



Inappropriate prescribing Top 5

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Disclosure

- Speaker: André Bonnici
- I have no present or past (10 years) commercial relationships with any pharmaceutical private company

Objectives

- Participants will:
 - Learn what are the most common inappropriate prescribing practices found in Canada
 - Understand the impact of inappropriate prescribing on patients, especially elderly patients
 - Learn how to potentially reduce risks of adverse drug reactions-related hospitalizations
 - Focus will be on the elderly population

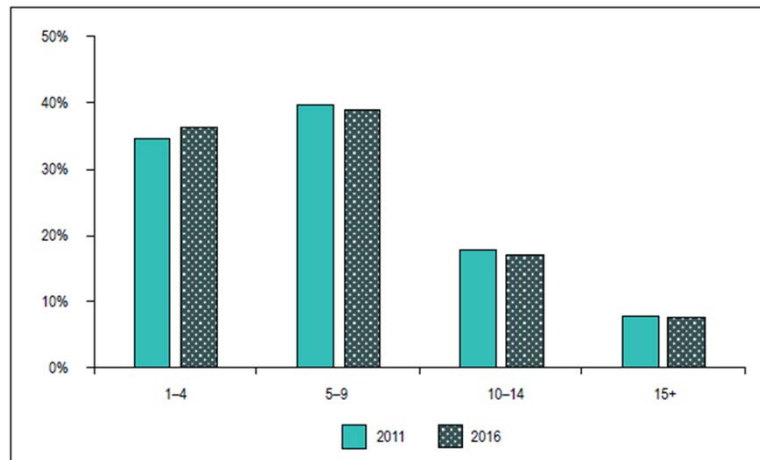
To start or not to start a drug...
a delicate balancing act



Report: Drug use among seniors in Canada 2016

- The Canadian Institute for Health Information (CIHI) is an independent, not-for-profit organization that provides essential information on Canada's health systems and the health of Canadians.

Figure 1 Percentage of seniors, by number of drug classes, Canada,* 2011 and 2016



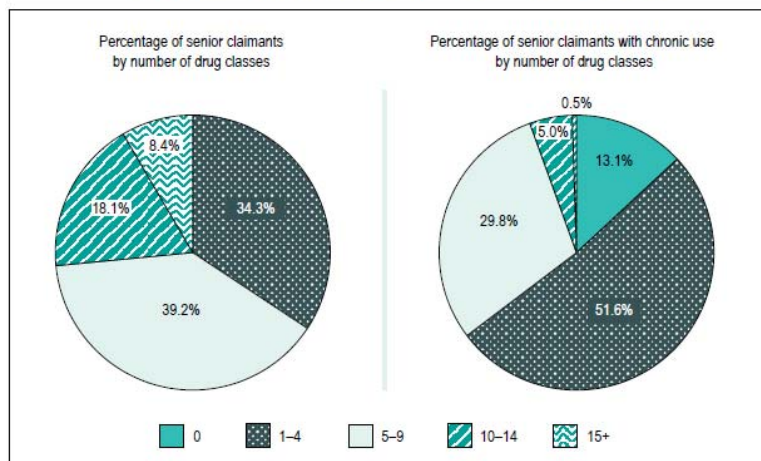
Note

* The Northwest Territories and Nunavut do not currently submit data to NPDUIS. Quebec has been excluded because data was not available prior to 2014.

Source

National Prescription Drug Utilization Information System, Canadian Institute for Health Information.

Figure 2 Percentage of seniors, by number of drug classes and number of chronic drug classes, Canada, * 2016



Note

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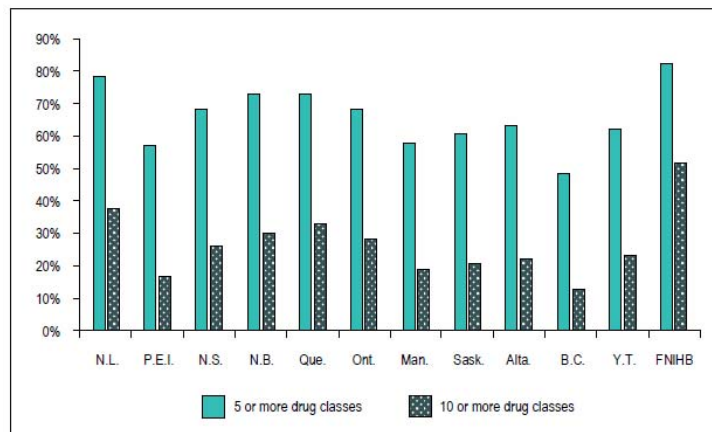
Sources

National Prescription Drug Utilization Information System, Canadian Institute for Health Information; Banque médicaments, Régie de l'assurance maladie du Québec.

Prescribing cascade

- Occurs when an adverse drug event is misinterpreted as a new condition, and a new drug or change of dose is prescribed to treat the adverse event.
- More likely to occur with chronic use of multiple drugs
- Common: hypertension as a result of NSAIDs.
 - In 2016: 71.4% of seniors using NSAIDs chronically were on antihypertensive VS 67.6% of seniors not using NSAIDs chronically (statistically significant)

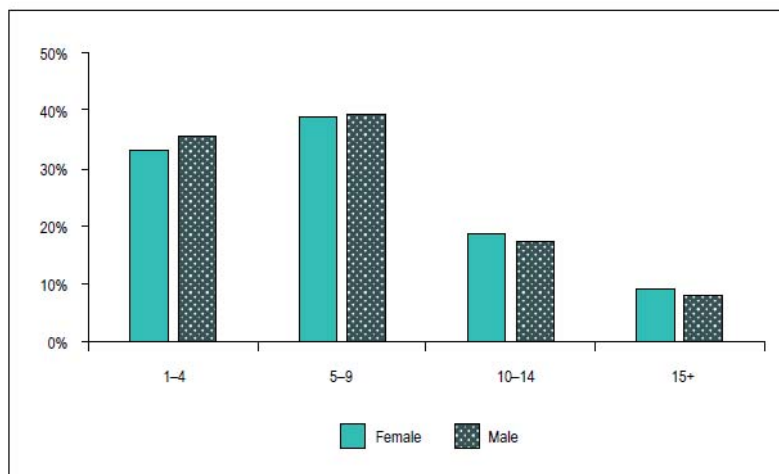
Figure 3 Percentage of seniors, by number of drug classes and jurisdiction, Canada,* 2016



Notes

* The Northwest Territories and Nunavut do not currently submit data to NPDUIS.
 Public drug programs in Newfoundland and Labrador, Nova Scotia and New Brunswick provide coverage to smaller proportions of seniors than those in other jurisdictions. Rates for these provinces may not be representative of the full seniors population. Comparing rates between jurisdictions should be done with caution. (For more information on public drug coverage available to seniors, see CIHI's [National Prescription Drug Utilization Information System Plan Information Document](#).)

Figure 4 Percentage of seniors, by number of drug classes and sex, Canada,* 2016



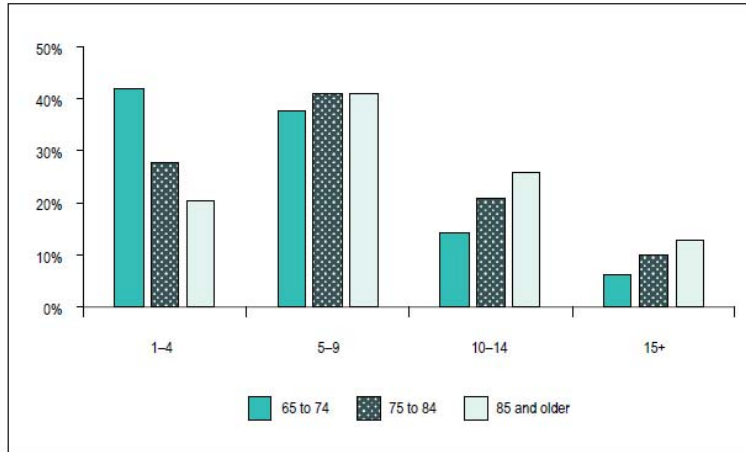
Note

* The Northwest Territories and Nunavut do not currently submit data to NPDUIS.

Sources

National Prescription Drug Utilization Information System, Canadian Institute for Health Information; Banque médicaments, Régie de l'assurance maladie du Québec.

Figure 5 Percentage of seniors, by number of drug classes and age group, Canada,* 2016



Note

* The Northwest Territories and Nunavut do not currently submit data to NPDUIS.

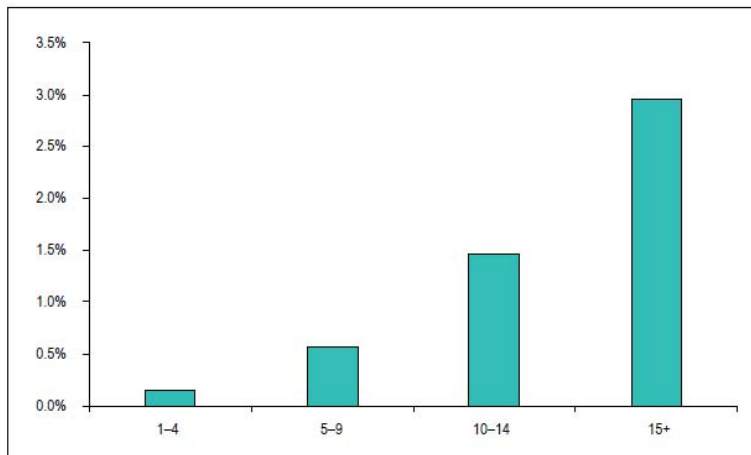
Sources

National Prescription Drug Utilization Information System, Canadian Institute for Health Information; Banque médicaments, Régie de l'assurance maladie du Québec.

Adverse drug reactions

- The number of drug classes prescribed to seniors is the factor most responsible for ADR-related hospitalizations (more than sex, age, # prescribers, number of pharmacies, prev. year hospitalization)
- In 2016, 0.7% of seniors were hospitalized for an ADR
- Seniors using 10 or more different drug classes made up 21% of seniors population but accounted for 58% of ADR-related hospitalizations

Figure 8 Percentage of seniors hospitalized for an ADR, by number of drug classes, selected jurisdictions,* 2016



Note

* There were 6 jurisdictions submitting linkable claims data to NPDUIS as of November 2017: Newfoundland and Labrador, Prince Edward Island, Manitoba, Alberta, British Columbia and Yukon.

Sources

National Prescription Drug Utilization Information System, Discharge Abstract Database and Hospital Morbidity Database, Canadian Institute for Health Information.

Which drugs cause most harm in seniors?

- **Anticoagulants** used for heart attacks and stroke prevention accounted for one quarter of all ADR-related Hospitalizations (23.9%) in seniors, mostly bleeding/coag disturbances.
- **Antineoplastics** (12.5%) which caused febrile neutropenia requiring hospitalization
- **Opioids** (8.1%) which caused mostly severe constipations and poisoning (OD). ***Seniors had the largest proportion of opioid-related poisoning related to therapeutic use than any other age group.

Table F1 Top 10 drug classes most commonly associated with seniors' ADR-related hospitalizations, Canada, 2016

Drug class	Common uses	Most common diagnosis related to hospitalization	Percentage of ADRs
Anticoagulants	Heart attack and stroke prevention	Coagulation defect, unspecified	23.9%
Other antineoplastic drugs	Cancer	Neutropenia	12.5%
Opioids and related analgesics	Pain management	Constipation	8.1%
Glucocorticoids and synthetic analogues	Asthma	Type 2 diabetes mellitus with poor control, so described	4.9%
Beta-adrenoreceptor antagonists, not elsewhere classified	Heart failure, high blood pressure, angina (chest pain)	Bradycardia, unspecified	3.5%
NSAIDs (excluding salicylates)	Arthritis, pain management	Acute renal failure, unspecified	3.3%
Loop (high-ceiling) diuretics	Heart failure, high blood pressure	Acute renal failure, unspecified	3.3%
Benzothiadiazine derivatives	High blood pressure	Hypo-osmolality and hyponatraemia	3.1%
Other diuretics	Heart failure, high blood pressure	Acute renal failure, unspecified	2.5%
Angiotensin-converting enzyme (ACE) inhibitors	High blood pressure, heart failure	Acute renal failure, unspecified	2.2%

Sources

Discharge Abstract Database and Hospital Morbidity Database, Canadian Institute for Health Information.

Inappropriate prescribing

- The Beers Criteria were first developed in 1991 by Mark H. Beers, MD, to decrease inappropriate prescribing and ADEs and, in particular, to identify medications or medication classes that should be avoided in older adults in nursing homes
- In January 2019, AGS published the latest update to the Beers Criteria for Potentially Inappropriate Medication Use in Older Adults
- [https://www.pharmacytoday.org/article/S1042-0991\(19\)31235-6/pdf](https://www.pharmacytoday.org/article/S1042-0991(19)31235-6/pdf)

Table 2. Incorporated changes of potentially inappropriate medications in older adults	
Medication or medication class	Recommendation; rationale (<i>changes to the 2015 criteria</i>)
Anticholinergics	
First-generation antihistamines	Avoid; clearance reduced with advanced age, and tolerance develops when used as hypnotic; risk of confusion, dry mouth, constipation, and other anticholinergic effects or toxicity
Antiparkinsonian agents (benztropine, trihexyphenidyl)	Avoid; not recommended for prevention of extrapyramidal symptoms with antipsychotics
Antispasmodics	Avoid; high anticholinergic and uncertain effectiveness
Antithrombotics	
Dipyridamole, oral short-acting	Avoid; may cause orthostatic hypotension, and more effective alternatives available; I.V. form acceptable to use in cardiac stress testing
Anti-infective	
Nitrofurantoin	Avoid in individuals with CrCL < 30 mL/min or long-term suppression; potential for pulmonary toxicity, hepatotoxicity, and peripheral neuropathy, especially with long-term use
Cardiovascular	
Peripheral alpha-1 blockers for treatment of hypertension	Avoid use as antihypertensive; high risk of orthostatic hypotension and associated harms, especially in older adults
Central-alpha agonists (clonidine, guanabenz, guanfacine, methyl dopa, reserpine > 0.1 mg/d)	Avoid clonidine as first-line antihypertensive. Avoid other CNS alpha-agonists as listed; high risk of adverse CNS effects; may cause bradycardia and orthostatic hypotension
Disopyramide	Avoid; may induce heart failure in older adults because of potent inotropic action; strongly anticholinergic
Dronedarone	Avoid in individuals with permanent atrial fibrillation or severe or recently decompensated heart failure; worse outcomes have been reported in patients who have permanent atrial fibrillation or severe or recently decompensated heart failure
Digoxin for first-line treatment of atrial fibrillation or heart failure	Avoid this rate control agent as first-line therapy for atrial fibrillation. Avoid as first-line therapy for heart failure. If used, avoid dosages > 0.125 mg/d. Atrial fibrillation: should not be used as first-line because <i>there are safer and</i>

Growth hormone	Avoid, except for patients diagnosed with growth hormone deficiency due to an established etiology; impact on body composition is small and associated with edema, arthralgia, carpal tunnel syndrome, gynecomastia, and impaired fasting glucose
Insulin, sliding scale (<i>insulin regimens containing only short- or rapid-acting insulin dosed according to current blood glucose levels without concurrent use of basal or long-acting insulin</i>)	Avoid; higher risk of hypoglycemia without improvement in hyperglycemia management regardless of care setting
Megestrol	Avoid; minimal effect on weight with increased risk of thrombotic events and possibly death in older adults
Sulfonylureas, long-acting (chlorpropamide, glimepiride, glyburide)	Avoid; chlorpropamide: long half-life and can cause prolonged hypoglycemia and SIADH; glimepiride and glyburide: higher risk of severe prolonged hypoglycemia
GI	
Metoclopramide	Avoid, unless for gastroparesis with duration not to exceed 12 weeks except in rare cases; can cause extrapyramidal effects, including tardive dyskinesia
Mineral oil, given orally	Avoid; potential for aspiration and adverse effects
PPIs	Avoid scheduled use for > 8 weeks unless for high-risk patients, erosive esophagitis, Barrett's esophagitis, pathological hypersecretory condition, or demonstrated need for maintenance treatment; risk of Clostridium difficile infection, bone loss, and fractures
Pain medications	
Meperidine	Avoid; not effective in dosages commonly used and has a higher risk of neurotoxicity, including delirium, than other opioids
COX nonselective NSAIDs, oral	Avoid chronic use, unless other alternatives are not effective and patient can take gastroprotective agent; increased risk of GI bleeding or peptic ulcer disease in high-risk groups, including those > 75 years or taking oral or parenteral corticosteroids, anticoagulants, or antiplatelet agents; can increase blood pressure and induce kidney injury
Indomethacin, ketorolac, includes parenteral	Avoid; increased risk of GI bleeding/peptic ulcer disease and acute kidney injury; indomethacin is more likely than other NSAIDs to have adverse CNS effects
Skeletal muscle relaxants	Avoid; poorly tolerated by older adults because some have anticholinergic adverse effects, sedation, and increased risk of fractures
Genitourinary	
Desmopressin	Avoid for treatment of nocturia or nocturnal polyuria; high risk of hyponatremia

Table 3. Incorporated changes of drug–drug, drug–disease, or drug–syndrome interactions in older adults

Medication or medication class	Recommendation; rationale (<i>changes to the 2015 criteria</i>)
Cardiovascular	
Heart failure (cilostazol, nondihydropyridine CCBs, NSAIDs, COX-2 inhibitors, thiazolidinediones, dronedarone)	Avoid; cilostazol; potential to increase mortality Avoid in HFrEF; nondihydropyridine CCBs; may promote fluid retention and/or exacerbate heart failure Use with caution in patients with asymptomatic heart failure; avoid in patients with symptomatic heart failure; NSAIDs, COX-2 inhibitors, and thiazolidinediones (may promote fluid retention and/or exacerbate heart failure); dronedarone (potential to increase mortality)
Syncope (AChEIs, nonselective peripheral alpha-1 blockers, tertiary TCAs, antipsychotics [chlorpromazine, thioridazine, olanzapine])	Avoid; AChEIs cause bradycardia; nonselective peripheral alpha-1 blockers cause orthostatic blood pressure changes; tertiary TCAs and antipsychotics increase risk of orthostatic hypotension and bradycardia
CNS	
Delirium (anticholinergics, antipsychotics, benzodiazepines, corticosteroids, H2-receptor antagonists, meperidine, Z drugs)	Avoid; potential of inducing or worsening delirium; avoid antipsychotics for behavioral problems of dementia and/or delirium unless nonpharmacological options have failed or are not possible and the older adult is threatening substantial harm to self or others; antipsychotics are associated with greater risk of cerebrovascular accident and mortality in patients with dementia
Dementia or cognitive impairment (anticholinergics, benzodiazepines, Z drugs, antipsychotics used chronically and “as needed”)	Avoid; adverse CNS effects; avoid antipsychotics for behavioral problems of dementia and/or delirium unless nonpharmacological options have failed or are not possible and the older adult is threatening substantial harm to self or others; antipsychotics are associated with greater risk of cerebrovascular accident and mortality in patients with dementia
History of falls or fractures (antiepileptics, antipsychotics, benzodiazepines, Z drugs, antidepressants [TCAs, SSRIs, SNRIs], opioids)	Avoid unless safer alternatives are not available; avoid antiepileptics except for seizure and mood disorders; avoid opioids except for pain management in setting of acute pain; may cause ataxia, impaired psychomotor function, syncope, additional falls
Parkinson disease (antiemetics [metoclopramide, prochlorperazine, promethazine], all antipsychotics except quetiapine, clozapine, and pimavanserin)	Avoid; dopamine-receptor antagonists with potential to worsen parkinsonian symptoms
GI	
History of gastric or duodenal ulcers (aspirin > 325 mg/d, COX-2 non-selective NSAIDs)	Avoid unless alternatives are not effective and patient can take gastroprotective agent; may exacerbate existing ulcers or cause new/additional ulcers

Kidney/urinary tract	
Chronic kidney disease stage 4 or higher, CrCL < 30 mL/min NSAIDs)	Avoid; may increase risk of acute kidney injury and further decline of renal function
Urinary incontinence in women (oral and transdermal estrogen, peripheral alpha-1 blockers)	Avoid in women; oral estrogen; lack of efficacy Peripheral alpha-1 blockers: aggravation of incontinence
Lower urinary tract symptoms, benign prostatic hyperplasia (strongly anticholinergic drugs, except antimuscarinics for urinary incontinence)	Avoid in men; may decrease urinary flow and cause urinary retention
Drug–drug interactions	
RAS inhibitor or potassium-sparing diuretics and another RAS inhibitor	Avoid routine use in those with chronic kidney disease stage 3a or higher; increased risk of hyperkalemia
Opioids and benzodiazepines	Avoid; increased risk of overdose
Opioids and gabapentin, pregabalin	Avoid; increased risk of severe sedation-related adverse events (respiratory depression and death)
Anticholinergic and anticholinergic	Avoid; increased risk of cognitive decline
Antidepressants (TCAs, SSRIs, and SNRIs), antipsychotics, antiepileptics, benzodiazepines, Z drugs, and opioids plus any combination of three or more of these CNS-active drugs	Avoid total of three or more CNS-active drugs; All: increased risk of falls Benzodiazepines and Z drugs: increased risk of fracture
Corticosteroids (oral or parenteral) plus NSAIDs	Avoid; increased risk of peptic ulcer disease or GI bleeding
Lithium plus ACEIs or loop diuretics	Avoid; increased risk of lithium toxicity
Peripheral alpha-1 blockers plus loop diuretics	Avoid in older women; increased risk of urinary incontinence
Phenytoin plus TMP-SMX	Avoid; increased risk of phenytoin toxicity
Theophylline plus cimetidine or ciprofloxacin	Avoid; increased risk of theophylline toxicity
Warfarin plus amiodarone or ciprofloxacin or macrolides (except azithromycin) or TMP-SMX or NSAIDs	Avoid when possible; increased risk of bleeding

Table 6 Top 10 chemicals from Beers list* prescribed to seniors, by rate of use and chronic use, Canada, † 2016

Chemical	Indicated uses	Beers criteria rationale (potential harm)	Rate of use	Rate of chronic use
Pantoprazole (PPI) (>8 weeks)	Gastroesophageal reflux disease, peptic ulcer disease	<i>Clostridium difficile</i> infection, bone loss, fractures	13.2%	10.3%
Lorazepam	Anxiety, insomnia	Cognitive impairment, delirium, falls, fractures	8.8%	3.6%
Nitrofurantoin	Antibiotic to treat urinary tract infection	Pulmonary toxicity, hepatotoxicity, peripheral neuropathy	5.0%	0.1%
Rabeprazole (PPI) (>8 weeks)	Gastroesophageal reflux disease, peptic ulcer disease	<i>Clostridium difficile</i> infection, bone loss, fractures	4.3%	3.5%
Amitriptyline	Depression	Sedation, orthostatic hypotension	2.9%	1.8%
Quetiapine	Schizophrenia, bipolar disorder	Cognitive decline, stroke, mortality	2.8%	1.7%
Omeprazole (PPI) (>8 weeks)	Gastroesophageal reflux disease, peptic ulcer disease	<i>Clostridium difficile</i> infection, bone loss, fractures	2.7%	2.2%
Zopiclone	Insomnia	Cognitive impairment, delirium, falls, fractures	2.4%	1.5%
Oxazepam	Anxiety, insomnia	Cognitive impairment, delirium, falls, fractures	2.4%	1.4%
Estradiol (oral/topical patch)	Menopause	Potential carcinogen (breast and endometrium)	2.1%	1.2%

Notes

* AGS Beers Criteria 2015 Updated Version, with modifications to make the measure of potentially inappropriate use more applicable to the Canadian market (see Appendix B).

† The Northwest Territories and Nunavut do not currently submit data to NPDUIS.

Sources

National Prescription Drug Utilization Information System, Canadian Institute for Health Information; Banque médicaments, Régie de l'assurance maladie du Québec.

Table G1 Top 10 chemicals from Beers list* prescribed to seniors, by rate of use and chronic use, by sex and age group, Canada, † 2016

Chemical	Common uses	Sex		Age group		
		Female	Male	65 to 74	75 to 84	85 and older
Pantoprazole (PPI) (>8 weeks)	Gastroesophageal reflux disease, peptic ulcer disease	13.8%	12.5%	11.2%	14.7%	17.7%
Lorazepam	Anxiety, insomnia	10.9%	6.2%	7.6%	9.6%	11.4%
Nitrofurantoin	Antibiotic to treat urinary tract infection	7.6%	1.7%	4.1%	5.5%	7.0%
Rabeprazole (PPI) (>8 weeks)	Gastroesophageal reflux disease, peptic ulcer disease	4.7%	3.8%	3.6%	5.1%	5.5%
Amitriptyline	Depression	3.7%	1.8%	3.1%	2.9%	2.0%
Quetiapine	Schizophrenia, bipolar disorder	3.0%	2.4%	2.1%	2.8%	5.2%
Omeprazole (PPI) (>8 weeks)	Gastroesophageal reflux disease, peptic ulcer disease	2.9%	2.3%	2.3%	2.9%	3.3%
Zopiclone	Insomnia	2.8%	2.0%	2.2%	2.6%	3.1%
Oxazepam	Anxiety, insomnia	3.0%	1.7%	1.7%	2.6%	4.2%
Estradiol (oral/topical patch)	Menopause	3.7%	0.0%	2.7%	1.5%	0.7%

Notes

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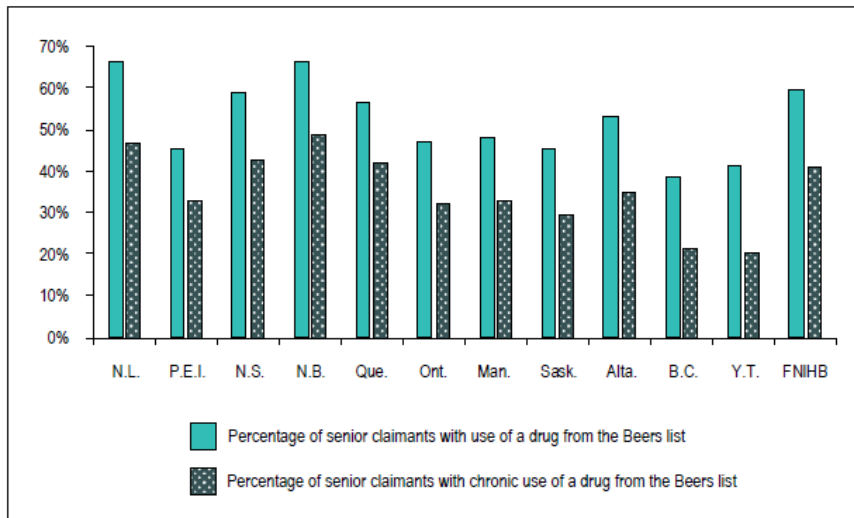
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Sources

National Prescription Drug Utilization Information System, Canadian Institute for Health Information; Banque médicaments, Régie de l'assurance maladie du Québec.

4 of the 10 most commonly prescribed chemicals from the Beers list are recommended to always be avoided in seniors.³⁷ Psychotropic drugs such as benzodiazepines, certain antidepressants and antipsychotics should be avoided as first-line treatment options for seniors in most situations because of their potential to increase the risk of falls, fractures and cognitive impairment. Despite this recommendation, lorazepam and oxazepam (benzodiazepines), zopiclone (a benzodiazepine-related drug) and quetiapine (an antipsychotic) are some of the chemicals from the Beers list most commonly used among seniors.

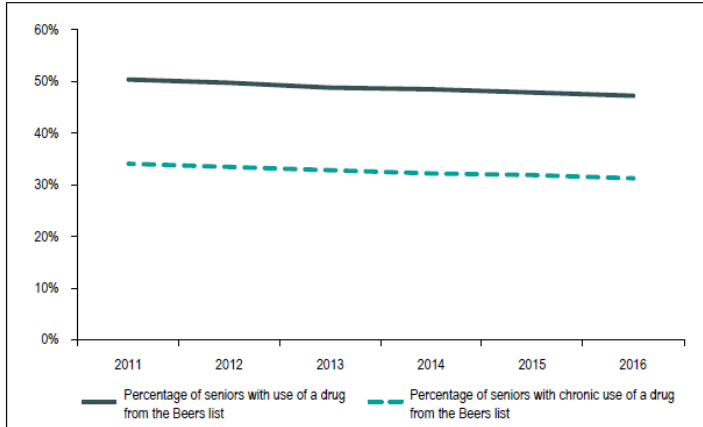
Figure 11 Seniors' usage rate of drugs from Beers list,* by jurisdiction, Canada,† 2016



Notes

* AGS Beers Criteria 2015 Updated Version, with modifications to make the measure of potentially inappropriate use more applicable to the Canadian market (see Appendix B).

Figure 10 Seniors' usage rate of drugs from Beers list,* Canada,†
2011 to 2016



Notes

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† The Northwest Territories and Nunavut do not currently submit data to NPDUIS. Quebec has been excluded because data was not available prior to 2014.

Source

National Prescription Drug Utilization Information System, Canadian Institute for Health Information.

How do we reduce risk of ADRs?

Top 5 take home messages

Take home #1

Too many drug classes = more ADR-related hospitalizations in seniors

- Regular medication reviews by MD and Pharmacist
- Avoid drug cascades (i.e. don't add a drug before you have ruled out if another drug is causing symptoms)
- Deprescribe (new admission, drug review using Beers list)

Top 5 take home...

Take home #2

Anticoagulants are the most implicated drug classes in ADR-related hospitalization in seniors

- Adjust dose to decreased renal function and decreased weight
- Check for drug-drug interactions
- Evaluate risk VS benefit of continuing in advanced age

Top 5 take home

Take home #3

Opioids are very frequently implicated in ADR-related hospitalizations in the elderly

- Avoid if possible (use acetaminophen?)
- If must , use them for short period and ADJUST dosage downward when advanced age and low weight or obesity
- Avoid combining opioids with other CNS depressants (or reduce dosage)
- Don't forget to prescribe laxatives!

Top 5 take home

Take home #4

Beware of corticosteroids in the elderly, frequent cause of ADR-related hospitalization (Hyperglycemia)

- Make sure glucose checked more frequently
- May need to adjust anti-diabetic drugs (if you add insulin, don't only use rapid sliding scale without baseline)

Top 5 take home

Take home #5

Use the Beers list!!

- Avoid chronic NSAIDS, especially when Creat clearance less than 30 ml/min
- Proton pump inhibitors stop after 8 weeks (unless Baretts , erosive esophagitis)
- Avoid benzodiapines (Falls, fractures)
- Avoid Amitripyline (anticholinergic)
- Avoid quetiapine and other antipsychotics (Stroke-death)
- Avoid Z-drugs (falls, fractures)

Other “good pratcices”

- Regular medication reviews by MD and Pharmacist
- Reassess and adjust medication dose to renal function, decreased weight etc...(especially in the elderly)
- Medication reconciliation (changes at transition of care)
- Patient teaching about medication by pharmacists
- Use software to guide - reduce number of drugs /drug classes (“Deprescribing” software Medstopper/Medsafer, Beers electronic tool from AGS)
- Article summarizing available tools (2020):
<https://onlinelibrary.wiley.com/doi/full/10.1002/jppr.1626>

Tools for deprescribing

- Example: Medsafer trial
- <https://pubmed.ncbi.nlm.nih.gov/31250427/>
 - Patients in the intervention arm had a "deprescribing opportunity report" generated by MedSafer and provided to their in-hospital treating team.

MED SAFER

Results: A total of 1066 patients were enrolled, and deprescribing opportunities were present for 873 (82%; 418 during the control and 455 during the intervention phases, respectively).

The proportion of patients with one or more PIMs deprescribed at discharge increased from 46.9% in the control period to 54.7% in the intervention period with an adjusted absolute risk difference of 8.3% (2.9%-13.9%).

Not all classes of drugs in the intervention arm were associated with an increase in deprescribing, and new PIM starts were equally common in both arms of the study.

Conclusion

- Physicians, Pharmacists, Nurses all should play an essential to reduce the risks of ADRs.
- With the aging population in Québec and Canada, it will become all the more crucial to reduce these risks , partly by re-thinking how we use medication to “first do no harm”.



