Deprescribing: the solution to irrational polypharmacy

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Deprescribing: the solution to irrational polypharmacy

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Videos of patients suffering from polypharmacy have been removed

Consent extended only to live presentation for health education
COI declaration
Thomas L. Perry, M.D., FRCPC

- part-time salary from UBC Therapeutics Initiative
- medical practice income
- medical-legal consultation
- consultant to litigation in USA and Canada against pharmaceutical manufacturers for fraudulent or inappropriate marketing
- no relationship with pharmaceutical companies

Mitigation: I try to seek truth and be sure what I say could withstand cross-examination
How would YOU respond to this situation?
Medication list: alphabetical order

1. Canagliflozin 300 mg/d
2. Celecoxib 200 mg/d
3. Compounded cream (amitriptyline, ketamine, etc.)
4. Cyclobenzaprine 10 mg/d
5. Gliclazide MR 30 mg/d
6. Insulin glargine 30 units bid
7. Metformin 500 mg bid
8. Mirtazapine 30 mg/d
9. Morphine SR 10 mg a.m., 20 mg p.m. (was 70 mg/d)
10. Nabilone 2 mg/d (as 1 mg)
11. Quinine sulfate 300 mg hs
12. Venlafaxine ER 150 mg/d

Age 67 (seen 2016):
- Chronic shoulder injury R > L
- Started morphine SR and IR 2002 at rehab program
- Referred re “appropriateness” of morphine 70 mg/d (stable dose)
- Also treated for “depression” and “insomnia”
Workshop objectives

1. Helping us all move from talk to action in:
   • Clinical deprescribing
   • Teaching others how to do it
   • Identifying barriers to inertia

2. Sharing ideas on what works or doesn’t work, and how we can enlist more younger prescribers and patients to resist irrational polypharmacy and encourage sensible deprescribing.
Satisfied patient and professional?

“They didn’t know what was keeping me alive then.”

“But I feel much more alive now!”

Courtesy Maud van Breemen, UBC TI
Canadian medical student - February 2017
(see “Choosing wisely: one person at a time” workshop Aug. 18, 2017)

“I'm on psychiatry and someone presented a case of a depressed patient. The number of drugs was astounding”:
Duloxetine, pregabalin, quetiapine, olanzapine, methadone 160 mg/day (not unusual in Canada)

“She was super sedated and the team's response was to start modafinil! ... I could not believe it. They were also discussing starting lithium (!) ... I asked a few questions but everyone was shocked when I brought up the possibility that the polypharmacy was a factor in her ongoing symptoms & ‘treatment resistance’.

“Anyway, just wanted to let you know your teaching has had a lasting effect!” (8 day elective was effective!)
Old doctor’s approach: Pontification 2014: probably ineffective – can’t compete with guidelines

1. Re-evaluate goals of therapy
2. Apply absolute risk differences
3. Consider simple pharmacology & physiology
4. Avoid unnecessary costs
5. Reassess ongoing value
6. Common sense & Golden Rule
7. Always stop at least 1 drug
Is a much simpler message better?

“They didn’t know what was keeping me alive then.”

“But I feel much more alive now!”
Deconstructing language helps!
(Another shameless plug for Aug 18th 14:30 h workshop)

“She will definitely benefit from an antidepressant”
• ??? (probability from RCT ≈ 10%)

“His diabetes should be treated aggressively.”
• Should we be “aggressive” in health care?

“Her gabapentin dose needs to be increased to ≥ 2400 mg/d!”
• Why? Probability of benefit is near zero, toxicity ≈ certain

“You’re gonna take these 23 new pills, and it’s gonna be great (fire and fury)!”
Experienced doctor’s simple approach:
Dr. Tom Finucane could not be here, but sent this advice

**Billion-dollar drugs that cause more harm than good: STOP**

1. **PPI for heartburn (same as GERD):**
   - chordates from sharks to humans have proton pumps – OK to disrupt them???

2. **Insulin for DM2:**
   - lots of known harm;
   - no RCT evidence of meaningful benefit;
   - ? carcinogenic;
   - harmfully expensive

See also Dr. Finucane forthcoming video lecture at:
http://gwcehp.learnercommunity.com/dcrx
Washington, DC - Centre for Rational Prescribing
Simple advice from Dr. Tom Finucane, Geriatrics, JHMI

Billion-dollar drugs that cause more harm than good (2): STOP

3. Antipsychotics in patients with psychotic symptoms, or delirium:
   • black box warning for death based on consistent, strong evidence;
   • SR shows no benefit in delirium;
   • worse suffering in palliative care delirium

4. Benzodiazepines:
   • cohort study suggests all cause mortality;
   • central benzo deficiency syndrome is rare

Dr. No (disguised as Dr. Yes)
Case 2: how would YOU handle this or teach others?

- This woman had profound tremor, asterixis, myoclonic jerks, some mild encephalopathy
- She recovered but developed withdrawal after pregabalin, tramadol, bupropion, nortriptyline, topiramate all stopped at once …
- Required brief hospitalization for fluids, and resentful of withdrawal, but recovered fast
- Would it have been better to “go slowly” and prolong intoxication?

Drugs for pain: pregabalin (Lyrica), tramadol SR, bupropion (Wellbutrin) for “HRT”, nortriptyline, topiramate (Topamax), esomeprazole (Nexium)
Practical tricks of the trade

1. Rank medication list quickly by priority:
   - probably useful
   - Irrelevant or uncertain
   - probably/potentially harmful

2. Recognize likely drug interactions (kinetic or dynamic); avoid potentially dangerous ones – e.g. multiple drugs that slow heart rate or impair K+ excretion or GFR

3. Use $T \frac{1}{2} \text{ elim}$ to plan safe deprescribing – see example

4. Challenge rather than worship unsupported, impractical, or potentially dangerous prescriptions originated by specialists.
You think YOUR life is complicated?

Polypharmacy after MVA (frighteningly common)

Young woman after car crash (pain):

1. Lansoprazole 20mg/d
2. Atorvastatin 40mg/d
3. Pregabalin 225mg at bedtime
4. Solifenacin 5mg/d
5. Topiramate 100mg at bedtime
6. Aripiprazole 5mg/d
7. Sertraline 250mg/d
8. Nortriptyline 40mg at bedtime
9. Vortioxetine 20mg at bedtime
10. Trazodone (100mg at bedtime)
11. Zopiclone (7.5mg at bedtime)
12. “prn” Cyclobenzaprine at bedtime
13. “prn: Ketorolac Injectable IM
14. “prn” hydromorphone 1-2 mg
15. “prn” Acetaminophen (paracetamol)
16. “prn” methocarbamol, THC pills, marijuana

If this list doesn’t frighten you, it should!

But what to do about it?
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Knowing the reason for a drug helps!

**Additional Discharge Medications**

<table>
<thead>
<tr>
<th>Details (Drug Name, Dose, Route, Frequency, Reason)</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lorsartan 25mg PO BID</strong> for HTN</td>
<td>Quantity: 30d Refill: Ø</td>
</tr>
<tr>
<td><strong>Lorsartan 50mg PO BID</strong> (total daily dose 100mg) for HTN</td>
<td>Quantity: 30d Refill: Ø</td>
</tr>
<tr>
<td><strong>Metformin 500mg PO BID</strong> for DMT2</td>
<td>Quantity: ___ Refill: ___</td>
</tr>
</tbody>
</table>
1. Let’s try ranking by priority – quickly! (or is it hopeless?)

Psychotropic drugs:

For pain?
- Pregabalin 225mg (? pain)
- Topiramate 100mg (? pain)
- Nortriptyline 40mg bedtime
- Cyclobenzaprine bedtime
- Ketorolac Injectable
- Hydromorphone 1-2mg
- Acetaminophen
- methocarbamol, THC, MJ

For depression?
- Aripiprazole 5mg/d
- Sertraline 250mg/d
- Vortioxetine 20mg/d

... psychotropic drugs:

For insomnia?
- Trazodone 100mg at bedtime
- Zopiclone 7.5mg at bedtime
- ? Nortriptyline 40mg bedtime

Drugs ? to counter AE:
- Lansoprazole 20 mg/d
- Solifenacin 5mg/d

Preventive drugs:
- Atorvastatin
It may not be hopeless if we challenge EVERYTHING!

But if we’re not the prescriber, it will require some kind of logic and plan ...

How much time is one human life worth?
Ranking drugs for symptoms by benefit

It should be easy for symptoms if we probe for straightforward answers and listen, e.g.:

• “That one really helps me” (me gusta mucho, c’est très bon, mycket bra, 很好, etc.)
• “They started them all at once, so I can’t tell!”
• “I never liked that one, but I really like my ...”

WHY DON’T WE ASK MORE OFTEN?
How would YOU respond to this situation?

85 y/o hospitalized for “alcohol w/d” has “high BP”, osteoporosis, “colitis”, insomnia, chronic pain, etc.

Regular psychotropics:
1. mirtazapine 45 mg/d (h.s.)
2. quetiapine 300 mg/d (h.s.)
3. zopiclone 15 mg/d (h.s.)
4. pregabalin 225 mg/d (divided doses)

Other drugs:
1. felodipine 2.5 mg/d
2. telmisartan 80 mg/d
3. T4 25 mcg/d
4. rabeprazole 20 mg/d
5. CaC03 twice/d
6. Vit D 800 units/d
7. risedronate 35 mg/week
8. KCL 8 mEq twice/d
9. 5’-ASA 6 tablets/d
Practical tricks of the trade

1. Rank medication list quickly by priority:
   • probably useful
   • Irrelevant or uncertain
   • probably/potentially harmful

2. Recognize likely drug interactions (kinetic or dynamic); avoid potentially dangerous ones – e.g. multiple drugs that slow heart rate or impair K+ excretion or GFR

3. Use $T_{1/2} \text{elim}$ to plan safe deprescribing – see example

4. Challenge rather than worship unsupported, impractical, or potentially dangerous prescriptions originated by specialists.
How would YOU respond to this situation?

LOOK AGAIN on the right

Regular psychotropics:

1. mirtazapine 45 mg/d
2. quetiapine 300 mg/d
3. zopiclone 15 mg/d
4. pregabalin 225 mg/d

1. felodipine 2.5 mg/d
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5. CaC03 twice/d
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9. 5’-ASA 6 tablets/d
Ranking drugs for symptoms – by harm

- This woman is Parkinsonized and sedated and has trouble even saying where she has pain
Considering **only her psychotropic drugs**, would YOU change anything?

<table>
<thead>
<tr>
<th>DRUG</th>
<th>STOP</th>
<th>REDUCE</th>
<th>CONTINUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mirtazepine 45 mg/d</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Quetiapine 300 mg/d</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zopiclone 15 mg/d</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregabalin 225 mg/d</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
What about now? How should we teach this?

The patient is much better, a “new woman”
Practical tricks of the trade

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2. Recognize likely drug interactions (kinetic or dynamic); avoid potentially dangerous ones – e.g. multiple drugs that slow heart rate or impair K+ excretion or GFR

3. Use T ½ elim to plan safe deprescribing – see example

4. Challenge rather than worship unsupported, impractical, or potentially dangerous prescriptions originated by specialists.
<table>
<thead>
<tr>
<th>Drug</th>
<th>Indication?</th>
<th>Toxicity?</th>
<th>Change</th>
<th>STOP?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morphine SR 30 mg/d</td>
<td>Shoulder pain</td>
<td>?</td>
<td>Added back to 60 mg/d</td>
<td>✓</td>
</tr>
<tr>
<td>Nabilone 2 mg/d</td>
<td>pain</td>
<td>?</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Celecoxib 200 mg/d</td>
<td>temporary</td>
<td>?</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Cyclobenzaprine 10 mg/d</td>
<td>pain</td>
<td>?</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Venlafaxine XR 150 mg/d</td>
<td>“depression”</td>
<td>?</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Mirtazapine 30 mg/d</td>
<td>“depression”/sleep</td>
<td>?</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Quinine 300 mg/d</td>
<td>Leg cramps</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canagliflozin 300 mg/d</td>
<td>DM2</td>
<td>? Low CBG</td>
<td>continued</td>
<td>later</td>
</tr>
<tr>
<td>Gliclazide MR 30 mg/d</td>
<td>DM2</td>
<td>Low CBG</td>
<td>continued</td>
<td>later</td>
</tr>
<tr>
<td>Insulin glargine 30 units bid</td>
<td>DM2</td>
<td>Low CBG</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Metformin 500 mg bid</td>
<td>DM2</td>
<td></td>
<td>continued</td>
<td></td>
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Practical tricks of the trade

1. Rank medication list **quickly** by priority:
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2. Recognize likely drug interactions (kinetic or dynamic); avoid potentially dangerous ones – e.g. multiple drugs that slow heart rate or impair K+ excretion or GFR

3. **Use T ½ elim to plan safe deprescribing** – see example

4. **Challenge rather than worship** unsupported, impractical, or potentially dangerous prescriptions originated by specialists.
Do you consider T ½ elimination or likely adverse effects to help you decide?

We may review briefly using a video:

- T ½ elim easy to find by internet or drug monograph
- Helps you know whether it’s safe to stop something ... long T ½ elim should not need taper!
- Kidneys more important than liver (except liver failure)
August 15, 2017

using clinical pharmacology rationally

Abstract

**Background and objective**

Chronic Low Back Pain (CLBP) is very common, with a lifetime prevalence between 51% and 80%. In majority, it is nonspecific in nature and multifactorial in etiology. Pregabalin (PG) and Gabapentin (GB) are gabapentinoids that have demonstrated benefit in neuropathic pain conditions. Despite no clear rationale, they are increasingly used for nonspecific CLBP. They necessitate prolonged use and are associated with adverse effects and increased cost. Recent guidelines from the National Health Service (NHS), England, expressed concerns on their off-label use, in addition to the risk of misuse. We aimed to assess the effectiveness and safety of gabapentinoids in adult CLBP patients.

**Benefits and safety of gabapentinoids in chronic low back pain: A systematic review and meta-analysis of randomized controlled trials**

Harsha Shanthanu, Ian Gilron, Manikandan Rajarathnam, Rizq AlAmri, Sriganesh Kamath, Lehana Thabane, Philip J. Devereaux, Mohit Bhandari
Gabapentin and pregabalin are NOT very effective

But let’s just think about their T ½ elimination:

- Gabapentin mean = 6 h
- Pregabalin mean = 6 h

Both excreted unchanged by kidney

Predicted equilibrium at any dose about 1 day
Effect of gabapentin, if any, is immediate
Same phenomenon when you look for it

Oxycodone > gabapentin = placebo for shingles


Maximum separation by 5 days
Reckless trial in PDPN (N = 325) – eventually published 2008?
final clinical study report dated February 7, 2000 (p. 53/3214)

Does this graph show a dose-response?

Does it show effect vs. placebo over time???

Does it show an effect of gabapentin?

![Graph showing weekly mean pain score](image-url)
eGFR 12 mL/min; he took ASA, candesartan, felodipine, furosemide, metoprolol, allopurinol, gliclazide, pioglitazone

• This man developed encephalopathy from gabapentin at 900 mg/d. The measured T½ elimination turned out to be 18 h ... but he was probably also very sensitive to gabapentin toxicity

• Drug stopped and recovery over several days
#4: celebrate reflex responses to “dogma alerts”

- “Adding a third-generation (...) will improve his (...)”
- “She needs to start ... bid”
- “I strongly recommend ... to prevent early death.”
- “Dual agent ... is indicated.”
- “Guidelines strongly recommend ... (Grade A recommendation, weak evidence)”