BETTER PRESCRIBING IN THE ELDERLY

Geneviève Lemay, MD, BScN, FRCP, geriatric medicine fellow, University of Ottawa, Ottawa, Ontario

Bill Dalziel, MD, FRCP, director, Geriatric Day Hospital, The Ottawa Hospital

Correspondence may be directed to gelemay@toh.on.ca.

Medication-related problems are common, costly, associated with poor outcomes, and potentially preventable in older adults. Potentially inappropriate medications (PIMs) continue to be prescribed and used as first-line treatments for the most vulnerable older adults despite better therapeutic choices and evidence of poor outcomes. Patients aged 60–79 years fill an average of 35 prescriptions per year, which is estimated to increase to 74 per year in patients over the age of 80 years, suggesting that the risk of adverse drug reactions (ADRs) is high (Figure 1).²

Inappropriate use of medications in elderly patients is of major concern to clinicians and public health authorities. Inappropriate prescribing is an important and possibly preventable risk factor for ADRs in the elderly and is associated with drug-related hospital admissions in up to 10–30% in older people.³ The incidence of PIMs is about 20% in community-dwelling elderly and up to 40% of long-term care residents (Figure 2).⁴ Moreover, ADRs occur during hospital admission in up to half of patients.⁵ The financial burden of ADRs to the health care system is substantial. A US study by Wu et al. calculated the mean cost of treating an ADR causing a hospital admission to be $9,491 per patient, with 60% of this cost being the room and board charges alone.⁶

A recent study found 42% of elderly in-patients were prescribed at least one drug without valid indication and that dosage or duration was inappropriate in about half of these patients.⁷ Conversely, medicines for conditions such as heart failure or osteoporosis remained under-prescribed in 20–70% of patients.³ Medication errors are also frequent during the transition between acute and post-acute care, in part due to incomplete discharge instructions.³ It is imperative to ensure good prescribing in primary care to avoid these costly consequences, both from a financial perspective and, more importantly, from a morbidity and mortality perspective.

The goal of this article is to present the importance of PIMs in the elderly, with a review of different criteria and tools developed over the last decade.
The Ottawa Top Ten Tool (OTT T) and the anticholinergic risk score (ARS) are two simplified guides that have been developed and are used to help clinicians enhance safer prescribing and reduce the risk of ADRs in their older patients (Table 1). The guides provide an approach to stopping PIMs through the use of a discontinuation algorithm.

**Try a “Trial of Discontinuation”**

There is a growing body of evidence showing that discontinuing specific medications in certain patient populations does not worsen outcomes, that it decreases the risk of ADRs, and that it reduces costs attributable to medications. Therefore, strategies to improve the discontinuation of medications and the need to integrate this process into health care are needed. This is why we want to introduce the concept of a “trial of discontinuation” (Figure 3). The outcomes of discontinuation can result in the patient feeling better (fewer side effects, lower drug cost), the patient feeling the same (less drug load and less cost), or the patient feeling worse (but recurrence of symptoms are predictable and the patient is able to monitor this).

**Measures and Tools to Decrease Inappropriate Prescribing**

To assist clinicians with a trial of discontinuation, two different indicators have been developed to assess the appropriateness of prescription: implicit criteria (judgement based) and explicit criteria (consensus based).

**Implicit Criteria**

Implicit criteria such as the medication appropriateness index (MAI) from Hanlon (1992) are used to assess each medication prescribed for a patient. The MAI consists of a 10-item checklist for consideration to determine the appropriateness of medication (Table 2). The index uses a three-point scale. For each criterion, a rating of 1 represents appropriate medication use, a rating of 2 represents marginally appropriate medication use, and a rating of 3 represents inappropriate use. Those reviewing a patient’s medications (often clinical pharmacists) need to have a comprehensive knowledge of medications to confidently determine their appropriateness.

**Explicit Criteria**

Explicit criteria are usually established by expert consensus to create a list of medications to be avoided in older adults, either in general or in specific situations.

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**Table 1. Why Are the Elderly at Such High Risk for ADRs?**

- Higher prevalence of chronic and multiple medical conditions leading to polypharmacy (≥6 medications increases significantly risk of ADRs) and increased side effects
- Age-associated physiological changes altering pharmacokinetics and pharmacodynamics (decreased GI transit, increased fat-to-lean body ratio, decreased oxidative phase of liver metabolism, reduced renal clearance and GFR)²⁶
- Homeostasis (decreased reserve in body system to adapt to change) with increased vulnerability to ADRs (delirium, CHF, etc.)²⁷

Increased risk of the following:
- Falls
- Prescribing cascades* (process whereby the side effects of drugs are misdiagnosed as symptoms of another problem resulting in more new medications and new side effects/drug interactions)
- Iatrogenic suffering
- Cognitive impairment – delirium and dementia
- Health care resource utilization (emergency room visits, hospitalization)
- Morbidity and mortality

*Exclusion from participation in pharmaceutical research, making dosing unclear, side effects uncertain and effectiveness ambiguous.²⁶ The typical drug trial patient is young, male, disease free, and on no other drugs. The typical recipient is old, is female, and has multiple comorbidities and medications.

**Summary:** Elderly people are at increased risk of suffering from polypharmacy, drug-drug interactions, drug-disease interactions, and ADRs.

ADR = adverse drug reaction; CHF = congestive heart failure; GI = gastrointestinal; GFR = glomerular filtration rate.


**Table 2. Medication Appropriateness Index**

<table>
<thead>
<tr>
<th>Index</th>
<th>Effectiveness</th>
<th>Dosage</th>
<th>Correct directions</th>
<th>Drug-drug interactions</th>
<th>Drug-disease considerations</th>
<th>Practical directions</th>
<th>Expense</th>
<th>Duplication</th>
<th>Duration</th>
</tr>
</thead>
</table>

Source: Data from Hanlon and Schmader.²³
the presence of specific comorbidities. These criteria are often easy to implement in routine clinical practice because only limited numbers of medications and clinical conditions are specified."Physicians familiar with explicit criteria may prescribe fewer PIMs when treating elderly patients. Throughout the years, explicit criteria have been proposed by groups around the world, such as PRISCUS, Nanjeo, Laroche's French consensus, McLeod, Winit-Watjana, Australian Prescribing, Zhan, ACOVE, HEDIS, DUR, STOPP-START, and Beers in 1991, 1997, 2003, and most recently 2012. In 2010, Chang and Chan looked at the seven most popular criteria/tools (Fick et al. – Beers, McLeod et al., Rancourt et al., Laroche et al., O'Mahoney et al. – STOPP and START, Winit-Watajana et al., and Rognstad et al. – Norwegian General Practice [NORGEP]) and identified similarities and differences. In their summary, they state that the STOPP, Rancourt, and Laroche criteria came closest to fully meeting the optimal explicit criteria (Table 3).

### Table 3. Similarities and Differences among Seven Criteria on PIMs

<table>
<thead>
<tr>
<th>Similarities</th>
<th>Differences</th>
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</thead>
<tbody>
<tr>
<td>Long-acting benzodiazepines:</td>
<td>Variation of inappropriateness of certain medications, Europe versus North America: amiodarone, doxazosin, fluoxetine</td>
</tr>
<tr>
<td>• Considered inappropriate by all 7 criteria</td>
<td>NSAIDs = nonsteroidal anti-inflammatory drugs.</td>
</tr>
<tr>
<td>• Associated with an increased risk of confusion, sedation, falls, and hip fracture</td>
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<tr>
<td>Short-acting benzodiazepines: strongly associated with fall-related injuries</td>
<td></td>
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<tr>
<td>Tricyclic antidepressants: strong anticholinergic effect introducing risks of impaired cognitive function, falls, constipation, urinary retention, and cardiotoxicity</td>
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<tr>
<td>Drug-disease interaction:</td>
<td></td>
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<tr>
<td>• Listed in at least 4 criteria</td>
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<tr>
<td>• Anticholinergic medications, NSAIDs, alpha-adrenoreceptor antagonists, and benzodiazepine listed for specific medical problems such as falls, peptic ulcers, urinary incontinence, or cognitive impairment</td>
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<tr>
<td>Drug-drug interactions: concomitant use of NSAIDs and warfarin was mentioned in 6 criteria</td>
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</tbody>
</table>

**Comparison among the Seven Explicit Criteria/Tools to Guide Initial Prescribing and Trial of Discontinuation**

In 2010, Chang and Chan looked at the seven most popular criteria/tools (Fick et al. – Beers, McLeod et al., Rancourt et al., Laroche et al., O’Mahoney et al. – STOPP and START, Winit-Watjana et al., and Rognstad et al. – Norwegian General Practice [NORGEP]) and identified similarities and differences. In their summary, they state that the STOPP, Rancourt, and Laroche criteria came closest to fully meeting the optimal explicit criteria (Table 3).
<table>
<thead>
<tr>
<th>Drug</th>
<th>Why Stop?</th>
<th>Alternatives</th>
<th>Indications to Continue</th>
<th>Special Monitoring/Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anticholinergics</strong> (not included in other categories):</td>
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<tr>
<td>H1 histamine blockers (diphenhydramine, hydroxyzine)</td>
<td>Potent anticholinergic properties Should not be used as hypnotics Impair cognition Delirium Falls Prolongation Q–T interval</td>
<td>Allergy symptoms: non-sedating non-anticholinergic anti-histamines (cetirizine, loratadine, desloratadine) Pain/muscle spasm: non-pharmacological muscle relaxation, physiotherapy, massage Nausea: ondansetron, low-dose domperidone</td>
<td>If diphenhydramine use for allergic reaction, use the smallest dosage possible Exception: anaphylaxis and transfusion reaction</td>
<td>Clinical monitoring for anticholinergic side effects: bladder outflow obstruction, constipation, delirium, worsening cognition in patients with dementia ECG for QTc</td>
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<tr>
<td>Benzotropine</td>
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<tr>
<td>Dimenhydrinate</td>
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<tr>
<td>See also Table 5</td>
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<tr>
<td><strong>Tricyclic antidepressants</strong></td>
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<tr>
<td>Amitriptyline, doxepin, imipramine, clomipramine, trimipramine</td>
<td>Strong peripheral anticholinergic side effects (constipation, dry mouth, orthostatic hypotension, cardiac arrhythmia) and central anticholinergic side effects (sedation, confusion, delirium) Cognitive deficit Increased risk of falling Can exacerbate glaucoma/BPH/heart block</td>
<td>SSRIs (citalopram, escitalopram, sertraline) Mirtazapine Non-pharmacological (behavioural therapy) SNRIs</td>
<td>Long use with no apparent side effects No cognitive issues Relapse with trial of discontinuation</td>
<td>Monitor for anticholinergic side effects, suicidality, fall risk, cognition ECG (QT prolongation, proarrhythmics) Therapeutic drug monitoring if risk of intoxication Avoid doses &gt;20 mg of citalopram, if used; monitor QTc for risk of prolongation</td>
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<tr>
<td><strong>Benzodiazepines</strong></td>
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<tr>
<td>Long-acting benzodiazepines: flurazepam, diazepam, bromazepam, clonazepam</td>
<td>Extreme long half-life producing prolonged sedation and reaction times Elderly more sensitive Risk of falls, fractures Psychiatric reactions can be paradoxical (agitation, irritability, hallucinations, psychosis) Cognitive impairment Depression May cause dependency</td>
<td>Sleep: very low-dose short-acting benzodiazepines for short duration only; low-dose zopiclone, trazodone Sedative antidepressant for concomitant insomnia and depression (mirtazapine) Non-pharmacological treatment of sleep disturbance/sleep hygiene Anxiety disorder; anti-depressant (citalopram, escitalopram, venlafaxine)</td>
<td>Use lowest possible dose, shortest possible duration of treatment May be appropriate for seizure disorders, ethanol withdrawal, and end-of-life care. Zolpidem, zopiclone: use for short period &lt;90 days</td>
<td>Clinical monitoring for adverse effects (cognitive function, vigilance, regular fall history, gait steadiness testing, psychopathology, ataxia) May exacerbate depression May worsen cognition If patient is on chronic benzodiazepines (over 1 month), yearly documentation and discussion of risks, and attempts to taper and discontinue For longer use (&gt;1 month), taper down slowly (may be done in consultation with specialist or pharmacist for complex cases)</td>
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<tr>
<td>Short-acting benzodiazepines</td>
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<td>(diphenhydramine, hydroxyzine)</td>
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<tr>
<td><strong>Older SSRIs/NDRIs</strong></td>
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<td>Fluoxetine, paroxetine Bupropion</td>
<td>Fluoxetine = long-half-life, multiple drug interactions – not unique to the elderly CNS side effects (nausea, insomnia, dizziness, confusion) Hyponatremia If risk of seizure (bupropion)</td>
<td>Another SSRI (sertraline, citalopram, escitalopram) Mirtazapine Non-pharmacological: (behavioural therapy)</td>
<td>Very good clinical response, no side effects, in consultation with geriatric psychiatrist</td>
<td>Clinical monitoring of CNS function Monitor of renal function and serum electrolytes Avoid doses &gt;20 mg of citalopram, if used; monitor QTc for risk of prolongation</td>
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<tr>
<td><strong>Antipsychotics</strong></td>
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<tr>
<td>Atypical: olanzapine, clozapine, risperidone, quetiapine – 40% lower mean oral clearance in the elderly Typical: haloperidol</td>
<td>Anticholinergic and EPS side effects (tardive dyskinesia), but less than typicals, parkinsonism, hypotonia, sedation, fall risk, all anti-psychotic agents associated with increased risk of all-cause mortality in patients with dementia Stroke, lowers seizure threshold Clozapine = increased risk of agranulocytosis and myocardiitis</td>
<td>Atypical antipsychotics with favourable risk/benefit profile (risperidone) Quetiapine = if used for insomnia, use low-dose trazodone (25–100 mg)</td>
<td>Short term (&lt;3 months) with reassessment of benefit/worsening/need to continue Advise patient/family of possible increased risk of stroke and mortality Haloperidol in acute psychosis (short duration: &lt;3 days), avoid single dose over 2 mg, avoid IV formulation (risk of postural hypotension and cardiovascular collapse)</td>
<td>Clinical monitoring for adverse effects, anticholinergic, and EPS Fall history Neurological and cognitive function (parkinsonism) Monitoring of cardiovascular function (hypotension, ECG/Q–T interval) Clozapine = blood pressure monitoring No psychoactive medication used to treat neuropsychiatric symptoms of dementia should be continued indefinitely, and attempts at drug withdrawal should be made regularly (e.g., every 3–6 months)19</td>
</tr>
</tbody>
</table>
Digoxin
Dosage >0.125 mg/d because of decreased renal clearance
Risk of toxicity
Dosage should not exceed 0.125 mg/d because of decreased renal clearance
Risk of toxicity
For tachycardia/atrial fibrillation use beta-blockers (metoprolol, bisoprolol, carvedilol)
Use for heart failure (NYHA III)
Use in difficult to control atrial arrhythmias
Monitor renal function
Monitor cardiovascular function
Therapeutic drug monitoring (target 0.5–1 ng/mL in elderly)
ONLY if renal dysfunction, ECG changes, drug-drug interaction, or signs/symptoms of toxicity

NSAIDs
Diclofenac, indomethacin, meloxicam, naproxen, ketorolac
Including OTC-NSAIDs: ibuprofen, naproxen
Indomethacin = most CNS side effects
Potential for GI bleeding/perforation, renal failure, hypertension, CHF
Avoid concomitant use of ASA/warfarin/dabigatran/clopidogrel
OTC not perceived by patient as dangerous; often not mentioned to physician
Acetaminophen, weak opioid (morphine, hydromorphone), tramadol
Avoid codeine – higher incidence of sedation, nausea, and constipation
Short duration (<14 days) 2-week trial: if no clinical significant benefit, discontinue as risk too high
Use in combination with PPI
Follow up GI manifestations (note that 70% of GI bleeds have no GI prodrome)
Monitor renal function
Monitor BP, signs of CHF

Urological spasmolytic agents
Oxybutynin, non-SR tolterodine, solifenacin
Anti-cholinergic side effects, sedation, weakness
ECG changes – prolonged Q–T
May worsen: prostatism, glaucoma, constipation, dementia
Non-pharmacological treatment (pelvic floor exercises, physical and behavioural therapies)
May use tolterodine SR with close monitoring if patient cognitively intact and good response to medication
Clinical monitoring for anticholinergic side effects (bladder outflow obstruction, constipation, cognition, falls)

Laxatives
Stimulant (senna, dulcolax)
Softener (docusate)
Long-term use results in cathartic colon and bowel dysfunction
Diarrhea, fecal incontinence, urgency
Refractory constipation, obstruction
Fibre, hydration
Osmotic laxatives (lactulose, polyethylene glycol 3350; magnesium hydroxide if GFR ≥60)
Short course during opioid use

Hypoglycemics
Long-acting sulfonylurea: glyburide chlorpropamide
TZDs: pioglitazone, rosiglitazone
Can cause severe prolonged hypoglycemia
Increase risk of HF and MI, avoid if liver disease
Metformin
Gliclazide
Repaglinide
Glucoscan
Avoid metformin if impaired renal function (adjust dose if GFR falls <60 mL/min, discontinue when GFR falls <30 mL/min)
TZDs – avoid if history of HF/edema/CAD
Note that insulin has been listed as a high-alert medication; use with close monitoring to avoid hypoglycemic episodes (often asymptomatic)

OTTT: Drug Classes Considered Inappropriate to Use in the Elderly
A thorough review of the literature and available tools and criteria for PIMs resulted in this summary of the top 10 drug classes considered inappropriate to use in the elderly. This simplified version is applicable in Canada, is arranged in categories, and concentrates on common high-risk drugs (with a higher potential for side effects and ADRs) for easier use. It includes simple explanations as well as safer alternatives. OTTT was created with the assistance and expertise of eight geriatric medicine specialists at The Ottawa Hospital and two expert geriatric pharmacists through use of rating scales for prioritization of relevance and importance, followed by formal discussions at geriatric academic rounds (Table 4).
Special Problem of Anticholinergic Load in the Elderly

Medications with anticholinergic properties have frequently been cited in the literature as causing an increase in adverse events. This often leads to consequences such as falls, hospitalization, and a loss of independence. Higher rates of cognitive dysfunction and delirium are found in patients experiencing a greater anticholinergic load. Evidence suggests that reducing anticholinergic medications is a modifiable risk factor to avoid associated morbidity. Rudolph and colleagues have developed an ARS that can be used in geriatric evaluation and management (GEM) as well as a primary care setting. It was demonstrated that a higher score increases the risk of anticholinergic adverse effects in GEM with a relative risk of 1.3 and in primary care of 1.9. A subsequent large study found greater risk of delirium, cognitive decline, and dementia with functional and behavioural issues in patients with a high anticholinergic load. These clinical side effects/symptoms later decreased if anticholinergics were decreased or discontinued.

The ARS ranks medications for anticholinergic potential on a three-point scale (1 = moderate, 2 = strong, 3 = very strong) for each medication based on its anticholinergic potential. The ARS score for a patient is the sum of points for his or her number of medications. The anticholinergic adverse effects are divided into central (falls, dizziness, confusion) and peripheral (dry mouth, dry eyes, and constipation). Table 5 presents a simplified version of the ARS created with the expertise of geriatric medicine specialists and pharmacists for use in conjunction with the OTTT. Modifications to the scale include the removal of medication rated as “0” for no anticholinergic risk and the inclusion of only the most common medications for 1, 2, and 3 points of risk.

Summary

In summary, prescribing medications is a complex phenomenon, particularly in the older population. The assessment and review of every patient’s medication list should be done every 6–12 months; all drugs should be reviewed, including over-the-counter drugs, and the pro re nata (PRN) should be key. Review should also be done at times of transitions: discharge from hospital, relocation to retirement home, or transfer to long-term care. There is no best tool for doing a medication review. The three simplified tools presented, MAI, OTTT, and ARS, could be incorporated together into routine practice as they are easy to use, relevant, accurate, and not time consuming. Appropriate initial prescribing, drug monitoring, drug regimen reassessment, and medication discontinuation are essential to optimizing prescribing and drug side effects in the elderly. Always consider drug side effects, including those of over the counter drugs, as a lead cause in the differential diagnosis of any new symptom.

Although criteria, prescribing tools, and guidelines provide invaluable information regarding prescribing for older patients, there are

### Table 5. Modified Anticholinergic Risk Scale

<table>
<thead>
<tr>
<th>3 Points</th>
<th>2 Points</th>
<th>1 Point</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitriptyline</td>
<td>Amantadine</td>
<td>Carbidopa-levodopa</td>
</tr>
<tr>
<td>Atropine/scopolamine</td>
<td>Baclofen</td>
<td>Entacapone</td>
</tr>
<tr>
<td>Benztropine</td>
<td>Cetirizine</td>
<td>Haloperidol</td>
</tr>
<tr>
<td>Chlorpromazine</td>
<td>Cimetidine</td>
<td>Methocarbamol</td>
</tr>
<tr>
<td>Clomipramine</td>
<td>Clozapine</td>
<td>Metoclopramide</td>
</tr>
<tr>
<td>Dicyclomine</td>
<td>Cyclobenzaprine</td>
<td>Mirtazapine</td>
</tr>
<tr>
<td>Diphenhydramine</td>
<td>Desipramine</td>
<td>Paroxetine</td>
</tr>
<tr>
<td>Doxepin</td>
<td>Loperamide</td>
<td>Pramipexole</td>
</tr>
<tr>
<td>Fluphenazine</td>
<td>Loratadine</td>
<td>Quetiapine</td>
</tr>
<tr>
<td>Flurazepam</td>
<td>Nortriptyline</td>
<td>Risperidone</td>
</tr>
<tr>
<td>Hydroxyzine</td>
<td>Olanzapine</td>
<td>Selegiline</td>
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<tr>
<td>Hyoscymine products</td>
<td>Prochlorperazine</td>
<td>Trazodone</td>
</tr>
<tr>
<td>Imipramine</td>
<td>Pseudoephedrine</td>
<td>Ziprasidone</td>
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<tr>
<td>Meperidine</td>
<td>Tiprolidine</td>
<td></td>
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<tr>
<td>Nitrazepam</td>
<td>Tolterodine</td>
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<tr>
<td>Oxybutynin</td>
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<tr>
<td>Perphenazine</td>
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<tr>
<td>Solifenacin</td>
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<tr>
<td>Trimipramine</td>
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</tbody>
</table>

Source: Adapted from Rudolph et al.

### Key Points

- There is a growing body of evidence showing that discontinuing specific medications in certain patient populations does not worsen outcomes, that it decreases the risk of ADRs, and that it reduces costs attributable to medications.
- Those reviewing a patient’s medications (often clinical pharmacists) need to have a comprehensive knowledge of medications to confidently determine their appropriateness.
- Medications with anticholinergic properties have frequently been cited in the literature as causing an increase in adverse events.
- Appropriate initial prescribing, drug monitoring, drug regimen reassessment, and medication discontinuation are essential to optimizing prescribing and drug side effects in the elderly.
important caveats concerning their use. No criteria should substitute for professional judgment or dictate prescribing for patients. When in doubt, consider consulting with a pharmacist or geriatrician.

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References