OPTIMIZE PRESCRIBING AND AVOID ADVERSE DRUG EVENTS IN ELDERLY PATIENTS

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*Views presented reflect only my own best professional opinion

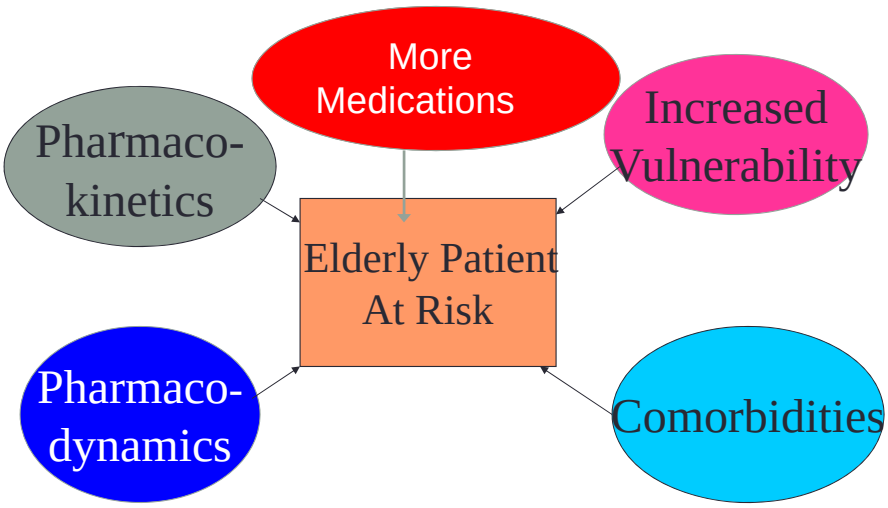
Objectives

- Identify physiologic changes with aging that put older patients at risk for Adverse Drug Events
- Identify the four most dangerous classes of medications for elderly patients and actions to decrease the risks of:
  - Anti-coagulants
  - Hypoglycemic medications including insulin
  - Cardiovascular medications
  - Antipsychotic medications
  - Other inappropriate medications
- Describe the special medication risks associated with transitions and nonadherence for elderly and best practices to reduce these risks
- Explain the importance of the Centers for Medicare and Medicaid Services initiative to reduce inappropriate use of antipsychotics in skilled nursing facilities

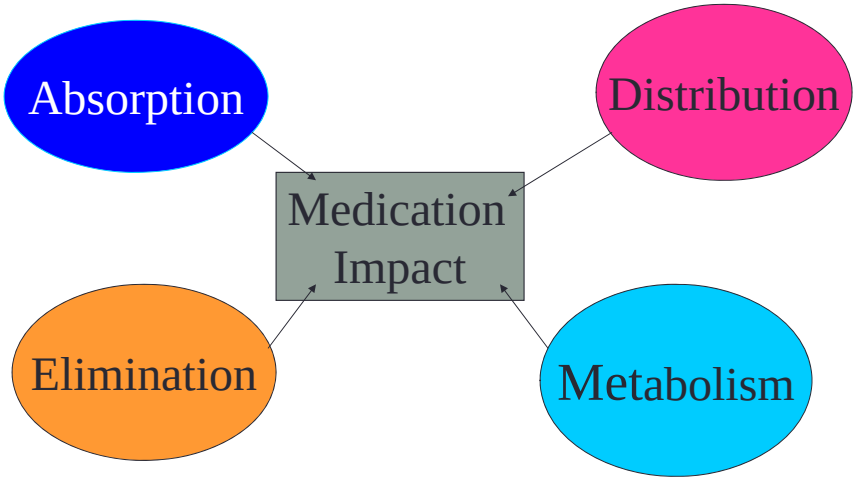
Medication Use in the Geriatric Patient: Pre-test

- Compared to a 30 year old patient what is the appropriate starting dose for an opiate analgesic for a 75 year old?
- Which pharmacologic factors is most affected by aging-- absorption, hepatic clearance, volume of distribution or renal clearance?
- Identify 3 highest risk medications in the elderly
- Name 5 reasons medication complications are more common at time of transition and steps to reduce risk
- Describe 5 steps to reduce antipsychotic prescribing in the nursing home

Why is the older patient different?



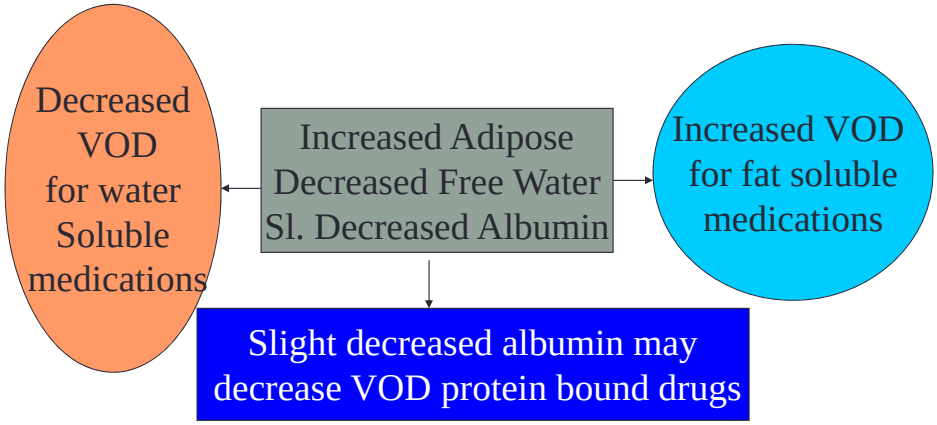
Pharmacokinetic Changes of Aging



Medication Absorption Changes Little with Aging

- Overall Bioavailability varies little with age
- Some alteration with changes with gastric pH (often due to medication)
- BUT If the stomach doesn't empty absorption may be greatly altered (Drug disease interaction where disease is related to aging)
- Drug/drug interactions may be significant: e.g. antacids decrease fluoroquinolone absorption

Volume of Distribution(VOD): Changes with Aging



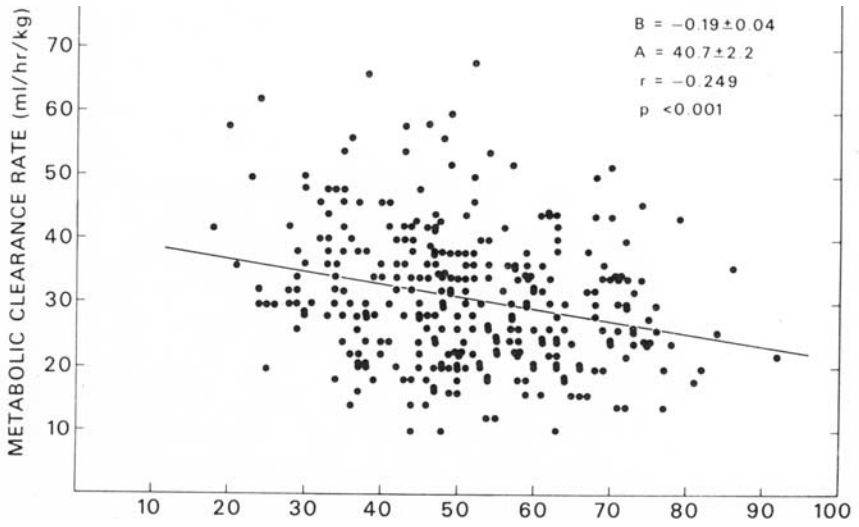
Volume of Distribution Changes with Aging – Summary

- More FAT-- Less Water
- Less albumin -- More Free Drug

Hepatic Metabolism Changes are Varied with Aging

- Clearance of medications slightly reduced overall due to decreased liver size and blood flow
- Phase 1 clearance most impacted (example: diazepam)
- Phase 2 seem less affected (example: lorazepam)
- Many other factors are usually more important including sex, ethnicity and diseases

Metabolic Clearance Rate by Age



Hepatic Metabolism May Be Altered Greatly By Drug-Drug Interactions

- Several Distinct C-P450 Isoenzymes may be affected by age
- CY3PA4 with likely significant decline
- CYP2D6 less change with age
- Many medications stimulate or inhibit C-P450 isoenzymes and often have greater impact than age alone
- Drug drug interactions especially of concern with erythromycin and anti-fungals
- LOOK THEM UP CONSISTENTLY!

Age has Significant Effect on Creatinine Clearance

- What is the calculated creatinine clearance of an 85 year old woman with a creatinine of 1.7?

Renal Clearance of Medication: Major Decline with Age

- To Calculate:

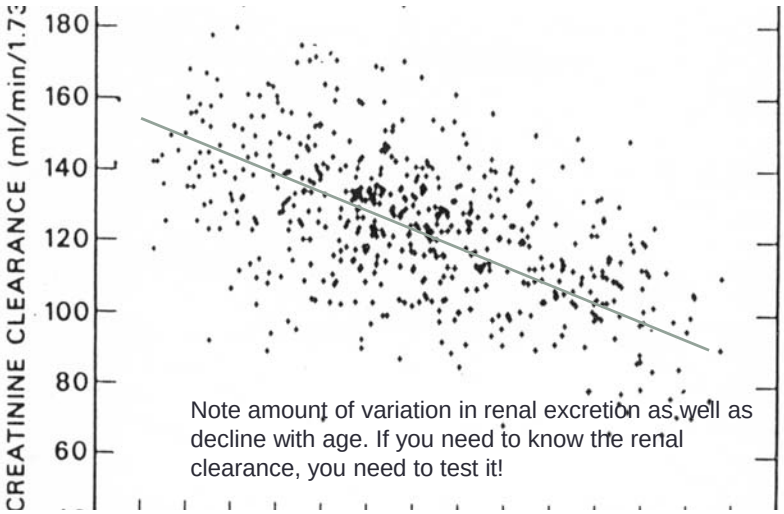
$$\frac{(140\text{-age}) \times (\text{Wt (kg)}) \times (.85 \text{ for women})}{72 \times \text{serum creatinine}}$$

Creatinine clearance of 85 year old woman with creatinine 1.7

$$\frac{(140\text{-}85)(50)(.85)}{(72)(1.7)} = 19$$

- Slightly high serum creatinine actually means near end stage renal disease

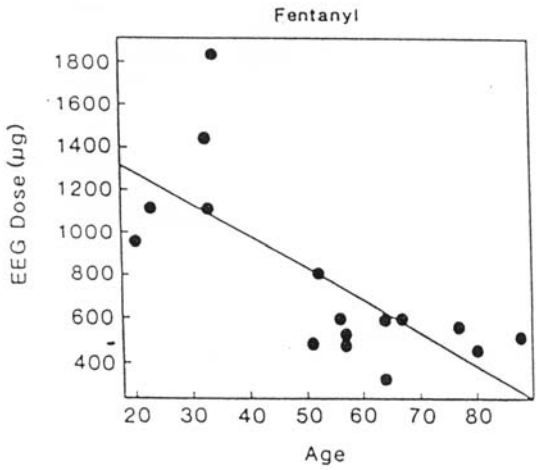
Creatinine Clearance by Age



Pharmacodynamic Changes with Aging

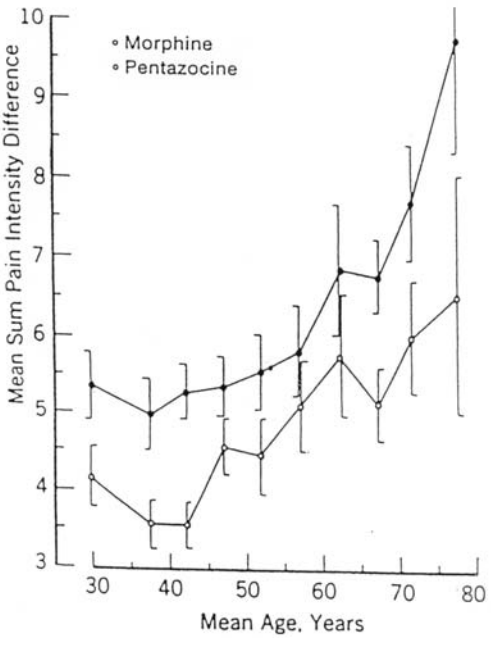
- B receptor responsiveness is reduced
- *Sensitivity to CNS and pain medications is generally substantially increased in the elderly**

EEG Response to Opiates by Age



Journal of Pharmacology and Experimental Therapeutics. 1977;240:159–66

Pain Response to Opiates by Age



JAMA. 1971;217:1835–41

Adverse Drug Event

- "An injury resulting from use of a drug"
- Estimated to cause 5-28% of all hospital admissions in elderly

Prevalence of Medication-Related Problems in the Elderly

- Elderly account for 49% of all days of hospital care
- 36% of reported Adverse Drug Events (ADE) involve an elderly patient
- 28% of hospitalizations of the elderly due to ADRs (17%) and non-compliance (11%)
- 32,000 elderly suffer hip fractures each year from falls due to medication-related problems
- Of elderly taking 3+ chronic medications, 33% re-hospitalized within 6 months of discharge from a hospital
  - ***20% of re-admits due to Medication Related Problems (MRP)***

From From Rollason V, Vogt N. Reduction of Polypharmacy in the elderly. Drugs Aging 2003:20(11):817-832.

Risk Factors for Adverse Drug Events

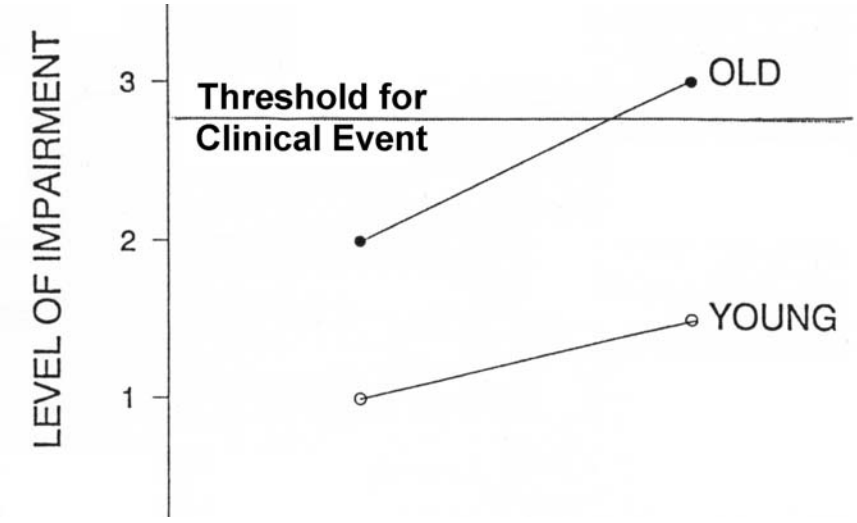
- Age >85
- Low body mass index
- > 6 diagnoses
- 9 or more medications
- 5-7 = Intermediate risk
- 12 or more doses per day
- History of prior ADE

From Geriatric Review Syllabus
AGS 7th edition

- Cognitive Impairment
- Heart Failure
- Living alone
- Substance abuse
- Psychologic disorder

Scott, IA, Amer J of Med; 2012 125, 529-537.

Increased Vulnerability is an Key Cause of Adverse Clinical Events in the Elderly



Specific ADE Vulnerabilities in the Elderly

- Delirium
- Falls
- Malnutrition
- Anti-cholinergic Side-effects
  - Confusion
  - Constipation
  - Urinary retention
  - Dry mouth
  - Other
- Orthostatic Hypotension
- Dehydration
- Metabolic Abnormalities

High Risk Medications and Actions to Avoid ADEs

USE

- Warfarin
- Appropriate for many older patients with atrial fibrillation and other problems
- Age is a risk factor for stroke
- Under-prescribing is an issue

ADR PREVENTION

- Monitor INR consistently especially with change in dose, change in diet or change in other medications
- Systems for monitoring are needed
- Watch for medication interactions (e.g. sulfa antibiotics, OTC aspirin, etc.)

Hypoglycemics

USE

- Set appropriate goals of therapy – little benefit to tight control in elderly
- HbdA1c goal of 8 or even higher is appropriate

ADE PREVENTION

- Avoid sliding scale Insulin
- Avoid long-acting, renally excreted hypoglycemics

Anti-psychotics in Dementia

USE

- Avoid whenever possible: no FDA indication and increased death rate in elderly
- Always use behavioral and other interventions first
- Use only with significant distress or patient risk
- Consider alternatives carefully
- Always obtain informed consent including risk of death

ADE PREVENTION

- Avoid use wherever possible: insist on behavioral interventions
- Effective monitoring needed to assess benefit
- Vigorously seek lowest dose and continue ongoing efforts to taper medication

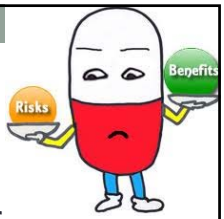
Avoiding Inappropriate Prescribing

- Survey show >20% of patient have at least one inappropriate med
- 10% of hospital admissions due to prescription of medication never or rarely appropriate

ACTION STEPS

- Review medication lists at each visit
- At least annual complete review:("everything in cabinet")
- Use software, pharmacists, Beers list, or START and STOPP lists to avoid inappropriate medications
- Medication reconciliation

Categories of Medication Related Problem



- Medical condition that requires new or additional drug therapy
- Wrong drug for patient's medical condition
- Correct drug – dose too low
- Correct drug – dose too high
- Adverse drug reaction
- Patient not taking the medication correctly
- Patient taking an unnecessary medication given present condition

From Janice Hoffman PharmD

Non-Prescription Drug Use in the Elderly

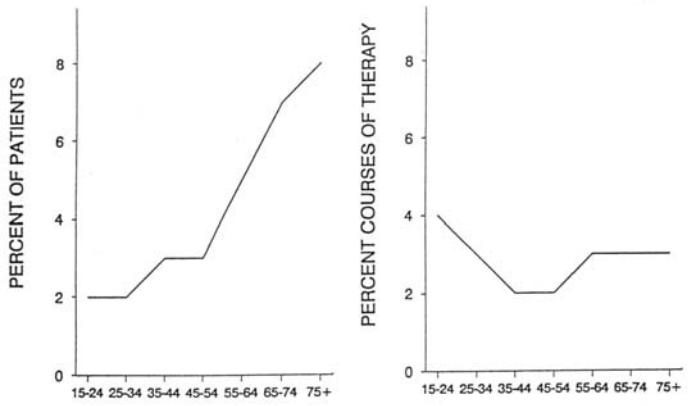
- 70% of elderly use daily OTCs
- OTCs = 40% of elderly medicine use
- Significant analgesic use

Thompson et al NEJM 1/20/83:13

What is Polypharmacy?

- Many perspectives…
- Some definitions based on number of medications
- "any time any medication is prescribed that increases risk of harm more than benefit"
- As patients become more frail or their life expectancy becomes shorter, the net benefit of many medications becomes negative
- As the number of meds increase potential interactions increase logarithmically

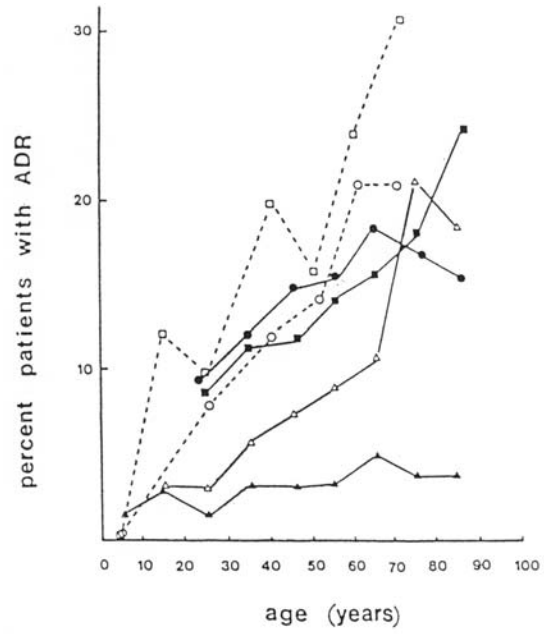
Unclear if Age Alone Causes ANY Increase in ADRs



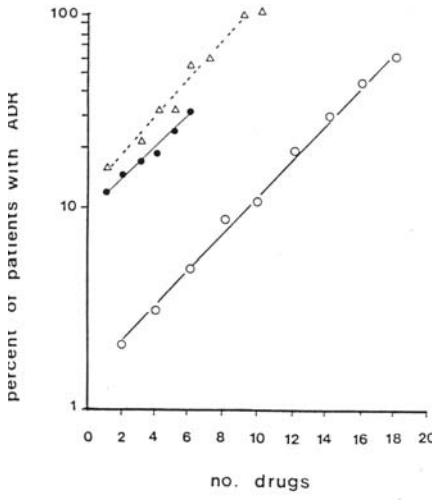
Adverse Drug Reactions

1 June 1991 • Annals of Internal Medicine • Volume 114 • 11

Adverse Drug Reactions Are Increased in the Elderly



Best Predictor of ADRs is Number of Medications



Reasons for Multiple Medications

Appropriate

Multiple disease states with effective medications

- Adverse impacts monitored less than patient centered benefit

Inappropriate

- Benefits of medication do not outweigh risks for this patient given functional status or adverse impacts of medicine

Examples of Medications Not Appropriate with Frail Elderly

- Vigorous blood pressure control in frail elderly[1]
- Vigorous blood glucose control in elderly
- Any time risk of catastrophic complication outweighs benefit of additional medicationsee Scott[2]
  - Medication errors are common and increase with # of meds
  - Non-adherence is serious problem
  - Falls are much more common in frail elderly
  - Cognitive impacts may lead to cascade of complications in frail

[1]See Musini et al Pharmacotherapy for hypertension in the elderly," Cochrane Database Syst Rev 2009;7(4):CD000028
[2]See Scott, IA et al Minimizing inappropriate Medications in older populations: a 10 step conceptual framework," Am J of Med 2012; 125: 529-537.

Love in the Time of Cholera

by Gabriel Garcia Marquez

He arose at the crack of dawn, when he began to take his secret medications: potassium bromide to raise his spirits, salicylates for the aches in his bones when it rained, ergosterol drops for vertigo, belladonna for sound sleep… in his pocket he always carried a little pad of camphor that he inhaled deeply when no one was watching to calm his fear of so many medicines mixed together.

Polypharmacy Case #1

Patient SMS is a 79 year old female who just developed high blood pressure. Dr. Salty prescribed her Lisinopril and then she gets dizzy. Dr. Salty prescribes Meclizine for dizziness.

What would you do?

From Janie Hoffman, PharmD

Ask Dr. Salty to hold off on the Meclizine. Start Lisinopril on a low dose and titrate up.

From Janie Hoffman, PharmD

Avoid using another medication to treat a side effect of another agent!

From Janie Hoffman, PharmD

CMS/CDPH and Others with Campaign to Reduce Antipsychotic Medication in SNFs

- On May 31, 2012 CMS launched national initiative to reduce antipsychotic use in patients with dementia
- **California Partnership to Improve Dementia Care and Antipsychotic Medication Reduction in Nursing Homes Collaborative**
  - **California Department of Public Health**
  - **California Association of Long Term Care Medicine**
  - **California Association of Health Facilities**
  - **California Advocates for Nursing Home Reform**
- 15% Target for reduction in 2012

Why Are Antipsychotic Rates So High in SNFs?

1. They do work in many patients for behavior problems
   (They also have a significant number of complications and increase the death rate)
2. Nothing else is shown to work; even behavioral and programmatic interventions are not “proven”
3. Many patients are distressed or present a real danger
4. Comfort may override function or longevity as primary goal
5. Prescribing physicians are often distant

Why are anti-psychotic medications used at rates higher than recommended?

6. The prescribing culture of the US and SNFs
7. Patients come to SNFs on anti-psychotics
8. Patients get medications when a situation is worse. “Regression to the mean” predicts that many of the patients will improve. “Post hoc ergo propter hoc” logic convinces staff that the intervention worked
9. Medications are tapered too slowly
10. Current incentives may encourage documentation to justify current use rather than reduce use

Mittelberger Plan for AS Reduction

1. Commit to reduction; measure use
2. Obtain true informed consent; engage family
3. Staff training/engagement and weekly follow-up
4. Environmental interventions
5. Care plan adjustments
6. Identify and treat other causes of behaviors
7. Certified Medical Director (CMD) and Pharmacy Review
8. Effective monitoring
9. Taper more rapidly than required (? Monthly)
10. Celebrate success

Multiple Interventions for Distressed Patients with Dementia

- Environment
  - Noise, light
  - Music
  - Familiar items
  - Friendly staff trained to respond appropriately
- Care plan
  - Rest and rewards
  - Activities and exercise
  - Family and other interactions
- Treatments
  - Pain
  - Anxiety, depression
  - Other

Dementia Behaviors: Avoid Reflex Medication Response

- Many behaviors will wax and wane
  - Avoid knee jerk “post hoc” prescription
- Try multiple alternatives before an anti-psychotic medication
  - Environmental
  - Social and Activities
  - Staff training
  - Treat pain and other problems

Medication Errors at Transitions of Care

REASONS for Errors:

1. Confusion about medications
2. Financial concerns or trouble obtaining medications
3. Duplication with prescribed medications at home
4. Patient vulnerability (usual medication not tolerated)
5. Patient diet changes (may impact BP and anticoagulation)
6. Inappropriate prescribed medications (eg sliding scale insulin)
7. Over the counter medications

See the work of Eric Coleman Care Transitions Intervention and Mary Naylor

Interventions to Reduce Errors at Transition

- Medication reconciliation with patient and caregiver
- Printed medication list
- Ask about all potential problems
  - Pharmacy and financial issues
  - Home medications
- Communicate with primary care provider
- Coach patient about side effects and encourage to take action if questions/problems arise
- Ensure effective monitoring program
- Limit number of dangerous medications (e.g. warfarin)
- Home health if appropriate

Quality Markers in Geriatrics Patients: ACOVE-3 Standards

- A complete medication list
- Drug regimen review at least annually
- Clear indication for each medication
- Patient education about each medication
- Documentation of response to therapy
- Medication Continuity
  - Follow up adherence, effectiveness and complications of every medication
- Avoid strong anticholinergics
- Avoid barbituates
- Antipsychotic medication response

From Wenger NA and ShekellPG, Measuring medical care to elders, JAGS 2007S247-S487

Medication Quality Indicators in Long Term Care

- Patients with antipsychotic medication without an accepted FDA indication (e.g. dementia)
- Patients without documented detailed consideration of alternatives to an anti-psychotic
- Patients without documented informed consent
- Patients with multiple antipsychotics without very strong documentation
- Patients without effective monitoring of antipsychotic medication
- CDPH survey focus with new audit tool (www.caltcm.org/resources/forms)
  - FF329 (inadequate indication for use)
  - F222 (chemical restraints)
  - F501 Inadequate Medical director oversight

Medication Use in the Geriatric Patient: Post-test

- Compared to a 30 year old patient what is the appropriate starting dose for an opiate analgesic for a 75 year old?
- Which pharmacologic factors is most affected by aging-- absorption, hepatic clearance, volume of distribution or renal clearance?
- What is the most important reason that elderly have more adverse drug reactions.
- Identify 3 markers of prescribing quality
- Identify 3 highest risk medications in the elderly
- Name 3 alternatives to antipsychotics in older patients with dementia

Medication Use in the Geriatric Patient: Pre-test

- Compared to a 30 year old patient what is the appropriate starting dose for an opiate analgesic for a 75 year old?
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- Describe 5 steps to reduce antipsychotic prescribing in the nursing home
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- Describe 5 steps to reduce antipsychotic prescribing in the nursing home

Medication Use in the Geriatric Patient: Post-test

- Compared to a 30 year old patient what is the appropriate starting dose for an opiate analgesic?
  - About 50% of the dose.
- Which pharmacologic factors is most affected by aging: absorption, hepatic clearance, volume of distribution or renal clearance?
  - Renal clearance is most affected.

Medication Use in the Geriatric Patient: Post-test

- Identify the 3 highest risk medications in the elderly
  - Warfarin
  - Insulin and hypoglycemics
  - Cardiovascular medications
  - Antipsychotic medications
- Five interventions at time of transition
  1. Complete medication reconciliation (with list with family)
  2. Ask and arrange for medication delivery
  3. Ask about duplicate and OTC home medications
  4. Establish monitoring and follow-up with PCP
  5. Coaching and/or patient follow-up at home

Post-test

- What is the most important reason that elderly have more adverse drug reactions.
  - Most important is number of medications
  - Also increased vulnerability to toxicity
- Identify 3 markers of prescribing quality
  - Complete medication lists,
  - Medication reconciliation, careful transition planning
  - Systematic medication review, No inappropriate medications; use of Beers list and/or STARTT/STOPP list
- Identify 3 highest risk medications in the elderly
  - Hypoglycemics, anti-coagulants, cardiac, antipsychotic
- Name 3 alternatives to antipsychotics in older patients with dementia
  - Behavioral, environmental, treat other problems causing behavior