Case Studies in Pharmacology

LaDonna S. Hale, PharmD
Associate Professor, Wichita State University

Learning Objectives

- Identify & discuss medications that may increase fall risk in older adults and the PTs' role in identifying & preventing medication issues in older adults
- Discuss new medications used in the management of acute pain, chronic pain syndromes, & osteoporosis
- Identify & discuss common medication-related issues that may affect rehabilitation therapies

Should we Care about Falls?

- An estimated one in three older adults (≥ 65 yrs) will fall annually
- An estimated one in two over the age of 80 years will fall annually
- Falls in older adults can have devastating consequences on the patient, family, and society
- Falls are the leading cause of injury-related death in older adults and the leading cause of nursing home placement
- 20-30% of falls result in severe injury with impaired mobility & independence
- Hip fractures are especially devastating; 25% will die within one year after the fracture and 40% will be unable to live independently
- ***One older adult dies every 35 minutes due to a fall***
- Fear of falling is the most common fear among older adults
- Fear of falling causes many older adults to limit their physical activity, causing further decreases in physical function, social isolation, and subsequent falls
- Fear of loss of independence causes many older adults to *not report* their falls.

Case Study 1

Case 1 – Simple Fall?

HPI: 62 y/o male was at home watching TV. He got up to answer the telephone and tripped on the single step leading into his kitchen. He was injured in the fall bumping his head & injuring his eye.
PMH: A-fib x 3 yrs; HTN x 5 yrs; BPH x 1 week

Home Medication	Therapeutic Use	Associated Fall Risk?
atenolol (Tenormin)		
warfarin (Coumadin)		
doxazosin (Carduara)		
zolpidem (Ambien)		
atorvastatin (Lipitor)		

Why was his injury so severe?

Discuss the factors that may have contributed to this patient's fall?

Are falls preventable or inevitable?

Evidence-based fall prevention guidelines exist

- National Council on Aging (NCOA)
- Centers for Disease Control (CDC)
- American Geriatrics Society (AGS)
  1. Medication review & modification
  2. Vision screening & referral
  3. Increasing physical activity & balance training
  4. Home safety evaluation & modification

Risk Factors Associated with Falls

- **Prior history of falls**
- **Age**
- **Muscle weakness**
- **Gait/Balance deficit**
- Impaired ADL/use of assistive devices
- Depression
- Cognitive impairment
- Visual deficit
- Arthritis pain
- Diabetes
- Parkinson's disease
- *Taking > 4 medications*
- *Recently starting a new medication or after a dosage increase*

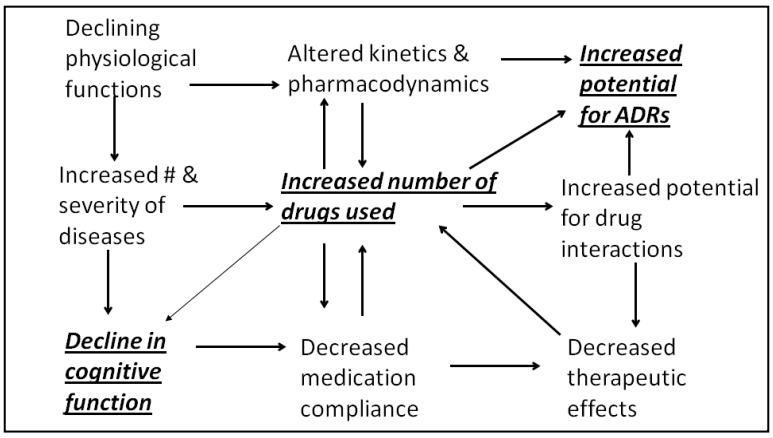
Older Adults often Respond Differently to Medications than Younger Adults

- Adverse drug reactions are 7 times more common in older adults than younger patients
- Half (50%) of all medication related deaths occur in those over the age of 65 years
- Up to 30% of hospitalizations in older adults are related to adverse drug reactions
- 45% of hospitalized older adults will experience an adverse drug reaction during their hospital stay

Why is the Rate of Adverse Drug Reactions so Much Higher?

- The liver and kidneys cannot clear the medication as quickly
- As we age our bodies change: changes in organ function, higher rates of liver failure, kidney failure, heart failure, COPD, HTN, diabetes, malnourishment, slowed reflexes, less muscle mass, poor vision, slowed orthostatic homeostasis, & weaker blood brain barrier
- Older adults tend to take more medications – polypharmacy. Polypharmacy increases the chances of drug interactions and risk of side effects. Although older adults constitute only about 13% of the U.S. population, they consume 30% of all prescription drugs and 40% of all OTC drugs purchased
- Rates of medication compliance are low. The risk of medication noncompliance increases with the more medications one takes and as the complexity of those medication regimens increases.

Snowball Effect: Medication – Age – Adverse Effects



Four Target Areas for Fall Prevention

1. Medication review & modification
2. Vision screening & referral
3. Increasing physical activity & balance training
4. Home safety evaluation & modification

1) What Role do Medications Play?

- Only a handful of studies have been able to demonstrate that reviewing & modifying medications *alone* will reduce the risk of falls
- The most effective interventions are multi-factorial
- Reducing the number of medications, particularly psychoactive medications, may reduce fall risk

2) What Role does Vision Screening & Referral Play?

- Poor vision is associated with falls but the effectiveness of this intervention as a strategy to actually reduce falls has been less well-studied (e.g. blurry vision, macular degeneration, glare)
- Loss of depth perception can make it difficult to navigate steps or curbs
- Loss of contrast sensitivity can make it difficult to see a curb/step, coffee table or other obstacles
- Vision can be monitored at home using an Amsler Grid
- Functional Vision Screening Questionnaire – asks questions like "Do you have trouble reading newsprint? Seeing the TV? Reading food labels? When crossing the street, do cars seem to appear very suddenly? etc…"to help assess functional vision

3) What Role does Physical Activity Play?

- Increasing physical activity is one of the most effective interventions. It works alone or in combination with other interventions
- Being physically active contributes substantially to healthy aging. Increasing physical activity can relieve arthritis pain, reduce obesity, HTN, depression, Type 2 diabetes, & strengthen bones
- In particular, targeted balance and strength training appears to be the most effective and well-studied fall prevention strategy available (lots of research with Tai Chi)
- Effective programs have been group programs, individualized programs, home exercise programs, lay person led (train-the-trainer), and expert led
- These programs also increase confidence in walking and confidence that if they do fall they will be able to get back up again

4) What Role does Home Safety Evaluation & Modification Play?

- More than half of all injuries occur in and around the home, and the home environment itself is implicated in more than one-third of falls
- Easy to use home safety check sheets are available from the CDC. Effectiveness is even higher when the home safety evaluation is conducted by a trained therapist
- Some home safety issues are easily and inexpensively fixed (e.g. non-slip mats, night lights, electrical cords, placing tape to mark doorways and steps)
- However other home safety issues may require additional assistance to fix (e.g. bathroom modifications, ramps, installation of an emergency response system)

Screening for Fall Risk

What tests do you use in your practice?

Which Medications Increase Fall Risk?

General Information

- Taking > 4 different medications per day
- Medications that cause side effects such as those listed in the table below
- Risk is highest after a new medication is added or the dosage is increased
- *Medications most often associated with falls when studied*: psychotropics & CNS active drugs, cardiovascular, skeletal muscle relaxants, and opioid analgesics

Adverse Effect	Medication Class and/or Examples
Hypotension	• Any antihypertensive, especially after a dosage increase • Taking more than two antihypertensives also increases risk
Orthostatic hypotension	• Any antihypertensive but especially the α-1 blockers: doxazosin (Cardura®), prazosin (Minipress®), terazosin (Hytrin®); clonidine (Catapres®); and hydrochlorothiazide • antipsychotics: e.g. haloperidol (Haldol®), risperidone (Risperdal®), ziprasidone (Geodon®), olanzepine (Zyprexa®), quetiapine (Seroquel®), clozapine (Clozaril®) • tricyclic antidepressants: e.g. amitriptyline (Elavil®), doxepin (Sinequan®) • opioid pain medications
Bradycardia (low pulse)	• β-blockers: e.g. propranolol (Inderal®), atenolol (Tenormin®), metoprolol (Lopressor®) • diltiazem (Cardizem®, Dilacor®), verapamil (Calan®, Verelan®, Isoptin®) • digoxin (Lanoxin®) • amiodarone (Cordarone®)
Cognitive Impairment	See one-page list of medications presented later in this document
Drowsiness	*Too many to list but here are several common causes* • sedatives/hypnotics *Long-acting* diazepam (Valium®), flurazepam (Dalmane®), *Short-acting*: lorazepam (Ativan®), oxazepam (Serax®), temazepam (Restoril®), alprazolam (Xanax®) • other sleep aids: e.g. diphenhydramine (Tylenol PM®, Advil PM®), zolpidem (Ambien®), zaleplon (Sonata®) • muscle relaxants: e.g. methocarbamol (Robaxin®), cyclobenzaprine (Flexeril®), orphenadrine (Norflex®) • anti-seizure medications: e.g. phenytoin (Dilantin®), carbamazepine (Tegretol®), gabapentin (Neurontin®), lamotrigine (Lamictal®) • antihistamines: diphenhydramine (Bendadryl®), chlorpheniramine (Chlor-Trimeton®), others
Osteoporosis	• high-dose inhaled corticosteroids and oral/systemic corticosteroids (> 6 months) • some anti-seizure medications: phenytoin (Dilantin®), phenobarbital, carbamazepine (Tegretol®) • warfarin (Coumadin®) – conflicting evidence
Visual disturbances	• amiodarone (Cordarone®) • α-1 blockers: doxazosin (Cardura®), prazosin (Minipress®), terazosin (Hytrin®), & tamsulosin (Flomax®) • bisphosphonates: e.g. alendronate (Fosamax®), ibandronate (Boniva®), risedronate (Actonel®) • corticosteroids: e.g. prednisone, dexamethasone, methylprednisolone • digoxin (Lanoxin®) • erectile dysfunction medications: sildenafil (Viagra®), tadalafil (Cialis®), vardenafil (Levetra®) • not all but some anti-seizure medications like tiagabine (Gabitril®), topiramate (Topamax®)
Low blood glucose	• Insulin, oral drugs to treat Type 2 diabetes
Movement awkwardness	• some antiemetics: metoclopramide (Reglan®), promethazine (Phenergan®) • anti-seizure medications: e.g. phenytoin (Dilantin®), carbamazepine (Tegretol®), gabapentin (Neurontin®), lamotrigine (Lamictal®) • antipsychotics: e.g. haloperidol (Haldol®), risperidone (Risperdal®), olanzepine (Zyprexa®), quetiapine (Seroquel®)

Antidepressants

- Tricyclic antidepressants (TCAs): amitriptyline (Elavil®), doxepin (Sinequan®)
    - Blurred vision, dizziness, memory loss, delirium, orthostatic hypotension, sedation
- Selective Serotonin Reuptake Inhibitors (SSRIs):
    - Would seem less likely to cause falls based upon their side effect profile; however, studies show they also increase fall risk
- Newer antidepressants:
    - Less is known about these related to fall risk
- So what should we do?

Benzodiazepines

- Long-acting benzodiazepines: diazepam (Valium®), chlordiazepoxide (Librium®), flurazepam (Dalmane®)
    - Half-lives of hundreds of hours
    - Delirium, sedation, dizziness, memory loss, movement awkwardness
    - Linked to falls, hip fractures, driving accidents
- Short-acting benzodiazepines: lorazepam (Ativan®), oxazepam (Serax®), alprazolam (Xanax®), temazepam (Restoril®)
    - Shorter half-lives; cleared more quickly
    - Delirium, sedation, dizziness, memory loss, movement awkwardness
- Non-benzodiazepine sleep aids: zolpidem (Ambien®), zaleplon (Sonata®), eszopiclone (Lunesta®)
    - Even shorter half-lives
    - Also shown to increase fall risk
- So what should we do?

Antipsychotics

- 1st generation antipsychotics: haloperidol (Haldol®)
    - High rate of extrapyramidal side effects
    - Orthostatic hypotension
    - Sedation
    - Anticholinergic side effects (blurred vision, memory loss, confusion)
- 2nd generation antipsychotics: risperidone (Risperdal®), ziprasidone (Geodon®), olanzepine (Zyprexa®), quetiapine (Seroquel®), clozapine (Clozaril®)
    - Lower rates of extrapyramidal side effects but still have other side effects
- So what should we do?

Skeletal Muscle Relaxants

- Examples: methocarbamol (Robaxin®), cyclobenzaprine (Flexeril®), orphenadrine (Norflex®)
    - Side effects include muscle weakness, drowsiness, dizziness, sedation, anticholinergic side effects
    - Associated with falls and fractures
- So what should we do?

Opioid Analgesics

- Any opioid can increase the risk of falls. A few particularly problematic ones in older adults include: propoxyphene (Darvocet®/Darvon®), meperidine (Demerol®), pentazocine (Talwin®), fentanyl patch (Duragesic®)
    - Dizziness, drowsiness, sedation, confusion, orthostatic hypotension

Cardiovascular Medications

- Antihypertensives: ACE-inhibitors, ARBs, CCBs, thiaizde diuretics, β-blockers, α1-blockers, & others
    - Risk is higher in patients taking two or more (which most people do by the way)
    - Risk is higher shortly after starting the medication or increasing the dose
    - Any antihypertensive can cause hypotension, but the vasodilators are most likely to be associated with falls and orthostatic hypotension. These include:
        - α-1 blockers: doxazosin (Cardura®), prazosin (Minipress®), terazosin (Hytrin®)
        - clonidine (Catapres®)
        - Hydrochlorothiazide (one of the most commonly used antihypertensives in the US)
    - β-blockers can cause bradycardia
- Antidysrhythmics: digoxin (Lanoxin®), amiodarone (Cordarone®)
    - Digoxin: bradycardia, blurred vision,
    - Amiodarone: bradycardia, spots in vision, movement awkwardness
- Nitrates for angina: nitroglycerin, isosorbide dinitrate (Isordil®), isosorbide mononitrate (Monoket®)
    - Vasodilators, orthostatic hypotension
- So what should we do?

Case Study 2

Case Study 2

HPI: 65 y/o male has rapidly progressive and severe loss of balance over two days

PMH: Suffered closed head injury in 1998 (coma x 3 days; rehab x several months); diagnosed with HTN, high cholesterol, depression, and alcoholism at that time

Social History: No alcohol use since 1998; smokes 1 ppd x 49 years

Medications: Currently takes no medications

For the first week, the source of the profound dizziness was thought to be uncontrolled HTN (BP 180/110). *Hydrochlorothiazide* is started. Two days later, *lisinopril* (BP 160/100) is started. Two days later *amlodipine* is started. After an MRI, it was discovered that he had two brain stem strokes. One week later, *simvastatin*, *bupropion* (Zyban®), *levothyroxine* (Synthroid®), and *dipyridamole/aspirin* (Aggrenox®) are started.

Therapy: Physical therapy three times weekly and speech therapy twice weekly are ordered.

Discuss his fall risk. List his risk factors. Can any of them be mitigated? What can you do?

The Physical Therapist's Role in Promoting Safe Medication Use

- PTs spend a significant amount of one-on-time time with patients. This may allow you to detect safety related medication problems. You may not be the one to correct these medication issues but you certainly can refer the issue to the appropriate person (family member, nurse, physician, etc)\
- Report (or encourage your patient to report) any adverse drug reactions (side effects). A good rule of thumb is to consider any new symptom the patient is experiencing to be a potential side effect until proven otherwise. Don't assume that aging is synonymous with constipation, dizziness, & confusion. These symptoms happen to be common side effects of drugs

You can always suggest some very simple things:

- Encourage patients to speak to their prescribers and pharmacists about their medications regularly and ask questions
- Bring a complete list of all medications to each medical appointment.
- Use of a pill box or medication calendar
- File of Life (www.folife.org) or Vial of Life (www.vialoflife.com): two similar tools to help patients keep track of medications and medical history and have it available for EMS & firefighters
- Encourage patients to take their medications as directed, read all the instructions that come with the medications, be knowledgeable about the medications, report any side effects to the doctor, throw out expired medicines, never take medications in the dark (have good lighting), keep medications separate from medications of other family members.

Non-compliance is a cause of Unsafe Medication Use

Signs of Non-compliance

- The patient does not seem to clearly understand his medications
- He does not know the name, dose, & purpose of his medications
- He often asks you questions about his medications
- He expresses concerns about his medications: lack of efficacy, side effects, high cost, bad taste, difficulty swallowing the pills, complexity of the regimen, difficulty "keeping up" with everything, difficulty reading the labels, etc.

Case Study 3

Case Study 3

HPI: 85 y/o female was found by her home aid in her living room, slumped over a chair. She is admitted to the skilled nursing facility where you work.

PMH: MI 5 years ago, CAD x 7 years, angina x 7 years, high cholesterol x 7 years, urinary incontinence x 3 years, early stage Alzheimer's dementia x 1 year

Ht = 5'4"; Wt = 52kg;

Social History: was in an assisted living facility; no EtOH, no smoking history

Home Medication	Therapeutic Use	Associated Fall Risk?
atenolol (Tenormin)		
clopidogrel (Plavix)		
docusate (Colace)		
levothyroxine (Synthroid)		
nitroglycerin patch		
simvastatin (Zocor)		
tolterodine (Detrol)		
zolpidem (Ambien)		

List this patient's risk factors for a fall:

How can those risk factors be mitigated?

Case Study 4

Case Study 4

HPI: 65 y/o male presents to the outpatient physical therapy clinic for energy conservation training and strength training related to his progressive muscle weakness. He is a regular client of yours.
Ht=5'9"; Wt=109kg

PMH: HTN x 8 yr; CHF x 2 yr; osteoarthritis; mild myasthenia gravis x 5 yrs; Type 1 DM since early childhood

Social History: lives w/ wife; retired; smokes 1ppd x 50 yr; sedentary life style; 3-4 drinks EtOH / day

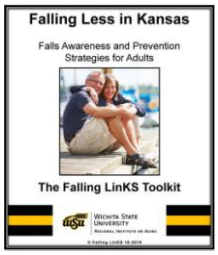
Home Medication	Therapeutic Use	Associated Fall Risk?
carvedilol (Coreg)		
ramipril (Altace)		
digoxin (Lanoxin)		
furosemide (Lasix)		
insulin injections		
ibuprofen prn		
neostigmine		
pyridostigmine		
prednisone		

List this patient's risk factors for a fall:

How can those risk factors be mitigated?

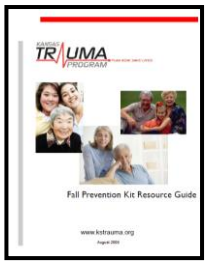
Knowledge is Power – Empower your Patients

Falls are NOT a natural part of aging. The risk of falls can be reduced. Many falls can be prevented
Feel comfortable asking questions of your healthcare providers
Specifically ASK your healthcare providers about fall risk
www.SafeAging.org
www.cdc.gov (Home & Recreational Safety)
www.StopFalls.org
Department of Veterans Affairs (National Center for Patient Safety Falls Toolkit)



The Falling Less in Kansas (Falling LinKS) toolkit is designed for use by older adults and their family. It contains information and tools in the areas of medication, exercise, vision, & home safety.

Available at the WSU Regional Institute on Aging website:
http:www.wichita.edu/aging/toolkit



The KS Trauma Program Fall Prevention Kit Resource Guide identifies and provides web address and contact information to excellent national fall prevention guidelines resources.

Available at the Kansas Trauma website:
http://www.kstrauma.org/download/Fall_Prevention_Guide_2009.pdf

Medications Associated with Cognitive Side Effects

Drug	Reported reactions	Examples* / Comments
Anticholinergics	Disorientation, confusion, delirium, memory impairment, blurred vision	atropine, scopolamine, oxybutynin (Ditropan®), tolterodine (Detrol®), hyoscyamine (Levsin®), some antihistamines, TCAs
Antiepileptics	Delirium, confusion, cognitive impairment, amnesia	phenytoin (Dilantin®), carbamazepine (Tegretol®), gabapentin (Neurontin®), lamotrigine (Lamictal®)
Anti-Parkinson drugs	Delirium, hallucinations, cognitive and behavioral problems especially late in disease or with multiple medications	levodopa/carbidopa (Sinemet®), selegiline (Eldepryl®), pergolide (Permax®), bromocriptine (Parlodel®), & anticholinergic Parkinson's drugs: trihexylphenidyl (Artane®), benztropine (Cogentin®)
Antipsychotics	Delirium, confusion, neuroleptic malignant syndrome	haloperidol (Haldol®). High anticholinergic activity with chlorpromazine (Thorazine®), thioridazine (Mellaril®) and clozapine (Clozaril®); lowest with risperidone (Risperdal®)
Barbiturates	Confusion, delirium, incoordination, withdrawal syndrome with hallucinations	Phenobarbital, secobarbital (Seconal®). Should be completely avoided in the elderly.
Benzodiazepines	Cognitive impairment, amnesia, excessive sedation, pseudodementia, lack of coordination, withdrawal syndrome with delirium, hallucinations	*Long-acting* high does increase risk of toxicity: diazepam (Valium®), flurazepam (Dalmane®), *Short-acting*: lorazepam (Ativan®), oxazepam (Serax®), temazepam (Restoril®), alprazolam (Xanax®)
Corticosteroids	Confusion, delirium, memory impairment	Case reports with large doses of any of the corticosteroids, e.g. > 60mg prednisone
Quinolone antibiotics	CNS stimulation, confusion	ciprofloxacin (Cipro®), levofloxacin (Levaquin®), ofloxacin (Floxin®), etc
Antihistamines (H1-blockers)	Impaired attention, decreased concentration, blurred vision	diphenhydramine (Bendadryl®, Tylenol PM®), chlorpheniramine (Chlor-Trimeton®), etc. Many have anticholinergic side effects. Fexofenadine (Allegra®), loratadine (Claritin®) least likely to cause CNS effects.
Acid blockers (H2-blockers)	Delirium, confusion	Many cases with cimetidine (Tagamet®), especially high doses
Non-steroidal anti-inflammatory drugs (NSAIDs)	Confusion, cognitive impairment, delirium, amnesia	ibuprofen (Motrin®), naproxen (Aleve®), but especially indomethacin (Indocin®)
Opioid agonists (Narcotic analgesics)	Delirium, impaired mental performance, confusion	Especially meperidine (Demerol®) pentazocin (Talwin®). Fentanyl patch (Duragesic®) causes confusion in 10% of long-term users.
Selective serotonin reuptake inhibitors (SSRIs)	Impaired concentration, confusion	fluoxetine (Prozac®), sertraline (Zoloft®), paroxetine (Paxil®). Fairly common, but reactions may be symptoms of depression; Less common than with tricyclics antidepressants.
Tricyclic antidepressants (TCAs)	Delirium, confusion, memory impairment, blurred vision	desipramine (Norpramin®) & nortriptyline (Pamelor®) have less anticholinergic SE than amitriptyline (Elavil®) or doxepin (Sinequan®)
Skeletal muscle relaxants	Sedation, confusion, blurred vision, hallucination	methocarbamol (Robaxin®), cyclobenzaprine (Flexeril®), orphenadrine (Norflex®)
Antiemetics	Delirium, confusion, restlessness, agitation	metoclopramide (Reglan®), promethazine (Phenergan®), meclizine (Antivert®), dimenhydrinate (Dramamine®)

* The list of examples is not all inclusive.

References

- Alexander BH, Rivara FP, Wolf ME. The cost and frequency of hospitalization for fall-related injuries in older adults. *Am J Public Health* 1992;82:1020–3.
- American Geriatrics Society, British Geriatrics Society, and American Academy of Orthopaedic Surgeons Panel on Falls Prevention. Guideline for the prevention of falls in older persons. *J Am Geriatr Soc* 2001;49:664-72.
- Cameron KA. *The Role of Medication Modification in Fall Prevention.* In: Falls Free: Promoting a National Falls Prevention Action Plan. Washington, DC: The National Council on the Aging; 2005
- Centers for Disease Control and Prevention. *Falls among Older Adults: An Overview*. Available at http://www.cdc.gov/ncipc/factsheets/adultfalls.htm. Accessed on Jun 1, 2008
- Dipiro JT, Talbert RL, Yee GC, et al. *Pharmacotherapy: A Pathophysiologic Approach, 7th ed*. McGraw Hill Medical. New York, NY 2008.
- Drugs that may cause cognitive disorders in the elderly. The Medical Letter 2000;42(Issue 1093)
- Gillespie LD, Robertson MC, Gillespie WJ, et al. Interventions for preventing falls in older people living in the community. *Cochrane Database Syst Rev* 2009;(2):CD007146.
- Hausdorff JM, Rios DA, Edelber HK. Gait variability and fall risk in community-living older adults: a 1-year prospective study. *Arch Phys Med Rehabil* 2001;82:105–06
- Hornbrook MC, Stevens VJ, Wingfield DJ, et al. Preventing falls among community-dwelling older persons: results from a randomized trial. *Gerontologist* 1994;34:16–23.
- Josephson K, Febacher D, Rubenstein LZ. Home safety and fall prevention. Clin Geriatr Med 1991; 7: 707-731.
- Kochera A. Falls among older persons and the role of the home: An analysis of cost, incidence, and potential savings from home modification. Issue Brief. Public Policy Institute American Association of Retired Persons. IB56:1-14. [Online] 2002 [cited 9/15/04]. Available from http://assets.aarp.org/rgcenter/il/ib56_falls.pdf.
- Pharmacotherapy choices for patients with dementia. *Pharmacist's Letter/Prescriber's Letter* 2008;24(5):240510.
- Shoba SR, Budhwar N, Ashfaque A. Osteoporosis in men. *Am Fam Phys* 2010;82:503-508
- Sterling DA, O'Connor JA, Bonadies J. Geriatric falls: injury severity is high and disproportionate to mechanism. *J Trauma* 2001;50:116–19.
- Stevens JA, Corso PS, Finkelstein EA, Miller TR. Cost of fatal and nonfatal falls among older adults. *Injury Prevention* 2006;12:290-5.
- Tinetti ME. Preventing falls in elderly persons. *New Engl J Med*. 2003;348:42-49.
- WSU Falling LinKS Research Team. The Falling LinKS Toolkit. 2010. Available at: http://www.wichita.edu/aging/toolkit
- 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;169:1952-60

Acknowledgments:

Much of the discussion regarding fall prevention strategies was adapted from materials developed through collaboration with the WSU Falling LinKS Research Team: Dr. Teresa Radebaugh (Principal Investigator), Dr. Candace Bahner, Dr. Deborah Ballard-Reisch, Mr. Michael Epp (Envision), Dr. LaDonna Hale, Mr. Rich Hanley (Harvey County Department on Aging), Ms. Karen Kendrick (Envision), Dr. Michael Rogers and Dr. Nicole Rogers. The Falling LinKS research team was supported by WSU Graduate Students: Ms. Ashley Archiopoli, Ms. Melissa Granville, Mr. Bobby Rozzell, Ms. Chigozirim Utah, and Ms. Katie Sue Williams. Falling LinKS was funded by the United Methodist Health Ministry Fund grant #20080427 (11-2008 to 10-2010) and the WSU Graduate School.

What's New in Osteoporosis Prevention/Management?

Calcium Supplementation

- Calcium supplementation may do more than prevent fractures. Low calcium intake has been associated with colon cancer, kidney stones, obesity, and hypertension
- ***Dose***: National Osteoporosis Foundation recommends 1200mg/day
- For best oral absorption take no more than 500 – 650 mg per dose
- Calcium citrate is best absorbed orally but calcium carbonate is cheaper
- Expensive forms of coral calcium have not been shown to be superior
- Calcium supplement should include Vitamin D

Calcium and Cardiovascular Risk

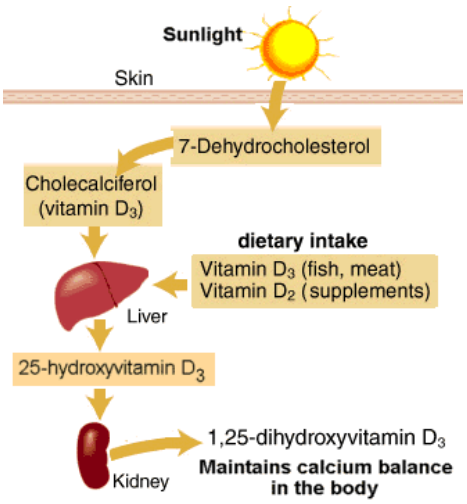
- A recent meta-analysis of 11 randomized, placebo-controlled trials evaluating calcium supplementation and cardiovascular outcomes was recently published. The authors concluded that calcium supplementation was associated with increased risk of myocardial infarction.
- The mechanism by which calcium supplementation may increase the risk is unknown.
- One theory is vascular calcification. This seems plausible; however, calcium calcification takes years to develop whereas the risk of MI increases acutely after calcium supplementation is begun.
- A second theory is that calcium supplementation may adversely affect blood coagulability or flow.
- This meta-analysis did not look at patients taking both calcium and vitamin D supplementation simultaneously as suggested.
- ***Numbers***: Based on data from this analysis, treating 69 patients with calcium for five years will cause one additional myocardial infarction. In comparison, treating 50 healthy postmenopausal women for five years with calcium will prevent one fracture.
- ***Real World***: Unanswered questions remain. Does vitamin D supplementation help mitigate the risk in some way? Are some patients at higher risk for CV disease than others? Is there an unsafe dose? Most clinicians are not going to stop recommending calcium supplementation just yet.

Vitamin D Supplementation

Vitamin D Dosing

- Vitamin D may do more than prevent fractures and falls. It may play a role in prevention of colon cancer and other cancers. Vitamin D deficiency has been associated with diabetes, hypertension, cardiovascular disease, and multiple sclerosis.
- Vitamin D receptors are found in muscle – muscle weakness is a symptom of vitamin D deficiency.
- There is a correlation between vitamin D deficiency & ***falls*** in older adults. It may reduce falls by simply improving strength and physical performance
- ***Dose***: National Osteoporosis Foundation recommends 800 IU/day for prevention of falls/fractures in older adults. A once yearly mega-dose of vitamin D (500,000 IU) was found to be *unsafe*, and actually increased falls.
- ***Numbers***: Treating 170 older adults with 800 IU of vitamin D daily for 1 to 7 years will prevent one nonvertebral *fracture*. Treating 15 patients with 800 IU of vitamin D daily for 2 months to 3 years will prevent one *fall*. That's fairly impressive and cost-effective.

Which vitamin D source is the best?



- "Vitamin D" refers to both Vitamin D2 and vitamin D3
- Vitamin D2 = ergocalciferol (OTC & Rx supplements & fortified foods)
- Vitamin D3 = cholecalciferol (OTC supplements & naturally in some foods)
- Vitamin D3 is better absorbed orally and is more effective in raising 1,25-dihydroxyvitamin D3 levels
- 1,25 dihydroxyvitamin D3 is the active form of Vitamin D
- Patients with end-stage kidney disease cannot convert Vitamin D3 into its active form. These patients should receive an Rx formulation of activated Vitamin 3 such as calcitriol (Rocaltrol®), doxercalciferol (Hectorol®), and paricalcitol (Zemplar®)

- American Academy of Dermatology recommends avoiding sunlight and getting vitamin D from food or supplements.
- Physicians can check vitamin D levels to screen for deficiency and assist in finding the correct dose. When vitamin D deficiency is identified, higher doses may be needed.
- ***Dose*** for Vitamin D deficiency: 50,000 IU of vitamin D2 or D3 given IM once weekly for six to eight months. This is becoming much more common as healthcare providers have started paying more attention to Vitamin D and actually screening for deficiency.
- Vitamin D toxicity is rare. Symptoms include nausea, vomiting, anorexia, confusion, constipation, weakness, and weight loss. (Don't worry, excessive sun exposure does not cause toxicity)

Prescription Medications to treat Osteoporosis

- Most of the evidence supporting medications used to treat osteoporosis has been conducted in postmenopausal women. There is far less evidence of their efficacy in corticosteroid-induced osteoporosis or in men
- Osteoporosis medications seem to be more effective in preventing vertebral fractures than hip fractures
- For prevention of vertebral fractures, good evidence supports the bisphosphonates, estrogen (e.g. Premarin®), teriparatide (Forteo®), and raloxifene (Evista®)
- For prevention of hip fractures, good evidence to supports both bisphosphonates and estrogen
- **Estrogen**: Of course, long-term estrogen has its issues and is no longer the treatment of choice

Bisphosphonates

- There isn't much new related to the bisphosphonates: alendronate (Fosamax®), ibandronate (Boniva®), risedronate (Actonel®). They are still the drugs of choice for treatment of osteoporosis. They may be taken orally daily, weekly, or monthly. Zoledronic acid (Reclast®) can be administered IV once a year.
- Non-compliance with patient instructions may account for therapy failures
- ***Patient instructions***: Take in the morning before breakfast, on an empty stomach. Take with a full glass of water (no juice, tea, coffee, or anything else). Remain upright for at least 30 minutes.
- ***Case Study 5***: Bisphosphonate-induced ulceration
- ***Osteonecrosis of the jaw***: Rare side effect. Usually occurs following trauma to the dental areas of the jaw (e.g. tooth extraction/dental surgery). The theory is that the bisphosphonates interfere with the bone's ability to heal

Case Study 5

Case Study 6

Case Study 6: 38 y/o female with long-standing juvenile rheumatoid arthritis, methotrexate x 10 years; prednisone x 10 years; alendronate x 5 years, calcium & vit D supplement x 5 years. X-ray shows right femoral shaft fracture. She had been complaining of pain in her that area for the last 6 months.

Bisphosphonates – interesting possible new side effect: Atraumatic mid-shaft fractures

- Long-term therapy may increase the risk of unusual long bone mid-shaft fractures.
- Evidence to support this side effect is weak (case reports & case series) but there is enough out there to justify further research and start paying attention. On the other hand, there are many long-term studies showing that alendronate is safe for long-term use, increases BMD, and causes no harm.
- The mechanism by with bisphoshonates may cause this side effect is unknown. Bisphosphonates decrease bone turnover, thus increasing BMD. It has been suggested that long-term reduced bone turnover might decrease bone strength by allowing microcracks to accumulate. there is increasing evidence to suggest that long-term bisphosphonate use may overly suppress bone metabolism, limiting repair of micro-damage and potentially increasing the risk for fractures in some patients.
- Some data indicate that patients concurrently taking corticosteroids are at an increased risk of developing these types of fractures.
- Some experts recommend a drug holiday after five years of bisphosphonate treatment. The duration of the holiday or the ability of the holiday to prevent these kinds of fractures has not been studied.
- Is there any way to detect this side effect before a fracture occurs? One case series showed that a significant number of patients experienced prodromal pain prior to the fracture. This may be something to watch for. Major changes in clinical practice are not likely to occur just yet.

New Drug: Denosumab (Prolia®) injection q 6 months

- This is a human IgG2 monoclonal antibody which inhibits the RANK ligand (RANKL). RANKL is a protein essential for the formation, function, and survival of osteoclasts. Osteoclasts are responsible for bone resorption. Denosumab binds to RANKL and prevents it from working; therefore, osteoclast formation is reduced.
- Denosumab is FDA approved for the treatment of postmenopausal women with osteoporosis at high risk for fracture or patients who have failed or are intolerant to other osteoporosis therapy.
- Just as with every other prescription osteoporosis treatment, adequate calcium and vitamin D supplementation is necessary for the medication to work effectively.
- Side effects were rare but include back pain, pain in the extremities, elevated cholesterol, musculoskeletal pain, infections, skin reactions, and osteonecrosis of the jaw.

References

- Bolland MJ, Avenell A, Baron JA, et al. Effect of calcium supplements on risk of myocardial infarction and cardiovascular events: meta-analysis. *BMJ* 2010;341:c3691.
- Calcium and cardiovascular risk. *Pharmacist's Letter/Prescriber's Letter* 2010;26(9):260901.
- Odvina CV, Levy S, Rao S, et al. Unusual mid-shaft fractures during long-term bisphosphonate therapy. *Clin Endocrinology*. 2010;72:161-168.
- National Osteoporosis Foundation. *2008 Clinician's Guide to Prevention and Treatment of Osteoporosis*. Available at http://www.nof.org/professionals/NOF_Clinicians%20_Guide.pdf
- Product info for Prolia. Amgen Manufacturing Limited, a subsidiary of Amgen Inc. Thousand Oaks, CA 91320.
- Safety of long-term bisphosphonate therapy. *Pharmacist's Letter/Prescriber's Letter* 2009;25(12):251205.
- Summary of the latest guidelines on bisphosphonate-induced osteonecrosis. *Pharmacist's Letter/Prescriber's Letter* 2009;25(3):250303.
- Vitamin D dosing: an update. *Pharmacist's Letter/Prescriber's Letter* 2010;26(7):260707.
- Vitamin D for fall prevention in the elderly. *Pharmacist's Letter/Prescriber's Letter* 2008;24(6):240604.
- Simonelli C, Clarke B, Kopher R, et al. Institute for Clinical Systems Improvement. Health care guideline: Diagnosis and treatment of osteoporosis. Sixth Edition. September 2008. Available at http://www.icsi.org/osteoporosis/diagnosis_and_treatment_of_osteoporosis__3.html

What's New in Pain Management?

Fentanyl (Duragesic®) patches leading to deaths despite strong warnings from the FDA

- Despite strong warnings from the FDA, patient deaths are still occurring due to overdoses fentanyl patches.
- Fentanyl patches are not effective for acute pain or mild pain.
- Fentanyl patches should not be started in opioid naïve patients. They should only be used in patients who have been taking 60mg/day or more of oral morphine for at least one week. All patients should be started on the lowest dose possible.
- Heat can dramatically increase absorption and lead to overdoses: heating pads, hot tubs, sunbathing, high fever, etc.
- Do not cut or removed just part of the back of the patch to try to titrate the dose.
- Do not put used patches in the trash – fold the patch sticky site together and flush it. Normally we don't like to flush medications, but for this one it's okay and actually safer.

Case Study 7

Case Study 7

PMI: 32 y/o female being treated for chronic cancer pain uses a fentanyl patch, 25mcg/day (the lowest dose available). She changes that patch every three days. She tells you that she generally feels extremely dizzy and lightheaded after her showers. You dig a little deeper and she tells you that she covers her patch with Saran wrap and tape during her showers so that it won't come off.

What's going on here?

New Opioid Formulations

- **Embed®**: extended-release morphine palate. There is an inner core that contains an opioid antagonist called naltrexone. Swallowing the capsules whole, slowly releases just the morphine. But if the pellets are crashed, the naltrexone is released and can blunt morphine affects. Patients taking Embeda must avoid alcohol, not because of the opioid, but because alcohol will dramatically increase the rate of release of the morphine from the pellets, possibly leading to fatal overdose.
- **tapentadol (Nucynta®)**: New opioid agonist and norepinephrine reuptake inhibitor – similar to tramadol. Nucynta is stronger and is considered a C-II controlled substance. Nucynta works about as well as oxycodone for acute pain with less constipation, but just as much drowsiness and dizziness.
- **tramadol (Ryzolt®)**: This is an extended-release tramadol product, basically just like Ultram ER

Topical NSAIDS

- Diclofenac topical solution and gel (Pennsaid®, Voltaren®, Solaraze®)
- As compared to oral, higher levels are achieved in the dermis and equal levels in the muscle. Some will reach the synovial fluid, but exactly how much is unknown. Systemic absorption is 150 times lower than oral. GI side effects are very rare. Absorption through the skin varies greatly from patient to patient. The most common side effect is topical dermatitis (10 – 15%). FDA approved for osteoarthritis pain.

References

- Safe use of fentanyl (Duragesic) patches. *Pharmacist's Letter/Prescriber's Letter* 2007:23(10):231010.
- Facts and Comparisons Online. Wolters Kluwer 2010. Available at: http://www.factsandcomparisons.com.
- Product information for Voltaren Gel. Novartis Consumer Health, Inc. Parsippany, NJ 07054-0622