Anticholinergic Side-effects of Medications
Common Classes of Culprits

1. **Anti-Histamines**: chlorpheniramine, diphenhydramine, promethazine (Phenergan), brompheniramine

2. **Anti-Psychotics**: a. Phenothiazines: chlorpromazine (Largactil), trifluoperazine (Stelazine),
   b. Atypicals: clozapine, olanzepine, quetiapine,

3. **Tricyclic Anti-depressants**: amitriptyline, clomipramine, doxepin (Sinequan, Deptran), trimipramine (Surmontil), imipramine (Tofranil), nortriptyline (Allegron)
4. **Bladder Storage**: Antispasmodics: darifenacin (Enablex – selective muscarinic M3 antagonist), oxybutynin (Ditropan), propantheline (Probanthene), tolterodine (Detrusitol), solifenacin (Vesicare)

5. **Anti-epileptic**: carbamazepine, oxcarbazepine

6. **Sundry**: atropine, benztropine, cyproheptadine, dimenhydrinate, hyoscyamine, paroxetine, scopolamine, amantadine, pethidine
Side-effects of anticholinergics

- Dry, sticky lips, need to lick lips to speak, difficulty chewing & swallowing
- Urinary, increased need for catheter
- Dry, pale, cool skin
- Insecure movements, falls, blurred vision
- Anxiety, rapid shallow breaths, tachycardia, arrhythmias
- Memory loss, disorientation, agitation, hallucinations, delirium, coma, circulatory collapse
2 year longitudinal study: Anticholinergic Burden Score (ACB):

Cognitive Decline:
Baseline: mean MMSE if ACB of 0 = 26.1, mean MMSE if ACB > 4 = 25
Mean change in MMSE = 0.8; for patients with ACB 4 or more, or on definite anticholinergic drug(s), mean change in MMSE = -1.15 (& -1.3 if baseline MMSE > 25)

Mortality: ACB = 0 -> 7% mortality; ACB 4 or more -> 20% mortality, & increased by 26% for every point > 4
>65yo, history of falls, 2 month follow-up after withdrawal of FRIDs especially CV & psychotrophic drugs:

RR of falls in withdrawal group vs continuation group = 0.48

For CV drugs RR 0.35

For psych drugs RR 0.56
You don’t have an Inferiority Complex.
You’re just inferior!
“..physicians often attribute anticholinergic symptoms in elderly people to ageing or age-related illness rather than to the effects of drugs.”

“Delirium can be caused by blockade of brain muscarinic receptors; drugs with anticholinergic activity are the most common cause of drug-induced delirium”

“In patients with dementia, anticholinergic drugs further inhibit cognitive performance & counteract the beneficial effects of cholinergic enhancers used to treat cognitive performance”

“The concept of AntiCholinergic Burden illustrates that side effects can be caused by combinations of drugs, even if the individual drugs do not cause obvious side-effects”
## ANTICHOLINERGIC DRUGS:

1. **antiemetics/anti-vertigo:**
   - Hyoscine
   - Cyclizine
   - Dimenhydrinate
   - Meclizine
   - Trimethobenzamide
   - Promethazine
   - Prochlorperazine

2. **antiparkinsonian:**
   - Benztropine
   - Benzhexol
   - Biperiden
   - Procyclidine
   - Trihexyphenidyl
   - Ethopropazine

3. **antispasmodics (genitourinary):**
   - Oxybutynin (urinary urge incontinence)
   - Flavoxate
   - Dicyclomine
   - Tolterodine (urinary urge incontinence)

3b **antispasmodics (gastrointestinal):**
   - Belladonna alkaloids
   - Clinidium bromide
   - Dicycloverine
   - Hyoscyamine
   - Methscopolamine bromide
   - Propantheline

4. **antimigraine:**
   - Belladonna alkaloids

5. **Bronchodilators:**
   - Ipratropium
   - Tiotropium

6. **pre-anaesthetics:**
   - Hyoscine (scopolamine)
   - Atropine

7. **mydriatics/cyclopegics:**
   - Atropine solution
   - Cyclopentolate
   - Homatropine
   - Tropicamide
   - Glycopyrrolate

8. **Miscellaneous:**
Survey of 20 clinic patients aged > 75 years:

0, 0, 0, 0, 6, 4, 4, 3, 0, 0, 0, 2, 2, 2, 3, 1, 6, 0, 2, 0

11 of 20 had at least 1 medication with potential anti-cholinergic effects

4 of 20 had ACB scores >= 4

Survey of 20 nursing home patients aged > 75 years:

4, 4, 3, 4, 4, 2, 4, 2, 3, 1, 1, 5, 6, 3, 2, 0, 7, 3, 1, 3

19 of 20 had at least 1 medication with potential anticholinergic effects

8 of 20 had ACB scores >= 4
Commonest drugs: (number of patients taking)

Clinic:
• antidepressants 5 (amitriptyline 3, mirtazapine, venlafaxine)
• opiates 3 (morphine, oxycodone, codeine);

Nursing Home:
• antipsychotics: 5 (risperidone, olanzapine, haloperidol)
• frusemide 4
• benzodiazepines 6 (oxazepam, temazepam)
• antidepressants 7 (mirtazapine, sertraline, paroxetine, citalopram)
• opiates 10 (oxycontin, morphine)

Only 1 patient (clinic) on bladder stabiliser
There is a growing body of evidence showing that discontinuing specific medications in certain patient populations does not worsen outcomes, decreases the risk of ADRs, and reduces costs attributable to medications. Therefore, strategies to improve discontinuing medications and integrate the discontinuation process into the health care system must be a top priority.

There are four distinct steps associated with discontinuing medications: (1) recognizing an indication for discontinuing a medication; (2) identifying and prioritizing the medication(s) to be targeted for discontinuation; (3) discontinuing the medication along with proper planning, communicating, and coordinating with the patient and in concert with the care of other clinicians; and, (4) monitoring the patient for beneficial or harmful effects. Indications that may warrant discontinuing a medication include (i) diminished benefit, such as cases of clinical improvement or stabilization, or (ii) increased risk, such as medication-related adverse effects, drug interactions, and unsafe use such as high-risk drugs in older adults.
To reduce the likelihood of an ADWE, it is recommended that many medications be tapered over the course of days to weeks, particularly medications used on a long-term basis.

Furthermore, while it may be possible to discontinue several medications concurrently, it is recommended that discontinuation be performed sequentially so that any withdrawal event can be easily attributed to the medication ceased. Using these basic principles, studies have consistently demonstrated that the overwhelming majority of medications can be discontinued safely and effectively without causing an ADWE.

The clinical consequences of geriatric polypharmacy are numerous and can be quite serious, including ADRs, medication errors, medication nonadherence, and excessive costs to both the individual and society. Rationally discontinuing medications in older adults is a logical approach to mitigate polypharmacy.
<table>
<thead>
<tr>
<th>Medications</th>
<th>Type of Reaction</th>
<th>Withdrawal Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha-antagonist antihypertensives</td>
<td>P</td>
<td>Agitation, headache, hypertension, palpitations</td>
</tr>
<tr>
<td>Angiotensin converting-enzyme inhibitors</td>
<td>P, D</td>
<td>Heart failure, hypertension</td>
</tr>
<tr>
<td>Antianginals</td>
<td>D</td>
<td>Angina (myocardial ischemia)</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>P, D</td>
<td>Anxiety, depression, seizures</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>P, D</td>
<td>Akathisia, anxiety, chills, coryza, gastrointestinal distress, headache, insomnia, irritability, malaise, myalgia, recurrence of depression</td>
</tr>
<tr>
<td>Antiparkinson agents</td>
<td>P, D, N</td>
<td>Hypotension, psychosis, pulmonary embolism, rigidity, tremor</td>
</tr>
<tr>
<td>Antipsychotics</td>
<td>P</td>
<td>Dyskinesias, insomnia, nausea, restlessness</td>
</tr>
<tr>
<td>Baclofen</td>
<td>P, N</td>
<td>Agitation, anxiety, confusion, depression, hallucinations, hypertonia, insomnia, mania, nightmares, paranoia, seizures</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>P</td>
<td>Agitation, anxiety, confusion, delirium, insomnia, seizures</td>
</tr>
<tr>
<td>Beta-blockers</td>
<td>P, D</td>
<td>Angina, anxiety, hypertension, myocardial infarction, tachycardia</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>P, N</td>
<td>Anorexia, hypotension, nausea, weakness</td>
</tr>
<tr>
<td>Digoxin</td>
<td>D</td>
<td>Heart failure, palpitations</td>
</tr>
<tr>
<td>Diuretics</td>
<td>D</td>
<td>Heart failure, hypertension</td>
</tr>
<tr>
<td>Histamine-2 blockers</td>
<td>D</td>
<td>Recurrence of esophagitis and indigestion symptoms</td>
</tr>
<tr>
<td>Narcotic analgesics</td>
<td>P</td>
<td>Abdominal cramping, anger, anxiety, chills, diaphoresis, diarrhoea, insomnia, restlessness</td>
</tr>
</tbody>
</table>
Nonsteroidal anti-inflammatory drugs  Dough recurrence of arthritis and gout symptoms
Sedative/hypnotics (e.g., barbiturates)  P  Anxiety, dizziness, muscle twitches, tremor
Statins  D, N  Cardiogenic shock, early neurological deterioration, heart failure, myocardial infarction, ventricular arrhythmia

Statin Discontinuation Might Increase Quality of Life in Patients with Advanced Life-Limiting Illness without Affecting Median Survival

Patients with advanced life-limiting illness & taking statins, randomised to continuation or cessation:

Outcome: This trial suggests that statin discontinuation may not influence survival or increase the rate of cardiovascular events in patients with advanced life-limiting illness, but may be associated with a small improvement in patient quality of life and significant monetary savings (mean $716 US per patient)
The incidence of ADRs in nursing homes ranges from 1.2 to 7.3 per 100 resident-months. Appropriately discontinuing medications in nursing-home residents is likely to result in more judicious medication use and will therefore reduce ADRs and costs attributable to medications.

There are many challenges to successfully discontinuing medications, including patient-, clinician-, and system-related barriers. Patients often become psychologically attached to a medication they have been taking for years to manage a chronic condition, and discontinuing this medication may be disconcerting to the patient. The patient and, in many cases, his/her family may perceive the medication discontinuation as substandard care or feel abandoned and that their condition is now terminal, treatment is futile, and death is imminent. Convincing patients and their families that a medication prescribed to manage a chronic condition is no longer essential and, in fact, could be harmful, is challenging.

From a system’s perspective, there is a paucity of data about discontinuing many medications; data may only be available from less robust findings in observational or retrospective studies.
Better documentation in patients’ medical records, especially at key points during transitions in care, would improve medication discontinuation by reducing unnecessary continuation of potentially harmful medications, and preventing medications from being inadvertently discontinued or restarted after discontinuation.

Pharmacists are important resources for prescribers and patients. Pharmacists provide information both to prescribers on a medication’s properties and how to taper or discontinue a medication and to patients about medication discontinuation, such as information about ADRs and ADWEs.
Possible Solutions
<table>
<thead>
<tr>
<th><strong>Medications With Strong ACh Properties</strong></th>
<th><strong>Alternatives</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>First-generation antihistamines for allergic rhinitis (eg, chlorpheniramine)</td>
<td>Second-generation antihistamines (eg, cetirizine, loratadine)</td>
</tr>
<tr>
<td>First-generation antihistamines for insomnia (eg, diphenhydramine)</td>
<td>Nonpharmacologic interventions (eg, eliminate caffeine, reduce daytime napping), low-dose trazodone, nonbenzodiazepine sedative-hypnotic (eg, eszopiclone, zolpidem)</td>
</tr>
<tr>
<td>Bladder antispasmodics for overactive bladder (eg, oxybutynin)</td>
<td>Nonpharmacologic interventions (eg, Kegel exercises, scheduled toileting)</td>
</tr>
<tr>
<td>Muscle relaxants for muscle spasms (eg, carisoprodol)</td>
<td>Nonpharmacologic interventions (eg, massage, physical therapy) and appropriate pain management (eg, acetaminophen, oxycodone)</td>
</tr>
<tr>
<td>TCAs for depression (eg, amitriptyline)</td>
<td>SSRI antidepressants (eg, citalopram, sertraline), SNRI antidepressants (eg, duloxetine, venlafaxine), TCAs with weak ACh properties (eg, nortriptyline)</td>
</tr>
<tr>
<td>TCAs for insomnia (eg, doxepin)</td>
<td>Nonpharmacologic interventions (eg, eliminate caffeine, reduce daytime napping), low-dose trazodone, non-benzodiazepine sedative-hypnotic (eg, eszopiclone, zolpidem)</td>
</tr>
<tr>
<td>TCAs for neuropathic pain (eg, amitriptyline)</td>
<td>Gabapentin, TCAs with weak ACh properties (eg, nortriptyline)</td>
</tr>
</tbody>
</table>
STOPP – Screening Tool of Older Person’s Prescriptions
START – Screening Tool to Alert doctors to Right Treatment

The STOPP/START Screening tools are based on the STOPP/START Prescription criteria which consist of a set of inappropriate combinations of medicines and disease (STOPP) and a set of recommended treatments for given conditions (START). Medicine prescription for the elderly is a complex problem as older patients tend to have more concurrent conditions. A greater number of conditions also leads to a greater number of concurrent drug treatments which increases the chance of dangerous complications in the patient case. Furthermore, there are often treatments which would be of benefit to an individual patient which are absent in their treatment plan. The STOPP/START criteria were developed to provide up-to-date, validated prescription information to doctors and pharmacists to ensure that elderly patients are given the best possible care.

**STOPP/START Screening Tool Software**

The STOPP/START screening software is a tool developed as part of this project which takes as input patient cases and prescription histories and first examines them for STOPP rule violations. These rule-violations are presented to the user (e.g. a pharmacist or general practitioner) and the particular dangers of the prescription plan are displayed. Following the STOPP screening, the software determines if there are any treatments which should be added to the prescription plan as per the START criteria. Any additions to the prescription plan are checked through the STOPP screening tool to discover if the additions may lead to violations of the STOPP criteria.

Alternatives: “Beers List”, “Canadian Criteria”
Sujita W. Narayan • Sarah N. Hilmer • Simon Horsburgh • Prasad S. Nishtala

J Am Geriatr Soc. 2008 Oct; 56(10): 1946–1952. Discontinuing Medications: A Novel Approach for Revising the Prescribing Stage of the Medication-Use Process; Kevin T. Bain, PharmD, ‡‡ Holly M. Holmes, MD, ‡§ Mark H. Beers, MD, †‡ Vittorio Maio, PharmD, MS, MSPH, † Steven M. Handler, MD, MS, ‡ and Stephen G. Pauker, MD ‡‡


CMAJ 2015: Effect of polypharmacy, potentially inappropriate medications and anticholinergic burden on clinical outcomes: a retrospective cohort study
Wan-Hsuan Lu MS, Yu-Wen Wen PhD, Liang-Kung Chen MD PhD, Fei-Yuan Hsiao PhD

- www.biomedcentral.com = source for composite ACB scoring chart
- http://www.ngna.org/_resources/documentation/chapter/carolina_mountain/STARTandSTOPP.pdf = options when STOPP flags a risk