

The 300 Medications Most Commonly Prescribed for Ontario's Seniors: an evidence-based review

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- read 'Bad Pharma' by Ben Goldacre (or his June 23/15 BMJ editorial, 350:h3397) for context.

- Polypharmacy, typically defined as 4 or more prescription medications daily, is an 80s concept associated with harm.
- Preventive polypharmacy is a 90s concept associated with benefit.
- Pharmatecture refers to minimizing medications to maximize results.
- Patient centred deprescribing is becoming a major geriatric primary care activity

Learning Objectives

- 1) Describe the 300 most commonly prescribed medications through ODB for Ontarians 65 and over, and their age-appropriate doses.
- 2) Review the evidence for, and against, the use of particular medications in clinical practice
- 3) Identify prescribing trends over time that are associated with better, or worse, outcomes

Data Source

-Ontario Public Drug Programs Division

All ODB recipients (distinct count) 65 and over
as of Apr 1/2017, through Mar 31,2018

(n=2.3 million) (97%!)

-topicals, inhalers, vitamins and eyedrops
excluded from analysis

Antihypertensives (“65%”)

- ACE inhibitors (29%), ARBs (24%), calcium channel blockers (28%), non-furosemide diuretics (25%); 48% of ontarians 65 and over are on 2 (or more) simultaneously.
- Most beta-blocker use (24%) is for AF/CHF/CAD, betablockers no longer recommended by CHEP for HTN over 75

ACE inhibitors (29%)

- Evidence that some ACE inhibitors reduce mortality in HTN (2.5-10 mg od ramipril 12%, 2-8 mg od perindopril 12%) is excellent. Evidence that lisinopril, enalapril, trandalopril, fosinopril (4% combined) reduce mortality in HTN is not as good. Quinapril and cilazapril (1.2% combined) may worsen cognition (Sink K, et al, Arch Int Med 2009)

Calcium channel blockers (28%)

- Evidence that some calcium channel blockers reduce mortality in HTN (2.5-10 mg od amlodipine 20%, felodipine .4%) is excellent, while there is no evidence that diltiazem 3.7%, nifedipine 3.1%, verapamil .4% reduce mortality, in HTN or CAD (Poole-Wilson PA, Lancet, 2004;364:849)

Diuretics (25%)

- HCTZ (alone or in combo)(19%) indapamide (5%), chlorthalidone (1%) all reduce mortality, but only when used at low dose with electrolyte monitoring
- Musini VM, et al, Cochrane Database Syst Rev 2014;CD003824 -although HCTZ demonstrates bigger BP effect at higher doses than 12.5 mg od (also way higher side effects) in the elderly, low dose chlorthalidone (6.25 mg), and indapamide (1.0 mg) are just as effective, and way better tolerated than higher doses.

Arbs (24%)

Altho' candesartan (5%), valsartan (5%), irbesartan (4%), telmisartan (5%), losartan (3%), and olmesartan (3%) are commonly used antihypertensives, there is good evidence that they do not reduce mortality for HTN (Elgendy IY, et al, Am J Hypertension 2014;PMID 25391580; meta-analysis of 16 ARB RCTs involving 113,000 patients age 65 and over. Increased risk of death/AKI with arbs, reduced risk of CHF hospitalization/stroke with arbs (all compared to placebo)

-Confirmed by Cheng J, et al, JAMA Intern Med 2014;174:773-785, and Li EC, et al, Cochrane Database Syst Rev 2014

Beta-blockers (24%)

- Metoprolol (25-200 mg/d) (8.2%), bisoprolol (1.25-10mg/d) (9.5%), carvedilol (3.125-25 mg bid) (.7%) are excellent choices proven to reduce mortality in systolic heart failure (Chatterjee S, et al, BMJ 2013;346:f55;Wikstrand J, et al, J Intern Med 2014;275:134). Bisoprolol may be superior to carvedilol/metoprolol if co-existent COPD (Su VY, et al, Medicine 2016;95:e2427). “the dose necessary to reduce resting heart rate by 10 bpm”
- Atenolol(4%) doesn't reduce mortality (Psaty, BM, JAMA;2006;295:1704), value of all beta-blockers for CAD much less than 20 years ago (Bangalore S, et al, Am J Med 2014;127:939-953)
- propranolol/acebutolol/nadolol/sotalol use all less than 1%

Oral Antibiotics (“60%”)

- Amox or amox/clav (19%), macrolides (12% - 7% azithromycin, 3% clarithromycin, 2% clindamycin) quinolones (10% - 5.5% cipro, 2% each levo/moxifloxacin, .7% norflox), cephalosporins (10% - 7% cephalexin, 2% cefuroxime, 1% cefprozil)
- Nitrofurantoin 6%, trimethoprim 3.2%, Metronidazole 2.8%, occasional Pen VK, cloxacillin, tetracycline (<2% combined)

-Azithromycin safer in the elderly than clarithromycin, which interacts with amlodipine, statins, digoxin, quetiapine, trazadone, tramadol -Wright AJ, et al, CMAJ 2011;183:303-307)

-both likely better (lower 30 day mortality) than alternatives for community acquired pneumonia (Trac MH, et al, CMAJ 2016:150901), which is >2/3 viral (Jain S, et al, NEJM 2015;373:1415)

Not trimethoprim for elderly UTI

- Increased risk for AKI/hyperkalemia in all elderly (Crellin E, et al, BMJ 2018;360:k341)
- Increased risk for death in elderly already on ACE/ARB/spironolactone (Antoniou T, et al, CMAJ 2015;187:E138; Fralick M, et al, BMJ 2014;349:g6196)

Analgesics (“60%”)

- Narcotics (24%)(tylenol#3’s/codeine - 10%,hydromorphone 6%, oxycodone 4%, hydrocodone 2%, morphine 1%, fentanyl .3%)
- NSAIDs (21%)(3-4% each naproxen, celecoxib, meloxicam, diclofenac, 1- 2% ketorolac, ibuprofen,indomethacin)
- Acetaminophen 12%
- Pregabalin/gabapentin 8.1%

- Hydromorphone .5 mg preferable to 30 mg codeine (equi-analgesic, but less nausea, constipation, abdominal pain, confusion)
- Antidepressants (but not ami/nortriptyline, doxepin, des/imipramine) safer than narcotics or gabas for chronic pain
- Naproxen (no max dose)/ibuprofen (max dose 800 mg/d) have lower CV risk than other NSAIDs (McGettigan P, et al, PLoS Medicine 2011;8:e1001098). topical NSAIDs safer than oral NSAIDs.

Statins (51%)

51% of all ontarians aged 65 and over got a statin last year, (25% rosuvastatin, 22% atorvastatin, 3% simvastatin, 1% pravastatin.

-mostly primary prevention (HTN, hyperlipidemic, diabetic)(treating to numbers beyond age 75?, vs. 5mg rosuvastatin/10 mg atorvastatin/10 mg simvastatin)

-only other lipid-lowering agents of note were ezetimibe (5%) and fenofibrate (1%)

- No evidence that ezetimibe or fenofibrate lowers mortality, even for secondary prevention in high risk patients (Cannon CP, et al, NEJM 2015;372:2387; Keech A, et al, Lancet 2005;366:1849)
- dose and age dependent diabetes risk, obesity risk, sedentary life style risk, pain/weakness risk with statins (Redberg RF, jama 2016)

- Ble A, et al, J Gerontol A Biol Sci Med Sci 2017;72:243 – a UK Clinical Practice Research Datalink project-10 year followup, 12,000 persons 60 years and older, statin users and matched controls, mostly secondary prevention.
- No effect on stroke, death, or dementia, 30% higher falls/fracture risk in persons 80 and over.
- Han BH, et al *jamainternmed*.2017.1442 – increased mortality with pravastatin for primary prevention in persons 75 and older

PPIs/H2 blockers (25%)

- 21% received PPI (pantoprazole 8%, rabeprazole 7%, omeprazole 3%, lansoprazole 3%), 4% ranitidine
- Both PPI use and H2 blocker use have been associated with cognitive impairment, and with increasing risk for B12 deficiency/osteoporosis (Lam JR, et al, JAMA 2013;310:2435; Gray SL, Arch Int Med, 2010;170:765-771) (? Put vitamins B12 and D in PPI). Recent evidence that PPIs increase mortality is very low quality.
- Effect of domperidone up to 20 mg po qid (2%) on QTc is tiny (3.4 milliseconds) (Biewenga J, Keung C, et al 2015)

Antidepressants (24%)

- Neither of the 2 most commonly prescribed antidepressants in the elderly (trazadone 5%, escitalopram 4%) are effective for depression in the elderly!
- Although citalopram (10-30 mg/d) (3%), venlafaxine (75-225 mg/d), duloxetine (30-90 mg /d), mirtazapine (15-45 mg hs), and sertraline (25-100 mg od) (each 2%), and fluoxetine (5-20 mg/d) (1%) are safe and effective in the elderly, there are serious safety concerns with amitryptiline/nortryptiline/doxepin (3.3% combined), bupropion and paroxetine (1% each)

Poquito mejor que nada – little better than nothing

Unfortunately, escitalopram (cipralex) is little better than nothing for mood in the elderly; still no positive RCTs in the elderly (now 6 decent ones: An H, et al, J Alzheimers Dis 2017;55:727; Choe YM, et al Int J Geriatr Psychiatry 2016;31:731; Angermann CE, et al, JAMA 2016;315:2683; Bose A, et al, Am J Geriatr Psych 2008;16:14-20, Kasper S, et al, Am J Geriatr Psych 2005;13:884-891, Lenze EJ, et al, JAMA 2009;301:295-303), involved over 1500 elderly subjects combined, and are all negative studies compared to placebo.

-antidepressants affecting norepinephrine (mirtazapine, venlafaxine) and capsaicin .075% are most effective for neuropathic pain (better pain relief/less side effects) over age 65 than gabapentin or pregabalin (Griebeler ML, et al, Ann Int Med 2014;161:639)

-Current use of gabapentin, pregabalin, baclofen (1.7%) in Ontario's seniors (9.8% in all) is rarely for seizure or spasm, far more likely to be used off-label for chronic pain/anxiety/substance dependence

-Johansen JE, [jamainternmed.2017.7856](https://pubmed.ncbi.nlm.nih.gov/277856/) – for every 1 elderly patient with improvement in neuropathic pain, 10 elderly patients will have worse cognition/mobility with gabapentinoids (all cause dizziness, drowsiness, falls, edema)

Constipation (22%)

- Most commonly prescribed drug (docusate 6%) ineffective (MacMillan TE, et al, Am J Med 2016;129:1001.e1-7)
- Safest, most evidence based drug for stimulant-cathartic naïve elderly (PEG 17-34 g/d) is not a benefit
- Senna ('as many 8.6 mg tablets at hs as it takes') (8%), bisacodyl (2%) are the most common stimulant-cathartics, lactulose (4%) and psyllium 1.3%) are the most common osmotics.

Sedatives (21%)

- No head to head data proving trazadone 25-75 mg hs safer than amitryptiline/nortryptiline/doxepin; virtually no overdose deaths, arrhythmias, urine retention with real world trazadone, however.
- Lorazepam .5 hg hs(7%), zopiclone 2.5 mg hs(4%) much more common than clonazepam (2%), oxazepam, temazepam, alprazolam, diazepam (each about 1%). Benzodiazepine/Z-drug use in ontario seniors has declined over 70% in 30 years, which is good, as benzo/Z-drug use increases dementia risk.

Other CAD/CHF/CRF meds(19%)

-Furosemide (9.4%) (stable over 10 years)(Ellison DH, NEJM 2017;377:1964), nitroglycerin (6%) (more nitropatch .2 to .4 mg/hr, less sublingual or oral), spironolactone 12.5-25 mg od(2.1%) (slow increase), digoxin .0625 mg od (1.5%) (slow decrease) use in Ontario's seniors, for symptomatic management of coronary disease, congestive heart failure, and/or chronic renal failure

Diabetic Medications(19% on orals, 7% on insulin)

- Metformin use (17.5%) no longer greater than use of gliclazide(5%), sita-/lina-/saxagliptin (10%), glyburide (.6%), 'tides and 'gliflozins' (3.3%) combined. (".085 not .070")
- Glargine/detemir (long-acting)(4%) insulin use greater than (aspart/lispro/30/70/isophane (short-acting)(3%) insulin use.
- 'tide' and 'gliflozin' efficacy needs to be determined in large RCTs of patients with control group receiving long-acting insulin and metformin ONLY.

Oral anticoagulants (“17%”)

- 5% on clopidogrel, most don't meet criteria (MI/stroke within 3 months, stent within a year)
- 9% on NOACs (3.9% rivaroxaban, 4.0% apixaban, 1.1% dabigatran), 3% on warfarin; most have AF, apixaban is safer/more effective than warfarin/rivaroxaban/dabigatran for AF (Lip GY, et al, Int J Clin Pract 2016;70:752; Graham DJ, et al, Circulation 2015;131:157)
- Dalte- enoxa- parin .5%, persantine .4%, ticagrelor .3% use rare, aspirin use mostly not captured.

Thyroid replacement

- 15.7% of all ontario seniors received a prescription for thyroid replacement in 2017-2018; ? the highest population prevalence for hypothyroidism ever recorded, OR a lot of elderly ontarians get a trial of levothyroxine for a borderline TSH (subclinical hypothyroidism – relatively safe, but probably ineffective, Stott DJ, et al, NEJM 2017;376:2534).

Osteoporosis medications (15%)

- Risendronate (7%), alendronate (3.2%), denosumab (3.5%), etidronate, zoledronic acid, pamidronate less than 1% combined.
- Optimal duration of use unclear
- Documentation of normal vitamin D levels before treatment often spotty.
- 2000 units vitamin D/day is a Health Canada recommendation for almost all Canadians aged 50 and over.

BPH meds (22%)

- Tamsulosin (.4 mg hs) (13%) is the safest of the alpha-blockers (falls/fractures), preferred to terazosin (2.6%), silodosin (2%), alfuzosin (1.2%), doxazosin (1.2%) (Welk B, et al, BMJ 2015;351:h5398)(effective for kidney stones, too!)
- Dutasteride (5.6%) or finasteride (3%) equally effective/safe as add on(takes 3 months to work) if prostate is large, but also equally likely to increase depression and ? dementia risk (Welk B, et al, JAMA Intern Med 2017;177:683)

Overactive bladder (4%)

- Tolterodine (.7%), solifenacin (.7%), oxybutynin (.5%) and fesoterodine (.7%) use are declining (all cause cognitive impairment), while mirabegron use (25-50 mg od) (1.8%) which does not cause cognitive impairment, is rapidly increasing (Oelke M, et al, Age Ageing 2015;44:745)

Oral estrogen

3.2% of all Ontario women 65 and over still receive oral conjugated estrogen (.3 or .625 mg), despite clear increase in breast cancer and dementia risk with doing so. (Espeland MA, et al, J Gerontol A Biol Sci Med Sci 2016;glw156;Chlebowski RT, et al, JAMA 2010 PMID 20959578; Marshall SF et al, Breast Cancer Res 2010 PMID 20064209)

Only 5.5% got antipsychotics!

- Quetiapine (2%), risperidone (1%), olanzapine (.8%), haloperidol (.8%), aripiprazole (.5%), methotrimeprazine (.4%) represents a >50% reduction in antipsychotic use over last 20 years. Elderly patients with dementia are now much more likely to receive trazadone or mirtazapine, citalopram or sertraline, often in combination, which are safer than quetiapine (<100 mg/d), which is safer than the other antipsychotics (Maust DT, et al, JAMA Psychiatry 2015;72:438).

Only 2.9% got acetylcholinesterase inhibitors!

- Donepezil (5-10 mg od)(2%), galanthamine (16-24 mg/d) (.7%), and rivastigmine (1.5 to 6mg bid) (.2%) use have all declined in Ontario over 5 years, reflecting lack of efficacy (Kennedy RE, et al, jamanetworkopen.2018.4080), high risk for side effects (weight loss, bowel and bladder incontinence)(Soysal P, et al, J Neurol Neurosurg Psychiatry 2016;PMID:27261502), and declining risk for dementia in old age (Salizabal CL et al, NEJM 2016;374:523-532)

- Drugs for gout prevention (allopurinol 4.5%), rheumatoid arthritis (methotrexate 1.1%), breast cancer in women (.8% letrozole, .6% anastrozole, .5% tamoxifen), prostate cancer in men (.8% leuprolide, .6% bicalutamide), and levodopa for restless legs/parkinson's (1.2%) were the only other medications prescribed for at least 1% of ontario's seniors.

Summary

- evidence based prescribing for ontario's seniors is a continuous quality improvement project; patient/pharmacist/prescriber/ministry of health/big pharma perceptions re: 'quality' are all different!
- creating a primary care and specialist billing code for 'deprescribing' (? with built in pharmacist followup) may improve quality from patient, pharmacist, prescriber, and ministry perspective (CMAJ articles by Chris Frank and Barb Farrell)

Thanks! Questions?