

# Recommendations for geriatric prescribing

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## General types of medication- related problems

- Unnecessary drug
- Not prescribing new needed Rx
- Contraindicated drug
- Dose too low or too high
- Adverse drug event/ drug interaction
- Nonadherence
- Prescribing cascade

From Williams CM, Am Fam Phys Nov 15, 2002

## Potentially Inappropriate Medications for Older Persons

- High Potential for
- Severe ADEs
  - Amitriptyline
  - Chlorpropamide
  - Digoxin > 0.125 mg/day
  - Disopyramide
  - GI antispasmodics
  - Meperidine
  - Methyldopa
  - Pentazocine
  - Ticlopidine
- High Potential for
- Less Severe ADEs
  - Antihistamines
  - Diphenhydramine
  - Dipyridamole
  - Ergot mesylates
  - Indomethacin
  - Meperidine, oral
  - Muscle relaxants


## Quality Prescribing

- Outcomes
  - Adverse Drug Events
  - Drug-Drug Interactions
  - Unrecognized symptoms
  - Decreased quality of life
  - Non-adherence
  - Cost
  - Adding beneficial medications

## BACKGROUND

Geriatric criteria based on WHO :

- Middle age : 45-59 Years
- Elderly : 60-74 Years
- Old : 75-90 Years
- Very old : > 90 Years



**Problema penggunaan obat pada lansia**

- makin bertambah usia
- penyakit penyerta
  - Kardiovaskular (CHD, CHF)
  - Degeneratif (OA)
  - Metabolik (DM), dll
- polifarmasi
  - ACE-inhibitor
  - OAINS
  - OAD, dll
- interaksi obat
- efek samping obat . . . ☠ ☠ ☠

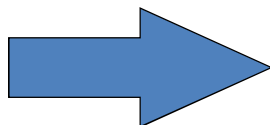
## Medications in the Elderly

### General

- 2/3 of elderly take Rx or OTC meds
- Avg of 5 Rx and 2 OTC/pt (more in NH)
- 30% of all RX written for pts > 65 yrs old
- Biochemistry of medications in the elderly
  - Longer duration of activity
  - More frequent adverse drug effects
  - Increase likelihood of drug toxicity
  - Lower doses needed to obtain therapeutic levels

## Adverse Drug Events in older adults

- Common
- May present differently than in younger adults
- May precipitate or mimic common geriatric disorders



- Under-recognition
- Increased morbidity
- ?Additional prescriptions

## Adverse Drug Events can mimic or precipitate geriatric syndromes

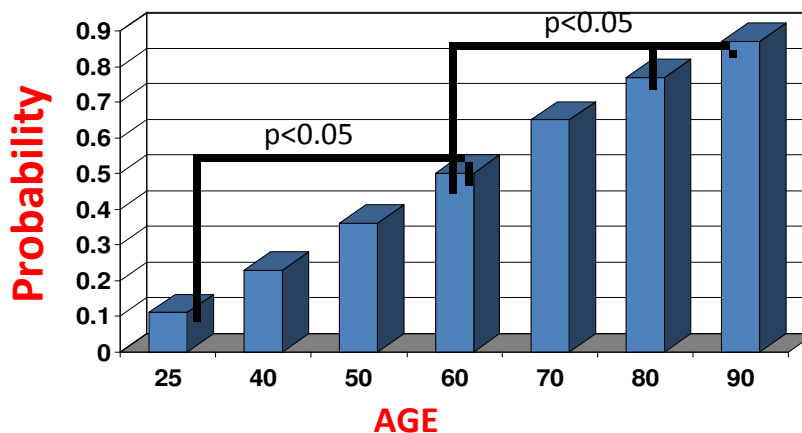
- Falls: psychotropics
- Urinary incontinence
  - Diuretics, caffeine, alcohol
  - Anticholinergic agents, including psychotropics
  - Sedative/hypnotics
  - Narcotic analgesics
  - Cardiovascular agents:
    - Alpha-adrenergic blockers and agonists
    - Beta-adrenergic agonists
    - Calcium channel blockers

## Dementia due to medications

- Psychotropics
  - Benzodiazepines, Antidepressants, Neuroleptics
- Analgesics
  - Meperidine, Indomethacin
- Antihypertensives
  - Methyldopa, HCTZ, propranolol
- Others
  - H<sub>2</sub> Blockers, Amantadine, Insulin

Larson et al, Ann Int Med 1987;107:169-173

## Major Toxicity after Chronic Theophylline Intoxication



Shannon M. Ann Intern Med 1993;119:1161-1167

## Why the elderly are at risk

- **Patient-level factors**
  - Age-associated changes in pharmacokinetics
  - Age-associated changes in pharmacodynamics
  - Comorbidity: drug-disease interactions
  - Polypharmacy: drug-drug interactions
  - Less physiologic reserve
  - Frailty
- **System level factors**
  - Fragmentation of care (Poly-doctoring)
  - Inadequate training in principles of geriatric practice

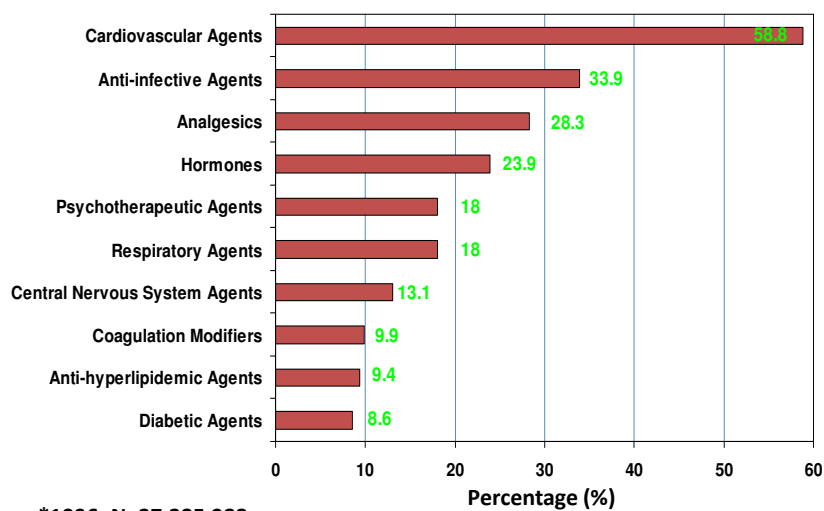
## Why the elderly are at risk

- **prescribing cascade**,
- see **several doctors**, each of whom may prescribe different medications
- use **over-the-counter** medication regularly including “**jamu**” containing “steroid”
- get medications from more than one pharmacy, or from **friends**

## Drug Use in the Elderly-Benefits Examples

- Antihypertensives
  - Reduce risk of heart failure and stroke
- $\beta$ -blockers and aspirin
  - Reduce risk of mortality and recurrent heart attack after a myocardial infarction
- Angiotensin Converting Enzyme (ACE) Inhibitors
  - Reduce mortality and risk of hospitalization in heart failure
- Biphosphonates
  - Reduce risk of hip and vertebral fractures in osteoporosis

## Drug Use in Community Dwelling Elderly\*



Moxey, Health Care Financing Review 2003

## Effective Therapies are Underutilized in Older Adults

- Thrombolysis for Acute MI
- Beta-blockers postinfarction
- Coumarin for Atrial Fibrillation
- Anything for osteoporosis
- Opioids for cancer pain

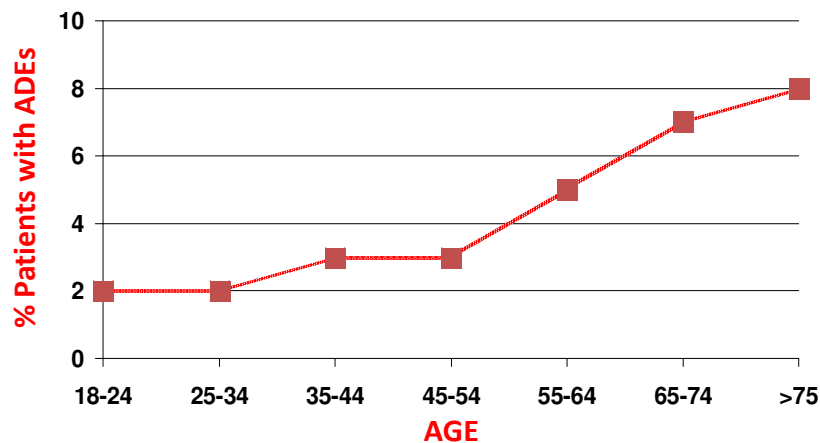


## Pharmacodynamic Changes

There is some evidence about increased drug sensitivity in elderly, which could be due to changes in:

1. Receptor number
2. Receptor affinity
3. Post receptor alterations and or
4. Homeostatic mechanisms impairment.

## ADEs: Aging or Age-related?

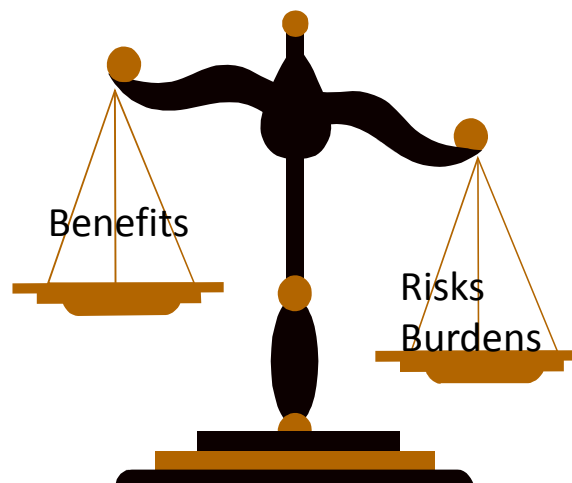


Hutchinson et al J Chronic Dis 1986;39:533-42

## What are the data for those $\geq 75$ yo?

- **No RCTs**
  - Fewer older adults with acute MI will meet criteria for thrombolysis
    - present without chest pain
    - present >3 hours after initial symptoms
  - Concern about intracranial hemorrhage
- **Observational studies:**
  - Prospective Cohort
  - Medicare databases

## Prescribing for Older Adults



## PROSES PENUAAN YANG MEMPENGARUHI FARMAKOKINETIK OBAT

Variable Body	Young Adults (20–30 years)	Geriatrics Adults (60–80years)
Body Water (% of body water)	61	53
Lean Body Mass (% of body weight)	19	12
Body Fat (% of bodyweight)	26-33 (woman) 18-20 (man)	38-45 (woman) 36-38 (man)
Serum Albumin (g/dl)	4,7	3,8
Kidney Weight (% of young adult)	100	80
Hepatic Blood Flow (% of young adult)	100	55-60

## Effects of Aging on Rx use (Absorption)

- Reduced gastric acid production
  - Raises gastric pH
  - May alter solubility of some drugs (ASA etc)
- Longer gastric emptying
  - Delay or reduce absorption
- Decreased esophageal motility
  - Capsules more difficult to swallow
- Loss of subcutaneous fat
  - Increased rate of absorption of topical medications
- Increased fragility of veins
  - IV administration more difficult

## Effects of Aging on Rx use (Distribution)

- Distribution
  - ↑ fat (18=>36% in men, 33=>45% women)
    - ↑ in VOD for lipid soluble drugs
    - ↑ concentration in body, longer  $T_{1/2}$
  - ↓ lean body mass
  - ↓ total body water – 10-15%
    - ↑ Na<sup>+</sup> space, ↑ serum/tissue levels of hydrophilic drugs
  - Albumin ↓, therefore ↓ binding and drug's free (unbound) form is more active

## Effects of Aging on Rx use (Metabolism)

- Difficult to predict, depends on
  - General health & nutritional status
  - Use of alcohol, medications
  - Long term exposure to environmental toxins/pollutants
- Aging causes decreased liver mass/ hepatic blood flow
  - Delayed/reduced metabolism of drugs
  - Higher plasma levels
- Lower serum protein levels
  - Loss of protein binding
- Idiosyncratic reactions

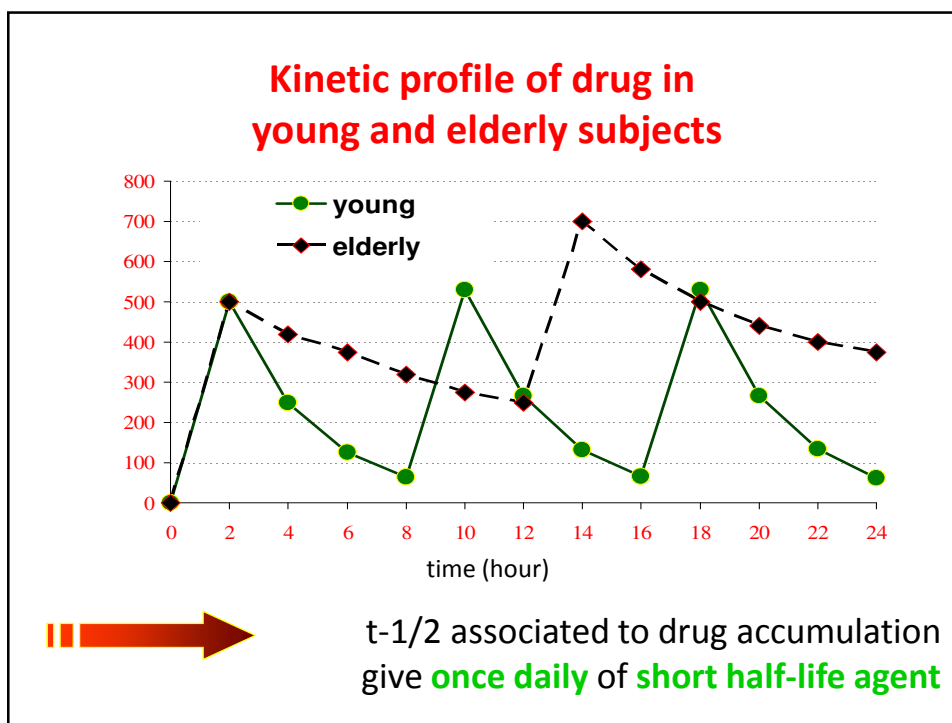
## Effects of Aging on Rx use (Metabolism)

Liver metabolism decreases with age

- ↓ in # of hepatocytes and enzymatic activity
- ↓ hepatic blood flow
- First-pass ↓ metabolism of some, not all drugs
- Phase I metabolism = CYP-450 system - produces active metabolites → this slows with age (30-40%)
- Phase II metabolism = Acetylation → inactive metabolites
  - this does NOT CHANGE with elderly
- Not possible to predict ability to metabolize a specific drug – commonly need to reduce doses by 30-40%

## Effects of Aging on Rx use (Excretion)

- Renal elimination
  - ↓ plasma blood flow
  - ↓ GFR (up to 30%)
  - Serum Cr is NOT a good measure of renal function -- a function of muscle breakdown (Elderly person with ↓ muscle → low cr)
  - Longer half-life of medications
  - Increased side effects
  - Increased potential for toxicity
- Est. Creatinine clearance: Males
  - $[(140 - \text{age}) \times \text{wt (kg)}] / [72 \times \text{Cr (mg/dl)}]$
  - Females = males X 0.85



## PK changes: So What?

- Decreased clearance
  - $Cl_{organ} = \text{Organ Blood Flow} \times \text{Extraction Ratio}$
  - Drug clearance is additive
  - Total clearance =  $Cl_{renal} + Cl_{hepatic} + Cl_{other}$
- è Increased steady-state concentration
- è Need to decrease dose

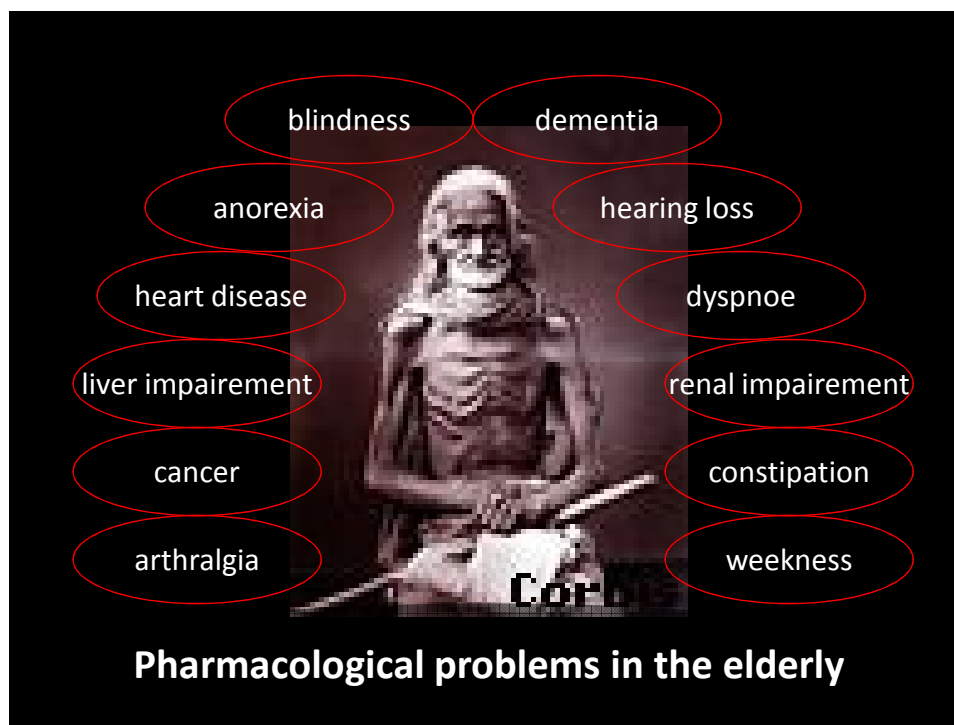
- Prolonged half life ( $t_{1/2}$ ) is common

$$t_{1/2} = \frac{0.693 \times V_d}{Cl}$$

- è Longer dosing interval
- è Longer
  - to steady state
  - until body is drug-free

## DOSIS OBAT UNTUK GERIATRIK

- 65-74 TAHUN : DOSIS LAZIM – 10%
- 75-84 TAHUN : DOSIS LAZIM – 20%
- > 85 tahun : DOSIS LAZIM – 30%



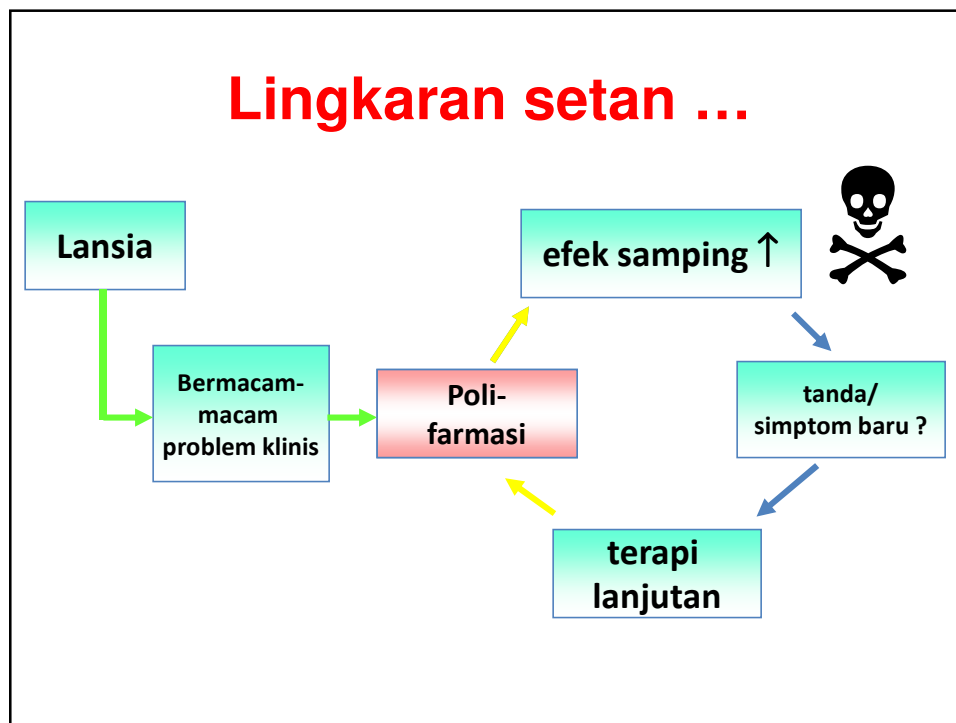
I have got them, but I forgot how to consume the drugs

Where are my medicines ?

Have I eaten them before?

**3 x 1 ≠ 1 x 3**  
**Efek terapeutik ≠ Efek samping obat**

Hindari pemakaian obat yang berbahaya . . . ☠️  
 ..... pilihlah obat yang aman  
 .. dengan regimen obat yang sederhana






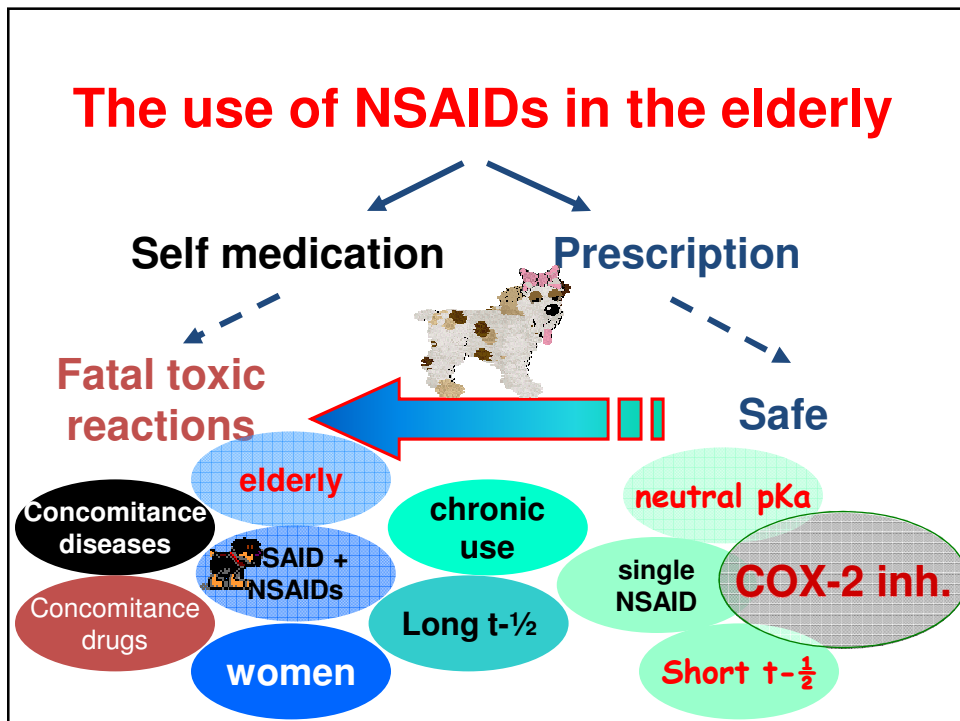
*Kurata et al., (1999)*

NSAID loxoprofen prescribed by an orthopedic to treat a patient with lumbago

Risk factors	Case
Age	Elderly (80 years)
Gender	Woman
Concomitant disease (CVS, kidney & liver)	hypertension
Concomitant drugs used	ACE-Inhibitor imidapril



**What next?** → The grandmother was **syncope** due to hyperkalemia, bradycardia



## Drug-Disease Interactions

- ↑ CHF: *NSAIDs*
- ↑ Claudication: *Beta blockers*
- ↑ Stress incontinence: *Alpha<sub>1</sub>blockers*
- ↑ Constipation
  - *CCB, anticholinergics, Betablockers, narcotics*
- ↑ BPH:
  - *Decongestants, anticholinergics, calcium channel blockers*
- Parkinsons or Dementia: *Anticholinergic delirium*

## Drug-Nutrient Interactions

- \ Protein-bound B<sub>12</sub> : *omeprazole*
- \ Folate and Vit D : *diphenylhydantoin*
- \ Thiamine: *furosemide*
- \ Coumadin effect: *Vitamin K*
- \ Calcium channel blocker bioavailability:  
*grapefruit juice*

## Drugs to Avoid in Older Adults

- Analgesics
  - Narcotics: Propoxyphene (Darvon™), Meperidine (Demerol™), pentazocine (Talwin™),
  - NSAIDs: Indomethacin, Phenylbutazone
- Muscle Relaxants
  - Robaxin™, Soma™, Ditropan™, Paraflex™, Skelaxin™, Flexeril™
- GI Antispasmodics
  - Bentyl™, Levsin™, Pro-Banthine™, DonnatoI™, Librax™

Beers M Arch Intern Med 1997;157:1531-1536

## Drugs to Avoid in Older Adults

- Cardio- or Cerebrovascular Drugs
  - Disopyramide (Norpace™)
  - Dipyridamole (Persantine™)
  - Methyldopa, Reserpine
  - Ticlopidine (??)
  - Hydergine, cyclospasmol
- Chlorpropamide (Diabinese™)
- Psychotropics
  - Antidepressants: Amitriptyline, doxepin
  - Sedatives: Meprobamate, chlordiazepoxide, diazepam, flurazepam, barbiturates
- H<sub>1</sub> Blockers (lipid soluble)
  - Chlorpheniramine, hydroxyzine, cyproheptadine, promethazine, dexchlorpheniramine, tripeleminamine

Beers M Arch Intern Med 1997;157:1531-1536

## BUT Remember . . . .

- è Prescribing is dynamic, not static.
- è Patients are dynamic, not static.

## Individualize Therapy

What is the patient's potential for:

- An adverse drug event?
  - An altered dose response?
  - A "drug interaction"?
    - drug-drug
    - drug-disease
    - drug-nutrient
  - Treatment non-adherence?
- All elders are not alike
    - Significant heterogeneity
      - greater among older individuals than younger
  - ADEs are common among older patients
  - ADEs can be minimized with strict attention to
    - ✓ risk factors
    - ✓ drug-drug interactions
    - ✓ drug-disease interactions
  - Start low, go slow

### Recommendations for geriatric prescribing

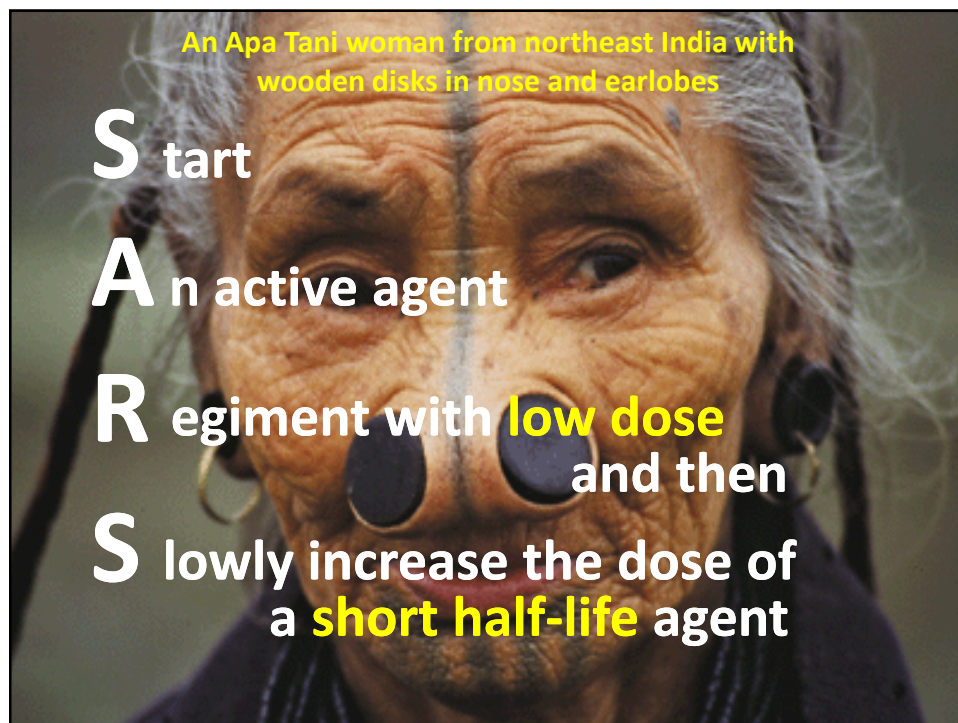
- Know your patient's medications and medication history.
- Individualize therapy.
- Reevaluate indications for continued drug use.
- Minimize dose and total number of drugs
- Start low, go slow. Use blood levels judiciously.
- Treat adequately. Do not withhold therapy for treatable diseases.
- Consider the possibility that any new symptom is an ADE.
- Know the drugs you and your patients use.
- Use new agents with caution.
- Encourage treatment adherence.

### The Obvious Do's and Don'ts

- Use effective medications to treat disease
- Use effective therapies to prevent disease
  
- Do not use unsafe medications
- Do not use ineffective medications

## Quality Prescribing

- Preventing excess morbidity and mortality by reducing harmful medications
  - Reduce total number of medications
  - Reduce complexity of regimen
  - Eliminate poorly tolerated medications
  - Eliminate drugs inappropriate for older adults
  - Avoid drug interactions



## CASE #1 (1 of 3)

- A 73 y.o. woman is seen for a routine visit.
- Blood pressure is 134/84 mm Hg; hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) is 8.1%.
- Metformin is increased to 500 mg twice daily, and other daily medications are continued: amlodipine (5 mg); timolol ophthalmic solution (1 drop bid); aspirin (81 mg); and calcium citrate (500 mg)
- At 6-mo. follow-up, blood pressure is 130/82 mm Hg, fingerstick blood glucose 93 mg/dL, and HbA<sub>1c</sub> 9.2%.

## CASE #1 (2 of 3)

- Which of the following is the most likely
- explanation for the increase in HbA<sub>1c</sub>?
- Incorrect choice of antidiabetic medication
- Inadequate dose of antidiabetic medication
- Long-term nonadherence with medication
- Altered pharmacokinetics
- Altered drug absorption

## CASE #1 (3 of 3)

- Which of the following is the most likely explanation for the increase in HbA<sub>1c</sub>?
- Incorrect choice of antidiabetic medication
- Inadequate dose of antidiabetic medication
- Long-term nonadherence with medication
- Altered pharmacokinetics
- Altered drug absorption

## CASE #2 (1 of 3)

- A 68 y.o. woman has a hx of Parkinson's disease, hypertension, and osteoarthritis.
- Daily medications are carbidopa-levodopa (25 mg/100mg tid); selegiline (5 mg bid); losartan (50 mg); celecoxib (200 mg); and a multivitamin
- In past 3 wk, she has taken diphenhydramine at bedtime for insomnia
- The patient now reports the onset of urinary incontinence



## CASE #2 (2 of 3)

- Which of the following is the most appropriate intervention?
- Discontinue celecoxib
- Discontinue diphenhydramine
- Discontinue losartan
- Substitute fosinopril for losartan
- Begin tolterodine

## CASE #2 (3 of 3)

- Which of the following is the most appropriate intervention?
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### **CASE #3 (1 of 3)**

**An 83 y.o. woman is brought to emergency because of dizziness on standing, followed by brief loss of consciousness. The patient now feels well.**

- **She has hypertension but is otherwise healthy**
- **Daily medications: metoprolol 50 mg; captopril 25 mg; nitroglycerin 0.4 mg sublingually prn.**
- **Blood pressure is 130/70 mm Hg sitting and 100/60 mm Hg standing. PE is otherwise normal. CBC, BUN, ECG, comprehensive metabolic panel are all normal.**

### **CASE #3 (2 of 3)**

- **Which of the following is the most likely**
- **cause of the syncopal episode?**
  
- **Sepsis**
- **Drug-related event**
- **Hypovolemic hypotensive episode**
- **Cardiogenic shock**
- **Unidentifiable cause**

### CASE #3 (3 of 3)

- Which of the following is the most likely cause of the syncopal episode?
- Sepsis
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- Hypovolemic hypotensive episode
- Cardiogenic shock
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### Individualization of Therapy

What is the patient's potential for:

- An adverse drug event?
- An altered dose response?
- A "drug interaction"?:
  - drug-drug
  - drug-disease
  - drug-nutrient
- Treatment non-adherence?

For some drugs, may be able to get  
same effect in older adults with  
lower dose

- Historical examples: Captopril, HCTZ?
- Lower doses but same blood levels
- Beta-blockers (Rochon study)
- ATLAS: Lisinopril
  - lower dose: same effect on mortality
  - higher dose: fewer hospitalizations for any reason as well as for CHF