cefadroxil Monohydrate, Cefazolin Sodium, Cefepime HCL, Cefixime, Cefoperazone Sodium, Cefotaxime Sodium, Cefoxitin Sodium, Cefprozil, Cephalexin Monohydrate, Cephalothin Sodium, Cephradine, Ciprofloxacin, Ciprofloxacin HCL, Ciprofloxacin HCL & Dexamethasone, Clarithromycin, 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 & Sulfisoxazole, Erythromycin Gluceptate, Erythromycin Lactobionate, Erythromycin Stearate, Flucloxacillin Sodium, Fluocinolone Acetonide & Neomycin Sulfate & Polymyxin B Sulfate, Framycetin Sulfate, Fusidic Acid, Fusidic Acid Sodium, Gatifloxacin, Gentamicin, Gentamicin & Colistin, Gentamicin Sulfate, Gramicidin & Neomycin Sulfate & Polymyxin B Sulfate, Gramicidin & Polymyxin B Sulfate, Grepafloxacin HCL, Levofloxacin, Linezolid, Moxifloxacin HCL, Mupirocin, Neomycin Sulfate, Neomycin Sulfate & Polymyxin B Sulfate, Netilmicin Sulfate, 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 & Trimethoprim, Spectinomycin HCL, Spiramycin, Streptomycin, Streptomycin Sulfate, Sulfabenzamide & Sulfacetamide & Sulfathiazole, Sulfacetamide Sodium, Sulfadiazine, Sulfadiazine & Trimethoprim, Sulfamethoxazole, Sulfamethoxazole & Trimethoprim, Sulfapyridine, Sulfisoxazole, Telithromycin, Tobramycin, Tobramycin Sulfate, Trimethoprim
6. Anticoagulant	Dabigatran Etexilate, Dalteparin Sodium, Danaparoid Sodium, Enoxaparin, Enoxaparin Sodium, Fondaparinux Sodium, Heparin, Heparin Calcium, Heparin Sodium, Lepirudin, Nadroparin Calc, Rivaroxaban, Tinzaparin Sodium
7. Anticonvulsants	Ethosuximide, Fosphenytoin, Gabapentin, Lacosamide, Levetiracetam, Magnesium Pyrogluconate, Magnesium Sulfate, Mephenytoin, Mephobarbital, Methsuximide, Oxcarbazepine, Phenobarbital, Phensuximide, Phenytoin, Phenytoin Sodium, Pregabalin, Primidone, Secobarbital Sodium, Topiramate, Vigabatrin
8. Antidepressants (SSRIs, SNRIs)	Act Venlafaxine XR, Apo-Venlafaxine XR, Auro-Venlafaxine XR, Citalopram Hbr, Citalopram Hydrobromide, Dom-Venlafaxine XR, Effexor Tablets, 37.5mg, Effexor Tablets, 50mg, Effexor XR, Escitalopram Oxalate, Fluoxetine, Fluoxetine HCL, Fluvoxamine, Fluvoxamine Maleate, Gd-Venlafaxine XR, Mylan-Venlafaxine XR,

	Nefazodone HCL, Ntp-Venlafaxine XR, Paroxetine, Paroxetine HCL, Phl-Venlafaxine XR, Pms-Venlafaxine XR, Pristiq, Ran-Venlafaxine XR, Riva-Venlafaxine XR, Sandoz Venlafaxine XR, Sertraline, Sertraline HCL, Teva-Venlafaxine XR, Venlafaxine Hydrochloride Extended-Release Capsules, Venlafaxine XR
9. Antidepressants (Other)	Amitriptyline, Amitriptyline HCL, Amitriptyline HCL & Baclofen, Amitriptyline HCL & Perphenazine, Amoxapine, Bupropion HCL, Clomipramine HCL, Desipramine HCL, Doxepin HCL, Duloxetine, Imipramine, Imipramine HCL, Isocarboxazid, Maprotiline HCL, Mirtazapine, Moclobemide, Nortriptyline, Nortriptyline HCL, Phenelzine Sulfate, Protriptyline HCL, Selegiline HCL, Tranylcypromine Sulfate, Trazodone HCL, Trimipramine, Trimipramine Maleate
10. Antiemetic	Metoclopramide HCL, Domperidone Maleate, Domperidone
11. Antineoplastic	Abatacept, Aldesleukin, Alemtuzumab, Altretamine, Aminoglutethimide, Anastrozole, Asparaginase, Azathioprine, Bicalutamide, Bleomycin Sulfate, Buserelin Acetate, Busulfan, Capecitabine, Carmustine, Chlorambucil, Cladribine, Cyclophosphamide, Cyproterone Acetate, Cytarabine, Dacarbazine, 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, Porfimer Sodium, Procarbazine HCL, Rituximab, Sirolimus, Sorafenib, Sunitinib Malate, Tacrolimus, Tamoxifen Citrate, Temozolomide, Thioguanine, Thiotepa, Tretinoin, Triptorelin, Triptorelin Pamoate, Vaccine - B.C.G., Vinblastine Sulfate, Vincristine Sulfate
12. Antiparkinson's Medications	Benserazide HCL & Levodopa, Bromocriptine, Bromocriptine Mesylate, Carbidopa & Entacapone & Levodopa, Carbidopa & Levodopa, Entacapone, Levodopa, Levodopa & Carbidopa, Neurological Disorders, Misc, Pergolide Mesylate, Pramipexole Dihydrochloride Monohydrate, Pramipexole HCL, Rasagiline Mesylate, Ropinirole HCL, Selegiline HCL, Tolcapone
13. Antiplatelet	Acetylsalicylic Acid & Dipyridamole, Clopidogrel, Clopidogrel Bisulfate, Dipyridamole, Prasugrel HCL, Ticlopidine, Ticlopidine HCL
14. Antipsychotic (atypical)	Aripiprazole, Quetiapine Fumarate, Risperidone, Olanzapine
15. Antipsychotic (other)	Chlorpromazine HCL, Clozapine, Codeine Phosphate & Phenylephrine HCL & Potassium Guaiacolsulfonate & Promethazine HCL, Codeine Phosphate & Potassium Guaiacolsulfonate & Promethazine HCL, Dextromethorphan HBR & Promethazine HCL & Pseudoephedrine HCL, Flupenthixol Decanoate, Flupenthixol HCL, Fluphenazine Decanoate, Fluphenazine Enanthate, Fluphenazine HCL, Guaiacolsulfonate Potassium & Phenylephrine HCL & Promethazine HCL, Haloperidol, Haloperidol Decanoate, Isopropamide Iodide & Prochlorperazine Maleate, Loxapine HCL, Loxapine Succinate, Meperidine HCL & Promethazine HCL, Mesoridazine Besylate, Methotrimeprazine, Olanzapine Tartrate, Paliperidone, Pericyazine, Perphenazine, Pimozide, Pipotiazine Palmitate, Potassium Guaiacolsulfonate & Promethazine HCL, Prochlorperazine, Prochlorperazine Dimaleate, Prochlorperazine Maleate, Prochlorperazine Mesylate, Promethazine, Promethazine HCL, Risperidone, Sulpiride, Thioridazine HCL, Thiothixene, Trifluoperazine HCL, Ziprasidone HCL, Zuclopenthixol Acetate, Zuclopenthixol Decanoate, Zuclopenthixol Dihydrochloride
16. Benzodiazepine	Alprazolam, Bromazepam, Chlordiazepoxide HCL, Chlordiazepoxide HCL & Clidinium Bromide, Clobazam, Clonazepam, Clorazepate Dipotassium, Diazepam, Diazepam & Methylcellulose, Estazolam, Flumazenil, Flurazepam HCL, Flurazepam Hydrochloride, Ketazolam, Lorazepam, Midazolam HCL, Nitrazepam, Oxazepam, Temazepam, Triazolam, Zaleplon, Zopiclone
17. Beta blockers	Acebutolol HCL, Atenolol, Atenolol & Chlorthalidone, Betaxolol HCL, Bisoprolol Fumarate, Brimonidine Tartrate & Timolol Maleate, Brinzolamide & Timolol Maleate, Carvedilol, Labetalol HCL, Metoprolol Tartrate, Nadolol, Oxprenolol HCL, Pindolol, Pindolol & Hydrochlorothiazide, Propranolol HCL, Propranolol HCL & Hydrochlorothiazide, Sotalol HCL, Timolol Maleate, Timolol Maleate & Travoprost
18. Bisphosphonate	Alendronate, Alendronate Sodium, Alendronate Sodium & Cholecalciferol, Calcium Carbonate & Etidronic Acid, Calcium Carbonate & Etidronic Acid Sodium, Calcium Carbonate & Risedronate Sodium, Clodronate Disodium, Clodronic Acid Disodium,

	Etidronate & Calcium Carbonate, Etidronate Disodium, Etidronic Acid Disodium, Ibandronate, Pamidronate Disodium, Pamidronic Acid Disodium, Risedronate Sodium, Risedronate Sodium & Calcium, Risedronate Sodium & Calcium & Vitamin D3, Zoledronic Acid
19. Calcium channel blockers	Amlodipine Besylate, Amlodipine Besylate & Atorvastatin, Diltiazem HCL, Erythrityl Tetranitrate, Felodipine, Flunarizine HCL, Nicardipine HCL, Nifedipine, Nimodipine, Verapamil HCL
20. Cholinesterase inhibitors	APO-Rivastigmine, Aricept, Exelon, Mylan-Galantamine ER, Mylan-Rivastigmine, Pat-Galantamine ER, PMS-Rivastigmine, Ratio-Rivastigmine, Reminyl, Reminyl ER, Sandoz-Rivastigmine, Teva-Rivastigmine
21. Coumadin	Warfarin
22. Digoxin	Digoxin
23. Glucocorticoids	Betameth, Budesoni, Cortison, Dexameth, Fludroco, Hydrocor, Methylpr, Predniso, Triamcin
24. Inhaled acetylcholine	Ipratropium Bromide, Tiotropium Bromide
25. Inhaled beta-agonist	Albuterol, Albuterol & Albuterol Sulfate, Albuterol Sulfate, Albuterol Sulfate & Ipratropium Bromide, Budesonide & Formoterol Fumarate, Fenoterol HBR, Fluticasone Propionate & Salmeterol Xinafoate, Foradil, Metaproterenol Sulfate, Oxeze, Pirbuterol Acetate, Procaterol HCL, Salmeterol Xinafoate, Terbutaline Sulfate, Zenhale
26. Inhaled corticosteroid	Beclomethasone Dipropionate, Budesonide, Ciclesonide, Flunisolide, Fluticasone Propionate, Triamcinolone Acetonide
27. Mood stabilizer	Lamotrigine, Lithium Carbonate, Lithium Citrate, Carbamazepine
28. 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 & Pentazocine 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, Bupivacaine & Fentanyl, Butorphanol Tartrate, Codeine, Codeine Phosphate, Codeine Sulfate, Dextromethorphan Hbr & Guaifenesin & Menthol, Dextropropoxyphene HCL, Dextropropoxyphene Napsylate, Diamorphine HCL, Fentanyl, Fentanyl & Baclofen, Fentanyl & Baclofen & Clonidine, Fentanyl & Bupivacaine, Fentanyl & Bupivacaine & Baclofen, Fentanyl & Bupivacaine & Clonidine, Fentanyl & Bupivicaine & Clonidine & Baclofen, Fentanyl & Clonidine HCL, Fentanyl Citrate, Hydrocodone Bitartrate & Ibuprofen, Hydromorphine & Bupivicaine & Clonidine, Hydromorphone, Hydromorphone & Baclofen, Hydromorphone & Bupivicaine, Hydromorphone & Bupivicaine & Baclofen, Hydromorphone & Bupivicaine & Baclofen & Clonidine, Hydromorphone & Bupivicaine & Clonidine, Hydromorphone Hbr, Hydromorphone HCL, Ibuprofen & Diphenhydramine HCL, Levorphanol Tartrate, Meperidine HCL, Morphine, Morphine & Baclofen, Morphine & Bupivicaine, Morphine & Bupivicaine & Baclofen, Morphine & Lioresal, Morphine HCL, Morphine Succinate, Morphine Sulfate, Nalbuphine HCL, Naloxone HCL & Oxycodone HCL, Narcotic Compound, Opium, Opium & Belladonna, Opium & Camphor, Opium Tincture, Oxycodone HCL, Oxymorphone HCL, Pentazocine HCL, Pentazocine Lactate, Propoxyphene HCL, Remifentanil HCL, Sufentanil Citrate, Tapentadol HCL, Tramadol, Tramadol HCL
29. Non-potassium sparing diuretics	Bumetanide, Chlorthalidone, Ethacrynic Acid, Furosemide, Hydrochlorothiazide, Indapamide, Methyldopa & Hydrochlorothiazide, Metolazone, Timolol Maleate & Hydrochlorothiazide
30. Nonsteroidal anti-inflammatories (excluding aspirin)	Cannabidiol & Dronabinol, Celecoxib, Diclofenac Sodium, Diclofenac Sodium & Misoprostol, Diflunisal, Etodolac, Fenoprofen Calcium, Floctafenine, Flurbiprofen, Glucosamine & Chondroitin, Ibuprofen, Indomethacin, Ketoprofen, Ketorolac Tromethamine, Mefenamic Acid, Meloxicam, Nabumetone, Naproxen, Naproxen

	Sodium, Oxaprozin, Phenylbutazone, Piroxicam, Rofecoxib, Sulindac, Tenoxicam, Tiaprofenic Acid, Tolmetin Sodium, Valdecoxib
31. Overactive bladder medication	Darifenacin, Flavoxate HCL, Oxybutynin, Oxybutynin Chloride, Solifenacin Succinate, Tolterodine Tartrate, Trospium Chloride, Trospium Hydroxide Chloride
32. Potassium sparing diuretics	Amiloride HCL, Amiloride HCL & Hydrochlorothiazide, Eplerenone, Spironolactone, Spironolactone & Hydrochlorothiazide, Triamterene, Triamterene & Hydrochlorothiazide
33. Proton Pump inhibitors	Amoxicillin Trihydrate & Clarithromycin & Lansoprazole, Dexlansoprazole, Esomeprazole Magnesium, Lansoprazole, Lansoprazole Sodium, Omeprazole, Omeprazole Magnesium, Pantoprazole, Pantoprazole Magnesium, Pantoprazole Sodium, Rabeprazole Sodium
34. Smoking cessation aid	Varenicline Tartrate, Bupropion HCL, Nicotine
35. Statins	Atorvastatin, Cerivastatin Sodium, Fluvastatin Sodium, Lovastatin, Pravastatin Sodium, Rosuvastatin Calcium, Simvastatin
36. Testosterone replacement	Androderm, Androgel, Methyltestosterone, Testim, Testosterone, Testosterone Cipionate, Testosterone Cypionate, Testosterone Decanoate, Testosterone Enanthate, Testosterone Powder, Testosterone Propionate

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. A 1 year lookback window relative to the index date was used.

Variable	Database	Codes
1. Bone mineral density test	OHIP	OHIP Fee Code: J654, J688, J854, J888, X149, X152, X153, X155, Y654, Y688, Y854, Y888
2. Bone scan	OHIP	OHIP Fee Code: J850, J650, J852, J862
3. Cardiac catheterization	CIHI-DAD	CCP: 4995, 4996, 4997
	OHIP	CCI: 3IJ30GP, 3HZ30GP, 2HZ24GPKJ, 2HZ24GPKL, 2HZ24GPKM, 2HZ24GPXJ, 2HZ28GPPL, 2HZ71GP
		OHIP Fee Code: G296, G297, G299, G300, G301, G304, G305, G306
4. Cardiac stress test	CIHI-DAD	CCP: 0341, 0342, 0343, 0344, 0605
	OHIP	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
5. Carotid endarterectomy	OHIP	OHIP Fee Code: N220, R792
6. Carotid ultrasound	CIHI-DAD	CCP: 0281
	OHIP	CCI: 3JE30, 3JG30
		OHIP Fee Code: J201, J501, J190, J191, J490, J491, J492
7. Chest x-ray	OHIP	OHIP Fee Code: X090, X091, X092, X195
8. CT head	OHIP	OHIP Fee Code: X188, X400, X401, X402, X405, X408
9. CT spine	OHIP	OHIP Fee Code: X128, X415, X416
10. Echocardiography	CIHI-DAD	CCP: 0282
	OHIP	CCI: 3IP30
		OHIP Fee Code: G560, G561, G562, G566, G567, G568, G570, G571, G572, G574, G575, G576, G577, G578, G581
11. ECT	OHIP	OHIP Fee Code: G478, G479
12. EEG	OHIP	OHIP Fee Code: G414, G415, G416, G417, G418, G540, G542, G544, G545, G546, G554, G555
13. Heart valve replacement	OHIP	OHIP Fee Code: R728, R735, R738, R772
14. Holter monitoring	CIHI-DAD	CCP: 0354
	OHIP	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
15. MRI head	OHIP	OHIP Fee Code: X421, X425
16. MRI spine	OHIP	OHIP Fee Code: X490, X492, X493, X495, X496, X498
17. Prostate-specific antigen (PSA) test	OHIP	OHIP Fee Code: L358
18. Pulmonary function test	OHIP	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
19. TRUS biopsy	OHIP	OHIP Fee Code: E780 , Z712
20. TURP	OHIP	OHIP Fee Code: S655, S654
21. Urine culture	OHIP	OHIP Fee Code: L633, L634, L641

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 OHIP, 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. Variables were included based on 1) an initial standardized difference >7%, 2) a potentially important relationship with study outcomes, or 3) a standardized difference >10% after initial matching.[1]

Demographics	**Reason for inclusion**
Age	SD > 0.07
Socioeconomic status	Potential confounder
Residing in a long-term care facility	SD > 0.07
Comorbid medical conditions	
BPH	SD > 0.07
Prostate Cancer	SD > 0.07 after initial matching
Alcoholism	Potential confounder
Acute urinary retention	SD > 0.07
Diabetes	SD > 0.07
Hypertension	SD > 0.07
UTI	SD > 0.07
Substance abuse	Potential confounder
Schizophrenia/delusional disorder	Potential confounder
Bipolar	Potential confounder
Personality disorder	Potential confounder
Comorbidity Index	
Charlson comorbidity score	SD > 0.07 after initial matching
John Hopkins Aggregated Diagnostic Groups (ADG)	SD > 0.07
Medication use	
Prostate specific alpha blocker	SD > 0.07
Antipsychotics	Potential confounder
Atypical Antipsychotics	Potential confounder
Mood stabiliser	Potential confounder
ACEI/ARB	SD > 0.07
Benzodiazepine	Potential confounder
Antineoplastic	SD > 0.07
Antibiotic	SD > 0.07
Androgen deprivation therapy	SD > 0.07
Overactive bladder medications	SD > 0.07
Narcotics	Potential confounder
Total number of unique medications	SD > 0.07
Hospital and physician utilization	
Number of hospital admissions	SD > 0.07
Number of psychiatric hospital admissions	Potential confounder
Number of emergency room visits	SD > 0.07
Number of family physician visits	SD > 0.07
Number of family physician mental health visits	Potential confounder
Number of psychiatry visits	Potential confounder
Number of urologist visits	SD > 0.07
Medical investigations and procedures	
Electroconvulsive therapy	Potential confounder
CT head	Potential confounder
MRI head	Potential confounder
Pulmonary function test	SD > 0.07
Urine culture	SD > 0.07
Prior TURP	SD > 0.07 after initial matching
Prostate specific antigen test	SD > 0.07
Transrectal ultrasound guided prostate biopsy	SD > 0.07

5ARIs in our study population are only indicated for the treatment of lower urinary tract symptoms from BPH. They may have also been used to treat gross hematuria in BPH patients, and although they may reduce the risk of prostate cancer[2], they were not approved, or widely used for this indication. The potential confounders of socioeconomic status, alcoholism, psychiatric diseases and medications, narcotics, electroconvulsive therapy and CT/MRI head were included due to a potential relationship with suicide or depression, although prior to the propensity score adjustment these were well balanced and therefore unlikely to confound our results. Exposed

men had a higher level of hospital/emergency room admissions, and family physician visits, which may have led to an increased risk of our secondary outcomes due to the increased health care contact leading to a greater propensity to diagnose depression or detect self-harm if they were not included in the propensity score. Similarly, exposed men tended to have more medical comorbidities, as measured by the John Hopkins ADG score, which is a risk factor for suicide.

References (eTable 3)

[1]Austin PC. Using the standardized difference to compare the prevalence of a binary variable between two groups in observational research. *Communications in Statistics - Simulation and Computation* 2009;38:1228–34.
[2] Thompson, I. M., Goodman, P. J., Tangen, C. M., Lucia, M. S., Miller, G. J., Ford, L. G., et al. (2003). The influence of finasteride on the development of prostate cancer. *The New England Journal of Medicine*, *349*(3), 215–224.

eTable 4. Coding definition for primary and secondary outcomes.

	Data sources	Codes
Suicide	ORGD	ICD 10 X60-X84
	NACRS	ICD 10 X60-X84 AND visdisp2002 = 10 or 11 (dead on arrival or death after arrival)
	OMHRS	Discharge reason = 2 (died from suicide)
	CIHI-DAD	ICD 10 X60-X84 AND dischdisp=07 (death after arrival) or suicide=1
Probable suicide	ORGD	ICD 10 Y10-32, Y34
	NACRS	ICD 10 Y10-32, Y34 AND visdisp2002 = 10 or 11 (dead on arrival or death after arrival)
	CIHI-DAD	ICD 10 Y10-32, Y34 AND dischdisp=07 (death after arrival)
Self-harm*	NACRS	ICD 10 X60-X84
	OMHRS	Self-injury attempts ≥1, Self-injury intent=true, Self-injury considered=true, Self-injury plan=true
Depression	CIHI-DAD	ICD 10 F32.0, F32.1, F32.2, F32.3, F32.8, F32.9, F33.0, F33.1, F33.2, F33.3, F33.4, F33.8, F34.1
	OHIP	≥2 family physician visits within 2 years, each with ICD 9 311 ≥1 psychiatry visit with ICD 9 311
	OMHRS	Axis I code for major depressive disorder (29620-29626, 29630-29636, 31100)

*Self-harm includes suicide attempts and para-suicide behavior that presents to the emergency room (ICD 10 X60-84), and men with a recent history of suicide attempt/para-suicide behavior that results in admission to a psychiatric hospital (Self-injury attempts ≥1). It also includes men who are admitted to a psychiatric hospital because of only thoughts of self-harm (Self-injury intent=true, Self-injury considered=true, Self-injury plan=true).

ORGD (Ontario register general death) contains cause of death for all residents based on death certificates. NACRS (National Ambulatory Care Reporting System, all emergency room visits), OMHRS (Ontario Mental Health Reporting System, all psychiatric hospitalisations after 2005), and CIHI-DAD (Canadian Institute for health informatics inpatient discharge abstracts) are based on data extracted from medical records by trained abstractors, and data quality is maintained though audit-feedback systems. Data on diagnoses are coded using ICD 10. For NACRS, OMHRS, and CIHI-DAD, up to 25 diagnoses can be coded per patient per admission/visit. Data elements have >80% agreement with medical records during reabstraction studies. [1-3]

A prior validation study[4] demonstrated that Ontario coroners had high inter-rater consistency when identifying deaths from hanging and carbon monoxide poisoning as suicide, however were more likely to code over the counter medication overdose, heroin intoxication, or drowning suicides as an undetermined cause of death. Older males in Canada who die from suicide tend to use methods with little equivocation as to intent (firearm, hanging, suffocation).[5] Coroner reports have been used in numerous studies to evaluate suicide rates and risk factors.[6]

Validation studies in the United Kingdom assessing the electronic coding accuracy of suicide as a cause of death, and self-harm behavior have suggested that the positive predictive value of suicide coding is 88% (78-94%) and the positive predictive value of self-harm coding is 89% (82 to 95%).[7] The ICD 10 codes used for suicide and self-harm have been used in several prior Ontario-based studies. [8-10]

A systematic review has summarised the results of validation studies for administrative data definitions of depression.[11] Positive predictive values for ICD 10 coding algorithms range from 89.5 to 91.1%, and jurisdiction specific algorithms were recommended. A Canadian study[12] validated the use of physician billing records and hospital discharge abstracts for identifying depression, and this definition was used for our study (with the addition of OMHRS data, which would be expected to improve the specificity of this algorithm further). The algorithm's sensitivity was 77.5%, specificity 93.0%, positive predictive value 91.6%, negative predictive value 80.7%, Kappa 0.71 (95% CI 0.64 to 0.77).

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eTable 5. Complete baselines for unmatched and matched cohorts.

		Pre-match					Post-match				
		Unexposed		Exposed		SD*	Unexposed		Exposed		SD
Demographics		N	%	N	%		N	%	N	%	
Age	Mean (SD)	74.85 (6.74)		75.52 (6.66)		0.1	75.84 (6.86)		75.56 (6.69)		0.05
	Median (IQR)	74 (69-79)		75 (70-80)			75 (70-81)		75 (70-80)		
	66-69.9	141589	26.8%	23803	22.4%	0.1	20133	21.6%	20832	22.4%	0.02
	70-74.9	143425	27.1%	28063	26.4%	0.02	24031	25.8%	24394	26.2%	0.01
	75-79.9	113329	21.4%	25338	23.8%	0.06	21612	23.2%	22126	23.7%	0.01
	80-84.9	77144	14.6%	17679	16.6%	0.06	15851	17.0%	15567	16.7%	0.01
	85-89.9	38173	7.2%	8580	8.1%	0.03	8283	8.9%	7602	8.2%	0.03
	≥90	14751	2.8%	2966	2.8%	0	3287	3.5%	2676	2.9%	0.03
Fiscal Year of Cohort Entry (index date)	2003	503	0.1%	127	0.1%	0.00	85	0.1%	91	0.1%	0.00
	2004	25682	4.9%	5991	5.6%	0.03	4349	4.7%	4455	4.8%	0.00
	2005	36221	6.9%	8319	7.8%	0.03	6436	6.9%	6429	6.9%	0.00
	2006	39863	7.5%	8971	8.4%	0.03	7184	7.7%	7164	7.7%	0.00
	2007	49914	9.4%	10858	10.2%	0.03	9009	9.7%	9003	9.7%	0.00
	2008	54721	10.4%	11590	10.9%	0.02	9879	10.6%	9907	10.6%	0.00
	2009	63501	12.0%	12927	12.1%	0.00	11397	12.2%	11477	12.3%	0.00
	2010	68260	12.9%	13432	12.6%	0.01	12618	13.5%	12492	13.4%	0.00
	2011	69859	13.2%	13201	12.4%	0.02	12458	13.4%	12478	13.4%	0.00
	2012	59317	11.2%	10697	10.1%	0.04	10133	10.9%	10061	10.8%	0.00
	2013	60570	11.5%	10316	9.7%	0.06	9649	10.4%	9640	10.3%	0.00
Rural Residence	N (%)	81763	15.5%	13996	13.2%	0.07	12741	13.7%	12610	13.5%	0.01
Socioeconomic Status	1 - Lowest	95324	18.0%	17781	16.7%	0.03	15773	16.9%	15740	16.9%	0.00
	2	107315	20.3%	20919	19.7%	0.02	18286	19.6%	18295	19.6%	0.00
	3	103899	19.7%	20839	19.6%	0.00	18483	19.8%	18493	19.8%	0.00
	4	108027	20.4%	22272	20.9%	0.01	19376	20.8%	19506	20.9%	0.00
	5 - Highest	112074	21.2%	24295	22.8%	0.04	21279	22.8%	21163	22.7%	0.00
	Missing	1772	0.3%	323	0.3%	0.08					
Residential status - Long-Term Care	N (%)	16755	3.2%	2098	2.0%	0.08	2255	2.4%	1990	2.1%	0.02
Comorbidities											
Acute kidney injury	N (%)	11500	2.2%	2564	2.4%	0.01	2526	2.7%	2236	2.4%	0.02
Acute urinary retention	N (%)	19682	3.7%	11988	11.3%	0.29	9683	10.4%	9397	10.1%	0.01
Alcoholism	N (%)	5421	1.0%	784	0.7%	0.03	739	0.8%	723	0.8%	0.00
Anxiety	N (%)	2284	0.4%	506	0.5%	0.01	426	0.5%	445	0.5%	0.00
Atrial fibrillation/flutter	N (%)	33939	6.4%	7018	6.6%	0.01	6764	7.3%	6157	6.6%	0.03
Benign Prostatic Hyperplasia	N (%)	123072	23.3%	72375	68.0%	1	62977	67.6%	59474	63.8%	0.08
Bipolar Disorder	N (%)	679	0.1%	115	0.1%	0.00	115	0.1%	98	0.1%	0.00
Cancer	N (%)	33583	6.4%	6849	6.4%	0.00	6480	7.0%	5977	6.4%	0.02

Bowel Cancer	N (%)	12493	2.4%	2308	2.2%	0.01	2122	2.3%	2031	2.2%	0.01
Brain tumor	N (%)	453	0.1%	94	0.1%	0.00	84	0.1%	83	0.1%	0.00
Breast Cancer	N (%)	1921	0.4%	365	0.3%	0.02	347	0.4%	324	0.3%	0.02
Lung Cancer	N (%)	8853	1.7%	1658	1.6%	0.01	1582	1.7%	1442	1.5%	0.02
Melanoma	N (%)	7792	1.5%	1772	1.7%	0.02	1551	1.7%	1572	1.7%	0.00
Prostate cancer	N (%)	61104	11.6%	13531	12.7%	0.03	13602	14.6%	12167	13.1%	0.04
Renal Cancer	N (%)	4619	0.9%	1146	1.1%	0.02	1251	1.3%	977	1.0%	0.03
Chronic kidney disease	N (%)	43161	8.2%	8853	8.3%	0.00	9246	9.9%	7819	8.4%	0.05
Chronic liver disease	N (%)	17923	3.4%	3692	3.5%	0.01	3344	3.6%	3202	3.4%	0.01
Chronic lung disease (including COPD)	N (%)	130423	24.7%	27689	26.0%	0.03	25306	27.2%	24047	25.8%	0.03
Congestive heart failure	N (%)	61684	11.7%	12260	11.5%	0.01	11560	12.4%	10814	11.6%	0.02
Coronary artery disease with angina	N (%)	205409	38.9%	41802	39.3%	0.01	38074	40.9%	36487	39.2%	0.03
Cranial head trauma	N (%)	11197	2.1%	2341	2.2%	0.01	2238	2.4%	2022	2.2%	0.01
Dementia	N (%)	48659	9.2%	9369	8.8%	0.01	9720	10.4%	8354	9.0%	0.05
Encephalitis/atypical CNS/MSA/PSP/PLS	N (%)	62	0.0%	7	0.0%	0.01	14	0.0%	<6	0.0%	0.01
Migraine	N (%)	1507	0.3%	341	0.3%	0.00	316	0.3%	273	0.3%	0.00
MS	N (%)	1225	0.2%	257	0.2%	0.00	272	0.3%	215	0.2%	0.02
Obesity	N (%)	23090	4.4%	4645	4.4%	0.00	4177	4.5%	4023	4.3%	0.01
Osteoporosis	N (%)	27394	5.2%	6889	6.5%	0.06	5941	6.4%	5880	6.3%	0.00
Peripheral vascular disease	N (%)	11069	2.1%	1770	1.7%	0.03	1867	2.0%	1578	1.7%	0.02
Personality disorder	N (%)	323	0.1%	46	0.0%	0.04	48	0.1%	37	0.0%	0.04
Prior depression	N (%)	16637	3.1%	3818	3.6%	0.03	3353	3.6%	3353	3.6%	0.00
Prior non-depression mental health (schizophrenia, bipolar, anxiety)	N (%)	4096	0.8%	777	0.7%	0.01	693	0.7%	683	0.7%	0.00
Prior self-harm	N (%)	1298	0.2%	255	0.2%	0.00	191	0.2%	191	0.2%	0.00
Rheumatoid arthritis	N (%)	19357	3.7%	4181	3.9%	0.01	3763	4.0%	3638	3.9%	0.01
Schizophrenia/ delusional	N (%)	1288	0.2%	181	0.2%	0.00	178	0.2%	163	0.2%	0.00
Seizure	N (%)	3209	0.6%	553	0.5%	0.01	597	0.6%	475	0.5%	0.01
Stroke or TIA	N (%)	15788	3.0%	3291	3.1%	0.01	2845	3.1%	2925	3.1%	0.00
Substance abuse	N (%)	766	0.1%	161	0.2%	0.03	144	0.2%	142	0.2%	0.00
Superficial head trauma	N (%)	24238	4.6%	4899	4.6%	0.00	4646	5.0%	4297	4.6%	0.02
Urinary tract infection	N (%)	101382	19.2%	38806	36.5%	0.39	33957	36.4%	32221	34.6%	0.04
Comorbidities by Medication use in 180 days prior to the index date											
Diabetes	N (%)	112395	21.3%	19293	18.1%	0.08	17385	18.7%	17352	18.6%	0
Hypertension	N (%)	314514	59.5%	59727	56.1%	0.07	54648	58.6%	52555	56.4%	0.04
Comorbidity Index (based on 3 year lookback window)											
Charlson comorbidity index	Mean (SD)	0.54 (1.24)		0.5 (1.17)		0.03	0.56 (1.21)		0.52 (1.2)		0.04
	Median (IQR)	0 (0-0)		0 (0-0)			0 (0-1)		0 (0-0)		
	0	403218	76.3%	82197	77.2%	0.02	69788	74.9%	71555	76.8%	0.04
	1	47531	9.0%	9863	9.3%	0.01	8510	9.1%	8705	9.3%	0.01
	2	39380	7.5%	7450	7.0%	0.02	8263	8.9%	6609	7.1%	0.07
	3+	38282	7.2%	6919	6.5%	0.03	6636	7.1%	6328	6.8%	0.01

Johns Hopkins ACG Aggregated Diagnosis Groups**	Mean (SD)	7.39 (3.67)		8.54 (3.68)		0.31	8.53 (3.72)		8.41 (3.69)		0.04
	Median (IQR)	7 (5-10)		8 (6-11)			8 (6-11)		8 (6-11)		
	0-4	124790	23.6%	14645	13.8%	0.25	13498	14.5%	13675	14.7%	0.01
	5-9	259863	49.2%	51297	48.2%	0.02	44331	47.6%	45224	48.5%	0.02
	10-14	123526	23.4%	33780	31.7%	0.19	29361	31.5%	28708	30.8%	0.02
	15-19	19634	3.7%	6467	6.1%	0.11	5769	6.2%	5381	5.8%	0.02
	≥20	598	0.1%	240	0.2%	0.03	238	0.3%	209	0.2%	0.02
Medication use (in the 180 days prior to the index date)											
ACE inhibitors or ARBs	N (%)	272316	51.5%	50769	47.7%	0.08	45255	48.6%	44849	48.1%	0.01
Alpha anatagonist (prostate specific)	N (%)	29646	5.6%	36906	34.7%	0.78	23078	24.8%	26396	28.3%	0.08
Alpha antagonist (non-specific)	N (%)	25807	4.9%	18112	17.0%	0.39	14880	16.0%	14244	15.3%	0.02
Androgen deprivation therapy	N (%)	9510	1.8%	630	0.6%	0.11	886	1.0%	620	0.7%	0.03
Antibiotic	N (%)	149521	28.3%	42635	40.1%	0.25	35233	37.8%	35443	38.0%	0
Anticoagulant	N (%)	5743	1.1%	1202	1.1%	0	1060	1.1%	1088	1.2%	0.01
Anticonvulsants	N (%)	10286	1.9%	1955	1.8%	0.01	1883	2.0%	1738	1.9%	0.01
Antidepressants (SSRIs, SNRIs)	N (%)	39474	7.5%	7783	7.3%	0.01	7306	7.8%	7057	7.6%	0.01
Antidepressants (Other)	N (%)	32272	6.1%	6835	6.4%	0.01	5909	6.3%	6229	6.7%	0.02
Antiemetic	N (%)	11204	2.1%	2876	2.7%	0.04	2315	2.5%	2506	2.7%	0.01
Antineoplastic	N (%)	20707	9.0%	2558	2.4%	0.09	2804	3.0%	2379	2.6%	0.02
Antiparkinson's Medications	N (%)	9990	1.9%	2290	2.2%	0.02	2089	2.2%	2012	2.2%	0
Antiplatelet	N (%)	34325	6.5%	7054	6.6%	0	5899	6.3%	6309	6.8%	0.02
Antipsychotics (Atypical)	N (%)	15096	2.9%	2306	2.2%	0.04	2277	2.4%	2127	2.3%	0.01
Antipsychotics (Other)	N (%)	4398	0.8%	773	0.7%	0.01	712	0.8%	687	0.7%	0.01
Benzodiazepine	N (%)	61667	11.7%	14116	13.3%	0.05	12254	13.1%	12216	13.1%	0
Beta Blockers	N (%)	165312	31.3%	30341	28.5%	0.06	28478	30.6%	26763	28.7%	0.04
Bisphosphonate	N (%)	27041	5.1%	6680	6.3%	0.05	5633	6.0%	5773	6.2%	0.01
Calcium channel blockers	N (%)	139096	26.3%	27852	26.2%	0.00	25139	27.0%	24542	26.3%	0.02
Cholinesterase inhibitors	N (%)	17216	3.3%	3060	2.9%	0.02	3305	3.5%	2753	3.0%	0.03
Coumadin	N (%)	48129	9.1%	10006	9.4%	0.01	9476	10.2%	8709	9.3%	0.03
Digoxin	N (%)	17307	3.3%	3474	3.3%	0	3129	3.4%	3039	3.3%	0.01
Glucorticoids	N (%)	27362	5.2%	5866	5.5%	0.01	5200	5.6%	5172	5.5%	0
Inhaled acetylcholine	N (%)	34371	6.5%	7294	6.9%	0.02	6340	6.8%	6407	6.9%	0
Inhaled beta-agonist	N (%)	59884	11.3%	12381	11.6%	0.01	11297	12.1%	10860	11.7%	0.01
Inhaled corticosteroid	N (%)	25962	4.9%	5462	5.1%	0.01	4913	5.3%	4815	5.2%	0
Mood stabilizer	N (%)	5807	1.1%	1074	1.0%	0.01	957	1.0%	943	1.0%	0.00
Narcotics	N (%)	81804	15.5%	17981	16.9%	0.04	15790	16.9%	15693	16.8%	0
Non-potassium sparing diuretics	N (%)	131761	24.9%	23498	22.1%	0.07	22872	24.5%	20787	22.3%	0.05
Nonsteroidial anti-inflammatories (excluding aspirin)	N (%)	77737	14.7%	16812	15.8%	0.03	14482	15.5%	14538	15.6%	0
Overactive bladder medication	N (%)	8375	1.6%	3395	3.2%	0.1	2983	3.2%	2855	3.1%	0.01
Potassium sparing diuretics	N (%)	19927	3.8%	3500	3.3%	0.03	3405	3.7%	3067	3.3%	0.02
Proton Pump Inhibitors	N (%)	116241	22.0%	25459	23.9%	0.05	22981	24.7%	22332	24.0%	0.02
Smoking cessation aid	N (%)	422	0.1%	79	0.1%	0	72	0.1%	75	0.1%	0
Statins	N (%)	263739	49.9%	50111	47.1%	0.06	45533	48.9%	44262	47.5%	0.03

Testosterone replacement	N (%)	2970	0.6%	708	0.7%	0.01	694	0.7%	601	0.6%	0.01
Number of unique DINs	Mean (SD)	6.71 (4.75)		7.48 (5.34)		0.15	7.41 (5.03)		7.39 (5.37)		0.00
	Median (IQR)	6 (3-9)		6 (4-10)			6 (4-10)		6 (4-10)		
Hospital and Physician Utilization (in the 365 days prior to the index date)											
Number of hospital admissions	Mean (SD)	0.49 (1.00)		0.68 (1.11)		0.18	0.66 (1.20)		0.65 (1.09)		0.01
	Median (IQR)	0 (0-1)		0 (0-1)			0 (0-1)		0 (0-1)		
	0	374346	70.8%	63876	60.0%	0.23	59134	63.5%	57466	61.7%	0.04
	1	93624	17.7%	25609	24.1%	0.16	19623	21.1%	21530	23.1%	0.05
	2	36679	6.9%	10056	9.4%	0.09	8041	8.6%	8449	9.1%	0.02
	3+	23762	4.5%	6888	6.5%	0.09	6399	6.9%	5752	6.2%	0.03
Number of psychiatric hospital admissions	Mean (SD)	0.01 (0.10)		0.01 (0.11)		0	0.01 (0.12)		0.01 (0.11)		0
	Median (IQR)	0 (0-0)		0 (0-0)			0 (0-0)		0 (0-0)		
	0	525366	99.4%	105683	99.3%	0.01	92589	99.3%	92536	99.3%	0
	1	2680	0.5%	644	0.6%	0.01	518	0.6%	573	0.6%	0
	2	278	0.1%	85	0.1%	0	63	0.1%	74	0.1%	0
	3+	87	0.0%	17	0.0%	0	27	0.0%	14	0.0%	0
Number of emergency room visits	Mean (SD)	0.55 (1.31)		0.74 (1.51)		0.13	0.72 (1.70)		0.72 (1.49)		0
	Median (IQR)	0 (0-1)		0 (0-1)			0 (0-1)		0 (0-1)		
	0	378034	71.5%	68434	64.3%	0.15	61634	66.1%	60660	65.1%	0.02
	1	87605	16.6%	19870	18.7%	0.06	17052	18.3%	17192	18.4%	0
	2	32539	6.2%	8746	8.2%	0.08	6984	7.5%	7457	8.0%	0.02
	3+	30233	5.7%	9373	8.8%	0.12	7527	8.1%	7888	8.5%	0.01
Number of family physician visits	Mean (SD)	8.55 (8.78)		10.05 (10.12)		0.16	10.03 (9.92)		9.87 (10.08)		0.02
	Median (IQR)	6 (3-11)		7 (4-12)			7 (4-13)		7 (4-12)		
Number of family physician mental health visits	Mean (SD)	0.22 (1.06)		0.27 (1.17)		0.04	0.26 (1.09)		0.26 (1.11)		0
	Median (IQR)	0 (0-0)		0 (0-0)			0 (0-0)		0 (0-0)		
Number of Geriatrician visits	Mean (SD)	0.09 (1.02)		0.17 (1.64)		0.06	0.12 (1.21)		0.17 (1.68)		0.04
	Median (IQR)	0 (0-0)		0 (0-0)			0 (0-0)		0 (0-0)		
Number of Neurologist visits	Mean (SD)	0.12 (0.85)		0.18 (1.1)		0.06	0.16 (0.92)		0.17 (1.07)		0.01
	Median (IQR)	0 (0-0)		0 (0-0)			0 (0-0)		0 (0-0)		
Number of Psychiatry visits	Mean (SD)	0.15 (1.92)		0.19 (2.46)		0.02	0.18 (2.30)		0.19 (2.32)		0.01
	Median (IQR)	0 (0-0)		0 (0-0)			0 (0-0)		0 (0-0)		
Number of urologist visits	Mean (SD)	0.47 (1.53)		1.38 (2.13)		0.49	1.23 (2.55)		1.21 (1.91)		0.01
	Median (IQR)	0 (0-0)		1 (0-2)			0 (0-2)		0 (0-2)		
Medical Investigations and Procedures											
Bone mineral density test	N (%)	20156	3.8%	5275	5.0%	0.06	4311	4.6%	4495	4.8%	0.01
Bone scan	N (%)	13119	2.5%	2979	2.8%	0.02	3440	3.7%	2564	2.8%	0.05
Cardiac catheterization	N (%)	10613	2.0%	2204	2.1%	0.01	1677	1.8%	1949	2.1%	0.02

Cardiac stress test	N (%)	63508	12.0%	14437	13.6%	0.05	12342	13.2%	12487	13.4%	0.01
Carotid endarterectomy	N (%)	494	0.1%	101	0.1%	0	87	0.1%	91	0.1%	0
Carotid ultrasound	N (%)	25083	4.7%	5999	5.6%	0.04	5122	5.5%	5230	5.6%	0
Chest x-ray	N (%)	163067	30.9%	38053	35.8%	0.1	33657	36.1%	32924	35.3%	0.02
CT head	N (%)	37024	7.0%	9613	9.0%	0.07	8414	9.0%	8298	8.9%	0
CT spine	N (%)	7121	1.3%	1977	1.9%	0.05	1594	1.7%	1718	1.8%	0.01
Echocardiography	N (%)	91549	17.3%	21512	20.2%	0.07	17958	19.3%	18853	20.2%	0.02
ECT	N (%)	111	0.0%	39	0.0%	0.07	29	0.0%	31	0.0%	0.02
EEG	N (%)	2451	0.5%	703	0.7%	0.03	590	0.6%	608	0.7%	0.01
Heart valve replacement	N (%)	793	0.2%	185	0.2%	0	156	0.2%	154	0.2%	0
Holter monitoring	N (%)	30489	5.8%	7885	7.4%	0.06	6417	6.9%	6870	7.4%	0.02
MRI head	N (%)	9812	1.9%	2478	2.3%	0.05	2140	2.3%	2153	2.3%	0
MRI spine	N (%)	8081	1.5%	2262	2.1%	0.05	1835	2.0%	1983	2.1%	0.01
PSA test	N (%)	40309	7.6%	15932	15.0%	0.24	13489	14.5%	14068	15.1%	0.02
Pulmonary function test	N (%)	45071	8.5%	10441	9.8%	0.05	9051	9.7%	9012	9.7%	0
TRUS biopsy	N (%)	5840	1.1%	6858	6.4%	0.28	4330	4.6%	4814	5.2%	0.03
TURP	N (%)	3551	0.7%	997	0.9%	0.02	1132	1.2%	934	1.0%	0.02
Urine culture	N (%)	74635	14.1%	34650	32.6%	0.45	27737	29.8%	27551	29.6%	0

*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.

**We used the Adjusted Clinical Group (ACG) scoring system to score comorbidity. The ACG is a population/patient case-mix adjustment system that provides a relative measure of the individual's expected consumption of health services. ICD-9/ICD-9-CM codes are categorized into 32 groups, called Ambulatory Diagnostic Groups (ADGs), based on clinical similarity, chronicity, likelihood of requiring specialty care, and disability. These groups are further reduced to 12 'Collapsed ADGs' or CADGs. Reference: The Johns Hopkins University Bloomberg School of Public Health, Health Services Research & Development Center. The Johns Hopkins ACG® Case-Mix System Version 10.0 Release Notes. (Editor in Chief: Jonathan P. Weiner). The Johns Hopkins University. 2011.

eTable 6. 5ARI medication utilisation details among the exposed cohort.

	Finasteride	Dutasteride
Number (%)	44692 (48.0%)	48505 (52.0%)
Median duration of use, years (IQR)	1.02 (0.23-3.58)	0.92 (0.22-2.70)
Number (%) of men that switched at least once to the other 5ARI during continuous use	2559 (5.7%) switched to dutasteride	938 (1.9%) switched to finasteride
Physician speciality initiating the 5ARI prescription		
Urology	15358 (34.4%)	23096 (47.6%)
Family physician	22087 (49.4%)	18994 (39.2%)
Other	7247(16.2%)	6415 (13.2%)

eTable 7. Significance of the potential effect modifiers of prior depression, and recent use of antidepressants on suicide between our matched cohorts of 5ARI users and non-users. Prior self-harm was such a rare event that the model could be fit. The interaction p-value indicates whether there is a significant difference in suicide based on these subgroups.

	Events/Number at Risk (%)		Hazard Ratio	P value for interaction
	5ARI users (Exposed cohort)	*Non-5ARI users (Unexposed cohort)*		
Prior depression				
Yes	*/3353	*/3353	2.00 (0.37 to 10.92)	0.32
No	*/89844	*/89844	0.81 (0.48 to 1.37)	
Recent use of antidepressants				
Yes	11/11882 (0.09%)	7/11882 (0.06%)	1.14 (0.41 to 3.15)	0.56
No	27/81315 (0.03%)	29/81315 (0.04%)	0.81 (0.45 to 1.44)	

*Individual numbers were not included for prior depression due to privacy regulations forbidding the reporting of any groups numbering less than 6.

eTable 8. Risk of suicide, self-harm and depression among men exposed to 5ARI medications compared to matched unexposed men after excluding matched pairs with evidence of prostate cancer.

	Death by suicide (primary outcome)		Self-Harm (secondary outcome)		Depression (secondary outcome)	
	5ARI users	*Non-5ARI users*	*5ARI users*	*Non-5ARI users*	*5ARI users*	*Non-5ARI users*
	n=69,699	*n=69,699*	*n=69,699*	*n=69,699*	*n=67,148**	*n=67,148*
HR	0.92 (0.51-1.64, p=0.77)	Reference	NA		NA	
Stratified HR**			0-1.5 years 1.95 (1.32-2.88, p<0.01) 1.5-3 years 0.57 (0.29-1.12, p=0.57) >3 years 1.11 0.59-2.10, p=0.75)	Reference	0-1.5 years 2.02 (1.77-2.30, p<0.01) >1.5 years 1.21 (1.05-1.39, p=0.01)	Reference

*Matched pairs with a prior history of depression were excluded from the cohort for this analysis.
**The secondary outcomes of self-harm and depression did not meet the assumption for proportional hazards, and as such the results were stratified by followup time. The overall HR in these cases represents an average HR over the entire followup period, and the stratified HR better represent the magnitude of risk associated with the specific time periods after 5ARI initiation.

eTable 9. Risk of suicide, self-harm and depression among men exposed to 5ARI medications compared to matched unexposed men, with adjustment for the competing risk of non-suicide mortality.

	Death by suicide (primary outcome)		Self-Harm (secondary outcome)		Depression (secondary outcome)	
	5ARI users	*Non-5ARI users*	*5ARI users*	*Non-5ARI users*	*5ARI users*	*Non-5ARI users*
	n=93,197	*n=93,197*	*n=93,197*	*n=93,197*	*n=89,844**	*n=89,844*
HR	1.06 (0.77-1.46, p=0.74)	Reference	NA		NA	
Stratified HR**			0-1.5 years 1.89 (1.48-2.41, p<0.01) 1.5-3 years 0.74 (0.52-1.07, p=0.11) >3 years 1.00 0.73-1.36, p=1.0)	Reference	0-1.5 years 1.90 (1.75-2.05, p<0.01) >1.5 years 1.09 (1.01-1.17, p=0.03)	Reference

*Matched pairs with a prior history of depression were excluded from the cohort for this analysis.
**The secondary outcomes of self-harm and depression did not meet the assumption for proportional hazards, and as such the results were stratified by followup time. The overall HR in these cases represents an average HR over the entire followup period, and the stratified HR better represent the magnitude of risk associated with the specific time periods after 5ARI initiation.

eResults. Example of SAS code used for primary analysis, and resulting raw output from SAS model.

```
proc phreg data=ari.outcomes;
     model suicide_fup*suicide(0) = exposure;
     strata pair;
     hazardratio exposure;
run;
```

The PHREG Procedure

Model Information	
Data Set	ARI.OUTCOME133
Dependent Variable	suicide_fup
Censoring Variable	suicide
Censoring Value(s)	0
Ties Handling	BRESLOW

Number of Observations Read	186394
Number of Observations Used	186394

Summary of the Number of Event and Censored Values

Stratum pair	Total	Event	Censored	Percent
Total	186394	74	186320	99.96

Convergence Status

Convergence criterion (GCONV=1E-8) satisfied.

Model Fit Statistics

Criterion	Without Covariates	With Covariates
-2 LOG L	85.950	85.692
AIC	85.950	87.692
SBC	85.950	89.996

Testing Global Null Hypothesis: BETA=0

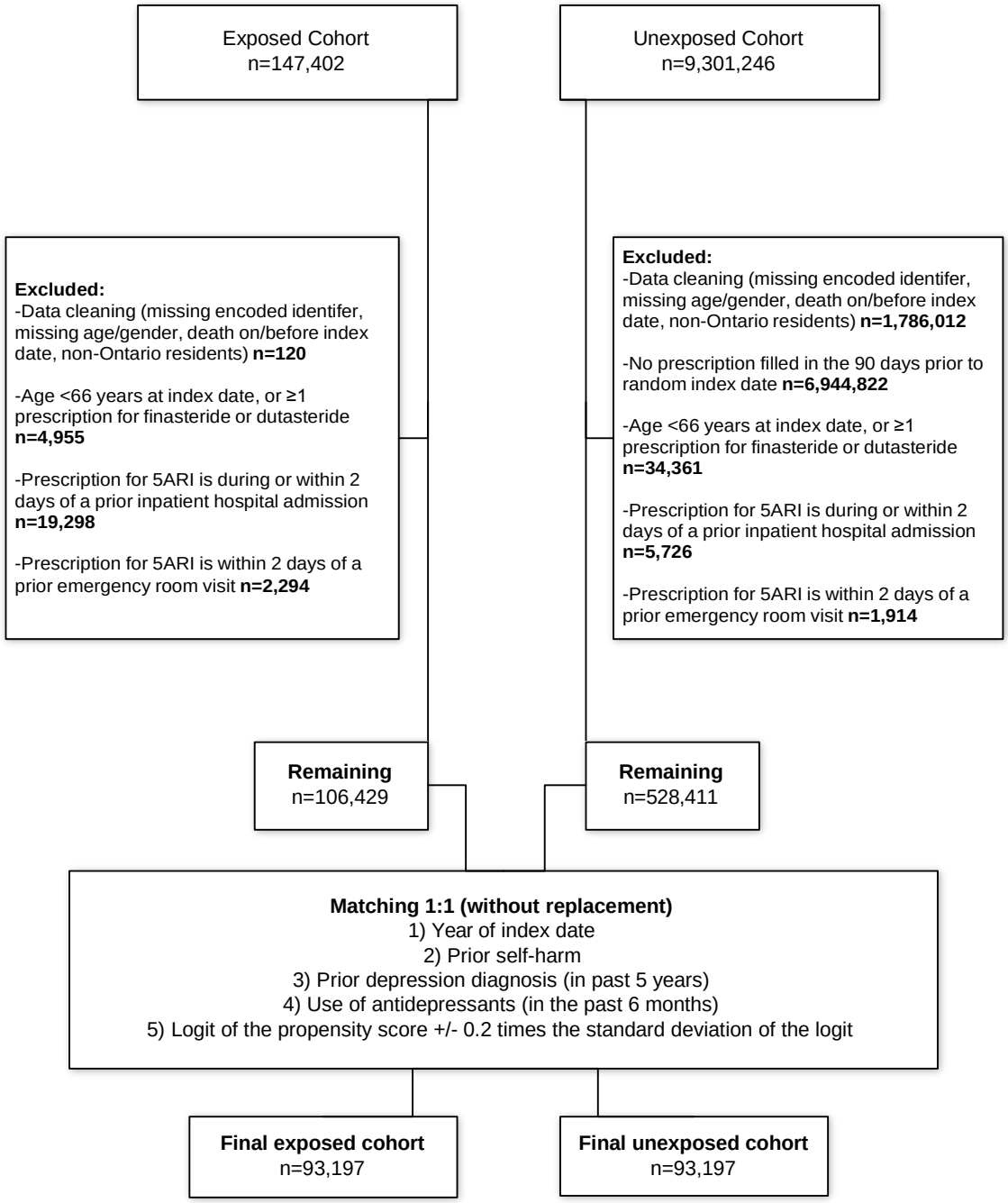
Test	Chi-Square	DF	Pr > ChiSq
Likelihood Ratio	0.2582	1	0.6113

Testing Global Null Hypothesis: BETA=0			
Test	Chi-Square	DF	Pr > ChiSq
Score	0.2581	1	0.6115
Wald	0.2577	1	0.6117

Analysis of Maximum Likelihood Estimates						
Parameter	DF	Parameter Estimate	Standard Error	Chi-Square	Pr > ChiSq	Hazard Ratio
exposure	1	-0.12921	0.25453	0.2577	0.6117	0.879

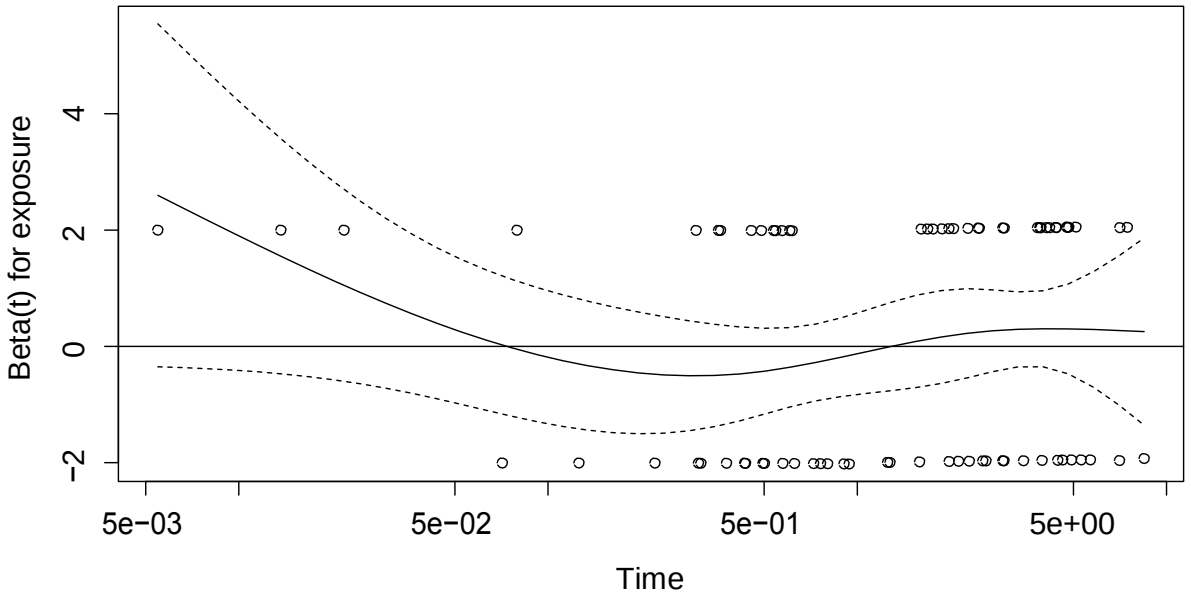
Hazard Ratios for exposure			
Description	Point Estimate	95% Wald Confidence Limits	
exposure Unit=1	0.879	0.534	1.447

eFigure 1. Cohort flow chart. The large number of patients excluded from the unexposed cohort are a result of a large number of men dying prior to their randomly assigned index date. Similarly, a large number of men were not over 66 years of age, and therefore were excluded because they did not have a prescription in ODB in the 90 days prior to the index date.

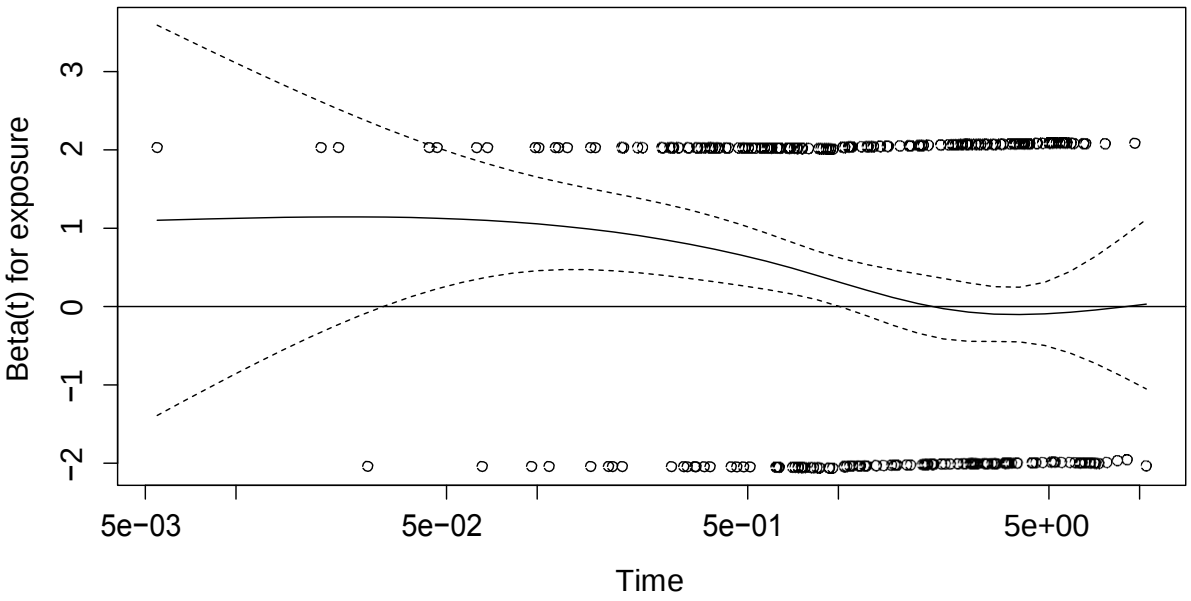


eFigure 2. Graph of Schoenfeld residuals for suicide, self-harm, and depression. Significant deviation of the plotted line (shown with 95% confidence intervals) from the straight dotted line at 0 on the y axis indicates a violation of the proportionality assumption. The statistical test for violation of the proportionality assumption (p value of a time varying covariate) is also included.

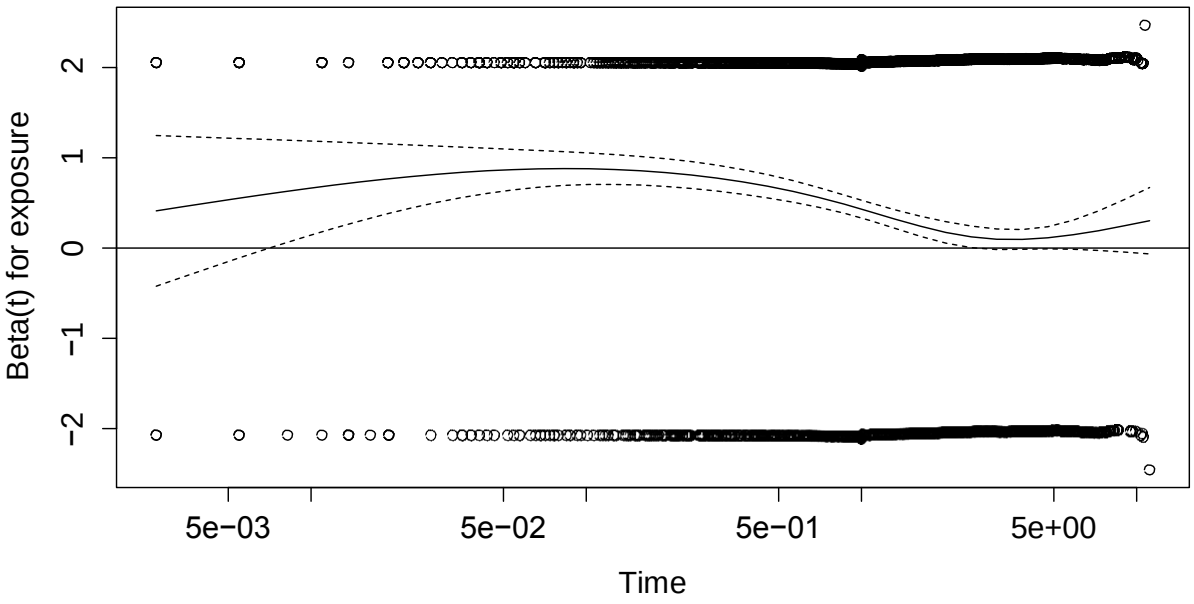
A) Suicide (p=0.54, suggesting no significant deviation from proportionality).



B) Self-harm (p<0.05, suggesting a significant deviation from proportionality).

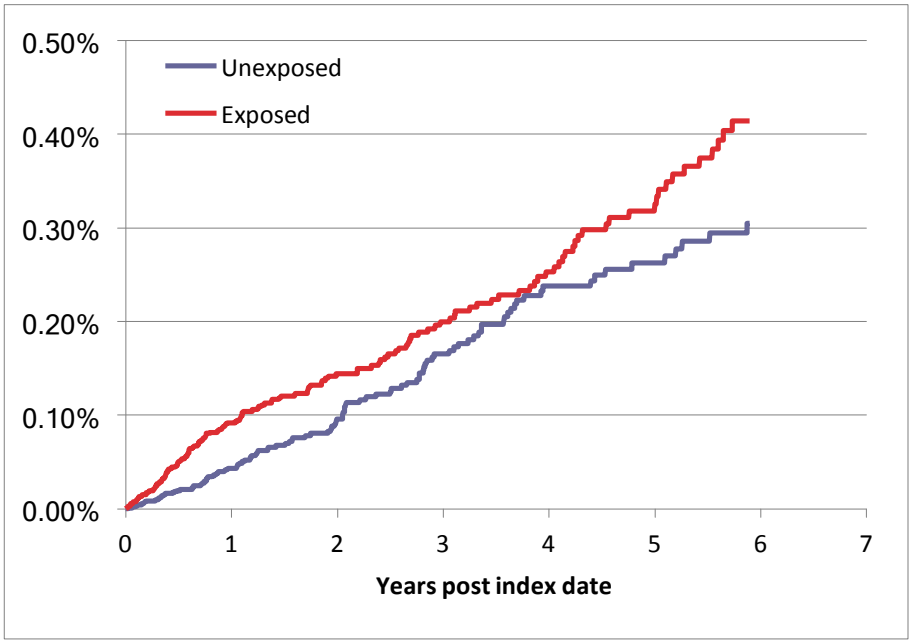


C) Depression (p<0.05, suggesting a significant deviation from proportionality).



eFigure 3. Kaplan meier graphs of self-harm and depression.

A) Self-harm



B) Depression