Unnecessary Drugs: An Overview of Potentially Inappropriate Prescriptions in the Elderly

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Objectives

1. Define what constitutes unnecessary medication use in older adults.
2. Review available tools and criteria used to identify unnecessary medication use in the long-term care setting.
3. Identify common inappropriate drugs/drug classes utilized in long-term care.
4. Explore pharmacological and non-pharmacological alternatives to inappropriate medications.
Unnecessary Medication Use

- Identified by CMS regulations as “any drug when used without adequate indications for its use.”
- “Without adequate indications for use” can include:
  - Lack of a clinical reason and/or documentation of rationale for medication use
  - Improper medication selection for indication being treated
  - Use of high-risk medications without justification of such use
  - Continued use of medications contributing to adverse drug reactions in an individual

Centers for Medicare and Medicaid Services, F-Tag 329, 42 CFR 483.25 (I)
Unnecessary Medication Use

• Additional circumstances that constitute unnecessary medication use:
  – Use of medications without appropriate monitoring
  – Drugs used in excessive doses
  – Use of multiple medications from the same pharmaceutical class and/or with similar action
  – Drugs used for an excessive duration
  – Drugs used in the presence of adverse consequences that indicate the dose should be reduced or discontinued

Centers for Medicare and Medicaid Services, F-Tag 329, 42 CFR 483.25 (l)
Clinical Tools

• Beers’ Criteria
  – Explicit list of medications to avoid in older adults
  – Updated by American Geriatric Society (AGS)
  – Most commonly used set of criteria in long-term care

• Screening Tool of Older Persons’ Potentially Inappropriate Prescriptions and Screening Tool to Alert doctors to the Right Treatment (STOOPP/START criteria)
  – Additional criteria used to identify inappropriate prescriptions and prescribing omissions in the elderly
  – Identified by AGS as a useful tool to be used in conjunction with Beers’ criteria


Barry PJ et al. START (Screening Tool to Alert doctors to the Right Treatment)—an evidence-based screening tool to detect prescribing omissions in elderly patients. Age Ageing. 2007;36:632-638.

Clinical Tools

| Medication Appropriateness Index |

Questions to Ask About Each Individual Medication

a. Is there an indication for the medication?
b. Is the medication effective for the condition?
c. Is the dosage correct?
d. Are the directions correct?
e. Are the directions practical?
f. Are there clinically significant drug–drug interactions?
g. Are there clinically significant drug–disease/condition interactions?
h. Is there unnecessary duplication with other medication(s)?
i. Is the duration of therapy acceptable?
j. Is this medication the least expensive alternative compared with others of equal utility?

Alpha Agonists

- clonidine, guanfacine, methyldopa
  - Clonidine identified by Beers’ criteria as a drug to avoid as a first-line agent due to high risk of CNS adverse effects, orthostatic hypotension, and bradycardia
  - Methyldopa may cause bradycardia, increased sedation, and may exacerbate depression in the geriatric population
  - As a class, alpha agonists are not recommended as routine treatment for hypertension
Alpha$_1$ Blockers

• Doxazosin, prazosin, terazosin
  – FDA approved indications: hypertension, benign prostatic hyperplasia (BPH)
  – Identified by Beers’ criteria as potentially inappropriate for use as antihypertensive agent in the elderly due to high risk of orthostatic hypertension, syncope, drowsiness, and dizziness
  – ALLHAT trial: compared treatment with diuretic, alpha blocker (doxazosin), and calcium channel blocker in patients ≥ 55 yrs with one or more CVD risk factors
    • Doxazosin arm stopped early due to 25% higher risk of CVD event


β-blockers

• Considerations:
  – Lipophilic vs. non-lipophilic: highly lipophilic β-blockers cross the blood brain barrier, leading to increased CNS effects such as fatigue, depression, and bizarre dreams
  – B-receptor selectivity in COPD patients: non-selective β-blockers may lead to increased bronchial constriction in patients with asthma or COPD
  – Decreased hypoglycemic awareness in diabetic patients
## Beta blocker Properties

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Immediate-release nifedipine

- Identified by Beers’ as drug to avoid due to high potential for hypotension and risk of precipitating myocardial ischemia; may also contribute to constipation
- Alternatives: When indicated, choose a long-acting dihydropyridine calcium channel blocker: felodipine, isradipine, nicardipine, extended-release nifedipine, nisoldipine


Appropriate Antihypertensive Treatment Options in the Elderly

- JNC 8 recommends low dose thiazide diuretics as first-line therapy for most patients without additional compelling indications.
- Other treatment options for elderly include: long-acting calcium channel blockers, ACE inhibitors or ARBs.
- Due to decreased baroreceptor and sympathetic neural responses, lower initial doses should be used with slower titration of antihypertensives.

First-generation antihistamines

- brompheniramine, chlorpheniramine, clemastine, diphenhydramine, doxylamine, hydroxyzine, promethazine, triprolidine
  - Increased risk of anticholinergic side effects (confusion, dry mouth, constipation, tachycardia)
  - Reduced clearance with advanced age
  - Development of tolerance when used as a hypnotic
  - Diphenhydramine and hydroxyzine: inappropriate when used for the management of anxiety or insomnia
Alternatives to first-generation antihistamines

- When used to treat or prevent allergic reactions, should be used cautiously and in the smallest effective dose
- When used for seasonal allergies, alternative treatment with less-sedating second-generation antihistamines may reduce, but not eliminate, unwanted side effects (cetirizine, fexofenadine, loratadine)
- Avoid excessive duration: antihistamines initiated for acute respiratory symptoms should be discontinued once symptoms resolve
Benzodiazepines

- Recent prospective study of elderly people who were free of dementia showed that new use of benzodiazepines was associated with a 50% increased risk of dementia
- Identified by Beers’ Criteria as drugs to avoid when used for treatment of insomnia, agitation, or delirium due to increased risk of cognitive impairment, delirium, falls, and fractures


Long-acting Benzodiazepines

• Chlorazepate, chlordiazepoxide, clonazepam, diazepam, flurazepam, quazepam
  – Can have an extended half-life in older adults, leading to accumulation of drug, excessive sedation, and increased risk of falls
  – Should not be used in older adults unless an attempt with a shorter-acting medication has failed
  – Exceptions: long-acting benzodiazepines used to withdraw residents from short-acting benzodiazepines or alcohol, diazepam used in neuromuscular syndromes, clonazepam used in bipolar disorder, nocturnal myoclonus, or seizure disorders
Short-acting Benzodiazepines

- Alprazolam, estazolam, lorazepam, oxazepam, temazepam, triazolam
- Should not be used, unless:
  - Other possible causes of distress have been ruled out (and documented)
  - Its use results in maintenance or improvement in the resident’s functional status
  - Daily use is less than four continuous months unless gradual dose reduction attempt is unsuccessful
  - Its use is for one of the following indications: GAD; panic disorder; symptomatic anxiety in residents with another diagnosed psychiatric disorder; cognitive disorders with associated behaviors indicating distress that pose a danger to the resident or others; sleep disorders; acute alcohol or benzodiazepine withdrawal
- When indicated for use, lorazepam and oxazepam are preferred agents due to water solubility
Oral Antidiabetic Agents

• First-generation sulfonylureas: chlorpropamide, tolazamide, tolbutamide
  – Chlorpropamide identified by Beers’ as medication to avoid due to prolonged half-life in older adults, prolonged hypoglycemia, and increased risk of SIADH leading to hyponatremia

• Long-acting second-generation sulfonylureas: glyburide
  – Prolonged half-life in elderly, leading to higher risk of severe prolonged hypoglycemia
Appropriate antidiabetic treatment options in the elderly

- Alternatives: ADA recommends metformin as first-line therapy in Type 2 diabetes
- When additional therapy is indicated, consider adding basal insulin, or sulfonylurea such as glipizide
- Antidiabetic therapy must include adequate monitoring of effectiveness of treatment (FBS, HgbA1c)

Megace (megestrol acetate)

- Identified by Beers’ criteria as drug to avoid due to minimal effect on weight and increased risk of thrombotic events
- Alternatives:
  - Nutritional supplements are safest option
  - Dronabinol- use is limited by significant CNS side effects, such as sedation, fatigue, and hallucinations

Skeletal muscle relaxants

• Carisoprodol, cyclobenzaprine, metaxolone, methocarbamol

• Identified by Beers’ as drug to avoid due to increased risk of sedation, falls, and fractures; questionable effectiveness at dosages tolerated by older adults

• Exceptions: periodic use (once every 3 months) for a short duration (not >7 days) may be appropriate


Centers for Medicare and Medicaid Services, F-Tag 329, 42 CFR 483.25 (I)
Acetaminophen

- Therapy with multiple sources of acetaminophen leading to increased risk of overdose and corresponding liver toxicity
- Alternative: Limit use of acetaminophen (from all sources) to <3 grams per 24 hours
Digoxin

- Appropriate indications: treatment of mild-to-moderate heart failure (or stage C); atrial fibrillation, atrial flutter, and paroxysmal supraventricular tachycardia
- Dosing:
  - Dependent on lean body mass and renal function
  - Elderly patients with low lean body mass may experience higher digoxin concentrations due to reduced volume of distribution
  - Beers’ criteria recommends avoiding doses >0.125mg/day in heart failure, due to increased risk of toxicity without established benefit
Digoxin

• Exceptions: Doses exceeding 0.125mg/day may be appropriate for the treatment of atrial arrhythmias

• Monitoring: Treatment must include routine monitoring of serum digoxin levels, keeping in mind that even therapeutic serum levels can cause side effects in the geriatric population
High Dose Antidepressants

• Decreased hepatic and renal function common in the elderly population predisposes them to unsafe drug levels and increased side effects.
• The lowest effective dose should be implemented and dose reductions should be attempted twice during the first year of therapy in separate quarters.
• Side effects
  – SIADH
  – Anorexia
  – Sedation
  – Serotonin syndrome
  – QTc prolongation
Preferred Antidepressants

• Zoloft (sertraline)
  – Less drug interactions than other SSRIs
  – Lower incidence of QT prolongation

• Celexa (citalopram) and Lexapro (escitalopram)
  – No significant Cytochrome P-450 interactions
  – FDA statement August 2011
    • Citalopram dose should not exceed 20mg/day in patients over 60 because of an increased risk of serious QTc prolongation and torsades de points
    • Risk is further increased in patients taking
      – Other medications known to prolong QT interval
      – Cyp 2C19 inh. (omeprazole, cimetidine, etc.)
Antidepressants to Avoid

- **Paxil (paroxetine)**
  - Significant interactions due to Cyp 2D6 inhibition

- **Luvox (fluvoxamine)**
  - Not indicated for depression (used to treat OCD)

- **Prozac (fluoxetine)**
  - Half-life of 6-9 days leads to greater buildup of the drug and its active metabolite
Antipsychotics

• Some elderly patients receive antipsychotic therapy for inappropriate behavior that is not necessarily psychotic.
• Prior to initiation of treatment, the physician should consider other causes of abnormal behavior such as: infection, confusion, stress, changes in drug therapy, or changes in the patient’s environment.
• Criteria for use:
  – Patient must have an approved diagnosis, and their clinical condition should meet one of the following:
    • 1) Symptoms are identified to be due to mania or psychosis
    • 2) Behavioral symptoms present danger to the patient or others
    • 3) Symptoms cause the patient to experience a significant decline in function, difficulty receiving care, or inexpressible or persistent distress
Typical Antipsychotics

• Higher incidence of anticholinergic symptoms than atypical antipsychotics
  – Confusion
  – Sedation (increased falls)
  – Postural hypotension (increased falls)
• Higher incidence of extrapyramidal symptoms than atypical antipsychotics
  – Dystonia
  – Parkinsonism
  – Akathisia
  – Tardive dyskinesia
Atypical Antipsychotics

• FDA Black Box Warning
  – Since 2005, all atypical antipsychotics carry a boxed warning indicating an increased death rate (1.6-1.7 times greater than placebo) in patients receiving atypical antipsychotics for dementia related psychosis. Death was typically due to heart failure, sudden death, or pneumonia.

• Lower incidence of EPS and anticholinergic symptoms than typical antipsychotics

• Cost is a greater concern with Atypicals vs. Typicals
PRN Antipsychotics

• Chemical Restraint
  – Any drug that is used for discipline or convenience and is not required to treat medical symptoms

• OBRA 1987
  – Individuals have the right to be free from physical or chemical restraint

• Approved Indications
  – Emergency care for brief periods
  – Resident’s unanticipated violent or aggressive behavior places him/her or others in imminent danger
    • Resident does not have the right to refuse restraints
Hypnotics

• Non-benzodiazepine hypnotics were once thought to be safer than benzodiazepines for treating insomnia.
• Recent research and the Beers criteria indicate that non-BZD hypnotics have similar incidences of delirium, falls, and fractures as BZDs.
• These agents typically provide minimal improvements of sleep latency and duration in the elderly.
• It is recommended that hypnotics be reserved only for patients that have failed to achieve symptom control with good sleep hygiene alone.
  – Good sleep hygiene includes:
    • Regular wake-up and bedtimes
    • Sleeping only enough to feel rested
    • Avoiding daytime naps
    • Increased daytime activity
Anticholinergic Medications

- Many medications have anticholinergic properties, which cause a blockade of the body’s natural cholinergic tone causing:
  - Confusion
  - Dry mouth
  - Constipation

- Medications with the most significant anti-ACH properties:
  - Tricyclic antidepressants
    - amitriptyline
    - nortriptyline
    - doxepin
  - MAOIs (also poses risk of QT-interval prolongation)
    - thioridazine
    - mesoridazine
  - First generation antihistamines
    - chlorpheniramine
    - diphenhydramine
    - doxylamine
    - hydroxyzine
    - promethazine
Alternatives to Anticholinergic Drugs

- **First generation antihistamines**
  - If used as an antiemetic
    - ondansetron (assesses patient’s risk of serotonin syndrome and QT-interval prolongation prior to initiation)
  - If used for insomnia
    - good sleep hygiene
    - trazodone
  - If used for allergies
    - fexofenadine or loratadine

- **MAOIs**
  - consider a weaker antidepressant (SSRI, SNRI, or tetracyclic) or combination therapy
    - consider the patient’s current medications and the new agent’s risk of QT-interval prolongation, drug interactions, and half-life before switching therapies

- **Tricyclic antidepressants**
  - If used for neuropathic pain
    - duloxetine, gabapentin, or pregabalin
  - If used for depression
    - SSRI (citalopram, sertraline, etc.)
Proton Pump Inhibitors

- Many patients are prescribed a PPI for ulcer prophylaxis during a hospital stay, and the medication is never discontinued despite the lack of a proper indication.
- Confirm that all PPIs have a proper indication and a dose reduction should be attempted 2 months post initiation (except pantoprazole, which is 3 months) – re-evaluate quarterly
- Side effects
  - increased risk of *Clostridium difficile* infection
  - bone loss (increased risk of hip fractures)
  - hypomagnesia
  - significant drug interactions due to Cytochrome P-450 inhibition
Alternatives to PPIs

- diet and lifestyle modifications
- Although H2 antagonists (famotidine, ranitidine, etc.) pose certain risks, they are generally better tolerated and have less drug interactions than PPIs.
- Antacids should be used to treat patients who experience symptoms less than twice weekly.
Anticoagulants

• Xarelto (rivaroxaban)
  – Similar efficacy in preventing stroke as warfarin
  – Higher rate of major GI bleed than warfarin
  – Unlike warfarin, there is no specific antidote
  – Contraindicated in patients with liver disease

• heparin
  – Associated with a 3 fold higher rate of heparin-induced thrombocytopenia than Low Molecular Weight Heparins
  – Preparations range from 1 unit/mL to 20,000 units/mL. This poses a higher risk of incorrect dose administration and adverse reactions.
  – All antithrombotics should have an appropriate stop date in the physician’s orders in order to prevent unnecessary and potentially dangerous therapy.

Nitrofurantoin

• Long term use is associated with increased pulmonary toxicity

• Efficacy is limited in patients with CrCl<60 mL/min due to subtherapeutic drug concentrations in the urine

• Alternatives
  – SMZ/TMP
  – Fluoroquinolones
  – For patients taking warfarin, ceftriaxone or amoxicillin/clavulanate are options to avoid interactions
Sliding Scale Insulin

• The goal of insulin therapy is to most closely mimic the body’s natural secretion of insulin. This includes a basal insulin level that elevates in response to carbohydrate consumption.
• Sliding scale insulin therapy does not provide a basal insulin that is present 24 hours per day.
• Beers’ criteria states that sliding scale insulin poses a higher risk of hypoglycemia without improvement of hyperglycemia management.
• A recent study found that sliding scale regimens were associated with a 3-fold higher rate of hyperglycemic episodes.

References

Centers for Medicare and Medicaid Services, F-Tag 329, 42 CFR 483.25 (l)


Barry PJ et al. START (Screening Tool to Alert doctors to the Right Treatment)—an evidence-based screening tool to detect prescribing omissions in elderly patients. Age Ageing. 2007;36:632-638.


