

INTRODUCTION

Objectives: (1) Number and most frequent “potentially inappropriate medications” (PIMs) and “potential prescribing omissions” (PPOs); (2) Number of admissions and readmissions; (3) Costs of all admissions; (4) Correlations of STOPP PIMs and START PPOs with admissions, readmissions and mortality. (5) Evidence-based deprescribing RCTs and correlations of deprescribing with changes in numbers of PIMs and PPOs, hospitalisations, mortality, and costs.

Design and participants: Retrospective database; all patients ≥ 65 admitted to 4 acute care Calgary hospitals 2013-2021.

Databases: (1) Alberta Health Services’ Data Integration, Management and Reporting (DIMR), (2) Pharmaceutical Information Network (PIN), (3) Discharge Abstract Databases, (4) STOPP PIM and START PPO criteria.

Outcome Measures: (1) PIMs and PPOs; (2) Readmissions; (3) Mortality; (4) Correlations of PIMs and PPOs with rehospitalisation and death; (5) Costs of PIMs, PPOs and correcting PPOs; (6) Money saved by deprescribing PIMs and PPOs and, therefore, ability to fund teams of deprescribing pharmacists and outreach nurses working with family physicians to improve patient health and reduce readmissions.

Ethics approval: Conjoint Health Research Ethics Board (REB15-2163).

RESULTS: READMISSIONS,COSTS, DIAGNOSES, 2013-2021

Admission	No of patients	Days in hospital	Died in hospital	Costs	VISITS	TOP 19 DISCHARGE DIAGNOSES
First	133738	10	3816 (2.65%)	\$1,619,667,484	12159	Heart Failure wo Cor Angio
2 nd	66807	11.9	2449 (3.66%)	\$854,260,441	10995	Chronic Obstructive Pulmon Dis
3 rd	36583	12.9	1511 (4.13%)	\$479,031,338	10139	Unilateral Knee Replacement
4 th	21194	13.5	920 (4.19%)	\$277,522,078	6019	Viral/Unspecified Pneumonia
5 th	12814	13.9	536 (4.18%)	\$171,730,025	5997	Part Excisn/Destr Prostate CA
6 th	7942	13.3	296 (3.72%)	\$101,554,275	5924	Unilateral Hip Replacement
7 th thru 39 th	16630	14.2	538 (3.24%)	\$220,839,556	5334	Lower Urinary Tract Infect
Total	295,797	12.8	10,084 (3.41%)	\$3,724,605,195	4892	Ischemic Event of CNS
					4032	Arrhythmia wo Cor Angio
					3791	Dementia
					3754	Fixation/Repair Hip/Femur
					3707	PCI w MI/Shock/Arrest/Hrt Fail
					3592	General Symptom/Sign
					3585	Pacemaker Implantation
					3572	Min Intv Upp Urin Trct Ext/ PO
					3277	Other/Unspecified Sepsis/Shock
					3216	Convalescence
					3143	Non-severe Enteritis

MEDICATION RESULTS

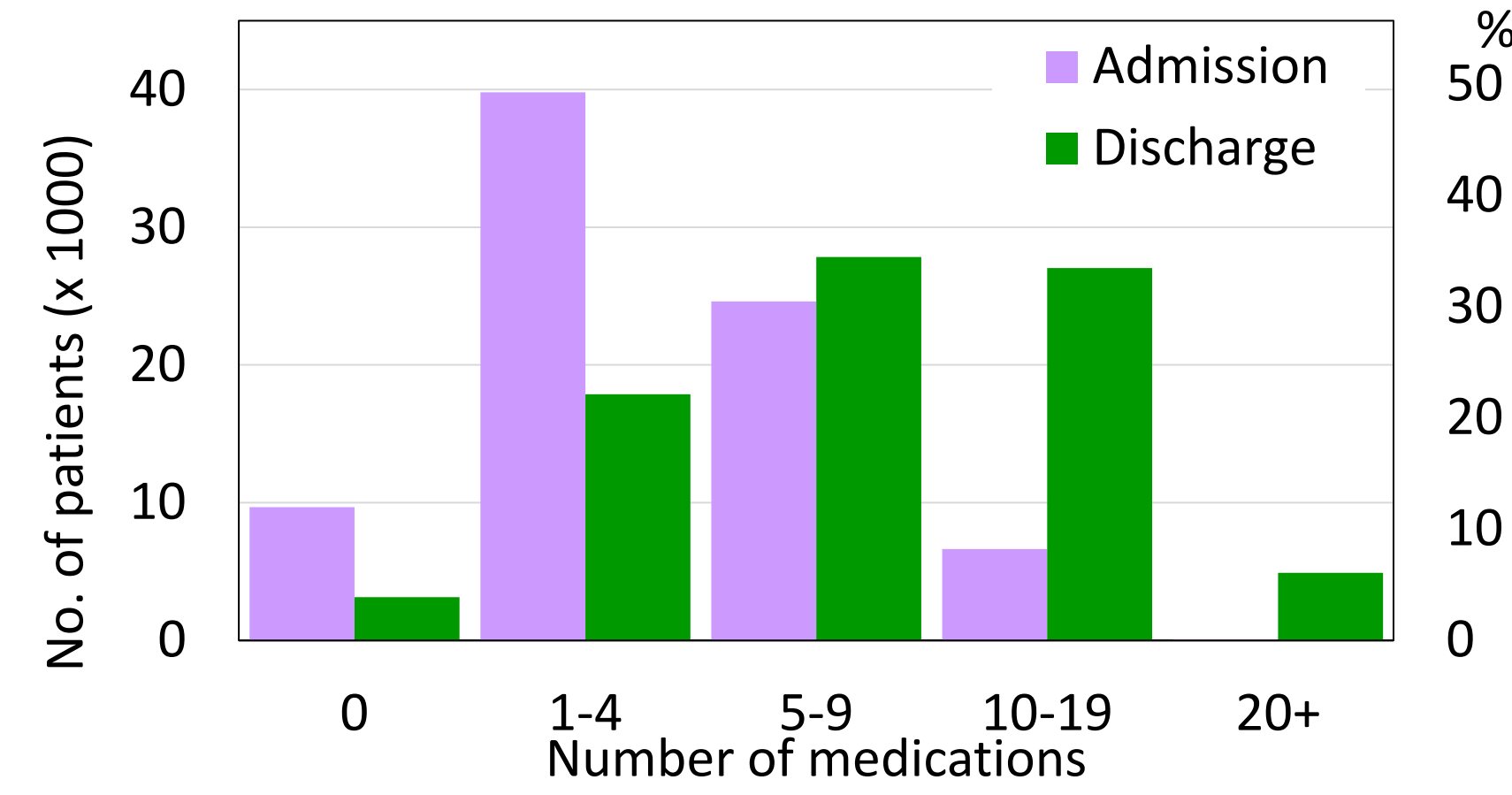


Figure 1. Frequency distribution of prescribed medications to patients. Admission meds: median 4 per patient, max 28. Discharge meds: median 9, max 63.

B) Frequently prescribed medication classes

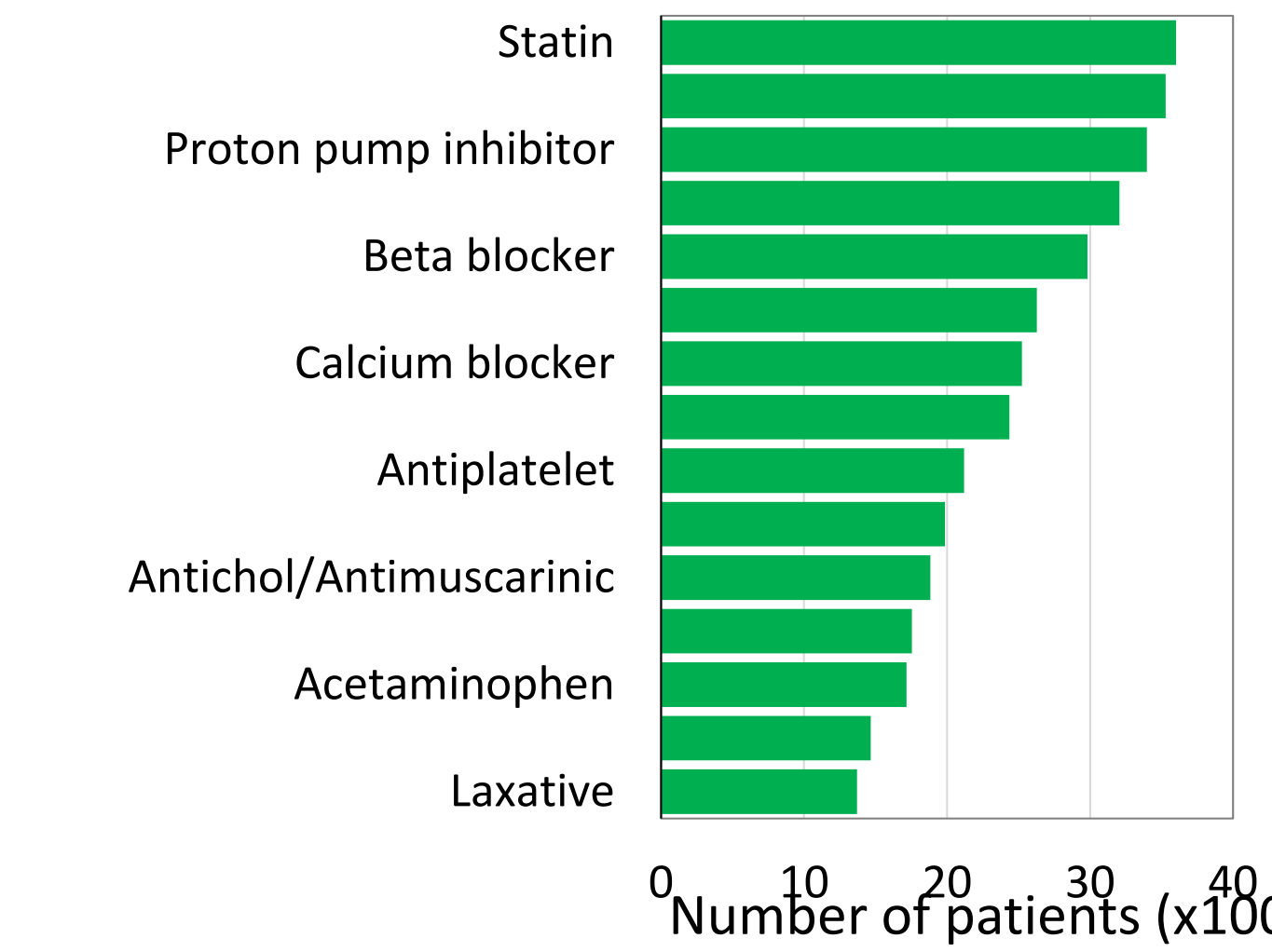


Figure 2. Common characteristics of elderly patient hospital visits.

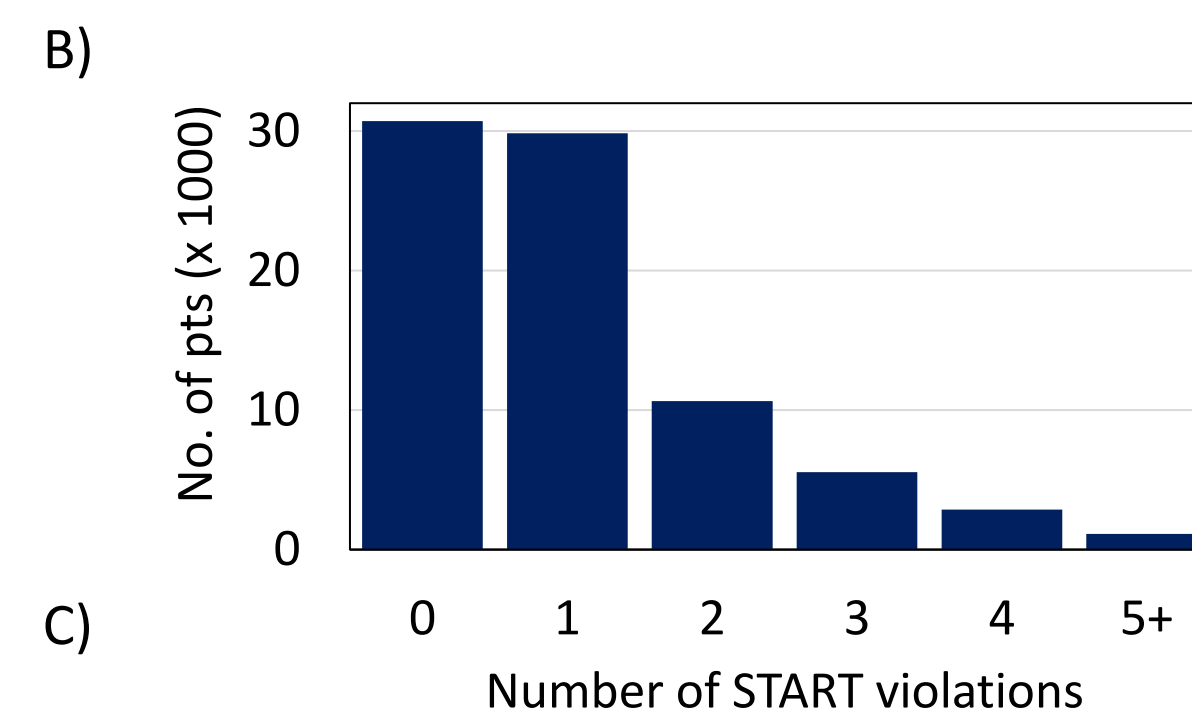


Figure 3. Evaluation of A) potentially inappropriate medications by STOPP violations, B) potential prescribing omissions by START violations. Distributions on the left, criteria on the right.

Odds ratios patient outcomes within 6 months of discharge

Independent variable	Outcome variable	
	Readmit 6M	Died 6M
Discharge medications	1.09 (1.09 – 1.09)	1.02 (1.02-1.03)
STOPP violations	1.14 (1.13 - 1.14)	1.07 (1.06-1.08)
START violations	1.10 (1.09 – 1.11)	1.33 (1.30-1.36)
START observances	1.20 (1.19 – 1.22)	1.05 (1.03-1.07)
BEERS avoid	1.26 (1.25 – 1.28)	1.30 (1.28-1.32)

CONCLUSIONS

- (1) Patients ≥65 years were discharged from Calgary hospitals 2013-21 with median 9 medications, and average 4 “potentially inappropriate medications” (PIMs). The most frequent were vasodilators, duplicate drug classes, opioids, anticoagulants, hypnotic Z-drugs, NSAIDs, benzodiazepines, beta-blockers, loop diuretics, neuroleptics and anticholinergics. The **first level in prescribing** is to use the STOPP/START and American Geriatric Society criteria, which summarise RCTs on these adverse drug interactions and were tested most recently in the 6 country SENATOR c-RCT.
- (2) The **second level in prescribing** is to identify which enzyme systems metabolise patients’ medications and ensure patients are not prescribed medications competing for the same enzyme or for enzymes which are induced or inhibited by other medications.
- (3) Two excellent free databases provide this information. The Flockhart Tables provide details of which medications induce or inhibit P450 enzymes and thus affect metabolism of other medications using those enzymes. DrugBank is > 13,500 peer-reviewed publications of drug metabolism, providing P450 enzyme metabolic pathways for some medications. For many 5-60 pathways not including P450 are provided so physicians need to know if no P450 pathway has been published and rely on monitoring symptoms and laboratory parameters after prescribing.
- (4) The **third level in prescribing** is to use data on the major differences in individual and ethnic group genomes how medications are metabolised. The NIH has funded personalised medicine in 10 major academic medical systems in the US. Mayo is the leader and provides patients with detailed advice about how their genome modifies metabolism of their medications. Canada needs to implement these three levels of prescribing and adopt the already tested Mayo software.

Key RCTs of comprehensive deprescribing

Author, date, country, Population	Intervention	Outcome
Cabezas CL 2006, Spain Hospitalised for heart failure, 2 hospitals. (IG 70, CG 64); avg age 75	RCT, 12 months. Pharmacist discharge interview with patient, carer: audiovisual and written material on CHF, diet education to reduce sodium, Infowin program explaining drug benefits and need for drugs, phone calls 2,4, 6 months	Readmissions reduced: 2 months (IG 9, CG 26, p = 0.034; 6 months IG 25, CG 54, p = 0.023. 12 months IG 39, CG 72, ns) Hospital stay costs/patient reduced (IG €997, CG €1,575)
Campins 2017, 2019, Barcelona, Spain. Community dwelling,; avg age 79; (IG 251, CG 252)	RCT, 12 months. Pharmacist evaluated all drugs, recommendations discussed with patient, face to face visit patient and physician.	Pharmacist recommended changes for 718/2709 drugs (physicians accepted 81%); (physicians accepted 70%) Fewer primary care visits at 0-3 months p = 0.001, and 0-6 months p = 0.048. Drug expenditure reduced by 14% IG€233, CG by 7 % €169/year. No differences hospitalisations
Gallagher 2016, Ireland University Hospital, ≥65, average age 77; (IG 361, CG 376)	c-RCT, 12 months, structured pharmacist review of medications, computerised STOPP/START decision support software (CDSS). Costs included pharmacist training and salary, physician and nurse review of pharmaceutical care plan, diagnosis-related group cost, support to implement CDSS	Hospital costs lower (IG €13,250; CG €15,465) Average number of adverse drug events/patient decreased (-0.064; -0.135, 0.008; p = 0.081); hospital mortality rate IG 4.7%, CG 4.5% (ns)
Gillespie 2009, Sweden Two university hospital internal medicine wards; ≥80 (IG 199, CG 201)	RCT, 12 months. Pharmacist medication reconciliation, drug review, advice to physician on drug selection, dosages and monitoring. Patient education. Fax on therapeutic goals, rationale for changes, monitoring needs for new drugs to primary care physician, phone call to patients 2 months after discharge. Primary goal reduction emergency department and hospital readmissions	IG: 16 % reduction in ED + hospital visits, 80% reduction drug-related admissions, 47% reduction ED visits. Most common reasons for drug-related admissions: sedatives, opioids and anticholinergics resulting in confusion and falls, and antihypertensives and diuretics resulting in bradycardia, hypotension and dehydration. Cost savings US\$ 230/patient, with pharmacist 0.5 full time.
Hyttinen 2019, 10% random sample of 64,250 ≥65 on Finnish Prescriptions register in 2000, with 10,333 who used PIMs precision matched with 10,333 who did not	Cohorts followed for 12 years	Pharmacists identified 476 drug-related problems (69% of suggested actions carried out by hospital physician, 6% by GP) Users of PIMs for 6 months had higher mortality (HR 1.81; 1.71, 1.92; p <0.001); PIM users higher 12 year hospital costs (€60,114; no PIM use €52,435, p <0.001)
Ravn-Nielsen 2018 Acute admission wards, Denmark, median age 72; (IG 476, basic intervention IG 493, CG 476)	RCT, 20 months then 6 month follow-up. Review and reconciliation, communication to primary care, counselling by phone	Drug counselling intervention reduced 30 day readmissions (IG 14%, CG 22%; (HR 0.62; 0.46, 0.84); Reduced 180 day readmissions (IG 40%, CG 49%; (HR 0.75; 0.62, 0.90) Reduced drug-related 30 day readmissions (IG 5%, CG 8%; (HR 0.65; 0.39, 1.09; ns); Reduced drug-related 180 day readmissions (IG 16%, CG 19%; (HR 0.80; 0.59, 1.08; ns); Mortality (HR 0.83; 0.22, 3.11; ns)
Scullin, 2007, 3 hospitals Northern Ireland; ≥ 65, taking ≥ 4 medications, hospital admission past 6 months. Avg age 70. (IG 371, CG 391)	RCT, 18 months. Integrated Medicines Management service group (5 pharmacists and 5 pharmacy technicians funded as QI project), received accelerated clinical training on major therapeutic topics, lecture and workshop by pharmacists, nurses, physicians, and study days at Postgraduate Centre. Audit showed service could be provided to 50% of patients. 1. Medication reconciliation (dosages, allergies, adverse effects). 2. Daily assessment of medications, chemical and hematological test results, individual patient counselling focusing on discontinued, new and high risk medications. 3. Pharmacist discharge summary to GP	5531 drug discrepancies identified. Counselling intervention reduced IG length of stay decreased by 2 days compared to CG (p = 0.003); Reduced IG readmissions over 12 months 40.8%, CG 49.3%, p = 0.027; NNT 11.7; Reduced costs by £2.8 million/year; No change in mortality over 18 months (IG 67, CG 76; p = 0.578)