Deprescribing: Protecting Patients from Polypharmacy

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Disclosures and Objectives

- I have no relevant disclosures
- Participants will be able to:
  - Identify polypharmacy and its consequences
  - Explain the ethical and practical framework for deprescribing
  - Make recommendations for deprescribing in specific clinical circumstances
  - Share anecdotes and support each other regarding experiences with polypharmacy and deprescribing

Case Study: PP

- PP is a 92-year-old female resident of a skilled nursing facility, who was recently diagnosed with colon cancer metastatic to lung, liver, and lymphatics.
- Comorbidities include:
  - Alzheimer's disease (FAST 6e)
  - Hypertension
  - Atrial fibrillation
  - Hyperlipidemia
  - Type-II diabetes mellitus
  - COPD
  - Glaucoma
  - Macular degeneration

PP's Medications

- donepezil (Aricept)
- memantine (Namenda)
- amlodipine (Norvasc)
- ramipril (Altace)
- metoprolol (Lopressor/Toprol)
- amiodarone
- rivaroxaban (Xarelto)
- simvastatin (Zocor)
- metformin (Glucophage)
- glipizide (Glucotrol)
- repaglinide (Prandin)
- sitagliptin (Januvia)
- insulin lispro (Humalog)
- albuterol (Proventil)
- ibuprofen (Spiriva)
- fosfomycin-salmetrol (Advair)
- docusate (Colace)
- nitrofurantoin (Macrobid)
- omeprazole (Nexium)
- dorzolamide (Trusopt)
- Ocuvite
- multivitamin
- vitamin D
- ferrous sulfate
- folic acid

Does this look like a patient you might know?

Polypharmacy

- “Taking over five prescribed drugs”
  - 30% of people over age 65 in developed countries!
- Sometimes appropriate…but...
  - 20% of drugs may be inappropriate...

...and it’s worse in our patients!

- 68% take 8+ meds
- 33% take 15+ meds

Polypharmacy

- “The single most important predictor of inappropriate prescribing and risk of adverse drug events in older patients is the number of prescribed drugs.”

(Scott et al. 2015)
Polypharmacy: Burdens

- Adverse drug events
- Unanticipated drug interactions
- Unknowable cumulative risk
- Ill health
- Disability
- Hospitalization
- Death
- Expense

(Notice that expense is conspicuously listed last)

Have you heard...

“When you hospice people get involved, you just stop everything.”

- Is that what we do?

- Or is referral to HPM just the first time anybody considers polypharmacy? 
  (Talabereza 2014)

- Prescribers are good at starting medications
- Prescribers are bad at stopping medications

My Guiding Principles

1. Allow the patient’s body to guide the plan of care
2. Weigh carefully the potential benefits and potential burdens of every potential intervention
3. Respect our obligation to protect the vulnerable from harms

Also consider...

- There are progressive physiological changes associated with aging and with advanced illness, causing alterations in pharmacokinetics/pharmacodynamics

Deprescribing

- The process of tapering or stopping drugs, aimed at minimizing polypharmacy and improving patient outcomes
  - Takes into account goals of care, functional status, prognosis, etc.

The Protocol

- Identify every drug and every indication
- Consider potential benefits vs. potential risks/burdens/harms of every drug
- Prioritize, discontinue, and observe
Many Things We Rarely Stop

- An effective treatment should be continued as long as the expected benefits outweigh the potential burdens
  - Antidepressants?
  - CHF/CAD meds?  
    - (Rossello et al. 2015)
  - Symptom-directed therapies?
  - Diuretics?
  - Thyroid meds?
  - Rate control meds in afib?

Applying Evidence

- What evidence?
  - None of the studies that established enshrined practices included patients in our population...
  - ...and so we might conclude these studies are not generalizable to our patients!!!
  - Like much of what we do, the evidence is lacking, and common sense must often be our guide

However...

- An emerging literature increasingly supports deprescribing as beneficial or non-inferior compared to continuing medications!
  - “Frail older adults deserve guidelines that take frailty into account while assessing the potential benefit and risks of treatment.”
    - (Mallery et al. 2014)

Two Types of Interventions

- Preventive
- Treatment
- (Always consider the time required to achieve benefit!)

Anticoagulants for Atrial Fibrillation

- A **preventive** intervention
  - Benefit is only achieved with prolonged chronic use
- In our population:
  - The risk of major bleeding is higher
  - The consequences of major bleeding may be more grave
  - The risk of falling is higher
  - The likely burdens (blood tests, injections or additional pills, minor bleeding and other complications) may run counter to the goals of care

Anticoagulants for Mechanical Valves

- Preventive...so be suspicious!
- A major study: Cannegieter et al. 1994
  - 13,088 patients with mechanical valves studied for 53,647 patient-years
  - For patients with no antithrombotic therapy:
    - Major embolism: 4 per 100 patient-years
    - Valve thrombosis: 1.7 per 100 patient-years
    - So...net risk of 5.7%/year...
  - In other words, the risk is 0.016%/day...
- So, if even THIS might be more burdensome than beneficial in many patients...
Anticoagulants for Clots

- Treatment rather than prevention, but...
- ...it takes at least weeks-to-months of treatment to derive any benefit!

Amiodarone for Atrial Fibrillation

- The opposite issue...
- The benefit persists long after discontinuation!
- With repeated dosing, the half-life of amiodarone is 58 days...
- ...and it takes four half-lives to clear a medication...
- ...and four half-lives is 238 days, or over seven months!

Dementia Medications

- Small benefit in mild-to-moderate dementia
- Questionable benefit in moderate-to-severe dementia
- No proven benefit in end-stage dementia!
  
  - Associated with increased syncope, hip fracture, arrhythmia, urinary retention, weight loss...
  
  - If there is zero benefit and there is more than zero burden, why is this done?

Antihypertensives: Almost Entirely Preventive

- Hypertension: unlikely to cause any acute complications/symptoms until SBP>180 or DBP >110
- Hypotension: uncomfortable, dangerous, and deadly
- Other common effects:
  
  - Weakness
  - Orthostasis
  - 30-40% increased risk of injurious falls!
- Also: blood pressure naturally decreases in the final phases of terminal illness

Antihypertensives: Blood Pressure Targets

- No evidence supports a SBP target <140 in patients over 80.
- No proven difference in all-cause mortality in patients over 80 with SBP <160mm Hg.
- "In the very frail with short life expectancy, a target systolic blood pressure of 160 to 190 mm Hg is reasonable".

Lipid-Lowering Medications

- A purely preventive intervention:
  
  - No acute benefits
  - Increased short-term morbidity/mortality?
  - Stopping statins is safe and associated with improved quality of life

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(Kutner et al. 2015)
Antihyperglycemics: Almost Entirely Preventive

- Hyperglycemia: In DM-II, rarely causes more than polyuria until extremely high (>600)
- Hypoglycemia:
  - (Collar et al. 2014)
  - Uncomfortable
  - Dangerous
  - Iatrogenic!
- Also: patients are eating less and renal function is declining

Antihyperglycemics: Which Agents are Worst?

- Insulin of any kind
- Agents that increase insulin:
  - Sulfonylureas such as glyburide and glipizide (Glucotrol)
  - Meglitinides such as repaglinide (Prandin)
  - DPP-4 inhibitors such as sitagliptin (Januvia)
- GLP-1 agonists such as exenatide (Byetta) and liraglutide (Victoza)
- Metformin (Glucophage): strictly contraindicated in even mild renal failure due to risk of lactic acidosis
- Alpha-glucosidase inhibitors such as acarbose are rarely used due to near-universal GI distress
- Thiazolidinediones such as pioglitazone (Actos) and rosiglitazone (Avandia) are rarely used due to cardiotoxicity, but may actually be the least risky in our patient population!

Antihyperglycemics: Blood Sugar Targets

- New ADA guidelines for hospice patients: between 200mg/dL and 300mg/dL (Phan et al. 2010)
- Personally: up to 450mg/dL if asymptomatic in DM-II
- "Tight glycemic control is more likely to harm rather than help patients with type 2 diabetes mellitus approaching the end of life." (Lee 2015)

Anemia Treatments

- Anemia: much better tolerated than widely recognized
- Physiological acclimation in chronic anemia
- Often treating numbers not patients
- Transfusions?
- Erythropoiesis-stimulating agents?
- Vitamins/supplements?
- Best supportive care?

Pulmonary Meds

- Advanced pulmonary disease is characterized by poor response to bronchodilators
- Bronchoconstriction may not be the issue at all
- Adverse effects are common and often under-recognized
  - Albuterol/LABA: anxiety, tachycardia, tremulousness
  - Ipratropium/tiopropium: urinary retention, delirium
- Can the patient even use proper technique?

Pulmonary Meds

- We have better options for managing dyspnea:
  - Systemic glucocorticoids
  - Opioids
  - Consider the benefit-burden ratio of those...
Antimicrobials

- Is it really bacterial? Is it really an infection at all?
- No good evidence that antimicrobials improve symptoms, yet...
  - 90% of hospitalized cancer patients in the last week
  - 42% of nursing home residents with advanced dementia in the last two weeks
  - 27% of hospice patients in the last week!
  (Juthani-Mehta et al. 2015)

- Even if they might improve symptoms, is this best appropriate palliative care?
- Our patients have:
  - Reduced likelihood of benefit
  - Increased likelihood of burden:
    - The burdens of workup
    - Antibiotic-associated diarrhea
    - Cdiff
    - Drug reaction
    - Drug interaction
    - Delirium!
      (Bhattacharyya et al. 2016)

- We have other options...

Anti-acid Medications

- Proton-pump inhibitors
- H2-receptor blockers
- Often started during a hospitalization for "GI prophylaxis" and just never stopped
- Deprescribing sometimes cures GERD/dyspepsia (imagine that!)
- Increase risk of Cdiff
- Kidney injury!
   (Antoniou 2014)
- Myocardial infarction!
   (Shah 2015)

Ophthalmic Meds

- Vision loss is permanent
- Vision loss is gradual
- Symptoms are rare

Vitamins/Supplements

- Poorly absorbed (patients are transitioning from anabolic to catabolic)
- Often contribute to nausea/vomiting, constipation, dyspepsia, etc.

Overcoming Obstacles

- "You're stopping everything"
- Discussion of benefit-burden ratio
- Exploration of the alternatives: what we suggest instead
- "I've taken this for 20 years"
- "It's done its job!"
- Empowering patient/surrogate
- Educating prescribers
- Establishing a standardized intervention
THANK YOU

- QUESTIONS?
- COMMENTS?
- CONCERNS?

Cited References