Polymedicine in the Elderly

Tracy Gutman
Geriatrician

Objective: Explain basic principles of aging and pharmacology
- Explain pharmacodynamic changes
- Explain pharmacokinetic changes including absorption, distribution, hepatic metabolism and renal clearance / excretion

Objective: Define polymedicine / polypharmacy
- Define polymedicine / polypharmacy and list some of the problems with inappropriate medication use
- Discuss risks and benefits of polymedicine
- List risk factors for polymedicine
- Discuss problems associated with polymedicine
Objective: Review adverse drug effects in the elderly; highlight and understand problem drugs in the elderly and drugs to avoid / closely monitor

- List risk factors for adverse drug reactions
- Describe age related changes that increase susceptibility to adverse drug effects in the elderly
- Define potentially inappropriate medications in the elderly using Beers and STOPP lists
- List the side effects of anticholinergic medications
- Give examples of medications with anticholinergic properties
- Give examples of specific problem drugs in the elderly, their negative side effects, and alternative options
- Define drug interactions and describe the impact of drug interactions in elderly patients
- Explain geriatric syndromes that can be caused by drugs

Objective: Discuss best practices for prescribing in older adults

- Define and give examples of the polymedicine or prescribing cascade to avoid
- Explain the utility of the BEERS list and STOPP and START lists
- Discuss medication adherence problems in the elderly and what can be done to improve adherence
- Explain best opportunities and practices for assessing medication use and reviewing medications in elderly patients

Objective: Define and discuss deprescribing

- List some of the barriers to deprescribing and avoiding polypharmacy
- Discuss overall principles of deprescribing and methods to attempt this practice
- Prioritize questions to ask when deciding on deprescribing
- Provide reasons to stop a medication or reduce the dose of a medication
- List some medications commonly associated with discontinuation syndromes requiring slow tapering
- Discuss a framework of determining drug utility
- Review principles for appropriate prescribing in end-of-life patients
Age-related changes that increase susceptibility to adverse drug effects

Pharmacodynamic changes (what the drug does to the body); altered sensitivity to medications; what factors affect whether medication will have a greater or lesser affect with same serum concentrations

Pharmacodynamic changes — physiologic and biochemical effects of drugs on the body

- Increased sensitivity to cardiovascular medications, anticoagulants, opioid analgesics, antipsychotics, benzodiazepines
- Altered concentration of neurotransmitters and receptors, altered receptor binding properties and responsiveness \( \Rightarrow \) results in exaggerated drug effects
- Functional reserves decline with age affecting cardiovascular, musculoskeletal, and CNS — exaggerated drug effects
- Impaired homeostatic mechanisms — more pronounced side effects; orthostatic hypotension with antihypertensives; lack of compensatory responses — impaired reflex tachycardia, impaired regulation of temperatures and electrolytes
- Side effects may develop over time because of these changes even in patients on stable doses of medications; side effects may be mistaken for new diseases with new medications added to treat

Pharmacokinetic changes (what the body does to the drug): alterations in factors that affect drug concentration at the target receptor or organ

- Absorption — minimal clinical relevance (little change due to aging alone) — generally if drug is swallowed, it will be absorbed but decreased active transport decreases bioavailability of some drugs (Calcium with achlorhydria); reduced first pass metabolism (reduced liver mass and blood flow) increases bioavailability of some drugs (metoprolol, propranolol, nortriptyline, calcium channel blockers, and tricyclic antidepressants); can be affected by medications and conditions common in older people
- Distribution — significant clinical relevance but not readily predictable
  1. Increased fat mass increases volume distribution and half life of lipophilic medications; increased body fat prolongs half life of fat soluble drugs (disopyramide, amitriptyline)
  2. Decreased total body water results in decreased volume of distribution and increased concentration of water soluble drugs (digoxin, ethanol, levodopa, morphine)
  3. Decreased fat-free mass/plasma protein leads to higher percentage of unbound (active) drug
Age-related decreases in metabolism and clearance of drugs

Hepatic Metabolism

- Decreased first-pass metabolism leads to increased concentration of drugs that typically have high levels of first-pass metabolism; i.e., hepatic clearance before reaching systemic circulation.
- Hepatic disease or reduced hepatic volume and blood flow results in reduced oxidative metabolism (reduced metabolism through CYP450) and higher steady-state concentrations of some drugs (diazepam, metoprolol, phenytoin, theophylline, alprazolam).

Excretion and Renal Clearance – significant impact

- Excretion – decreased cardiac output (e.g., heart failure) results in less perfusion of kidneys and liver which reduces elimination (imipramine, morphine, propranolol).
- Increased concentration of renally cleared drugs.
- Serum creatinine alone does not provide adequate information to guide dosing.
- Use Cockcroft-Gault to estimate glomerular filtration rate; more conservative than other calculators, e.g., MDRD, less likely to overestimate eGFR especially in frail older patients; drug company renal dose recommendations are based on eGFR.
- Reduced kidney function reduces elimination of renally excreted drugs or metabolites (digoxin, cephalaxin, morphine, meperidine, gabapentin, sotalol, Lisinopril, Ramipril, diuretics, metformin).
Kidneys!

- Decrease in renal drug clearance corresponds to decline in creatinine clearance
- May be difficult to distinguish age related changes from disease related changes – diabetes, hypertension, CAD may also account for diminished kidney function in the elderly
- Even if a dosage is decreased appropriately based on age-related pharmacokinetic changes, physiologic changes and decreased homeostasis can cause greater sensitivity to drug interactions

Polymedicine or Polypharmacy

- Defined as taking 5 or more medications a day
- Use of more medications than are clinically indicated
- Use of unnecessary medications
- Use of inappropriate medications that have greater potential risk for harm than benefit, are less effective or more costly than available alternatives, or do not agree with accepted medical standards
- Can be considered an age-related geriatric syndrome and is a predictor of malnutrition, hospitalization, nursing home placement
- Can be conceptually perceived as a disease with possibly more serious consequences than the diseases the different drugs are prescribed for
- Leads to increase in mobility impairment, risk of falls, adverse drug events, and to morbidity and death

Polymedicine or Polypharmacy

- Limitations to this terminology:
  - I use polymedicine: Homage to the clinical pharmacist I worked with running a polymedicine clinic
  - Problems with the word Polypharmacy:
    - Poly – many; many pharmacies
    - Connotation of negative, inappropriate use of medications; unnecessary; medication does not meet diagnosis
    - Vague – e.g. excessive medication use could mean: frequency, dosage, unintentional overuse, intentional misuse or abuse, use of drug when non drug therapy is more appropriate
    - Does not include qualitative differences between different drug classes and inappropriate drug use
Polymedicine — critical, systematic, thoughtful review of medications can sometimes involve need for multiple medications

--Medication reviews and appropriate prescribing involve prescribing appropriate combinations sometimes of multiple medications — e.g., polymedicine can be appropriate (START guidelines)

--Elderly have many chronic conditions that increase with age — stroke, cardiovascular diseases, musculoskeletal disorders and dementia: more medications needed

--Don’t forget the guidelines (even though they don’t always apply and are problematic — see next slide): guidelines for secondary prevention and targeting goals for blood pressure, diabetes, lipids, osteoporosis: more medications

--Polymedicine — multiple medications that are appropriate / clinically indicated

Difficulties in prescribing for older adults: Lack of Evidence

• Lack of data to guide use of medications in older adults because they are rarely included in RCTs

• Elderly are underrepresented in drug trials even though they are the greatest users of medications

• Most evidence based clinical guidelines are extrapolated from younger populations

• Even when older adults are included, healthy elderly subjects do not represent frail older patients typically using these medications

• Guidelines do not always make sense for frail elders and very old; following guidelines in these patients adds medications without considering life expectancy, goals of care, time to potential benefit

Polymedicine

• More than 50% of female Medicare beneficiaries took 5 or more medications daily

• 20-65% of older adults take potentially inappropriate medications


• More than 50% of older adults in institutions and 27% of older adults in the community are taking more than five prescribed medications daily; proportion increases with age

• One national survey of US nursing home resident – 40% received 9 or more medications
• The US Center for Medicare and Medicaid Services estimates that polymedicine costs more than $50 billion dollars annually

In the US
• 60% of older patients receive 5 or more drugs
• 20% receive 10 or more drugs
• About 1 in 3 older patients living in the community and taking at least 5 drugs will experience an adverse drug reaction
• Up to 20% of older patients living in the community receive at least 1 inappropriate medication as do 1/3 of hospitalized patients and as many as 50% of those living in residential care facilities

Risk factors for polymedicine
1. Demographic: advancing age, female gender, low education level
2. Health status markers: recent hospitalization, multiple comorbidities, depression; involvement of multiple prescribers; greater health care utilization; difficulties with IADLs; frailty
Why is this a problem?

- Evidence indicates that using more medications is associated with increased medication side effects and adverse health events
- Polymedicine is associated with increased risk of adverse drug reactions and interactions, inappropriate prescribing, inappropriate drug use, nonadherence, impaired balance and falls, hospitalization, increased risk of cognitive impairment, institutionalization, mortality

Problems associated with Polymedicine

- adverse drug reactions
- drug-drug interactions
- drug-disease interactions
- higher risk of using potentially inappropriate medications
- decreased adherence
- increased risk of medication errors
- increased cost
- increased morbidity and mortality
- Risk factor for dementia; risk of dementia increases with number of drugs used
- Elderly people can develop cognitive and functional impairment as a result of their medications

Drug Interactions / Adverse Drug Reactions

- increased vulnerability to drug interactions due to underlying comorbid conditions
- Use of multiple medications increases the risk of adverse drug reactions: 13% among patients taking five medications v. 6% among those taking one or two

Those at highest risk of adverse drug reactions:

- patients prescribed 8 or more medications
- previous adverse drug reaction
- 4 or more medical co-morbidities
- liver disease
- heart failure
- renal disease
- receiving high risk drugs: anticoagulants, insulin or oral hypoglycemic drugs, psychotropic medications, sedatives / hypnotics, cardiovascular drugs (digoxin, nitrates, vasodilators), NSAIDs
- cognitive impairment
- living alone
- history of nonadherence
- known psychological disorders or substance abuse

Drug Interaction

- A clinically meaningful alteration in the effect of one drug as a result of coadministration of another drug; interactions can be beneficial but may also increase effects of a drug causing toxicity or inhibit the effects of a drug leading to diminished benefit

Examples of Drug Interactions / Effects in the Elderly

- Warfarin interactions: many elderly take warfarin to reduce stroke risk from atrial fibrillation or to decrease risk of recurrent thromboembolic disease or thrombotic risk due to mechanical heart valves
- Proton Pump Inhibitors – increased risk of MI?, reduce absorption of medications and supplements including thyroid hormone, calcium, magnesium; increased fracture risk in PPI users; reduce vitamin B12 absorption; increased risk of B12 deficiency; associated with diarrhea (C diff) and pneumonia
Examples of drug side effects in elderly

• SSRIs – more likely to develop hyponatremia; SNRIs as well; increased risk of GI bleed
• Quinolones – CNS side effects (anxiety, restlessness, insomnia, hallucinations, psychosis, seizures); higher risk for tendonitis and tendon rupture; implicated as a cause of peripheral neuropathy
• Bactrim – at risk for the development of hyperkalemia especially if taking Ace inhibitor or ARB and with renal insufficiency

Be careful even with common drugs

• Elderly patients who take ace inhibitors are 20 fold more likely to be hospitalized for hyperkalemia if they receive a potassium sparing diuretic in the prior week
• Elderly patients who take an ace inhibitor or ARB are nearly 7 fold more likely to be hospitalized with hyperkalemia if they have recently received SMX/TMP

Geriatric syndromes that can be caused by drugs

• 1. Falls: sedatives, hypnotics, anticholinergics, antihypertensives, antidepressants, antidiabetics
• 2. Cognitive impairment: anticholinergics, benzodiazepines, antihistamines, tricyclic antidepressants
• 3. Incontinence: alpha-blockers, sedatives (benzos), diuretics
• 4. Constipation: anticholinergics, opioids, tricyclic antidepressants, calcium channel blockers, calcium supplements
• 5. Delirium: antidepressants, antipsychotics, antiepileptics
• 6. Diarrhea: antibiotics, proton pump inhibitors, allopurinol, SSRIs, ARBs, anxiolytics, antipsychotics
• 7. GI bleeding: NSAIDs, oral anticoagulants
Medication Adherence Issues

- high number of drugs and regimen complexity – limit number of medications; try to simplify regimen to daily dosing when possible
- inadequate patient understanding – include drug indication on prescription; explain rationale for every new drug started and anticipated duration of therapy
- prescription not congruent to patient goals, cost barriers – what are patient goals
- memory problems, poor organization – medication organizers, medisets, blister packs, electronic dispensing devices, cues / calling, monitoring, drug administration
- difficulty taking (vision or dexterity problems or dysphagia) – order easy to remove bottle caps, larger font labeling, magnifying glass, spacer for inhalers or nebs; consider smaller tablets, solutabs, liquid versions

What do we do about it?

- Carefully evaluate risk benefit of each medication given lack of guidelines / evidence based medicine that includes frail, older adults
- Medication regimens should fit patient preferences and goals of care
- Reduce the number of inappropriate drugs prescribed

What do we do about it? Think carefully

- Given the large risks of adverse drug reactions in the elderly, think about the drugs you are prescribing
- The drugs should be absolutely necessary to achieve well defined goals and given at the lowest effective doses
- Discontinue drugs that do not achieve desired end points and that are no longer needed
Problem Drugs

- Two-thirds of adverse drug effects that result in ER visits and hospitalizations for older adults are due to 4 medications: warfarin and antiplatelet medications (bleeding); insulin and sulfonylurea agents (hypoglycemia)
- Consider stopping aspirin in patients with stable coronary artery disease on warfarin; continuing both aspirin and warfarin doubles the risk of bleeding without conferring additional cardioprotection

Problem Drugs

- Muscle relaxants (e.g., cyclobenzaprine, methocarbamol) – sedation, anticholinergic, increased fall and fracture risk, uncertain efficacy
- Iron more than once daily – increased GI side effects (nausea, constipation), usually outweigh small marginal gains in iron absorbed when daily dose increased to twice a day
- Chronic daily NSAIDs – GI bleed, renal insufficiency, fluid retention, blood pressure elevation; short term use may be appropriate

Problem Drugs

- First generation antihistamines (e.g. Benadryl) – sedating, anticholinergic effects: confusion, dry mouth, dry eyes, constipation, urinary retention
- Glyburide – higher risk of hypoglycemia (including episodes requiring hospitalizations and causing death)
- Benzodiazepines – confusion, memory loss, dizziness, daytime sleepiness, falls and fractures, depressed mood, functional impairment, dependency / withdrawal
Problem Drugs: Anticholinergic Meds

• increased blood-brain barrier permeability and age related declines in cholinergic transmission are contributing factors
• Patients with dementia are more susceptible to the effects of anticholinergic medications and are more likely to receive them

Problem Drugs: Anticholinergic Meds

• Falls
• Sedation
• Confusion, delirium
• Urinary Retention
• Constipation
• Dry mouth
• Glaucoma, dry eyes, blurred vision
• Memory impairment / cognitive dysfunction
• Dizziness
• Impulsive behavior
• Loss of independence

Medications with Definite Anticholinergic Effects

• Amantadine
• Amitriptyline
• Amoxapine
• Atropine
• Benztrapine
• Brompheniramine
• Carbamazepine
• Chlorpheniramine
• Chlorpromazine
• Clozapine
• Cyclobenzapine
• Desipramine
• Dicyclomine
• Diphenhydramine
• Doxepin
• Hydroxyzine
• Imipramine
• Methscopolamine
• Metoclopramide
• Nortriptyline
• Olanzapine
• Oxcarbazepine
• Oxypertine
• Perphenazine
• Promethazine
• Quetiapine
• Sontolamine
• Thioridazine
• Tolterodine
• Trihexypene
Anticholinergic, don’t forget
Second generation antihistamines such as cetirizine and loratidine; H2 blockers like ranitidine; avoid if possible but better than first generation

Examples of problem drugs and their alternatives

Antihistamines: First Generation: Side effects
First Generations Antihistamines
• Brompheniramine
• Carboxamine
• Chlorpheniramine
• Clemastine
• Diphenhydramine
• Dimenhydrinate
• Hydroxyzine

Alternatives:

Allergies or Itching – Use
Loratidine or Cetirizine
Insomnia
• Sleep hygiene
• Melatonin
• Mirtazapine
• Trazodone
Antidepressants

- Amitriptyline
- Amoxapine
- Clomipramine
- Desipramine
- Doxepin
- Imipramine
- Nortriptyline
- Paroxetine
- Trimipramine

- SSRIs: sertraline, citalopram (max 20 mg), lexapro
- SNRIs: venlafaxine, duloxetine
- Other: mirtazapine, bupropion

Pain

NO NSAIDS!!!!!!!!!!!!!!

- Kidney damage
- GI bleeding
- Hypertension
- Edema
- MI

Avoid anticholinergic muscle relaxants:

- Cyclobenzaprine
- Methocarbamil

First Line: Acetaminophen scheduled

- Neuropathic pain – gabapentin; pregabalin
- Consider duloxetine (watch renal function and don’t use with liver issues)
- Topical
- Physical therapy
- Alternatives: chiropractic, acupuncture, Tai Chi

Problem Drugs for Older Adults

AGS BEERS CRITERIA
FOR POTENTIALLY INAPPROPRIATE MEDICATION USE IN OLDER ADULTS
Dealing with Problem Drugs: Reducing Polypharmacy and Appropriately Prescribing

- STOPP: prevent overprescribing
- START: prevent underprescribing—to avoid not giving an elderly patient a medication that is clearly indicated

STOPP and START criteria – for detecting potentially inappropriate prescribing in old age; 2003

STOPP screening tool of older persons (potentially inappropriate) prescriptions = potential errors of prescribing commission

START screening tool to alert to right treatment = potential error of prescribing omission

STOPP screening tool of older persons (potentially inappropriate) prescriptions = potential errors of prescribing commission
8. Gastrointestinal System

- Loperamide, an antidiarrheal agent, for treatment of diarrhea in patients with severe inflammatory bowel disease (risk of exacerbation, inappropriate antidiuretic hormone, dehydration, electrolyte imbalance, hypovolemia).

- Midodrine, an alpha-adrenergic agonist, for treatment of orthostatic hypotension (risk of hypertension, orthostatic intolerance).

- Gastrointestinal drugs with anticholinergic activity (risk of urinary retention, constipation, dry mouth, confusion, delirium, mydriasis).

- Gastrointestinal drugs with histamine H2 receptor antagonist activity (risk of gastritis, dyspepsia, nausea, vomiting).

- Antacids, aluminum hydroxide, and magnesium hydroxide, for treatment of acid-base disturbances (risk of diarrhea, constipation, nephrotoxicity).

- Proton pump inhibitors (PPIs), such as lansoprazole, pantoprazole, and esomeprazole, for treatment of chronic acid-related disorders (risk of bone fracture).

- NSAIDs, such as ibuprofen and celecoxib, for treatment of arthritis or osteoarthritis (risk of gastrointestinal bleeding, renal dysfunction, hypertension).

- Antidiarrheal agents, such as loperamide and diphenoxylate/atropine, for treatment of chronic diarrhea (risk of constipation, overdose).

9. Endocrine System

- Antihypertensive drugs, such as angiotensin-converting enzyme inhibitors (ACE inhibitors), angiotensin receptor blockers (ARBs), and calcium channel blockers (CCBs), for treatment of hypertension (risk of hypotension, electrolyte disturbances).

- Antihypertensive drugs, such as diuretics (thiazide, loop, or potassium-sparing diuretics), for treatment of chronic heart failure (risk of fluid retention, electrolyte disturbances).

- Antihypertensive drugs, such as beta-blockers (non-selective and selective), for treatment of hypertension and angina pectoris (risk of bradycardia, conduction defects).

- Antihypertensive drugs, such as alpha-blockers, for treatment of hypertension (risk of hypotension, postural hypotension).

- Antihypertensive drugs, such as angiotensin II receptor antagonists (ARBs), for treatment of hypertension (risk of hypotension, electrolyte disturbances).

- Antihypertensive drugs, such as aldosterone inhibitors (spironolactone), for treatment of hypertension (risk of fatigue, hyperkalemia).

10. Drugs that may affect the central nervous system in patients with dementia or other cognitive disorders

- Antipsychotic drugs, such as atypical antipsychotics (clozapine, risperidone), for treatment of agitation and aggression in patients with dementia (risk of extrapyramidal side effects, sedation, dystonia).

- Antiepileptic drugs, such as lamotrigine and valproic acid, for treatment of seizures (risk of hematologic disorders, skin rashes).

- Opioid analgesics, such as morphine and fentanyl, for treatment of pain (risk of respiratory depression, sedation).

- Benzodiazepines, such as lorazepam and diazepam, for treatment of anxiety and agitation (risk of sedation, respiratory depression).

- Psychostimulants, such as methylphenidate and atomoxetine, for treatment of attention-deficit/hyperactivity disorder (risk of insomnia, agitation).

- Anticholinergic drugs, such as scopolamine and benztropine, for treatment of parkinsonian symptoms (risk of blurred vision, dry mouth, constipation).

11. Contraindications and precautions

- Contraindicated in patients with allergy to the drug (risk of anaphylaxis).

- Contraindicated in patients with severe renal impairment (risk of accumulation, toxicity).

- Contraindicated in patients with severe hepatic impairment (risk of accumulation, toxicity).

- Contraindicated in patients with a history of stroke or transient ischemic attack (risk of exacerbation of symptoms).

- Contraindicated in patients with a history of cardiac arrhythmia (risk of exacerbation of symptoms).

- Contraindicated in patients with a history of glaucoma (risk of exacerbation of symptoms).

- Contraindicated in patients with a history of urinary tract obstruction or bladder outlet obstruction (risk of exacerbation of symptoms).

- Contraindicated in patients with a history of malignant hyperthermia (risk of exacerbation of symptoms).

- Contraindicated in patients with a history of peptic ulcer disease (risk of exacerbation of symptoms).

- Contraindicated in patients with a history of gastrointestinal bleeding (risk of exacerbation of symptoms).
Examples:

• Loop diuretic for edema
• Loop diuretic as first line therapy for hypertension
• Aspirin greater than 150 mg per day: increased bleeding risk, no increased efficacy
• TCAs
• Long term benzodiazepines
• Prolonged use of first generation antihistamines
• Long term NSAID use

START – screening tool to alert to right treatment = potential error of prescribing omission

• Warfarin for atrial fibrillation
• Aspirin for ASCVD
• Statin for ASCVD where the patient’s functional status remains independent for ADLs and life expectancy is greater than 5 years
• Ace inhibitor for CHF and after MI
• Calcium and vitamin D for osteoporosis
• Metformin

Polymedicine Cascade

• Consider any new symptom as a possible drug side-effect; any new symptoms in an elderly patient should be considered a drug effect unless proven otherwise; treating a new symptom that may be drug related with another medication can lead to polymedicine where patient is taking excessive and unnecessary medications
Avoid the Prescribing Cascade

- An adverse effect of one drug is misinterpreted as a new medical condition that leads to prescription of another drug, a new medication is added to manage side effects of current medications
- It is easy to overlook medication adverse side effects when patients are having so many symptoms that could be attributed to their complex chronic diseases
- Before starting a medication, ask, is this medication possibly being prescribed to treat the side effects of an existing medication
- Thorough history; timing of new symptoms in relation to medication starts or changes

Prescribing cascades – treating side effects of medications with other medications

- E.g. Furosemide → urinary frequency → oxybutynin
- Ibuprofen → hypertension → antihypertensive
- Metoclopramide → parkinsonism → levodopa/carbidopa
- Risperidone → parkinsonism → benztropine
- Amlodipine → edema → furosemide

- Gabapentin → edema → furosemide
- Ciprofloxacin → delirium → antipsychotic
- Lithium → tremor → propranolol
- Bupropion → insomnia → mirtazapine
- Donepezil → urinary incontinence → oxybutynin
- Meperidine → delirium → antipsychotic
- Beta blocker → depression → antidepressant
- Amitriptyline → decreased cognition → donepezil
- NSAID → heartburn → H2 blocker or PPI; increased salt retention and renal effects – increased blood pressure – blood pressure medication
- Omeprazole → low B12 → B12 replacement
- Subbed → urinary retention → alpha blocker
- Antipsychotic → akathisia, activation, agitation → more psychoactive medications
Prescribing for the older adult

• Consider nonpharmacologic approaches – try to avoid unnecessary drugs
• Consider the risk versus the benefit before prescribing any drug
• Set specific goals and timelines for assessing drug therapy outcomes
• Discontinue unnecessary or ineffective therapy
• Think carefully about medications that carry a substantially higher risk of adverse effects; Use safer alternatives instead of high risk drugs
• When initiating new agents, start with lower doses, titrate slowly, increase as indicated
• Include pharmacists on the interdisciplinary team

Prescribing for the older adult

Match each medical condition with medications being taken to identify
• overuse (no indication or medications with no clear evidence-based indications) – Stop
• underuse (clear indication but no suitable drug being offered)
• misuse (administration of a different drug may be more effective with less side effects)
Currently prescribed medications could be discontinued if original diagnosis / condition does not still exist or the medications are having little or no therapeutic effect

Prescribing for the older adult

Where life expectancy is less than 12 months, medications that usually take longer than this to have benefit may be inappropriate
• bisphosphonate therapy to prevent osteoporotic fractures or statins to prevent cardiovascular events
Identify and try to discontinue medications that are of little or no benefit or potentially harmful
Prescribing for the Older Adult

• Be less aggressive in reaching rigid target goals (blood sugar, blood pressure, lipids)
• Focus on quality of life and patient / family preferences
• Start slow and go slow but go
• Stop most and reduce dose
• Sometimes a problem drug (potentially inappropriate medication) is appropriate if benefit outweighs risk to patient

Look at the big picture

• Many older adults experience increasing numbers of incurable comorbidities, disability, and suffering for increasingly prolonged periods before death
• The model of one disease – one therapy / guideline does not work for these patients
• Almost half of people older than 65 years have 3 chronic conditions, with 21% having 5 or more
• Single disease approach leads to polypharmacy


Medication Review

• brown bag review – both prescription and over the counter medications
• contacting pharmacies; utilizing home health nurses
• medication review appointments – consider each medication and whether it is effective, tolerated and appropriate for the patient
Medication Review

- Any patient interaction can be an opportunity for critical medication review
- Transitions of care between care settings
- Changes in overall health of patient that affect life expectancy, diagnosis of terminal condition or progression of dementia or clinical frailty; eliminate medications that are unlikely to provide meaningful benefit to the patient in their remaining time

What are your goals of care?

- Disease centered approach – often leads to polymedicine
- Consider patient's current condition and longer term goals of care; consider prognosis, time to benefit, potential adverse effects – more important with advancing age
- Multiple medications may be needed – improve function, control symptoms, limit disease progression, extend life
- Assess function, health, goals of care – ongoing review of medications is needed

Questions to Ask:

- Is the drug clearly indicated and effective?
- What are the therapeutic end points?
- What are the potential benefits – what is the clinical indication, what is the appropriateness of the medication; what do the guidelines say?
- What are the potential harms – adverse drug reactions / adverse events
- Do the benefits outweigh the risks?
- Is the drug being used to treat side effects of another drug?
Questions to Ask

• Could it interact with underlying diseases or other drugs in the regimen?
• Consider adherence and cost; Drug utilization – duration of use? Adherence? If poor, then stop if patient remains stable off
• Does the patient / caregiver know indication for drug, how to take it, and adverse effects?
• What are possible ADWEs – adverse drug withdrawal events – clinically significant symptoms / signs caused by stopping a medication; cardiovascular and central nervous system drug classes are most common medications associated with ADWEs

Discontinuing Medications

• But be aware of recurrent or new symptoms; educate patients to report
• 74% of medication discontinuations are well tolerated; reducing medications has been shown to decrease hospitalization and mortality rates; no significant adverse events of deaths have been attributed to discontinuation
• Studies have shown that discontinuing medications can be done safely with no significant adverse events and there are reports of subjective clinical, functional, mood, and cognitive improvement
• 88% of patients reported global improvement in health
• Slow tapers; e.g. beta blockers, SSRIs, opioids, benzodiazepines
• Communicate medication discontinuation to the pharmacy; it is not uncommon for patients to refill and take medications that have been discontinued

• Discontinuing anticholinergics and benzodiazepines has been shown to decrease risk of cognitive decline
• Stopping some medications in older patients does not necessarily worsen clinical outcomes, is not usually associated with withdrawal syndromes, and can improve some outcomes including falls, behavioral issues, and cognitive status
• Consider stopping unnecessary medications and medications that cause side effects
Consider trying to reduce pill burden

- Reduce pill burden – pill burden is the total number of pills or doses a patient must swallow during the day
- Complex regimens and poor timing or unnecessary separation of multiple medications can lead to error in medication administration and affect quality of life
- Consider using combination products or switching from multiple times daily to once daily formulations

Deprescribing: active review process; determine risks and benefits and stop meds

Deprescribing

- Positive, patient-centered, inherently ambiguous
- Requires shared decision making; informed consent
- Close monitoring of effects
- Address the cumulative risk from multiple drugs
- Benefits: reduction in falls and improvement in cognitive and psychomotor function
How to Deprescribe

• Prioritization – reconsider which medications are really needed; consider adverse drug reactions, patient nonadherence, no clear indication, lack of benefit, use of medication to treat adverse reaction to another medication that can be changed, severity of condition being treated, risk of withdrawal symptoms

• Discontinuation – medications that can be stopped; get rid of duplicative drugs; consider changing drugs to prn if not really needed routinely (e.g. prn pain meds for arthritis, prn PPI for GERD, prn allergy meds)


• Goals of care – end of life / palliative versus curative; What are the patient’s values and preferences; emphasis on shared decision making
• Simplification of medication regimen improves adherence
• The only way to determine if a medication is needed may be stop it
• Guideline recommended drugs may not make sense in older adults with multiple comorbidities at end of life


• Assess frequency and magnitude of benefit, time to attain benefit versus burdens – frequency and magnitude of adverse effects, adherence burden, costs
• Try a behavioral intervention – e.g. for insomnia; bladder behavior therapies / timed voiding
• Benefit unlikely to be realized in patient’s lifetime – e.g., bisphosphonate, statins for primary prevention (statin in patient with limited life expectancy less than 5 years; bisphosphonate in patient with limited life expectancy less than 2 years)

Determine which medications are still providing benefit

- Ask about the symptoms for which each symptom based drug is being used
- Look at signs – for example blood pressures and blood glucose to help determine whether medications used to treat hypertension and diabetes are needed; watch out for hypoglycemia and hypotension – avoid these – use more conservative targets for blood pressure and blood sugar

Questions to ask when trying to determine drug utility: What is the strength of the indications?

1. Provides immediate relief of distressing symptoms (e.g. analgesics, antiemetics)
2. Effectively modifies an acute condition that is life threatening or will soon result in distressing symptoms if not treated (e.g., antibiotics for sepsis, diuretics for CHF, bronchodilators for asthma)
3. Effectively modifies a chronic condition that might progress to become life threatening or cause distressing symptoms if not treated; e.g. methotrexate for RA, ace inhibitors for CHF

Disease and/or symptom control drugs – those that control active disease and symptoms and maintain quality of life (e.g. analgesics, antianginals, anti-heart failure drugs, levothyroxine); if treatment with drugs ceased, patients may become symptomatic or lose function from worsening disease; but drugs could be stopped if they are ineffective or reduced in dose or used prn if disease is mild and symptoms intermittent

4. Has the potential to prevent serious diseases or adverse events in the future without immediate effect / preventive drugs; e.g. antiplatelet agents to prevent CVD, bisphosphonate to prevent osteoporotic fracture, antihypertensive to prevent stroke; prevent future morbid events; consider risks, benefits, life expectancy, time to benefit, goals of care
5. Is unlikely to be useful in either the short or long term; e.g. vitamin supplement
6. Is prescribed where a non-drug therapy (e.g. PT instead of NSAID) is more beneficial
What is the likelihood of misuse, toxicity, non adherence?

1. Is associated with little benefit and high risk of toxicity in most older patients – e.g. Beers, STOPP
2. Is a duplicate in drug therapy (second drug from same class)
3. Is prescribed for an adverse drug reaction
4. Is a potentially beneficial drug but is prescribed at a dose likely to cause toxicity
5. Has the potential for significant drug-drug or drug-disease interactions
6. Is taken more often than once daily
7. Can be safely administered as a combination medicine
8. Is causing significant problems with adherence

Use care if you and your patient / family decide to stop a medication

• Balance clinical impact (reduction in side effects) with the risk of adverse drug withdrawal events – clinically significant signs of symptoms caused by stopping a drug – e.g. physiologic withdrawal reactions (e.g. tachycardia with beta blocker discontinuation); appearance of new symptoms (e.g. sweating with antidepressant withdrawal); exacerbation of an underlying condition (e.g. worsening angina after stopping nitrates)
• ADWE more likely with long duration of use, higher dose, and short half life

Stop / discontinuing / deprescribing usually means tapering

• Taper medications to reduce risk and severity of ADWEs; do gradual tapers
• Consider tapering bp meds, e.g. CCBs, beta blockers; anticonvulsants; antidepressants; antipsychotics; corticosteroids; digoxin; diuretics; gabapentin; hypnotics; narcotics; PPIs; these meds have higher risk of ADWE
• Monitor for withdrawal effects; may need several attempts at withdrawal; regular follow up
Develop a weaning strategy

- Identify adverse effects from discontinuation of medication
- Identify recurrence of original symptoms
- If need to restart, consider best drug in class for older people
- Do brown bags reviews to assess what drugs are being taken and how

Medications commonly associated with discontinuation syndromes requiring tapering

- Alpha blockers – agitation, headache, hypertension, palpitations
- ACE inhibitors – Heart failure and hypertension
- Antianginal agents – Angina
- Antidepressants – Anxiety, depression and seizures
- Antipsychotics – Dizziness, insomnia, nausea and restlessness
- Anticholinergics – Anxiety, nausea, vomiting, headache and dizziness
- Baclofen – Agitation, anxiety, confusion, depression, hallucinations, hypertension, insomnia, mania, nightmares, paranoia and seizures
- Benzodiazepines – Agitation, anxiety, confusion, delirium, insomnia and seizures
- Corticosteroids – Anorexia, hypotension, nausea, weakness, hypothalamic-pituitary-adrenal axis suppression and inflammatory states
- Digitalis – Heart failure and palpitations
- Diclofenac – Heart failure and hypertension
- Nausea analgesics – Abdominal cramping, anger, anxiety, chills, diaphoresis, diarrhea,
- Insomnia and restlessness
- NSAIDs – Recurrence of gout and arthritis

Clinical pharmacist colleagues are crucial!

- Talk to your pharmacist: Medication reviews by pharmacists conveyed to physicians – evidence that this reduces number and cost of medications
Deprescribing is hard

- Bias toward the status quo; hard to stop a medication that has already been prescribed
- Patient may see a specialist and start a medication – may have unclear directions and length of use
- Prescribers are reluctant to change drugs other prescribers start
- There are few data on the safety and best ways to discontinue medications
- Patients may be psychologically and physically attached to their medications
- Stopping a medication may be perceived by patient / family as providing inadequate care
- Beware of prescribing inertia – tendency to automatically renew a medication even when the original indication is no longer present

End of life care / Palliative Care

- Many frail elders are essentially suffering from non curable diseases and the goal is to relieve suffering
- Advanced age, multiple medical problems, progressive, advanced disease with limited prognosis
- Focus of care is on quality of life
- End of life patients are at risk of adverse drug effects due to polymedicine, declining organ function, multiple co-morbidities, malnutrition, changes in body composition
- Lack of evidence to guide care
- The risk of polymedicine may outweigh the combined benefits of the medications
- Consider changing mantra of start low and go slow to stop most and reduce dose

Consider getting rid of drugs at end of life

- Avoid / discontinue drugs aimed at prolonging life or preventing disease especially if time to benefit long and not offering symptomatic benefit
- Focus on medications that have a positive impact on symptoms and quality of life
End of life prescribing

1. Life-extending drugs are usually not appropriate (unless helping with symptom control)
2. Drugs for primary or secondary prevention usually not appropriate unless time to benefit is shorter than life expectancy and adverse effects are not significant
3. Prescribing more than 5 regular daily drugs should be avoided
4. Patient or caregiver help define most problematic symptoms in order to focus medications on the most burdensome symptoms first
5. Make changes to drug regimen over time
6. Start or withdraw medications step wise – one by one – to assess adverse reactions and impact on symptoms
7. Use simple dosing schedules; can use liquids, buccal, subcutaneous, to tailor treatment


• Reduce number of drugs at end of life
  ---lipid lowering drugs
  ---drugs used for osteoporosis
  ---anti-platelet drugs
  --cholinergic drugs; memantine?? (carefully)
  ---iron and vitamin supplements
  ---vaccines
  ---chemotherapeutic drugs
• But if drug is controlling symptoms, then keep as goals are prevention of suffering

Difficult decisions involving preferences and trade offs
References


References


References

- Weng MC, Tsai CF, Suh KL, Lee YT, Lee HC, Tsang SL, ... Chen SC. (2013). The impact of number of drugs prescribed on the risk of potentially inappropriate medication among outpatient older adults with chronic diseases. QJM, 106(11), 1009-1015.