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COMMONLY PRESCRIBED MEDICATIONS IN THE ELDERLY & THEIR COMPLICATIONS

Donna M Boreen PharmD

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OBJECTIVES

- How common in the elderly is complications from drugs?
- Why is it so challenging to prescribe to the elderly?
- What is cascading?
- List one drug/drug class which is considered inappropriate for use in the elderly and their alternatives.
- What can you do to help?

HOW COMMON IS POLYPHARMACY IN ELDERLY?

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- How many meds do the elderly use*:
  - 81% use at least 1 medication
  - 50% use more than 5 medications
  - 46% also use OTCs
- Frequency of Adverse Drug Reactions:
  - Outpatients 10 – 35%
  - Post Discharge – 15%
  - Hospital – 6.7%
- 72% of adverse drug events (ADEs) in primary care and 42% of ADEs in long-term care are preventable.
- Potentially Inappropriate Medications: 7.2 billion
- 4^{th} or 5^{th} most common cause of death

*N Engl J Med 2004; 351:2870

WHY IS POLYPHARMACY SUCH AN ISSUE WITH THE ELDERLY?

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- Premarketing drug trials often exclude geriatric patients
  - Approved doses may not be appropriate for older adults
- Kidney function declines
- Drug clearance declines
- Toxic metabolites increase
- Protein levels change = more “free drug”
- More fat = change in kinetics of drug clearance
- Multiple illnesses mean multiple medications
- Multiple meds = multiple drug interactions

PRESCRIBING CASCADE

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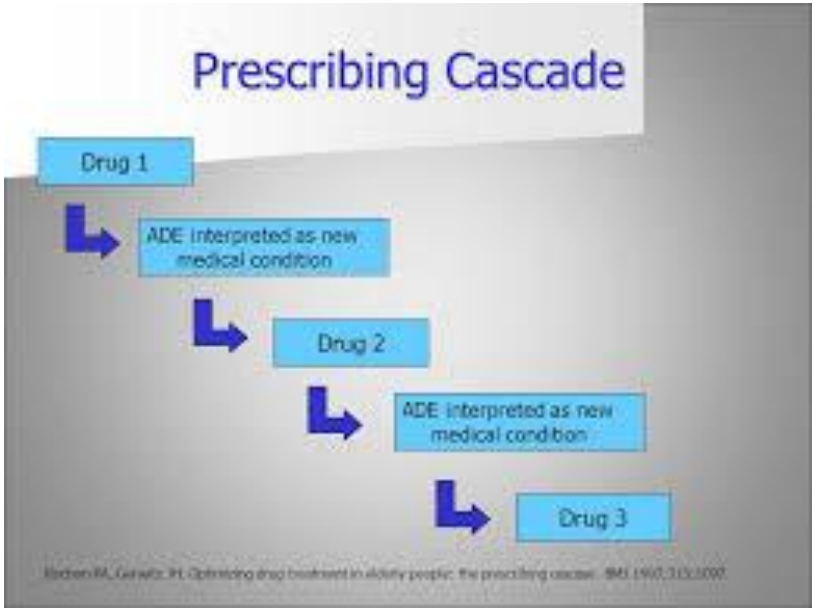
Prescribing cascades occur when a new drug is prescribed to treat symptoms arising from an unrecognized adverse drug event related to an existing therapy.

Then patient is at risk for developing additional Adverse drug events



Examples of prescribing cascades

Initial drug therapy	Adverse drug event	Subsequent drug therapy
Antipsychotics	Extrapyramidal signs and symptoms	Antiparkinsonian therapy
Cholinesterase inhibitors	Urinary incontinence	Incontinence treatment
Thiazide diuretics	Hyperuricemia	Gout treatment
NSAIDs	Increased blood pressure	Antihypertensive therapy

Medication prescribing cascades occur when patients are prescribed medications to treat the adverse side effects of previously prescribed medications. This leads to polypharmacy and further increases the risk for adverse drug events. Periodic review of medication lists, especially in older adults, can minimize this risk.

Data from: Rochon PA, Gurwitz JH. Optimizing drug therapy for elderly people: the prescribing cascade. BMJ 1997; 315:1096 and Gill SS, Mamdani M, Naglie G, et al. A prescribing cascade involving cholinesterase inhibitors and anticholinergic drugs. Arch Intern Med 2005; 165:808.

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LIVE FEARLESS℠

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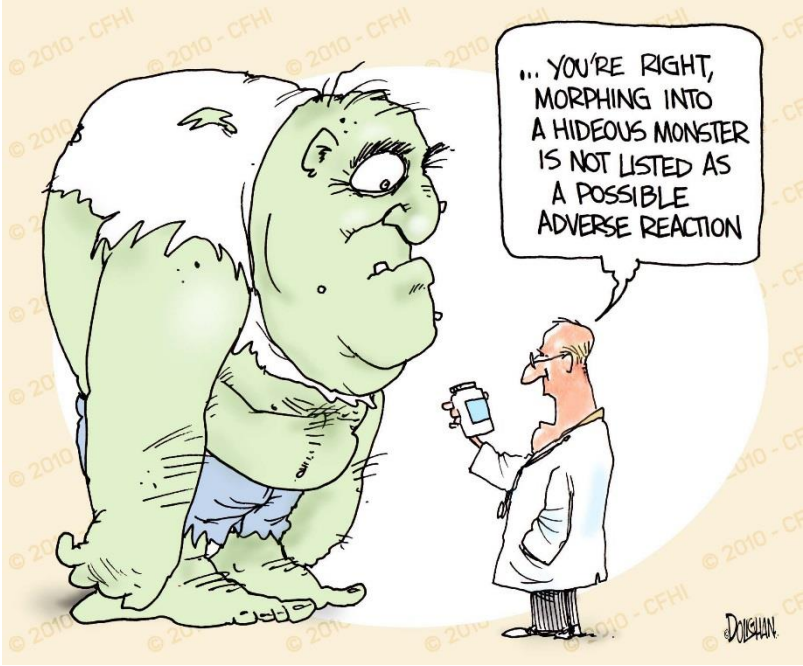
MEDICATIONS THAT MAY CAUSE ISSUES IN THE ELDERLY

Frequency of adverse drug events by type

Type	Total adverse drug events (n = 815) N (percent)	Preventable adverse drug events (n = 338) N (percent)
Neuropsychiatric	199 (24)	97 (29)
Hemorrhagic	159 (20)	53 (16)
Gastrointestinal	140 (17)	55 (16)
Renal/electrolytes	80 (10)	40 (12)
Metabolic/endocrine	64 (8)	35 (10)
Cardiovascular	36 (4)	15 (4)
Dermatologic	36 (4)	4 (1)
Extrapyramidal symptoms	30 (4)	7 (2)
Fall with injury	21 (3)	17 (5)
Fall without injury	21 (3)	11 (3)
Infection	19 (2)	1 (<1)
Syncope/dizziness	16 (2)	8 (2)
Anticholinergic	9 (1)	3 (1)
Ataxia/difficulty with gait	9 (1)	5 (2)
Hematologic	8 (1)	3 (1)
Respiratory	6 (1)	4 (1)
Anorexia	3 (<1)	2 (<1)
Functional decline	3 (<1)	2 (<1)
Hepatic	1 (<1)	1 (<1)

Adverse drug events could manifest as more than one type. Neuropsychiatric events include oversedation, confusion, hallucinations, and delirium. Anticholinergic effects include dry mouth, dry eyes, urinary retention, and constipation.

Reproduced with permission from: Gurwitz, MD, Field, T, Judge, J, Rochon, P, et al. The incidence of adverse drug events in two large academic long-term care facilities. Am J Med 2005; 118:251. Copyright © 2005 Excerpta Media.

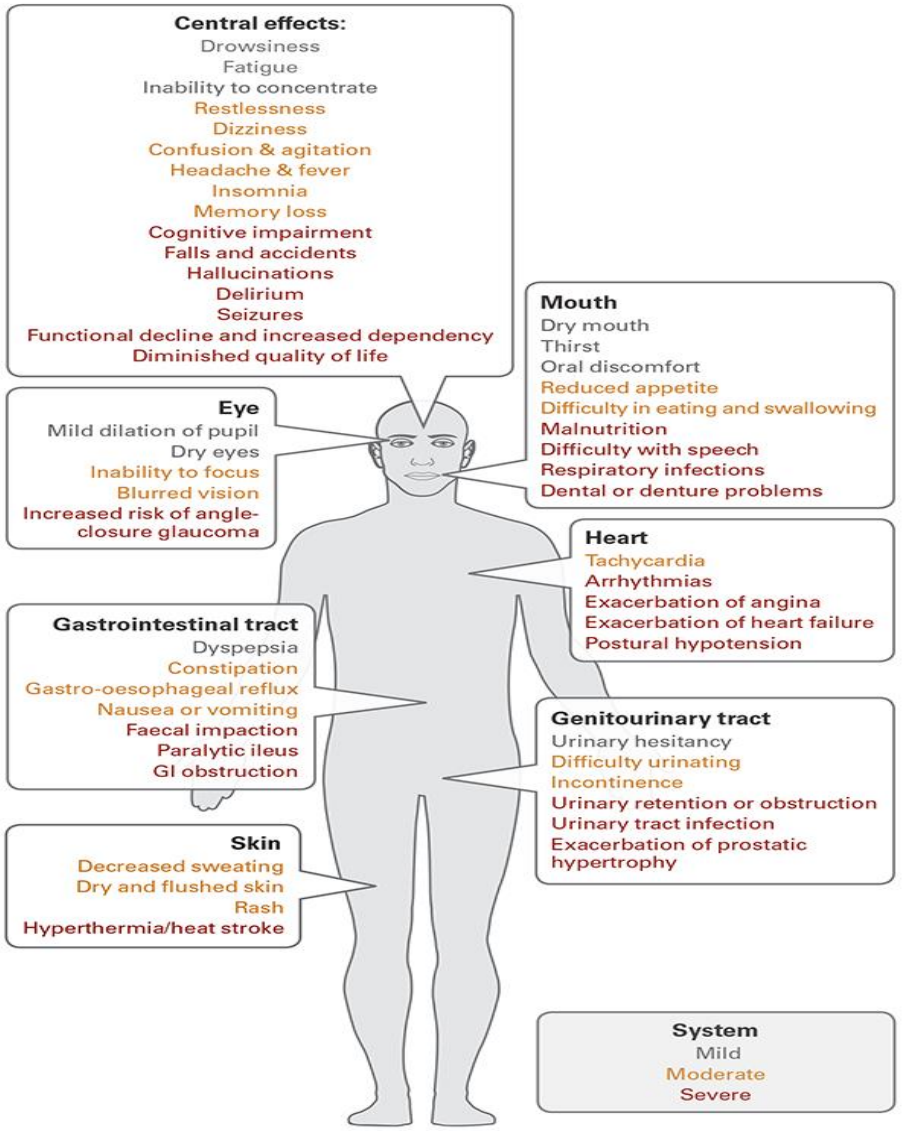


ANTICHOLINERGIC

- More than 7 million Americans suffer from dementia or mild cognitive impairment
  - 50% are coping with at least 2 additional chronic diseases that require treatment with more than 5 medications
- Elderly population is sensitive to experiencing drug related adverse effects that can negatively impact their cognitive function, i.e. anticholinergics
- Over 9 million older Americans, including those with cognitive impairment are prescribed at least one anticholingeric with negative cognitive effect

ANTI CHOLINERGIC SIDE EFFECTS

- Dry Eyes
- Dry Mouth
- Tachycardia
- Constipation
- Urinary Retention
- Confusion and Delirium
- Tremulousness and Twitching



Drugs believed to cause or prolong delirium or confusional states*

Analgesics
Nonsteroidal anti-inflammatory agents
Opioids (especially meperidine)
Antibiotics and antivirals
Acyclovir
Aminoglycosides
Amphotericin B
Antimalarials
Cephalosporins
Cycloserine
Fluoroquinolones
Isoniazid
Interferon
Linezolid
Macrolides
Metronidazole
Nalidixic acid
Penicillins
Rifampin
Sulfonamides
Anticholinergics
Atropine
Benztropine
Diphenhydramine
Scopolamine
Trihexyphenidyl
Anticonvulsants
Carbamazepine
Levetiracetam
Phenytoin
Valproate
Vigabatrin
Antidepressants
Mirtazapine
Selective serotonin reuptake inhibitors
Tricyclic antidepressants
Cardiovascular and hypertension drugs
Antiarrhythmics
Beta blockers
Clonidine
Digoxin
Diuretics
Methyldopa

Corticosteroids
Dopamine agonists
Amantadine
Bromocriptine
Levodopa
Pergolide
Pramipexole
Ropinirole
Gastrointestinal agents
Antiemetics
Antispasmodics
Histamine-2 receptor blockers
Loperamide
Herbal preparations
Atropa belladonna extract
Henbane
Mandrake
Jimson weed
St. John's Wort
Valerian
Hypoglycemics
Hypnotics and sedatives
Barbiturates
Benzodiazepines
Muscle relaxants
Baclofen
Cyclobenzaprine
Other CNS-active agents
Disulfiram
Cholinesterase inhibitors (eg, donepezil)
Interleukin-2
Lithium
Phenothiazines

* Not exhaustive, all medications should be considered.

Anticholinergic activity of medications and other substances

Class	Drugs	Relative anticholinergic potency
Antihistamines	H_1 receptor antagonists (1st generation, eg, brompheniramine, carbinoxamine, chlorpheniramine, clemastine, cyproheptadine, dimenhydrinate, diphenhydramine, doxepin, doxylamine, hydroxyzine, meclizine, triprolidine, others)	High
	H_1 receptor antagonists (2nd generation, eg fexofenadine, cetirizine*, loratadine, desloratadine, levocetirizine, others)	Low
Antiparkinson	Benztropine, trihexyphenidyl	High
	Amantadine, bromocriptine, entacapone	Low
Analgesic	Opioids (eg, codeine, hydrocodone, fentanyl, meperidine, methadone, morphine, oxycodone, tramadol, others)	Low
Antimuscarinic, overactive bladder	Darifenacin, fesoterodine, oxybutynin, solifenacin, tolterodine, trospium	High
Antimuscarinic, spasmolytic	Atropine, clidinium-chlordiazepoxide, dicyclomine, hyoscyamine, glycopyrrolate, homatropine, methscopolamine, propantheline, scopolamine (hyoscine)	High
Antimuscarinic, inhaled bronchodilator	Ipratropium, tiotropium	High (local effect)
Antimuscarinic, ophthalmic drops (mydriatic/cycloplegic)	Atropine, cyclopentolate, homatropine, scopolamine	High (local effect)
Cardiovascular	Disopyramide	Low
Gastrointestinal	Antiemetics (eg, hydroxyzine, meclizine, promethazine, scopolamine); also refer to 1st generation antihistamines above	High
	Domperidone, loperamide, prochlorperazine	Low
	H_2 receptor antagonists (ranitidine, cimetidine, famotidine¶)	Low
Muscle relaxant	Orphenadrine, tizanidine	High
	Cyclobenzaprine*, baclofen, methocarbamol	Low
Psychotropic	Antipsychotics 1st generation: chlorpromazine, fluphenazine, loxapine, methotrimeprazine (levomepromazine), thioridazine, trifluoperazine	High
	Antipsychotics 1st generation: haloperidol, perphenazine*, others	Low
	Antipsychotics 2nd generation: clozapine	High
	Antipsychotics 2nd generation: (eg, olanzapine*, quetiapine, iloperidone, risperidone, others)	Low
	Benzodiazepines: chlordiazepoxide, clonazepam, temazepam, triazolam	Low
	Selective serotonin reuptake inhibitors (SSRI) antidepressants: citalopram, fluoxetine, fluvoxamine, paroxetine*	Low
	Tricyclic antidepressants (eg, amitriptyline, clomipramine, desipramine, doxepin, imipramine, nortriptyline, others)	High
Other neurologic	Carbamazepine, lithium, nefazodone, oxcarbazepine, phenelzine, trazodone	Low
Other substances		
Plants	Angel's trumpet (*Brugmansia* species); Deadly nightshade (*Atropa belladonna*); Henbane (*Hyoscyamus niger*); Jimson weed (*Datura stramonium*); Mandrake (*Mandragora officinarum*); Moonflower (*Datura inoxia*); Muscarinic mushroom species (particularly *Clitocybe* and *Inocybe;* other muscarine-containing mushrooms include: *Amanita, Entoloma, and Mycena* species); Nightshade species: American nightshade (*Solanum americanum*), Bittersweet woody nightshade (*Solanum dulcamara*), Black (common) nightshade (*Solanum nigrum*)	

A large number of medicines are reported to have some anticholinergic activity and considerable variation exists in potency rankings assigned to specific drugs using available anticholinergic risk scales and in expert lists; this list is not exhaustive. Increasing dose and additive effects from simultaneous use of more than one anticholinergic drug can alter the anticholinergic activity rating provided in this table.

* Classified as moderate or high anticholinergic potency in some references or variable effects reported.
¶ Intravenous famotidine use has been associated with central nervous system (CNS) effects (eg, delirium and confusion) in hospitalized older adults and patients with renal function impairment; this may be due to a central anticholinergic effect.

Courtesy of Paula A Rochon, MD and Stephen J Traub, MD with additional data from:

1. *Durán CE, Azermai M, Vander Stichele RH. Systematic review of anticholinergic risk scales in older adults. Eur J Clin Pharmacol 2013; 69:1485.*
2. *Salahudeen MS, Hilmer SN, Nishtala PS. Comparison of anticholinergic risk scales and associations with adverse health outcomes in older people. J Am Geriatr Soc 2015; 63:85.*
3. *United States prescribing information available at US National Library of Medicine DailyMed website (http://dailymed.nlm.nih.gov/dailymed/index.cfm).*
4. *American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 updated Beers Criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2015; 63:2227.*

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HRM: MUSCLE RELAXANTS USE IN THE ELDERLY

- Why are muscle relaxants a concern for older adults?
  - Can lead to grogginess and confusion
  - Increase risk of falls
  - Can also cause constipation, dry mouth, and problems urinating
- Plus…
  - Little evidence that they work well
  - NO study on muscle relaxant medications has ever focused on an elderly population.
  - Never been consistently demonstrated to improve muscle spasms in older adults.

HRM: MUSCLE RELAXANTS

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Muscle Relaxants considered HRMs:

- Metaxalone (Skelaxin)
- Carisoprodol (Soma, Carisoma, Sodol)
- Methocarbamol (Marbaxin, Robaxin)
- Chlorzoxazone (Parafon Forte, Remular)
- Orphenadrine (Flexon, Norgesic, Norflex)
- Cyclobenzaprine (Flexeril)

ALTERNATIVES within Muscle Relaxants

- **Baclofen (Lioresal, Baclosan)**
- **Tizanidine (Zanaflex)**

QUESTIONS FOR MUSCLE RELAXANTS

- Do you fell tired or groggy?
- Sleeping more in the daytime? Falling as
  unexpectedly?
- Explain what confusion is…
  - Inability to think as clearly or quickly as yo
    normally do.
  - May feel disoriented and have difficulty
    paying attention, remembering, and maki
    decisions.

ALTERNATIVES FOR MUSCLE RELAXANTS

- **For Spasticity:**
  - Baclofen
  - Tizanidine
- **For Musculoskeletal Pain**:
  - Oral NSAIDs, Voltaren gel, Cymbalta
  - May consider non-pharmacologic treatments, such as cryotherapy, heat, massage, stretching/exercise, and transcutaneous electrical nerve stimulation (TENS)

NON-BENZODIAZEPINE HYPNOTICS

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- Non-Benzodiazepine Hypnotics include: Eszopiclone (Lunesta), Zolpidem (Ambien), Zaleplon (Sonata)
- There is currently no evidence to support the long-term use of these agents. These medications are meant to be taken on an as needed basis (generally no more than 3 days per week), not every night.
- The efficacy and safety of these medications have not been proven when using these agents for longer than 3 months.
- In general, these medications are recommended for short-term use (1-4 weeks). They have limited value in improving sleep when used for longer periods of time.

NON-BENZODIAZEPINE HYPNOTICS

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- What are the risks associated with taking these medications?
  - Increased risk of falls (especially at night)
  - Memory impairment
  - Headaches
  - Cognitive impairments/amnesia
  - Daytime sedation
  - Motor incoordination
  - Complicated sleep behaviors (Increased risk of motor vehicle accidents, sleep eating)
  - Addiction
  - Development of tolerance
  - Rebound insomnia

NON-BENZODIAZEPINE HYPNOTICS

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- What are some pharmacological alternatives to the medications listed above?
  - Rozerem
  - Silenor
- Encourage member to discuss the medications listed above with their doctor or pharmacist.
- Encourage member to address possible root causes of their sleeping problems (ie. other medical conditions, medications) with their doctor.
- Encourage member to try nonpharmacological alternatives (with the guidance of their doctor) to aid in treating their sleeping problems

NON-BENZODIAZEPINE HYPNOTICS

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- What are some alternative ways to manage insomnia?
  - Don’t watch t.v. before bed or while trying to fall asleep
  - Don’t eat right before going to bed; have a light snack if hungry
  - Sleep in a dark and quiet room at a cool temperature; try using a fan or other machine that will provide a white noise to help you fall asleep
  - Try relaxation techniques while lying in bed
  - Reflect on attitudes and beliefs about sleep
  - Avoid taking long afternoon naps

NON-BENZODIAZEPINE HYPNOTICS

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- Address any mental health concerns such as depression and/or anxiety
  Keep a sleep log
- Get up at a consistent time and go to bed at a consistent time
- If you find that you cannot fall asleep within 30 minutes, try reading or another quiet activity until you become sleepy
- Exercise each day, but not before bedtime
- Limit or eliminate alcohol, caffeine, nicotine, especially within 4 hours of bedtime
- Get into a bedtime routine in preparing for bedtime
- Wear something comfortable to bed

ANTI-HYPERTENSIVES

- Studies typically do not include elderly population when determining appropriate dosing
  - Low risk of fall injuries reported in clinical trials with healthy adults or healthy older adults is not reflective the risk in an older adult with multiple chronic diseases
- Some clinical trials have associated with serious fall injuries (including hip and other major fractures, …)
- Many elderly require multiple anti-hypertensives to reach treatment goals, but this can change as they age
  - Loss of weight, decreased renal function,……
- Postural changes in blood pressure or low blood pressure
- Monitor blood pressure, sit at the side of the bed prior to standing, evaluate risk vs benefit of multiple meds (serious fall injury morbidity vs CV event)

DIABETES IN THE ELDERLY

- Epidemiology
  - Prevalence of Diabetes in >65 yrs of age around 30% depending on diagnostic criteria used
  - Projected to increase by 4 fold before 2050
- Those >75 years of age have double the rate of ER visits for hypoglycemia than the general population with Diabetes
- Why is there more concern
  - With decreased cognitive function, visual impairments, decreased renal function, polypharmacy…..all make it difficult to perform complex self care and complications from treatments
    - Glucose monitoring, adjusting insulin dosing, appropriate timing and content of meals……..

DIABETES IN THE ELDERLY

- Comparative effectiveness studies of medication to treat diabetes in the elderly is lacking
- Metformin
  - lower incidence of hypoglycemia
  - GI issues and weight loss
  - Typically need to have dose reduced
- Sulfonylureas
  - Risk of hypoglycemia
  - Glyburide has highest risk of severe prolonged hypoglycemia (on HRM list)
  - Chlorpropamide
  - Alternatives: short-acting sulfonylureas (glipizide), metformin
    - Short acting SU dose with meals may help those that eat sporadic

DIABETES IN ELDERLY

- Thiazolidinediones (pioglitazone)
  - Edema, heart failure, bone fractures,….)
- Insulin
  - Risk of hypoglycemia
    - Insulin, sliding scale is on HRM list due to higher risk of hypoglycemia without improvement of hyperglycemic control (regardless of settings)
  - Visual or manual dexterity may be barriers to insulin therapy (pen devices help but costly)
  - Hypoglycemia risk is somewhat lower with analog compared to human insulin, but more expensive

Selected high-risk drugs

Drug	Potential harm	Comment
Insulin	Hypoglycemia	May often be appropriate; however, aggressive glycemic control may often yield greater harms than benefits in older adults.[1-3]
Sulfonylureas	Hypoglycemia	Older hospitalized patients at significant risk for hypoglycemia; avoid or use with great caution.[4]
Warfarin	Gastrointestinal, intracranial bleeding	Although a high-risk drug, benefits of warfarin therapy often outweigh harms; maintenance of prothrombin time/international normalized ratio in therapeutic range tightly linked to risk/benefit ratio.[5]
Digoxin	Impairment of cognition, heart block	May have a third-line role in management of systolic heart failure; suboptimal choice for rate control in atrial fibrillation.
Benzodiazepines	Falls	Associated with as much as a 60 percent increase in fall risk.[6]
Diphenhydramine, other first-generation antihistamines	Impaired cognition, urinary retention in men	Poor choice as sleep aid due to anticholinergic effects, next-day sedation, impact on performance including driving; close medication reconciliation important because patients may also obtain over-the-counter drugs.
Opioid analgesics	Constipation, sedation, confusion, cardiorespiratory depression, seizures	Codeine, meperidine, pentazocine, butorphanol and nalbuphine are poor choices for analgesia. Fentanyl, morphine, or oxycodone are often appropriate with careful dose adjustment.
Antipsychotics	Death, pneumonia	Elevated risk of death when used to treat behavioral complications of dementia, although in selected cases, benefits may exceed risks if consistent with patient goals of care.[7]
Chemotherapeutic agents	Myelosuppression (neutropenia, anemia), hepatotoxicity, cardiotoxicity	Comprehensive assessment is required for determining goals of treatment, particularly in light of comorbidities. When indicated, chemotherapy dose and schedule should be carefully individualized for organ function and anticipated toxicities of treatment. In general, greater treatment-related toxicity is accepted when the expected outcome of treatment is cure.
Selected antimicrobials		
Fluoroquinolones	Tendon inflammation and rupture, hypoglycemia, cardiac arrhythmias, *C. difficile*-associated diarrhea, exacerbation of myasthenia gravis	Elevated risk of tendon rupture in combination with glucocorticoids.
Nitrofurantoin	Pulmonary toxicity, hepatotoxicity	Therapeutic concentrations are not attained in urine of patients with renal insufficiency (CrCl <60 mL/minute).
Trimethoprim-sulfamethoxazole (co-trimoxazole)	Hyperkalemia, hypoglycemia (with sulfonylurea), severe dermatologic reaction (rare)	Drug interactions include warfarin (↑ INR), agents that increase serum potassium, and sulfonylureas (↑ hypoglycemic effect).

References:

1. *Brown AF, Mangione CM, Saliba D, Sarkisian CA; California Healthcare Foundation/American Geriatrics Society Panel on Improving Care for Elders with Diabetes. Guidelines for improving the care of the older person with diabetes mellitus. J Am Geriatr Soc 2003; 51:S265.*
2. *Greenfield S, Billimek J, Pellegrini F, et al. Comorbidity affects the relationship between glycemic control and cardiovascular outcomes in diabetes. Ann Intern Med 2009; 151:854.*
3. *Gerstein HC, Miller ME, Byington RP, et al; Action to Control Cardiovascular Risk in Diabetes Study Group. Effects of intensive glucose lowering in type 2 diabetes. N Engl J Med 2008; 358:2545.*
4. *Deusenberry CM, Coley KC, Korytkowski MT, et al; Hypoglycemia in hospitalized patients treated with sulfonylureas. Pharmacotherapy 2012; doi: 10.1002/j. 1875-9114.2011.01088.x (ePublished ahead of print May 8, 2012).*
5. *Mant J, Hobbs FD, Fletcher K, et al; BAFTA Investigators; Midland Research Practices Network (MidReC). Warfarin versus aspirin for stroke prevention in an elderly community population with atrial fibrillation (the Birmingham Atrial Fibrillation Treatment of the Aged Study, BAFTA). Lancet. 2007; 370 (9586):493-503.*
6. *Woolcott JC, Richardson KJ, Wiens MO, et al. Meta-analysis of the impact of 9 medication classes on falls in elderly persons. Arch Intern Med 2009; 169:1952.*
7. *Schneider LS, Dagerman KS, Insel P. Risk of death with atypical antipsychotic drug treatment for dementia. JAMA 2005; 294:1934.*

Revisions and additional information included with data from: Steinman MA, Hanlon JT. Managing medications in clinically complex elders: "There's got to be a happy medium." JAMA 2010; 304:1592.

WHAT CAN YOU DO?

- Often, members left on HRM because they are ***tolerating it***
- The medical community still needs to exercise caution:
  - Contribution of HRMs to other disease states (delirium, dementia, constipation, urinary retention) may occur slowly and subtly, so difficult to relate medication's contribution to the patient's current problem.
  - If used chronically, adverse effects will become less tolerable as the patient ages.

We need your help to reevaluate the risk vs. benefits of the continued use of these HRMs every year.

WHAT CAN YOU DO (CONT'D)

- Review member's medications and if you see one of the HRMs we talked about today:
  - Talk about the side effects of that particular HRM:
    - Can be done in person or via telephone.
    - Ask if they have had any of the specific side effects we listed today.
    - If you sense they are not able to answer, ask family or friends or a caregiver.

MEDICATION MANAGEMENT PRINCIPLES

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- The Eight Rights
  - Right Patient
  - Right Medication
  - Right Dose
  - Right Route
  - Right Time
  - Right Documentation
  - Right Reason
  - Right Response

HOW YOU CAN HELP

- If side effects exist…
  - Encourage member/family to call MD to discuss risk vs. benefits of the medication.
  - If you are comfortable with this, contact the provider yourself.
  - Provide handouts to the family. This will help encourage the conversation with their provider.
  - Refer member to plan's MTM program
  - If it is a BCBSMN member and they are not eligible for MTM, email Donna Boreen. She may be able to assist.

HOW YOU CAN HELP

- If member is in an LTC setting:
  - Each LTC facility has a clinical pharmacist. They review member's medications once a month. You could leave a note in the RPh "box" requesting the RPh to evaluate the benefit versus risk of the HRM. The Director of Nursing should be able to assist you as to where you can leave your note.
  - Utilize the nursing staff. Ask them if they note side effects issues.
  - MTM is also available to eligible members in an LTC facility.
- **Member should *NOT* stop taking the HRM UNLESS instructed by their provider.**

THANK YOU.