POLYPHARMACY AND DEPRESCRIBING

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CASE STUDY: MRS. D

A 77 YEAR OLD OBESE WOMAN WITH DIABETES, HIGH BLOOD PRESSURE, HEART FAILURE, MODERATELY SEVERE KIDNEY DISEASE, HIGH CHOLESTEROL, HEART BURN, SEVERE KNEE ARTHRITIS, BURNING NEUROPATHY IN HER FEET, GLAUCOMA, DEPRESSION, AND INSOMNIA.

IN ADDITION TO HER PRIMARY DOCTOR, SEEN BY AN ENDOCRINOLOGIST, CARDIOLOGIST, NEUROLOGIST, PSYCHIATRIST, AND OPHTHALMOLOGIST.

• Mrs. D’s Medications
  • Metformin 1000 2 X daily
  • Gliclazide 60 mg daily
  • Metoprolol 50 mg 2 X daily
  • Lisinopril 40 mg daily
  • Frusemide 40 mg daily
  • Simvastatin 80 mg daily
  • Amitriptyline 25 mg at bedtime
  • Duloxetine 20 mg daily
  • Clonazepam 0.5 mg 2 X daily
  • Gabapentin 600 mg 3 X daily
  • Ranitidine 150 mg 2 X daily
  • Paracetamol 500mg/Codeine 30mg 4X daily prn
  • Timolol 0.5% 1 drop to both eyes daily
  • (OTC) Diphenhydramine 25 mg at bedtime
  • (sleeper)

ANYTHING POTENTIALLY INAPPROPRIATE?
Why Potentially Inappropriate?

Amitriptyline
  confusion
Clonazepam
Ranitidine
Diphenhydramine
Codeine

Metformin at her dose with moderate-severe kidney failure
  risk of kidney damage
Metoprolol (for high blood pressure) + timolol (for glaucoma)
  decrease BP
Simvastatin
  dose adjust?
Gliclazide
  hypoglycaemia
WHY IS POLYPHARMACY A PROBLEM?

• 1 in 4 older persons are hospitalised for medication related problems¹

• In the community 1 in 3 people receiving more than 5 medications suffer an adverse drug reaction (ADR)²

• Up to 18% inpatients deaths are in part attributed to ADR’s³

¹ Kalisch et al Int J Qual Health Care 2012 24 239-49
³ Buajordet et al J Intern med 2001 250 327-41
BENEFITS OF DEPRESCRIBING

- Adverse Drug Reactions (ADR)
- Drug Interactions
- Medication Non-Adherence
- Declining Functional Status
- Impaired Cognitive Status
- Falls
- Incontinence
- Worsening Nutrition
- Increased Healthcare costs
MECHANISMS LEADING TO PHARMACOKINETIC VARIATIONS OF DRUG EFFECTS IN THE ELDERLY
HARMS OF DEPREScribing

- Adverse drug withdrawal reactions
- Change pharmacokinetic and pharmacodynamics of existing drugs.
- Return of Medical Condition
Results summary: A systematic review of 31 clinical trials in older people concluded that specific classes of medications like Antihypertensives, Benzodiazepines and Psychotropic drugs could be withdrawn successfully without causing harm in people aged 65 years and older.
Results summary: Evaluations of the use of medications in 190 geriatric patients led to discontinuation of 322 drugs in 119 patients with no significant adverse effects after 12 months. Drugs discontinued with no adverse effects included NSAIDs, analgesics, statins, oral hypoglycemics, carbamazepine and digoxin.
Why is it so hard to stop?

Patient barriers

Patients may:
• Be psychologically attached to a medication
• Be physically dependent on a medication
• Feel abandoned if the medication is stopped
• Consider that it is because death is imminent
• Not understand why a chronic treatment may no longer be useful

Although patients may:
• Be unsure of the reasons for medications
• Have other medications added to treat side effects
• Be non-adherent to the treatment
• Hate taking his medications
Why is it so hard to stop?
Prescribers barriers

Prescribers may be:

• Concerned with patients’ resistance to change

• Concerned with other clinicians’ resistance to change

• Fear adverse drug reactions and withdrawal events

• Reluctant to stop medications when they have been started by a colleague or when their length of use or original indication is unclear

• Unsure if the drug can be stopped abruptly or should be tapered
THE PRESCRIBING CASCADE

- can occur as a result of treating a side effect of a medication by another medication
BE AWARE OF THE “PRESCRIBING CASCADE”

NSAID -> HTN-> antihypertensive therapy
Metoclopromide-> Parkinsonism -> carbidopa/levodopa
Dihydropyridine-> oedema -> frusemide
NSAID -> H2 blocker -> delirium -> Haloperidol
HCTZ -> gout-> NSAID -> 2nd antihypertensive
pseudoephidrine -> urinary retention -> alpha blocker
### Examples of medication to be used with caution in the elderly

**InnovAiT** 9(2) 69-77 2016

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<tr>
<th>Medication</th>
<th>Caution</th>
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<tr>
<td>Non-steroidal anti-inflammatories e.g. naproxen, ibuprofen</td>
<td>- Risks: Gastrointestinal bleeding, cardiac failure, nephrotoxic&lt;br&gt;- Suggested action: Avoid where possible. If essential, offer short courses with proton pump inhibitor cover</td>
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<tr>
<td>Hypnotics e.g. benzodiazepines</td>
<td>- Risks: Drowsiness, confusion, poor balance and increased risk of falls&lt;br&gt;- Suggested action: Avoid where possible or offer a short course only</td>
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<tr>
<td>Diuretics e.g. furosemide</td>
<td>- Risks: Hypotension, increased risk of falls, nephrotoxic. Diuresis can be difficult for patients with poor mobility&lt;br&gt;- Suggested action: Review renal function regularly and ensure good hydration status</td>
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<tr>
<td>Anti-cholinergics e.g. tricyclic antidepressants, antihistamines, oxybutynin</td>
<td>- Risks: Postural hypotension, dizziness, increased falls, urinary retention, constipation and confusion. Associated with increased risk of dementia&lt;br&gt;- Suggested action: Stop where possible and consider alternative</td>
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<td>Anti-depressants e.g. tricyclics, selective serotonin reuptake inhibitors (SSRI)</td>
<td>- Risks: Confusion, dizziness, hypotension and falls. May be toxic in overdose. Can be cardiotoxic and increase risk of stroke and heart attack&lt;br&gt;- Suggested action: If necessary, opt for SSRI</td>
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<tr>
<td>Hypoglycaemic diabetic mediation e.g. sulfonylureas</td>
<td>- Risks: Hypoglycaemia&lt;br&gt;- Suggested action: Target HbA1c of 7.5% or 58 mmol/ mol if life expectancy less than 10 years</td>
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<tr>
<td>Anti-coagulants</td>
<td>- Risks: Warfarin interacts with many drugs and foods&lt;br&gt;- Suggested action: Careful counselling and consider risk of falls</td>
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<tr>
<td>Cardiac glycosides e.g. digoxin</td>
<td>- Risks: Caution in renal impairment as increased risk of toxicity&lt;br&gt;- Suggested action: Start with lower doses in the elderly. Monitor renal function</td>
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<tr>
<td>Anti-psychotics</td>
<td>- Risks: Cognitive impairment, sedation, cardiac arrhythmias, parkinsonism, increased risk of stroke and heart attack, osteoporosis&lt;br&gt;- Suggested action: If used for a mental health disorder, review regularly. Avoid for behavioural disturbance in dementia</td>
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A patient-centred deprescribing process


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<tr>
<th>Step 1: Compile comprehensive medication history</th>
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<td>- Obtain an accurate list of all regular, when required and intermittent medications (prescription and non-prescription)</td>
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<tr>
<td>- Document indications for each medication</td>
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<td>- Identify possible ADRs and non-adherence</td>
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<th>Step 2: Identify potentially inappropriate medications</th>
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<td>- Assess the potential harms and benefits in the individual (e.g., causing ADRs, no indication)</td>
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<td>- Use lists of medications that are high risk in the elderly (e.g., Beers list, STOPP criteria)</td>
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<td>- Take into account life expectancy and the patient’s treatment goals when reviewing preventive medications</td>
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<th>Step 3: Determine whether medication can be ceased, and prioritise</th>
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<td>- Appropriate timing of withdrawal (otherwise medically stable)</td>
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<td>- Gain patient consent (highlight potential benefits of medication cessation, confirm that it is a trial and medication can be restarted if necessary)</td>
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<td>- Stop one medication at a time</td>
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<th>Step 4: Plan and initiate withdrawal</th>
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<td>- Tapering is recommended to reduce adverse drug withdrawal reactions, increase patient comfort and identify lowest effective dose</td>
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<td>- Ensure the patient (and carer) is comfortable with the plan and is aware of what steps to take if symptoms return</td>
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<th>Step 5: Monitor, support and document</th>
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<td>- Monitor the patient for adverse drug withdrawal reactions and return of symptoms, short and long term</td>
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<td>- Ensure that the patient has a contact number for questions and concerns</td>
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<tr>
<td>- Implement non-pharmacological therapies</td>
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<td>- Document the process and outcome and communicate to all relevant parties</td>
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The CEASE deprescribing framework

- **Current medicines** – ascertain all medicines the patient is currently taking and the reasons for each one (also termed medication reconciliation).
- **Elevated risk** – consider the potential for this patient to be harmed by the medicines being prescribed in determining required intensity of deprescribing intervention:
  - Consider risk factors such as total number of drugs, age, presence of drugs associated with high risk (e.g. opiates, benzodiazepines, psychotropics, anticoagulants, hypoglycaemic drugs, cardiovascular drugs), past non-adherence, multiple prescribers, impaired cognition and poor social support, substance abuse, mental health problems.
- **Assess** each medicine for its usefulness in relation to its risk by considering:
  - Indications for the drug (is the continued prescribing of the drug justified on the basis of a verified diagnosis and robust evidence of effectiveness for this indication in this patient?);
  - Effects of the drug to date on the underlying disease process and/or its symptoms;
  - Future benefit–harm trade-offs in the context of life expectancy, time until benefit (for preventive medications), goals of care (symptom relief vs disease modification vs cure), and patient values and preferences.
- **Sort** – prioritise those medicines for discontinuation with lowest utility (or highest disutility) and greatest ease of discontinuation, while taking patient preferences into account.
- **Eliminate** – implement a discontinuation regimen, and monitor patients closely for improvement in outcomes or onset of withdrawal or rebound syndromes.
Summary of the four principles of medicines optimisation. Reproduced with permission from the Royal Pharmaceutical Society.
UNDER-PRESCRIBING IN THE ELDERLY!

- Falls and Anticoagulation
Despite nearly 20 years of evidence many people are still not anticoagulated!

There is no good evidence that patients should not be denied oral anticoagulation solely on the basis of high risk for falls. For patients with valid indications for anticoagulation, benefit generally outweighs risk. For example, an analytic model suggests that older patients (age, ≥65) who have a 5% annual risk for stroke (i.e., CHADS2 score of 2–3) and are taking anticoagulants would need to fall approximately 295 times yearly for risks of fall-related subdural hemorrhages to outweigh benefits of stroke prevention (Arch Intern Med 1999; 159:677). In addition, providers should be aware of risks conferred by polypharmacy in patients taking anticoagulants and should discontinue unnecessary medications, monitor patients more closely, or both.
Oral anticoagulants have been demonstrated to reduce the incidence of, and mortality secondary to, embolic strokes associated with atrial fibrillation. Despite this, oral anticoagulants are underprescribed with some estimates suggesting as few as 40% of eligible patients receive therapy. The risk of falls is the most commonly cited reason for not providing oral anticoagulation, although the risk of bleeding associated with falls on oral anticoagulants is still debated. In this study Donzé et al evaluated a prospective cohort of elderly individuals requiring oral anticoagulation at a single European centre.

A total of 515 patients were enrolled with a mean age of 71. Falls risk was assessed with the use of 2 validated questionnaires with nearly 60% of the population deemed to be at high risk. Follow-up was for 12 months with the primary outcome being the time to a first major bleed. A total of 35 patients had a first major bleed during follow-up (incidence rate: 7.5 per 100 patient-years). Comparing patients at high risk of falls with patients at low risk, there was no significant difference in major bleeding (8.0 vs 6.8 per 100 patient-years, P=0.64). Similarly, using multivariate analysis a high falls risk was not associated with the risk of a major bleed (HR, 1.09; 95% CI, 0.54-2.21). Overall, only 3 major bleeds occurred directly after a fall (incidence rate: 0.6 per 100 patient-years).

Conclusions
In this prospective cohort study, patients on oral anticoagulants at high risk of falls did not have a significantly increased risk of major bleeding. These findings suggest that being at risk of falls is not a valid reason to avoid anticoagulation therapy.

An 86 yo lady with hypertension, osteoporosis, and mild cognitive impairment presents with episodes of palpitations and heart “fluttering.” These episodes occur 1 to 2 times per week, last for up to several hours, and are associated with mild shortness of breath and reduced exercise tolerance. She is widowed and lives in a retirement facility, but she is independent in activities of daily living. She has fallen twice in the past year without significant injury. An electrocardiogram demonstrates sinus rhythm with left ventricular hypertrophy. A 30 day event monitor reveals several episodes of paroxysmal atrial fibrillation that correspond with her symptoms. A subsequent echocardiogram shows normal left ventricular systolic function, mild diastolic dysfunction, and no significant valvular abnormalities. Laboratory studies, including thyroid-stimulating hormone, are normal. What is this patient’s risk of stroke? What is her risk of major bleeding from anticoagulation? How should falls risk be addressed in the decision making process?

As noted above, our patient has a high risk of stroke and a moderate risk of bleeding, and multiple lines of evidence indicate that the benefits of anticoagulation (i.e., prevention of stroke and systemic embolization) substantially outweigh the risks of bleeding. Although she has a history of falls, which may seem to muddy the waters, this factor should not play a major role in decision making. Moreover, her advanced age should, if anything, be considered a point in favor of anticoagulation. So from the scientific standpoint, anticoagulation is the clear winner.
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