Managing Polypharmacy: Evidence-based Dissection of Pharmaceuticals

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Disclosure

I have no relevant financial relationships to disclose.

Objectives

- To understand polypharmacy: its prevalence, causes, and outcomes
- To be able to better assess the pharmaceutical profile of patients
- To develop a process by which pharmaceutical profiles can be modified to contain the most appropriate medications for each patient
Agenda

- Definition and Prevalence
- Causes
- Effects and Outcomes
- Pharmacokinetics and Pharmacodynamics
- Tools

Polypharmacy - Definition(s)

- Medications used concurrently or excessively
- More medications than are indicated for a specific problem – consider ALL medications, preparations, lotions, potions, nutraceuticals regardless of source
- More than a specific number
  - Threshold ≥ 5
  - Excessive ≥ 10

Polypharmacy - Definition

- Consider the appropriateness of the medication regimen
  - Was the medication once appropriate → is the medication still appropriate?
  - Is the medication still clinically indicated?
  - Does anyone (patient, family, clinician) know why the medication is being taken?
  - Is the medication effective – either by patient report or in literature?
  - Is the medication duplicative?
Prevalence

- Polypharmacy is more common than expected
- Multiple statistics from multiple sources
  - 1998-99: 25% of US population took >5 medications; 5% >10
  - 2005-2006: 29% took >5 meds
  - 20-35% of community-dwelling elders took >10 meds
  - ~40% of elderly hospital inpatients were taking at least 1 inappropriate medication; of these, 33% lacked indication

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Causes - Patient Factors

- Age
  - Population is aging and acquiring more medical conditions
  - More medical conditions = More medical interventions
  - Add treatments for primary and secondary prevention
  - 40-49 yo: 18.5% polypharmacy prevalence
  - 80-89 yo: 78% polypharmacy prevalence
Causes - Patient Factors

Self-medication
- 33% of people >75 yo take ≥ 3 OTC daily
  - Analgesics
  - Nutritional supplements, vitamins, complementary medications
  - Interventions touted online, Dr. Oz, infomercials

Causes - Patient Factors

Sharing medications - “This helps me, so maybe it will help you”

Expectation that everything can be made better by a pharmaceutical
  - “Better living through chemistry”
  - Antibiotics for viral infections

Causes - Physician Factors

Tyranny of Evidence
- Evidence-based quality measures must be followed
  - Physicians tracked and rated on these measures
  - Reimbursement will be tied to measures and outcomes
  - HTN: ACE and ARBs
  - DM: HbA1c < 7

Guidelines
- Each focuses on one disease process
  - Multiple conditions → Multiple guidelines → Multiple medications
  - However... not tested on elderly
  - Following multiple guidelines can harm rather than benefit the patient
Causes - Physician Factors

Medicalization
- Every symptom MUST be treated with a medication.
- Ex: terminal secretions with anticholinergics.
- Expectation that every patient/physician encounter MUST end with a prescription.
- "The doctor didn’t do anything for me."
- Using antibiotics to treat viral syndromes.
- Unnecessary analgesics/opioids.

Causes - Physician Factors

Medication Cascade
- Prescription of Drug A → Side Effect 1
- Side Effect 1 seen as a new symptom or disease.
- Drug B Prescribed → Side Effect 2
- Side Effect 2 seen as another new symptom or disease.
- Drug C Prescribed → Side Effect 3...
- Consider any new symptom in a patient to be a medication side effect until proven otherwise.
- Consider stopping an existing medication rather than prescribing a new one.

Causes - Physician Factors

Physician Behavior
- Physicians tend not to take a full medication history - limits information.
- Physicians lack knowledge of side effects.
- Professional courtesy:
  - Physicians often reluctant to change orders of another physician.
  - "There had to be some reason the medication was prescribed."
Causes - Physician Factors

- Fragmentation of Healthcare Infrastructure
- Multiple transitions with different clinicians at each stage
- Often no one physician knows the patient's narrative
- Multiple providers → Lack of continuity
- Multiple providers may use different pharmacies → duplicate medications

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Effects of Polypharmacy

Decrease in physical and cognitive function
- The greater the number of medications taken (≥ 5), the greater the decrease in function.
- Age-matched populations:
  - Fewer medications: 50% had decreased function in IADLs
  - Five or more medications: 75% had decreased function in IADLs
- Decrease in function/IADLs → Decrease in independence
- Progression to loss of ADLs → greater assistance required → losses for the person; increased caregiver responsibility; caregiver burnout; increased financial burden on person, caregiver, system
Effects of Polypharmacy

- Delirium - when a patient becomes delirious, look at the medication list first
- Falls - increased risk with psychotropic or cardiovascular medications
- Decreased Nutrition
  - Medications cause anorexia, nausea, dry mouth
  - Medications cause increased appetite with increase in non-nutritious intake

Effects of Polypharmacy

Adverse Drug Events

- When inappropriate medications are prescribed, the risk of ADE outweighs potential clinical benefits
- When multiple medications are prescribed, the risk for drug-drug interactions also increases
- More medications = More chances for adverse events or errors

Effects of Polypharmacy
Effects of Polypharmacy

Errors lead to:
- Emergency Department visits
- Acute care hospital admissions
- Premature stoppage of drug
- Need for more medications
- Deterioration of underlying disease
- Non-adherence
- Falls – injury is 5th leading cause of death, many due to falls
- Cognitive decline
- Death

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Pharmacokinetics & Pharmacodynamics

- Aging associated with changes in body and organ function:
  - DNA damage due to lifetime of oxidative stress
  - Telomere shortening
  - Changes in gene expression
  - Up-regulation of cell apoptosis
  - Studies of drug effects do not account for these changes
  - Elderly and debilitated usually excluded from trials
  - Test subjects for efficacy trials for life expectancy of decades
Pharmacokinetics

- Absorption
  - Decreased due to decreased GI blood flow, GI motility, gastric emptying, gastric acid production
  - First pass effect also decreased due to decreased liver mass

- Distribution
  - Altered protein binding
    - Increased in α-1 acid glycoprotein (CA, inflammation)
    - Decrease in albumin
  - Less binding = more free drug (warfarin)

- Metabolism
  - Liver size decreases by 1/3, hepatic blood flow decreases by 40% = decreased metabolism of β-blockers, Ca-channel blockers, TCAs
  - Cytochrome P450 decreased = prolonged metabolic clearance (alprazolam)

- Excretion
  - Kidney size decreases by 30-30%
  - Effects of disease (CKD)
  - Prolonged clearance

Pharmacodynamics

Cardiovascular Medications

- Ca-channel blockers - increased hypotensive effect without rebound tachycardia
  - Think: FALLS
- Decreased baroreceptor sensitivity
  - Think: FALLS
- Loop diuretics less effective
Pharmacodynamics

- CNS Medications
- Increased sensitivity to benzodiazepines, atypical antipsychotics
- Underlying alterations of receptors in brain:
  - Dopamine, GABA, NMDA
  - Lead to increased risk of sedation, extrapyramidal signs, confusion, insomnia, falls

Pharmacodynamics

- Medications that prolong QT interval
  - Increased risk of torsades de pointes and V. fib
  - Antipsychotics, antiarrhythmics, antidepressants, antibiotics...
- Hypoglycemia
  - Keeping HbA1c < 7 increases risk of falls
  - Multiple hypoglycemic episodes lead to worsening of cognitive impairment
  - Sulfonylureas are secretagogues
  - Can accumulate in renal insufficiency with increased risk of hypoglycemia

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Medication Review

- Should be done at regular intervals, especially with any transition of care
- Goal: the right medications - not too many, not too few
  - Patient comorbidities
  - Patient goals of care
  - Patient preferences
  - Patient ability to adhere to regimen

“Brown Bag Review”

- “Bring me everything you put into or onto your body to treat something, make you feel better, or prevent something.”
- Not just asking about medications

Medication Review

- Beware the trap of Ageism
  - >75% of elders have capacity
  - >80% of elders understand their medications
- Falls, confusion, and lethargy are not part of normal aging
- Match everything in the brown bag to a diagnosis or symptom
  - Look for overtreatment - what is there - expected/unexpected?
  - Look for undertreatment - what is missing?
  - Look for orphan drugs - what are they doing there?
Medication Review

- Review for adherence - how often do you miss taking a dose of your medications?
- Review for Adverse Drug Effects
  - Any new symptom in an elder should/could be considered a drug side-effect until proven otherwise
  - Patients often do not relate ADRs to the medication, as symptoms may not start for weeks after starting
  - May need to describe symptoms to patients, families

Medications to Think About

- Warfarin/Other Anticoagulants
  - One-year risk of CVA in a fib decreased from 4% to 2%
  - Risk of intracranial or GI bleed 8% in debilitated patients
  - Risk further increased with frequent falls
- Statins
  - How much more benefit does patient with limited life span derive from lipid control?
  - How much increased debility from muscle pain or weakness?

Medications to Think About

- Clopidogrel
  - Evidence exists for up to 6 months of treatment after stent placement
  - NNT for 2 years to prevent 1 CVA = 200
- Furosemide
  - Best indication in stable heart failure
  - Risk: decreased renal blood flow, increased dehydration, falls
Medications to Think About

- **Bisphosphonates**
  - No added benefit for use beyond 3-5 years
  - Adherence: can patient remain upright for 30 minutes?
- **Donepezil**
  - Clinically marginal increase in cognition
  - Side effects: nausea, anorexia, syncope

Medications to Think About

- **Sulfonylureas** - glimepiride, glipizide
  - Secretagogues; can cause occult hypoglycemia
  - Increase in cognitive impairment, delirium, dizziness, falls
- **Vitamins E, A, β-carotene**
  - Can cause fatigue, weakness, bleeding (vit E)
  - Associated with increase in all-cause mortality
  - Large pills

Medications to Think About

- **Antihypertensives**
  - Is patient frail? No evidence of association between blood pressure control and mortality
- **Psychotropic medications** (benzodiazepines, TCAs, SSRIs)
  - Increased confusion, increased falls
“Sharp Dissection of Pharmaceuticals”
ABCD Method - Glenn Ross

A medications = must have medications
- Medications necessary for symptom control
- Patient should remain on these
- Plan = continue

B medications = nice to have medications
- Medications currently necessary for symptom control but need to be reviewed on regular basis
- Oral medications that do not have parenteral form
- Medications with limited efficacy as patient declines
- Plan = continue for now

C medications - why is this here?
- Medications with no known indication or resolved condition
- Medications used inappropriately or for wrong indication
- Medications which are duplicative
- Medications used for primary or secondary prevention following guidelines that no longer apply to the patient
- Medications that increase anticholinergic or serotonin burden
- Plan = develop a process to discontinue medications safely and in an orderly fashion

D medications - oh no!
- Medications which are harmful to the patient or place the patient at high risk of severe complications
- Medications which need to be stopped quickly
- Plan = discontinue medications as quickly and safely as possible
Discontinuing Medications: Deprescribing

Less is more

- Start low, go slow
- Use judgment
- Plan to discontinue one medication at a time
- Stop abruptly or taper as the medication dictates
- Monitor for side effects:
  - Withdrawal symptoms
  - Reappearance of previous symptoms
  - Worsening of underlying condition
- If adverse reaction appears, restart medication and move on
- If no adverse reaction appears, move on

Study of Nursing Home Residents
- Discontinuation of medications provoked no adverse reactions
- Only 10% of medications had to be restarted

Study of Community-Dwelling Elders
- Mean number of medications stopped per patient: 5
- 66% of patients had all planned medications stopped
- Only 2% of these medications had to be restarted

With appropriate information, consultation, critical thinking, and planning, deprescribing can be successful.
Discontinuing Medications

- Check out Bohemian Polypharmacy (by James McCormack, PharmD; james.mccormack@ubc.ca)
- https://www.youtube.com/watch?v=spJp3is0z8

References

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References


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