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Supplementary Appendix

Exploring high priority potentially inappropriate prescribing cascades in older adults: a population-level retrospective cohort study

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

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eAppendix 1

Description of How Individual Drug Therapies within Drug Classes were Identified

Variations in how drug classes are named and described in the literature can impact which individual drugs may be relevant to a prescribing cascade as the initial drug or subsequent drug, and therefore to include in our analysis. For some prescribing cascades, drug classes identified were clearly named and defined (e.g. diuretics). For other prescribing cascades, drug classes were unclear. This was either because the drug class was so broad that it encapsulated many more drugs than relevant for the prescribing cascade (e.g. antiemetics in the 'antihypertensives --> orthostatic hypotension/dizziness --> antiemetics' prescribing cascade), or alternatively, the drug class was poorly defined due to the generic description (e.g. cough remedy, sleep agent). Combination products were included.

For our analysis, the following process was used to decide which individual drugs to include in the above instances of unclear drug classes. If a published list of individual drugs for the drug class was available, the list was used to capture the broadest sense of that drug class. If no list of single drugs was available for that drug class, the effect or symptom described in the prescribing cascade was used as an indication, and individual drugs used to treat that indication (as defined by the Compendium of Pharmaceuticals (eCPS)[1] were included (e.g. cough remedy). Finally, if a pre-existing list of individual drugs for a drug class was available from previous ICES projects, this list was used (e.g. sleep agents)[2]. A detailed list of the drug classed and individual drugs used to identify each of the 65 prescribing cascades was prepared and archived at ICES. (available on request)

eAppendix 2

Prescription Sequence Symmetry Analysis Formula Description

Prescription sequence symmetry analysis (PSSA) approach, first described in 1996[3], has been successfully used to determine the presence of potential prescribing cascades and the strength of the association [4,5] For the PSSA analysis, the initial drug and the subsequent drug were included. The crude sequence ratio (SR) was calculated by dividing the number of individuals who had an initial drug before the subsequent drug (suggesting a prescribing cascade) by the number who had a subsequent drug before the initial drug (not consistent with a prescribing cascade). Given that prescribing trends and drug utilization over time may influence the sequences of drug initiation, a corrective measure called a null effect SR was calculated. The null effect SR provided a background rate for the sequence of two drugs with the assumption that there was no causal relationship between them, specifically that subsequent drug followed initial drug. The adjusted sequence ratio (aSR) was calculated by dividing the crude SR by the null effect SR and providing 95% confidence intervals (CIs), resulting in an estimate in the presence of temporal trends of drug initiation. An aSR >1 indicated the presence of a potential prescribing cascade[6].

To quantify the likelihood of the prescribing cascade, sequence ratio was defined as the main parameter of analysis using PSSA[3,7,8] . The prescribing cascade specific cohort was classified into those where the initial drug was initiated before the subsequent drug and those where the initial drug was initiated after subsequent drug. The crude SR was calculated by dividing the number of individuals who had initial drug first over the number of individuals who had subsequent drug first. Taking incidence trends into account, a null-effect SR was calculated as follows:

$$\text{null-effect SR} = a/(1-a)$$

$$a = \frac{\sum_{m=1}^{\mu}[DA_m \times (\sum_{n=m+1}^{\mu} DB_n)]}{\sum_{m=1}^{\mu} DA_m \times \sum_{m=1}^{\mu} DB_m}$$

where:

m or n= consecutive days of the accrual period

μ=the last day of the accrual period

DA_{index}=number of individuals presenting their first initial drug on the index day

DB_{index}=number of individuals presenting their first subsequent drug on the index day

To account for the non-causal baseline prescribing trends over time, an aSR is calculated by dividing the crude SR over the null-effect SR (crude SR/null-effect SR).

eTable 1. Data Sources

Continuing Care Reporting System Long-Term Care (CCRS-LTC) database	The CCRS-LTC database is compiled by the Canadian Institute for Health Information (CIHI) and is used to identify individuals living in long-term care.
Ontario Drug Benefit (ODB) program database	The ODB database contains prescription medication claims for those covered under the provincial drug program, mainly: those aged ≥65 years, long-term care home residents, patients receiving services under the Ontario Home Care program, those receiving social assistance, and residents eligible for specialized drug programs (e.g., programs which cover the costs of medications for individuals whose medication costs exceed 4% of their net household income and for individuals with rare, serious conditions). Each medication claim has an associated prescriber identifier which indicates the health practitioner who wrote the prescription, as well as fields that identify the type, quantity and duration of treatment. An audit of 100 randomly selected prescriptions dispensed from 50 Ontario pharmacies determined that the ODB had an error rate of 0.7%, and none of the pharmacy characteristics examined (locations, owner affiliation, productivity) were associated with coding errors.[9]
Ontario Health Insurance Plan (OHIP) Claims History Database	The OHIP claims database contains information on inpatient and outpatient services provided to Ontario residents eligible for the province's publicly-funded health insurance system by fee-for-service health care practitioners (primarily physicians) and "*shadow billings*" for those paid through non-fee-for-service payment plans. Billing codes on the claims identify the care provider, their area of specialization and the type and location of service. OHIP billing claims also contain a 3-digit diagnosis code – the main reason for the service – captured using a modified version of the ICD, 8th revision.
Ontario Health Insurance Plan (OHIP) Registered Persons Database (RPDB)	The OHIP RPDB provides basic demographic information (age, sex, location of residence, date of birth, and date of death for deceased individuals) for those issued an Ontario health insurance number. The RPDB also indicates the time periods for which an individual was eligible to receive publicly funded health insurance benefits and the best known postal code for each registrant on July 1st of each year.
The DRUGLIST file (DIN)	The file contains a near exhaustive list of DINs (Drug Identification Numbers) used in Canada from 1990 forward. It contains information on drug and product names, subclass information, PCG codes, Drug strength, Route of Administration, First and Last dispensing dates from ODB, etc based on two sources of data: The DIN file from IQVIA Solutions Canada Inc, and the ODB data. IQVIA's file is created by

	contacting drug manufacturers and going through current and historic drug formularies from 1990 forward. It can be used to obtain a list of DINs which fall under generic drug names, drug subclasses, or PCG codes. It can be also used to look up properties of a drug, such as strength, to gather information about actual dose of drug dispensed in an ODB claim.
Postal Code Conversion File (PCCF)	Converts any Canadian postal code to a Statistics Canada standard geographical area, including Dissemination Area/Enumeration Area, Census Division, and Latitude/Longitude, as well as an urban/rural flag and neighborhood income quintile. Canadian postal codes are six-character alphanumeric codes. The first three letters represent the forward sortation area (FSA), the first character of the FSA represents the specific area in a major geographic region or province, the second character represents whether the address is urban or rural, and the third character specifies a specific area within a city or town. The last three characters of the postal code are the local delivery unit (LDA). In an urban area, the LDA may indicate a specific city block, single building, or large-volume mail receiver; in a rural area, the LDA may indicate a specific rural community.

eTable 2. The 65 Potentially Inappropriate Prescribing Cascade (PIPC) List Organized by Physiological System.

Cardiovascular System	
Drug Class	
1	Angiotensin converting enzyme inhibitor to cough to cough remedy
2	Antihypertensive to orthostatic hypotension/dizziness to antiemetic
3	Beta blocker to depression to antidepressant
4	Beta blocker to erectile dysfunction to Phosphodiesterase-5 inhibitor
5	Calcium channel blocker to edema to diuretic
6	Calcium channel blocker to constipation to laxative
7	Diuretic to gout or hyperuricemia to anti-gout agent
8	Diuretic to urinary incontinence to overactive bladder medication
9	HMG Co-A reductase inhibitor to myalgia/myositis to pain reliever
10	HMG Co-A reductase inhibitor to myalgia/myositis to mineral supplement
11	HMG Co-A reductase inhibitor to myalgia/myositis to quinine sulfate
12	HMG Co-A reductase inhibitor to insomnia to sleep agent
Individual Drug	
13	Digoxin to nausea to antiemetic
14	Midodrine to hypertension to antihypertensive
Central Nervous System	
Drug Class	
15	Anticonvulsant to rash to topical corticosteroid
16	Anticonvulsant to nausea to antiemetic
17	Antipsychotic to extrapyramidal symptoms to beta-blocker
18	Antipsychotic to extrapyramidal symptoms to antiparkinsonian agent
19	Antipsychotic to extrapyramidal symptoms to anti-tremor antimuscarinic
20	Antipsychotic to akasthisia or tardive movements sedative
21	Antipsychotic to arrhythmia to antiarrhythmic
22	Antipsychotic to hyperglycemia to antihyperglycemic
23	Benzodiazepine to cognitive impairment to cholinesterase Inhibitor
24	Cholinesterase Inhibitor to urinary incontinence to overactive bladder medication
25	Cholinesterase Inhibitor to insomnia to sleep agent
26	Cholinesterase Inhibitor to gastrointestinal upset to antiemetic
27	Cholinesterase Inhibitor to gastrointestinal upset to bismuth subsalicylate
28	Cholinesterase Inhibitor to diarrhea to antidiarrheal
29	Cholinesterase Inhibitor to rhinorrhea to antihistamine
30	Dopaminergic antiparkinsonian agent to psychotic symptoms, hallucinations to antipsychotic
31	Gabapentinoid to peripheral edema to diuretic
32	SSRI/SNRI to urinary incontinence to overactive bladder medication
33	Tricyclic antidepressant to cognitive impairment to cognitive impairment to cholinesterase Inhibitor
34	Tricyclic antidepressant to constipation to laxative
35	Tricyclic antidepressant to urinary incontinence to overactive bladder medication
Individual Drug	

36	Flunarizine to depression to antidepressant
37	Lithium to extrapyramidal symptoms to antiparkinsonian agent
38	Venlafaxine to hypertension (dose-related) to antihypertensive
39	Venlafaxine to tremor to benzodiazepine
Endocrine System	
Drug Class	
40	DPP-4 Inhibitor to joint pain to Nonsteroidal anti-inflammatory drug
41	SGLT2 inhibitor to mycotic infection to antifungal
Individual Drug	
42	Metformin to diarrhea antidiarrheal
43	Pioglitazone or Rosiglitazone to oedema to diuretic
44	Rosiglitazone to heart failure to diuretic
Gastrointestinal System	
Drug Class	
45	Anticholinergic antiemetics to urinary retention to alpha-1-receptor blocker
46	Antidopaminergic antiemetic to extrapyramidal symptoms to antiparkinsonian agent
47	Laxative to diarrhea antidiarrheal agent
48	Proton pump inhibitor to osteoporosis/fractures to vitamin supplement
49	Proton pump inhibitor to vitamin or mineral deficiency to vitamin or mineral supplement
Musculoskeletal System	
Drug Class	
50	Bisphosphonate to gastritis, gastric ulcer, gastrointestinal bleed to gastroprotective agent
51	NSAID to gastroprotective agent
52	NSAID to nausea to antiemetic
53	NSAID to hypertension to antihypertensive
54	NSAID to worsening of heart failure to heart failure agent
55	Opioid to depression to antidepressant
Urogenital System	
Drug Class	
56	Alpha-1-receptor blocker to orthostatic hypotension to vestibular suppressant
57	Urinary anticholinergic to dry mouth to saliva substitute
Miscellaneous System	
Drug Class	
58	Carbapenem to seizures to anticonvulsant
59	Corticosteroid to insomnia to sleep agent
60	Corticosteroid to psychosis to antipsychotic
61	Corticosteroid to hypertension to antihypertensive
Individual Drug	
62	Acitretin to vulvo-vaginal candidiasis to antifungal
63	Erythromycin to arrhythmia to antiarrhythmic
64	Fludrocortisone to hypertension to antihypertensive
65	Iron supplement to constipation to laxative

HMG Co-A: Hydroxymethylglutaryl-coenzyme A; SSRI/SNRI: Selective serotonin reuptake inhibitor / Serotonin and norepinephrine reuptake inhibitor; DPP-4 inhibitor: Dipeptidyl Peptidase 4 Inhibitor; SGLT2 inhibitor: Sodium-glucose cotransporter-2 inhibitor; NSAID: Nonsteroidal anti-inflammatory drug

eTable 3. The 24 Prioritized Potential Inappropriate Prescribing Cascades (PIPCs) and their Population Prevalence, Incidence of Prescribing Cascade, and Adjusted Sequence Ratios by Age Group.

Potentially Inappropriate Prescribing Cascade Initiating to Subsequent Drug		Age: 66-74			Age: 75-84			Age: 85 or older		
		Prevalence rate of Initial Drug, %	Incidence of prescribing cascade, % (95% CI)	Adjusted sequence ratio (95%CI)	Prevalence rate of Initial Drug, %	Incidence of prescribing cascade, % (95% CI)	Adjusted sequence ratio (95%CI)	Prevalence rate of Initial Drug (%)	Incidence of prescribing cascade, % (95% CI)	Adjusted sequence ratio (95%CI)
Cardiovascular System										
Drug Class										
Antihypertensive to antiemetic		58.6	1.7 (1.6-1.8)	1.40 (1.29-1.52)	72.4	2.1 (1.9-2.2)	1.60 (1.45-1.76)	79.6	3.6 (3.3-3.9)	3.24 (2.77-3.79)
HMG Co-A reductase inhibitor	to pain reliever	51.5	11.0 (10.8-11.2)	1.16 (1.13-1.20)	60.2	10.7 (10.5-11.0)	1.16 (1.12-1.20	55.5	10.6 (10.2-11.1)	1.29 (1.20-1.39)
	to sleep agent		3.8 (3.7-3.9)	1.30 (1.24-1.36)		4.5 (4.3-4.6)	1.31 (1.24-1.38)		7.1 (6.7-7.6)	1.88 (1.70-2.07)
Angiotensin converting enzyme inhibitor to cough remedy		25.1	2.1 (2.0-2.2)	1.46 (1.31-1.61)	29.4	2.2 (2.0-2.3)	1.53 (1.36-1.73)	30.0	1.8 (1.6-2.1)	1.35 (1.10-1.66)
Beta blocker to antidepressant		20.1	4.3 (4.2-4.5)	1.20 (1.13-1.27)	30.9	5.2 (5.0-5.4)	1.22 (1.16-1.29)	38.8	7.6 (7.3-7.9)	1.42 (1.32-1.53)
Calcium channel blocker	to diuretic	19.2	6.7 (6.6-6.9)	1.68 (1.60-1.76)	26.8	7.6 (7.4-7.8)	1.60 (1.52-1.68)	33.6	9.1 (8.7-9.4)	1.74 (1.62-1.86)
	to laxative		7.1 (6.9-7.3)	1.25 (1.19-1.30)		7.5 (7.3-7.7)	1.17 (1.12-1.22)		8.8 (8.5-9.2)	1.40 (1.32-1.50)
Central Nervous System										
Drug Class										
SSRI/SNRI to overactive bladder medication		13.4	3.2 (3.0-3.4)	1.27 (1.18-1.38)	13.6	3.0 (2.8-3.2)	0.94 (0.87-1.02)	14.1	2.7 (2.5-2.9)	0.93 (0.82-1.05)
Gabapentinoid to diuretic		8.0	3.9 (3.8-4.1)	1.22 (1.15-1.28)	9.9	5.2 (5.0-5.4)	1.21 (1.15-1.27)	10.7	7.2 (6.9-7.5)	1.22 (1.14-1.31)
Anticonvulsant to antiemetic		5.2	3.2 (3.0-3.3)	1.14 (1.05-1.24)	5.9	3.3 (3.2-3.5)	1.28 (1.18-1.40)	6.3	4.1 (3.8-4.5)	1.72 (1.49-1.97)
Endocrine System										
Drug Class										
Dipeptidyl Peptidase 4 (DPP-4) Inhibitor to Nonsteroidal anti-inflammatory drug		9.1	6.5 (6.2-6.9)	1.21 (1.12-1.31)	10.7	4.8 (4.5-5.2)	0.99 (0.90-1.09)	8.7	3.0 (2.6-3.5)	0.92 (0.74-1.14)
Sodium-glucose cotransporter-2 (SGLT-2) inhibitor to antifungal		8.8	6.3 (6.1-6.5)	2.20 (2.06-2.34)	7.8	6.9 (6.7-7.1)	2.09 (1.97-2.23)	4.0	7.1 (6.7-7.5)	2.06 (1.87-2.27)

Individual Drug										
Metformin to antidiarrheal		18.2	1.0 (0.9-1.1)	1.61 (1.36-1.92)	19.0	1.4 (1.2-1.5)	1.45 (1.21-1.74)	13.5	1.8 (1.5-2.2)	1.78 (1.28-2.47)
Gastrointestinal System										
Drug Class										
Proton pump inhibitor	to vitamin supplement	26.8	1.6 (1.6-1.7)	1.31 (1.24-1.40)	33.6	1.9 (1.8-2.0)	1.28 (1.20-1.36)	37.8	2.2 (2.0-2.3)	1.47 (1.32-1.64)
	to vitamin or mineral supplement		3.8 (3.7-3.9)	1.27 (1.22-1.32)		5.0 (4.8-5.1)	1.25 (1.20-1.30)		6.6 (6.4-6.9)	1.32 (1.24-1.40)
Laxative to antidiarrheal agent		8.9	1.9 (1.9-2.0)	2.68 (2.50-2.87)	13.4	2.3 (2.2-2.4)	2.54 (2.37-2.71)	21.2	2.4 (2.3-2.5)	2.32 (2.11-2.55)
Musculoskeletal System										
Drug Class										
Opioid to antidepressant		14.7	5.3 (5.2-5.4)	1.36 (1.32-1.40)	15.5	6.4 (6.2-6.5)	1.34 (1.30-1.38)	16.0	8.1 (7.9-8.3)	1.14 (1.09-1.18)
NSAID	to gastroprotective agent	14.7	7.1 (7.0-7.2)	1.27 (1.24-1.31)	13.4	6.3 (6.2-6.4)	1.18 (1.14-1.22)	8.8	6.1 (5.8-6.4)	1.29 (1.20-1.38)
	to antiemetic		1.6 (1.5-1.6)	1.65 (1.56-1.75)		1.7 (1.7-1.8)	1.62 (1.51-1.73)		2.4 (2.2-2.6)	2.11 (1.85-2.41)
	to antihypertensive		3.3 (3.2-3.3)	1.12 (1.08-1.16)		2.8 (2.7-2.8)	1.06 (1.01-1.11)		2.6 (2.4-2.8)	1.11 (1.00-1.23)
	to heart failure agent		3.6 (3.6-3.7)	1.18 (1.14-1.23)		3.4 (3.3-3.5)	1.14 (1.09-1.19)		3.9 (3.7-4.2)	1.24 (1.14-1.35)
Miscellaneous System										
Drug Class										
Corticosteroid	to sleep agent	21.4	5.0 (4.9-5.1)	1.31 (1.28-1.35)	24.6	5.7 (5.6-5.8)	1.30 (1.26-1.33)	24.4	7.4 (7.2-7.6)	1.43 (1.37-1.49)
	to antipsychotic		1.7 (1.7-1.8)	2.51 (2.38-2.65		2.5 (2.4-2.6)	2.68 (2.55-2.83)		5.0 (4.8-5.1)	2.58 (2.43-2.75)
Individual Drug										
Iron Supplement to laxative		3.9	12.5 (12.2-12.9)	1.20 (1.15-1.25)	7.2	12.0 (11.7-12.3)	1.13 (1.09-1.18)	11.6	10.8 (10.4-11.2)	1.16 (1.10-1.22)

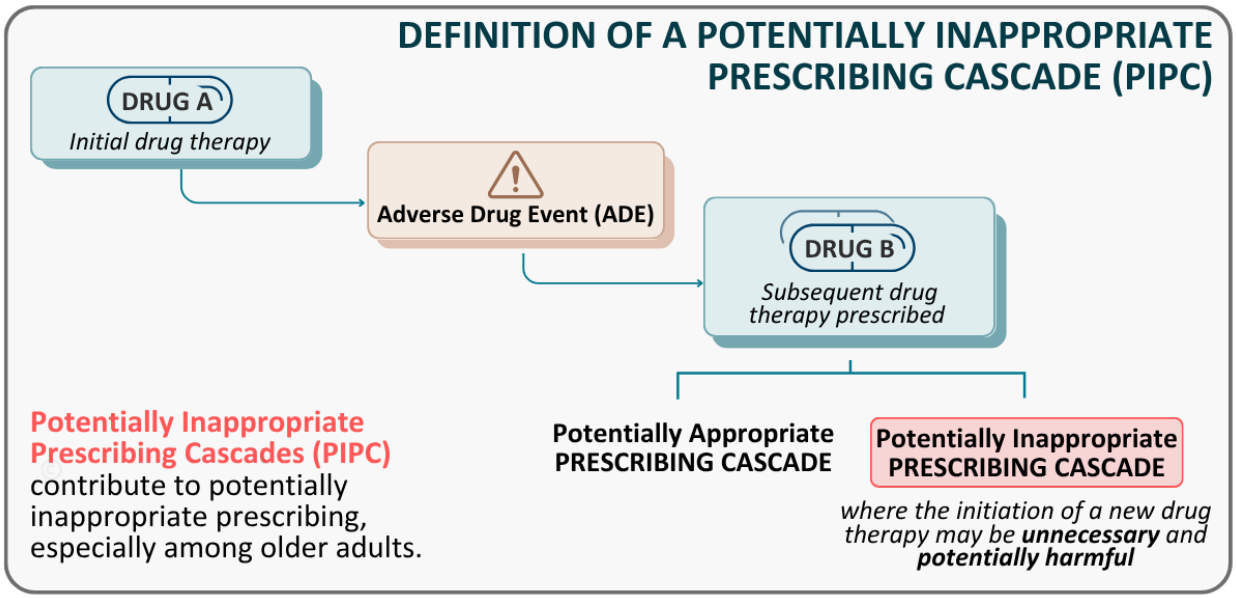
eTable 4. The Sensitivity Analyses on the 24 Prioritized Potentially Inappropriate Prescribing Cascades (PIPCs) with 180 day Exposure Window

Potentially Inappropriate Prescribing Cascade		Prescription Sequence Symmetry Analyses				
		Initial drug dispensing before subsequent drug, number	Initial drug dispensing after subsequent drug, number	Crude Sequence Ratio	Null-effect Sequence Ratio	Adjusted sequence ratio (95%CI)
Cardiovascular System						
Drug Class						
Antihypertensive to antiemetic		2,066	1,316	1.57	0.97	1.62 (1.52-1.74)
HMG Co-A reductase inhibitor	to sleep agent	4,812	3,852	1.25	0.91	1.37 (1.31-1.42)
	to pain reliever	11,949	10,563	1.13	0.91	1.24 (1.21-1.27)
Angiotensin converting enzyme inhibitor to cough remedy		1,197	722	1.66	1.06	1.56 (1.42-1.71)
Beta blocker to antidepressant		4,847	3,830	1.27	0.97	1.30 (1.25-1.36)
Calcium channel blocker	to diuretic	7,953	4,615	1.72	0.99	1.73 (1.67-1.80)
	to laxative	7,240	5,545	1.31	0.98	1.33 (1.28-1.38)
Central Nervous System						
Drug Class						
SSRI/SNRI to overactive bladder medication		1,942	1,691	1.15	1.03	1.11 (1.04-1.19)
Gabapentinoid to diuretic		5,359	4,299	1.25	0.99	1.26 (1.21-1.31)
Anticonvulsant to antiemetic		2,046	1,596	1.28	0.95	1.35 (1.26-1.44)
Endocrine System						
Drug Class						
DPP-4 inhibitor to NSAID		1,313	1,296	1.01	0.87	1.16 (1.08-1.26)
SGLT2 inhibitor to antifungal		4,871	2,156	2.26	0.97	2.34 (2.22-2.46)
Individual Drug						
Metformin to antidiarrheal		459	284	1.62	1.02	1.58 (1.36-1.83)
Gastrointestinal System						
Drug Class						
Proton pump inhibitor	to vitamin supplement	3,358	2,509	1.34	0.96	1.40 (1.33-1.47)
	to vitamin or mineral supplement	8,822	6,894	1.28	1.01	1.27 (1.23-1.31)
Laxative to antidiarrheal agent		5,320	2,003	2.66	0.96	2.77 (2.63-2.92)
Musculoskeletal System						
Drug Class						
Opioid to antidepressant		18,245	13,182	1.38	1.00	1.38 (1.35-1.41)
NSAID	to antiemetic	3,542	2,128	1.66	0.96	1.73 (1.64-1.82)
	to gastroprotective agent	14,405	11,376	1.27	0.97	1.31 (1.28-1.34)
	to heart failure agent	7,251	6,084	1.19	1.00	1.19 (1.15-1.23)
	to antihypertensive	6,145	5,399	1.14	1.01	1.13 (1.09-1.17)

Miscellaneous System						
Drug Class						
Corticosteroid	to antipsychotic	8,936	3,730	2.40	0.97	2.47 (2.37-2.56)
	to sleep agent	19,186	14,977	1.28	0.96	1.33 (1.30-1.36)
Individual Drug						
Iron Supplement to laxative		9,575	7,682	1.25	0.99	1.26 (1.23-1.30)

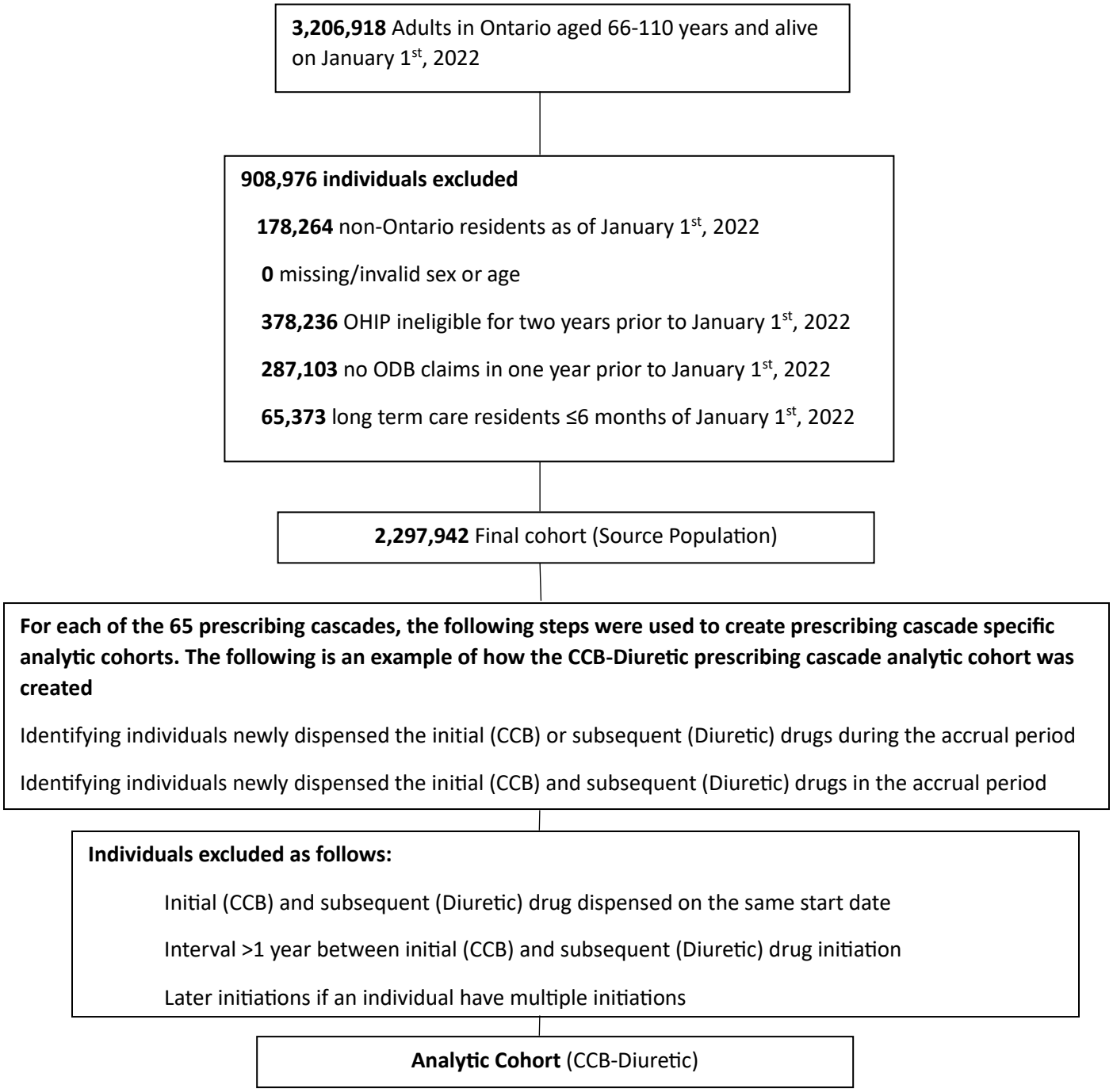
CI: confidence interval; HMG Co-A: Hydroxymethylglutaryl-coenzyme A; SSRI/SNRI: Selective serotonin reuptake inhibitor / Serotonin and norepinephrine reuptake inhibitor; DPP-4 inhibitor: Dipeptidyl Peptidase 4 Inhibitor; SGLT2 inhibitor: Sodium-glucose cotransporter-2 inhibitor; NSAID: Nonsteroidal anti-inflammatory drug

eFigure 1. Definition of a Potentially Inappropriate Prescribing Cascade



Legend: A visual representation of the definition of a Potentially Inappropriate Prescribing Cascade.

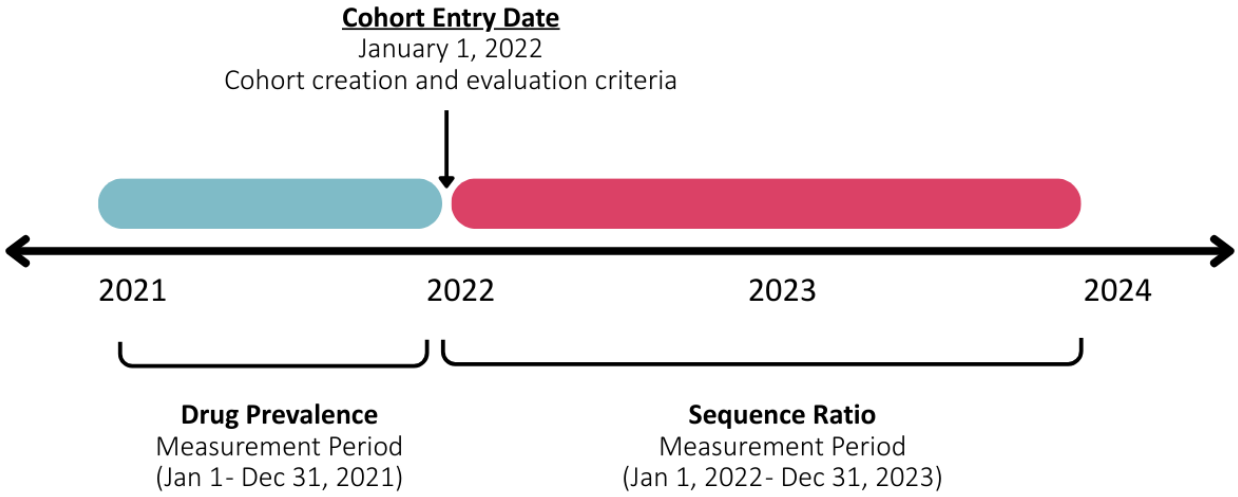
eFigure 2. Study Flow Diagram Used to Identify the Cohort



Legend: The Figure describes the steps used to identify the cohort.

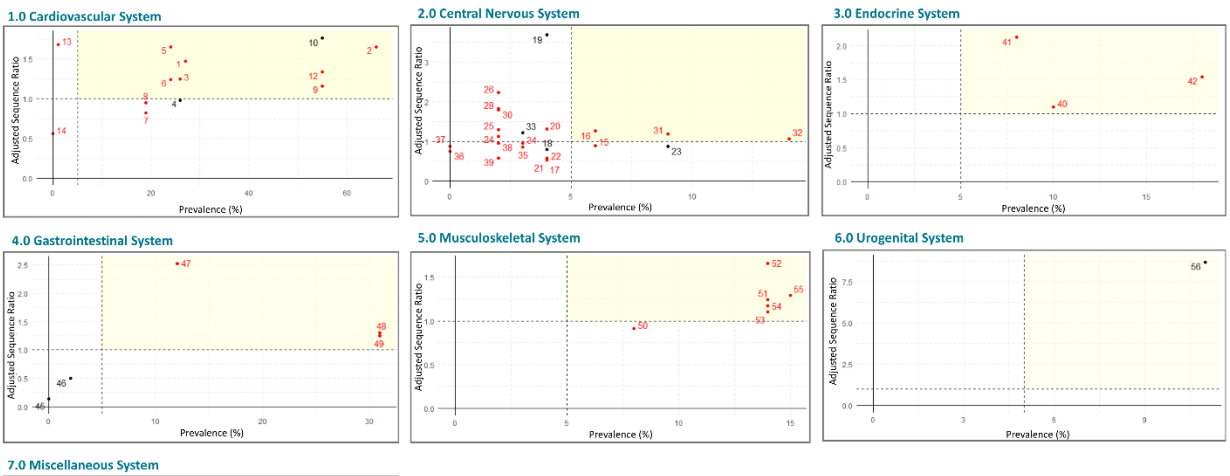
OHIP, Ontario Health Insurance Plan; ODB, Ontario Drug Benefit; CCB, calcium channel block

eFigure 3. Study Design Schematic



The figure shows the measurement period for identifying the prevalence of initial drug and sequence ratio.

eFigure 4. The 24 Prioritized Potentially Inappropriate Prescribing Cascades (PIPCs) organized by seven Physiological Systems.



Prescribing Cascade with high incidence (≥1%)
Prescribing Cascade with low incidence (<1%)
Prescribing Cascades in this quadrant have high prevalence (≥5%) of initial drug and high likelihood (aSR>1)
Prioritized Prescribing Cascade with high incidence, high prevalence and an Adjusted Sequence Ratio >1

1.0 Cardiovascular System

Drug Class

1 Angiotensin converting enzyme inhibitor to cough remedy
2 Antihypertensive to antiemetic
3 Beta blocker to antidepressant
4 Beta blocker to Phosphodiesterase-5 inhibitor
5 Calcium channel blocker to diuretic
6 Calcium channel blocker to laxative
7 Diuretic to anti-gout agent
8 Diuretic to overactive bladder medication
9 HMG Co-A reductase inhibitor to pain reliever
10 HMG Co-A reductase inhibitor to mineral supplement
11 HMG Co-A reductase inhibitor to quinine sulfate*
12 HMG Co-A reductase inhibitor to sleep agent

Individual Drug

13 Digoxin to antiemetic
14 Midodrine to antihypertensive

2.0 Central Nervous System

Drug Class

15 Anticonvulsant to topical corticosteroid
16 Anticonvulsant to antiemetic
17 Antipsychotic to beta-blocker
18 Antipsychotic to antiparkinsonian agent
19 Antipsychotic to anti-tremor antimuscarinic
20 Antipsychotic to sedative
21 Antipsychotic to antiarrhythmic
22 Antipsychotic to antihyperglycemic
23 Benzodiazepine to cholinesterase Inhibitor
24 Cholinesterase Inhibitor to overactive bladder medication
25 Cholinesterase Inhibitor to sleep agent
26 Cholinesterase Inhibitor to antiemetic
27 Cholinesterase Inhibitor to bismuth subsalicylate*
28 Cholinesterase Inhibitor to antidiarrheal
29 Cholinesterase Inhibitor to antihistamine*
30 Dopaminergic antiparkinsonian agent to antipsychotic
31 Gabapentinoid to diuretic
32 SSRI/SNRI to overactive bladder medication
33 Tricyclic antidepressant to cholinesterase Inhibitor
34 Tricyclic antidepressant to laxative
35 Tricyclic antidepressant to overactive bladder medication

Individual Drug

36 Flunarizine to antidepressant
37 Lithium to antiparkinsonian agent
38 Venlafaxine to antihypertensive
39 Venlafaxine to benzodiazepine

3.0 Endocrine System

Drug Class

40 Dipeptidyl Peptidase 4 (DPP-4) Inhibitor to Nonsteroidal anti-inflammatory drug
41 Sodium-glucose cotransporter-2 (SGLT-2) inhibitor to antifungal

Individual Drug

42 Metformin to antidiarrheal
43 Pioglitazone or Rosiglitazone to diuretic*
44 Rosiglitazone to diuretic*

4.0 Gastrointestinal System

Drug Class

45 Anticholinergic antiemetics to alpha 1 receptor blocker
46 Antidopaminergic antiemetic to antiparkinsonian agent
47 Laxative to antidiarrheal agent
48 Proton pump inhibitor to vitamin supplement
49 Proton pump inhibitor to vitamin or mineral supplement

5.0 Musculoskeletal System

Drug Class

50 Bisphosphonate to gastroprotective agent
51 Nonsteroidal anti-inflammatory drug (NSAID) to gastroprotective agent
52 NSAID to antiemetic
53 NSAID to antihypertensive
54 NSAID to heart failure agent
55 Opioid to antidepressant

6.0 Urogenital System

Drug Class

56 Alpha-1 receptor blocker to vestibular suppressant
57 Urinary anticholinergic to saliva substitute*

7.0 Miscellaneous System

Drug Class

58 Carbapenem to anticonvulsant*
59 Corticosteroid to sleep agent
60 Corticosteroid to antipsychotic
61 Corticosteroid to antihypertensive

Individual Drug

62 Acitretin to antifungal
63 Erythromycin to antiarrhythmic
64 Fludrocortisone to antihypertensive
65 Iron Supplement to laxative

*The adjusted sequence ratio could not be calculated due to the small number of the individuals newly started on both the initial and subsequent drug. Therefore, these prescribing cascades were not displayed in the figure.

Legend: This scatterplot shows the prevalence rate of the initial drug, incidence of prescribing cascade, and adjusted sequence ratio for each of the 65 Potentially Inappropriate Prescribing Cascades (PIPC) in each of the seven physiological systems. The physiological systems align with the systems used in the STOPP/START Version 3 criteria[8].

The numbers on the figure correspond to the PIPCs listed at the bottom of the figure.

Each dot in the figure represents one PIPC. The x-axis shows the population prevalence of the initial drug. The Y-axis shows the adjusted sequence ratio. Dots located in the upper-right (yellow) quadrant represent PIPCs with high initial drug prevalence (≥5%) and a high likelihood of a prescribing cascade (aSR >1). Red dots indicate PIPCs with a high incidence of prescribing cascades (≥1%). Black dots indicate PIPCs with a low incidence of prescribing cascades (<1%). Red dots within the upper-right (yellow) quadrant represent the prioritized PIPCs.

eReferences

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