Stopping Drugs in the Elderly

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Disclosures

- No financial relationships with commercial interests to disclose
Stopping Drugs in the Elderly
Clinical Practice Gaps & Objectives

• Gap: the elderly often receive inappropriate medications and experience the vast majority of adverse drug events

• Objective: Optimize drug therapy by considering consensus panel recommendations regarding polypharmacy, drug interactions, and medication use in elderly
Stopping Drugs in the Elderly: The Agenda

- Briefly review relevant pharmacokinetic & pharmacodynamic changes with aging
- Identify medications that frequently cause problems in the elderly
- Review & Apply approaches to avoid polypharmacy in older adults
  - Prescribing tips in the elderly
Pharmacodynamics

• Response that occurs when a drug interacts at its receptor
Pharmacodynamic Changes with Aging

- Increased response
  - Opiates
  - Warfarin
Pharmacodynamic Changes with Aging

- Increased response
  - Opiates
  - Warfarin

- Decreased response
  - Beta-agonists
Pharmacokinetics

- Drug concentration at the site of action
Pharmacokinetics

• Drug concentration at the site of action

• 4 Determinants:
  – Absorption --- minimal clinical relevance
  – Distribution
  – Metabolism --- marginal clinical relevance
  – Elimination
Pharmacokinetic Changes with Aging

• **Distribution**
  - ↑ fat mass
  - ↓ muscle mass
  - ↓ total body water
  - ↓ albumin (binds acidic drugs)
  - ↑ alpha-1 glycoprotein (binds basic drugs)

• Clinically important, not fully predictable
Effects of Aging on Volume of Distribution: Muscle and Fat mass Δ’s

64 yr old woman

20 yr old woman

Cross-section CT Thighs

J Nutr 1997 127:990S
Effects of Aging on Volume of Distribution (VD)

- ↓ body water → lower VD for hydrophilic drugs
- ↓ lean body mass → lower VD for drugs that bind to muscle
- ↑ fat stores → higher VD for lipophilic drugs
- ↓ plasma protein (albumin) → higher percentage of drug that is unbound (active)
Pharmacokinetic Changes with Aging

• Elimination
  - ↓ renal mass, renal blood flow
  - ↓ glomerular filtration rate (10 cc/decade)

• Clinically important & predictable
  - ↑ concentration of renally cleared drugs
  - Serum creatinine alone does not provide adequate information to guide dosing
  - Use Cockcroft-Gault (CG) to estimate GFR in older adults
    - More conservative estimate than MDRD, esp frail
    - Drug company renal dose recs are based on CG
Polypharmacy in the Elderly: Objectives

- Briefly review relevant pharmacokinetic & pharmacodynamic changes with aging
  - Identify medications that frequently cause problems in the elderly
  - Review & Apply approaches to avoid polypharmacy in older adults
    - Prescribing tips in the elderly
Hx: 83 yo F with DM (A1C 7.2% on glipizide) & HTN (well controlled w/HCTZ) presents with dysuria & frequency. Low grade fever, no chills, no n/v. NKDA.

Exam: T 100°F BP 136/78  HR 88  Wt 55kg
Mild low abdominal discomfort to palpation, (-) CVAT, o/w unremarkable

Labs:  U/A 10-30 WBC, nitrate (+), electrolytes nl, Bun/Cr 24/1.3
Drug Prescribing in the Elderly

Which of the following is the least appropriate choice for empiric tx of her UTI?

A. Cephalexin
B. Nitrofurantoin
C. TMP/SMX
D. Levofloxacin
Drug Prescribing in the Elderly

Which of the following is the least appropriate choice for empiric tx of her UTI?

A. Cephalexin

B. Nitrofurantoin – calculated GFR 28cc/min, efficacy ↓ with ↓ GFR < 60cc/min, ↑ potential for side-effects, on (the dreaded) Beer’s list & HEDIS list of high risk meds in the elderly

C. TMP/SMX

D. Levofloxacin

HEDIS Ref: http://www.ncqa.org/tabid/1274/default.aspx
The Beers List of Potentially Inappropriate rx\textsuperscript{es} in older adults

- First generation antihistamines (eg, diphenhydramine)
- GI antispasmodics (eg, hyoscyamine)
- Muscle relaxants
- Benzodiazepines
- Nonbenzodiapine sleepers: avoid use > 90 days
- Tertiary TCAs (eg, amitriptyline, doxepin > 6mg)
- Chronic use non-COX selective NSAIDS (unless other rx’s not effective & pt can take gastroprotection rx)
- Digoxin > 0.125mg/d
- Central alpha agonists (eg, clonidine)

Can I tell you about use of a few drugs in old people that really gets under my skin?
Three Meds I hate to see in older pts

• Muscle relaxants
  - Sedating, anticholinergic, falls/fx, ?’able efficacy

• Iron more than once daily (or w/PPIs)
  - Marginal gain BID/TID iron, ↑ adverse GI effects
  - ↓ H+ → ↓ absorption

• Megestrol acetate (Megace)
  - minimal effect on wt, takes months, ↑ thrombotic events, possibly ↑ death

“One of the first duties of the physician is to educate the masses not to take medicine”
- Sir William Osler
When to Just Say No

• NSAIDS - other than short-term use
• PPIs – if possible avoid chronic use
• Benzodiazepines
• Sedating antihistamines
• 1\textsuperscript{st} generation tricyclics
• Iron > 325mg/d
• Muscle relaxants
Scope of the Problem

Elderly Bear ↑ Burden of Injuries from Rx’s

- ADEs are responsible for 5% - 28% of acute geriatric hospital admissions
- 30-50% felt to be predictable/preventable

Emergency Hospitalizations for Adverse Drug Events (ADEs) in Older Americans

- National electronic ADE surveillance 2007-09
- Hospitalization rates after ED visits for ADEs
- Pts age 65+ had 100,000 admits/yr d/t ADEs
- Four meds/classes causes 2/3 of the mayhem
  - Warfarin 33%
  - oral antiplatelet drugs 13%
  - insulins 14%
  - oral hypoglycemics 11%
- “high risk” meds implicated in only 1% of admits
- Recs for addressing the 4 above meds/classes

NEJM 2011;365:2002-12
Anticoagulation & Antiplatelet Issues

Case: 87 yo F hx stable CAD, HTN, ↑ lipids, hx iron deficiency (2007, declined GI w/u) falls → hip fx
Meds PTA: ASA 81mg, metop 25mg BID, Lisinopril 20mg, simvastatin 20mg, omeprazole 20mg
Course: 3 wks post-op develops DVT

Question: After initial LMWH tx, best approach to manage her anticoagulant/antiplatelet tx is:
1) Warfarin and continue ASA for CAD
2) LMWH for 3 months minimum
3) Warfarin and stop ASA
4) Caval Filter (anticoag too risky)
Warfarin + Aspirin in Elderly: Oil and Water?

After acute tx with LMWH the best approach to manage her anticoagulant/antiplatelet therapy is:

1) Warfarin and continue ASA for CAD
2) LMWH for 3 months minimum
3) Warfarin and stop ASA – warfarin provides cardioprotection in stable CAD pt, combination more than doubles bleed risk w/o clear additional benefit
4) Caval Filter (anticoag too risky)
Warfarin + Aspirin in Elderly: Oil and Water?

Benefits: Warfarin and ischemic heart dz

1° prevention: Warfarin ↓ angina > ASA in ↑ risk pts

2° prevention CAD pts: Warfarin INR 2-3 vs control
- Mortality risk ↓ 18% (95% CI, −6% to 37%)
- MI risk ↓ 52% (95% CI, 37%-64%);
- Stroke risk ↓ 53% (95% CI, 19%-73%)

2° prevention s/p MI RCT: W INR 2.8-4.2 vs ASA 160mg
- W ↓ reinfarction 26%, CVA 48%, mortality NS Δ

Arch Intern Med. 2002;162:88
JAMA. 1999;282:2058-2067
NEJM 2002; 347(13):969
“... one can infer that OAC alone targeted to an INR of 2-3 can provide substantial protection against recurrent CAD

Chest 2012;141;531S
Warfarin + Aspirin in Elderly: Oil and Water?

Risks: Warfarin + aspirin vs warfarin alone

- Kaiser cohort study: 2500 pts W vs 1600 pts W + ASA
  - OR$_{adj}$ hemorrhagic events: 2.75 (95% CI 1.44 - 5.28)
  - OR$_{adj}$ coronary events 0.99 (95% CI, 0.37- 2.62)

- “There is a cost to adding aspirin to OAC… a doubling of bleeding risk”

*Chest 2008;133:948-954*

*Chest 2012;141;531S*
Weigh Risks & Benefits Carefully

- **Case F/U**: Coumadin added, ASA continued, Hct drop 29 to 20 w/retroperitoneal bleed.

- **Conclude**: Carefully weigh need to continue antiplatelet rx in elderly pts with new indication for coumadin (eg, new AF, DVT, P.E.)

- **Caveats**: Pertinent to stable CAD, n/a to pts w/ACS, s/p stents, etc
DM Management in Older Adults

- AGS Choosing Wisely recs:
  - $A_1c$ target 7-7.5% if healthy & life expect > 10yr
  - $A_1c$ 7.5%-8% w/mod comorbidity & life exp < 10 yr
  - $A_1c$ 8%-9% w/multiple comorbidities/limited life-expectancy

- Avoid meds other than metformin to ↓ $A_1c$ < 7.5%

DM Management in Older Adults

ADA recommends

• Healthy: HbA$_{1c}$ target of $< 7.5$

• or slightly higher (8% target) in pts
  - With limited life expectancy ($< 10$ yrs?)
  - Extensive comorbid conditions
  - At ↑ risk for serious hypoglycemia (eg ↑ age, ↓ function, cognitive impairment)

Diabetes Care 2012; 35:2650  Diabetes Care 2013;36(S1):S11
DM Management in Older Adults

• Hypoglycemia risks ↑ w/age & w/tighter control
  ➢ 20 severe events/1000 pts age 80+ w/DM 10+ yrs
  ➢ Hypogly assoc w/↑ dementia, CV events, falls, etc

• Yet recent VA study of 650K high risk pts
  ➢ high risk: age 75+ & Cr > 2, or ↓ cognition/dementia
  ➢ tx’ed with insulin and/or sulfonylurea in 2009
  ➢ 50% had A1C < 7%

• Appears we are over-treating DM in older adults!

Diabetes Care 2013;36:3535   JAMA Intern Med online Dec 2013
Adverse Drug Reactions

7-fold increased risk in the elderly

- Changes in pharmacodynamics/kinetics
- Drug-disease and drug-drug interactions
- Related to Polypharmacy!
  - 13% population use 30% rx’s, 50% OTC agents
  - 60% elderly on 5+ meds
  - 20% elderly on 10+ meds

Exponential Relation Between Polypharmacy and ADRs

# of Drugs Taken

Percent of Patients with an ADR

Polypharmacy in the Elderly: Objectives

✓ Briefly review relevant pharmacokinetic & pharmacodynamic Δ’s that occur w/aging
✓ Identify medications that frequently cause problems in the elderly

• Review & Apply approaches to avoid polypharmacy in older adults
  - Prescribing tips in the elderly
Optimizing Therapies and Care Plans

Recognize opportunities to stop meds

- Review existing meds before starting new rx
- Annual/semiannual medication review
- Care transitions are key opportunities
  - Is pt managing current care plan?
  - Is complexity impacting adherence & safety?
  - Have pt preferences changed?
  - 44% pts rx’ed ≥ 1 unnecessary drug at d/c

Inpt & Transitions in Care Opportunities to ↓ Meds: PPIs

Choosing Wisely: Society of Hospital Medicine

• Don’t rx meds for stress ulcer prophylaxis to medical inpt unless high risk for GI comps (eg ICU)

• My Corollary: d/c PPI if used for inpt prophylaxis

• Additional corollary: d/c the prn sleeper as well!
  ➢ hospitalization ↑ risk chronic benzo use 5-fold
  ➢ 13 % new benzo use rx’ed at hospital d/c

http://www.choosingwisely.org

Int J Geriatr Psych 2013;28(3):248
Problems with Chronic PPI use

- ↑ Risk C. difficile
- ↑ Risk PNA (HCAP, possibly CAP)
- ↓ absorption of nutrients
  - ↓ Calcium/↑ hip fracture risk
  - ↓ iron (give Fe supps w/VitC or OJ)
  - ↓ B12 (check level)
  - ↓ magnesium absorption
- ↓ absorption meds: thyroid hormone, ketoconazole, itraconazole

Am J Gastroenterol. 2009;104:S5
How about stopping chronic PPI use?

- PPIs appropriate for erosive esophagitis, frequent symptoms (2+ episodes/wk), and/or severe sxms
- Severe erosive dz or Barretts’s continue rx
- GERD/Dyspepsia – consider d/c after asxm 12+ wks
  - taper by 50%/wk if on high dose or BID dosing
  - be aware of risk temporary ↑ sxms d/t “acid rebound” when stopping PPI’s used > 8wks
  - Δ to H2 block (scheduled or prn) or PPI prn
  - Success rates d/c acid-suppression variable: 14-35%
    - 1 RCT: 31% success w/taper, 22% w/o taper

Guidelines for the diagnosis and management of GERD
How Do I Cut Down on Meds?
Apply clinical practice guidelines with caution!

- Almost all existing guidelines have single dz focus
- Application of CPGs to hypothetical 79yo pt w/COPD, DM, HTN, OP, OA → 12 medications, complicated regimen → $406 monthly cost
- Studies rarely include frail elderly, mult comorbid dz
- Risks (drug-drug, drug-dz interactions) likely are ↑
- Do CPGs address short & long term goals?
- Pt preferences?

JAMA 2005;294:716
How Do I Cut Down on Meds?

Apply clinical practice guidelines with caution!

- CHF Guidelines: based on excellent RCT data
- Issue: Older Adults w/CHF often w/comorbid dz
- Characteristics 2.5 million Medicare Beneficiaries Hospitalized for Heart Failure, 2001-2005
  - mean age 80 years old, nearly 60% women
  - 2/3 of pts w/chronic atherosclerosis
  - 67% HTN
  - 42% COPD
  - 42% diabetes mellitus
  - 30% renal failure
  - 14% dementia

Arch Intern Med 2008;168(22):2481-8
Interactions Among CPGs Likely

84 yo w/CHF, DM, OP, CKD, AD c/o fatigue/insomnia

Fatigue
- Glipizide
- Metformin
- Metoprolol
- Simvastatin
- Donepezil
- Zolpidem
- Alendronate

Diabetes

Heart Failure

Osteoporosis

Kidney dz

Am J Geriatr Soc 2012;60:1957
EBM for the Frail Older Adult

Does the Emperor have any clothes?

- Evidence for the best care of frail older pts w/multimorbidity is often lacking
- "Absence of evidence is not evidence of absence" -- Carl Sagan, Astronomer (and Donald Rumsfeld)
Reducing Polypharmacy

Tools to identify potentially inappropriate meds

- Beers Criteria
  - J Am Geriatr Soc 2012;60:616-31

- STOPP/START

- “Good Palliative-Geriatric Practice Algorithm”
  - Arch Intern Med Oct 2010;170:1648
STO**PP**/START

**STO**PP  Screening Tool of Older Persons’ Prescriptions

**START**  Screening Tool to Alert Doctors to Right Treatment

- List of potentially inappropriate meds by organ system

- RCT 400 inpts age 65+ at time of d/c
  - Screen w/STO**PP**/START w/recs to attending MD
  - Uneccessary polypharm, incorrect doses, & potential drug-drug & drug-disease interactions ↓ 36%
  - Undertx reduced by 21%

Clin Pharmacol Ther 2011 Jun;89(6):845
Reducing Polypharmacy in the Elderly

- Polypharmacy & inappropriate meds common
- Results in ↓ compliance, ↑ D.I.s, ↑ ADEs
- RCTs: Rx reviews by PharmDs ↓ ~ 1 rx
- “Good Palliative-Geriatric Practice algorithm”
  - NH: n=119, \( \bar{x} \) age 83, \( \bar{x} \) 7 meds ↓ by 3
    - 10% resumed, hosp ↓ (30 v 12%), mort ↓ (45 v 21%)
  - Outpt: n 70, \( \bar{x} \) age 83, \( \bar{x} \) 8 meds ↓ by 4, 19 mo f/u
    - 2% failed rx d/c, resumed d/t sxms, no ↑ M&M
“Good Palliative-Geriatric Practice Algorithm”

Discuss the following with the patient/guardian

- An evidence-based consensus exists for using the drug for the indication given in its current dosing rate in this patient's age group and disability level, and the benefit outweighs all possible known adverse effects

  No/Not sure

  Indication seems valid and relevant in this patient's age group and disability level

    No

    Do the known possible adverse reactions of the drug outweigh possible benefit in old, disabled patients?

      Yes

      STOP DRUG

      No

      Any adverse symptoms or signs that may be related to the drug?

        Yes

        SHIFT TO ANOTHER DRUG

        No

        Is there another drug that may be superior to the one in question?

          Yes

          REDUCE DOSE

          No

          Can the dosing rate be reduced with no significant risk?

            Yes

            Reduce dose

            No

            Continue with the same dosing rate
If a Medication is Stopped...

- Taper if necessary
- D/C it from the EMR
- Make sure the pt/family knows
  - In writing + updated med list
- Communicate with the pharmacy
  - Ask pharmacy to d/c further refills
  - 1.5% electronically d/c\(^{ed}\) meds were subsequently dispensed

Polypharmacy in the Elderly: Objectives

- Briefly review relevant pharmacokinetic & pharmacodynamic Δ’s that occur w/aging
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Prescribing Tips in the Elderly

• The Prescribing cascade
• Avoiding drug-drug interactions
• Be aware of non-adherence
• Patient education
• MD Education: Know what your pt is taking
Avoid the Prescribing Cascade

Drug 1

Adverse effect misinterpreted as new medical condition

Drug 2

BMJ 1997; 315:1096
Avoid the Prescribing Cascade

- HCTZ – Allopurinol
- NSAIDs – Antihypertensives
- Metoclopramide – Carbidopa/Levodopa
- Cholinesterase inhibitors – Tolterodine
Prudent Prescribing: Beware of Drug-Drug Interactions

- 100% chance of DDI with 8 drugs
- Nearly 50% of community-dwelling geriatric patients had at least one DDI
- DDI can result in ADRs or suboptimal dosing
- A key: Avoid Polypharmacy
Drug-Drug Interactions
Sulfonylurea, abx & hypoglycemia: Who knew?

- Risk of severe hypoglycemia (ED visit)
- Pts on glipizide tx’ed for infxn (ref cephalexin)
  - TMP/SMX: OR 3.1 (1.8-5.4)
  - Clarithromycin: OR 2.9 (1.7-5.0)
  - Fluconazole: OR 2.5 (1.2-5.2)
  - Levofloxacin: OR 2.1 (1.3-3.3)
- MOA: ↓ hepatic metabolism by CYP2C9 inhib
  (and possibly effects on P-Glycoprotein & CYP3A4)
- Similar to worse effects in pts on glyburide

Clin Pharmacol Ther. 2010; 88(2): 214
Prescribing Tips in the Elderly

• The Prescribing cascade
• Avoiding drug-drug interactions
• Be aware of non-adherence
• Patient education
• MD Education: Know what your pt is taking
Adherence Issues

- ~50% of people w/chronic dz consistently take their meds as prescribed
- HTN & HLD adherence as low as 30-40% at 1yr
  Drugs Aging 2008;25: 885
- “Medicines will not work if you do not take them”
  C Everett Koop

WHO: Adherence to long-term therapies
Adherence to Anti-hypertensive Regimen

Medication Adherence after MI in Elderly

mean age 80yo

Improving Medication Compliance

Why aren’t pts more compliant?

- **Number of meds the key factor**
- Complexity of med regimen
- Other potential factors
  - lack of information/understanding
  - side-effects
  - forgetfulness
  - emotional factors
  - costs

NEJM 2005;353:487
Relation Between Polypharmacy and Compliance
Improving Medication Compliance

Why aren’t pts more compliant?

- Number of meds the key factor
- **Complexity of med regimen**
  - daily really is better than BID
    - J Manag Care Pharm. 2012;18:527
- **Other potential factors**
  - lack of information/understanding
  - side-effects
  - forgetfulness, memory problems
  - depression, emotional factors
  - costs

NEJM 2005;353:487
Prudent Prescribing: Improving Medication Compliance

Explain why, what and when of any new rx

• MDs often fail in this regard
  ➢ FP and IM docs observed for 243 new rx’s
  ➢ ¼ never stated name of new med
  ➢ explicit directions, duration ≈ 50% of time

• Write indication ON RX→ it will be on bottle!
  ➢ Lisinopril to improve heart function
  ➢ Metoprolol to help prevent heart attack

Arch Intern Med 2006;166:1855
Other Methods to Improve Compliance

- Other predictors of ↓ medication adherence
  - # of prescribers
  - # pharmacies and less refill consolidation

- Advise
  - 1 pharmacy
  - Synchronize refill dates

Other Methods to Improve Compliance

- Cost, even w/Med D & ↓ gap, likely still matters
  - 13% elderly w/cost related non-adherence (gen do not inform MD)
  - Eliminating copay for essential meds after MI did ↑ adherence

- ↑ frequency of clinic visits

- Pill boxes, reminders (data mixed, helps monitoring)

Arch Intern Med 2006;166:1829  NEJM 2011;365:2088
Adherence: Is anyone keeping score?

- New 2012 CMS measure of adherence to help assess quality of Medicare Advantage programs

- 1-5 stars: 5 = 75% enrollees get 80+% of their ---
  - oral hypoglycemic
  - antihypertensive
  - cholesterol lowering meds

- Doesn’t come w/strategies to improve adherence!

- Unlikely to improve w/o multi-faceted approach
  - MDs alone won’t do it (but we can help!)

Ann Intern Med 2012;157:580
Prescribing Tips in the Elderly

- The Prescribing cascade
- Avoiding drug-drug interactions
- Be aware of non-adherence
- Patient education
- **MD Education: Know what your pt is taking**
How can we improve our knowledge of patient drug use?
1. Accurately ascertain all current drug use
   • ‘brown paper bag’ medication reconciliation

2. Identify patients at risk of, or suffering, ADR
   • at risk: ≥8 medications
     advanced age (>75 years)
     high-risk medications
   • assess for current, past or highly likely future toxicity

3. Estimate life expectancy
   • clinical prognostication tools or lifespan calculators

4. Define overall care goals
   • consider current functional status and quality of life with
     reference to estimated life expectancy

5. Verify current indications for ongoing treatments
   • perform diagnosis-medication reconciliation
   • confirm diagnostic labels against formal diagnostic criteria
   • ascertain, for each confirmed diagnosis, drug appropriateness

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All three at-risk criteria – aim for ≤ 5 drugs
Discontinue drugs for which there is unequivocal evidence of past, current or future toxicity
(eg triple whammy of NSAID, diuretic, ACE inhibitor)

If life expectancy less than 2 years, preservation of function and quality of life predominate over
prolonging life and avoiding future complications as goals of care

Discontinue drugs for which the diagnosis is wrong or
totally unsubstantiated or where, for a confirmed
diagnosis, the drug is ineffective

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Evid Based Med 2013;18(4):121
<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
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<tbody>
<tr>
<td>6.</td>
<td>Determine need for disease-specific preventive medications</td>
</tr>
<tr>
<td></td>
<td>- estimate clinical impact and time to future treatment benefit</td>
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<tr>
<td></td>
<td>- compare this estimate with expected lifespan</td>
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<tr>
<td>7.</td>
<td>Determine absolute benefit-harm thresholds of medications</td>
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<tr>
<td></td>
<td>- reconcile estimates of absolute benefit and harm using prediction tools (see <a href="http://www.mdcalc.com">http://www.mdcalc.com</a>)</td>
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<tr>
<td>8.</td>
<td>Review the relative utility of individual drugs</td>
</tr>
<tr>
<td></td>
<td>- rank drugs according to the relative utility from high to low based on predicted benefit, harm, administration and monitoring burden</td>
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<tr>
<td>9.</td>
<td>Identify drugs to be discontinued and seek patient consent</td>
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<tr>
<td></td>
<td>- reconcile drugs for discontinuation with patient preferences</td>
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<tr>
<td>10.</td>
<td>Devise and implement drug discontinuation plan with close monitoring</td>
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</table>

**TEN STEP APPROACH**

- Discontinue preventive drugs whose time until benefit exceeds expected lifespan
- Discontinue drugs whose absolute level of harm exceeds absolute level of benefit; in ‘line-ball’ cases elicit patient preferences
- Discontinue drugs of low utility
- Discontinue drugs patients are not in favour of taking
ANY Questions!
Evidence-based “deprescribing”

- Physician-pt individualized process
- Some specific recs, eg meds requiring slow taper

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<thead>
<tr>
<th>Med</th>
<th>Type</th>
<th>Clinical Sxms</th>
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<tbody>
<tr>
<td>α - block</td>
<td>Withdrawal(W), rebound (R)</td>
<td>HTN, palpitations, headache</td>
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<tr>
<td>Antianginal</td>
<td>Dz recrudescence (D)</td>
<td>angina</td>
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<tr>
<td>Anticonvulsant</td>
<td>W, D</td>
<td>Anxiety, depression, sz’s</td>
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<tr>
<td>Antidepressant</td>
<td>W, D</td>
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<td>Anticholinergics</td>
<td>W</td>
<td>Anxiety, n/v, HA, dizziness</td>
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<tr>
<td>Baclofen</td>
<td>W,R</td>
<td>Agitation, anxiety, confusion, other</td>
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<tr>
<td>Benzodiazepines</td>
<td>W</td>
<td>Agitation, anxiety, delirium, other</td>
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<tr>
<td>β-block</td>
<td>W, D</td>
<td>Angina, anxiety, HTN, tachycardia</td>
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<tr>
<td>Digoxin or diuretic</td>
<td>D</td>
<td>CHF, palpitations, HTN</td>
</tr>
<tr>
<td>Opiates</td>
<td>W</td>
<td>Chills, anxiety, insomnia, anger, other</td>
</tr>
</tbody>
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PPI          R, D

Evid Based Med 2013;18(4):121
Simplifying Meds: The Polypill

• RCT 2000 pts w/multiple CV risk factors
  ➢ Fixed dose polypill: ASA 75mg, simvastatin 40mg, lisinopril 10mg, & atenolol 50% or hctz 12.5mg
  ➢ vs usual care

• Adherence at 15m: 86% vs 65%

• If poor adherence at entry: 77% vs 23%

• SBP & LDL better, no Δ in CV events or mortality

JAMA 2013;310:918
Screening Tool of Older Person’s Prescriptions

Cardiovascular System

1. Digoxin > 125µg/day w/impaired renal funx
2. Loop diuretic for dependent ankle edema only i.e. no clinical signs of heart failure
3. Loop diuretic as 1st line mono-tx of HTN
4. Thiazide diuretic w/hx of gout
5. Non-cardioselective β-blocker w/COPD
6. Beta-blocker in combination w/verapamil
7. Diltiazem or verapamil w/NYHA Class III or IV CHF
Screening Tool of Older Person’s Prescriptions

Cardiovascular System

8. Calcium channel blockers w/chronic constipation
9. Use of aspirin & warfarin combi w/o H2 block or PPI
10. Dipyridamole as mono-tx for CV 2^0 prevention
11. ASA w/hx of PUD w/o H2 block or PPI
12. ASA dose > 150mg day
13. ASA w/o hx coronary, cerebral or peripheral vascular symptoms or occlusive arterial event
14. ASA to treat dizziness not clearly d/t CVD
Screening Tool of Older Person’s Prescriptions

Cardiovascular System

15. Warfarin for 1st DVT for > 6 months duration
16. Warfarin for 1st first uncomplicated PE > 12 months
17. Aspirin, clopidogrel, dipyridamole or warfarin with concurrent bleeding disorder (*high risk of bleeding*).

---- and that’s just the CV system

- CNS and psychotropics drugs, GI, respiratory, endo, GU, MSK, Falls, analgesics each have their own lists
STOPP/START

Screening Tool to Alert Drs to Right Treatment

Cardiovascular: should rx/tx ---
1. Warfarin w/Afib w/o contraindication
2. ASA w/Afib where warfarin contraindicated
3. ASA or clopidigrel w/hx CAD, CVD or PVD
4. HTN hx w/SBP > 160 & tx not contraindicated
5. Statin tx pts w/ CAD, CVD, PVD & life expectancy > 5 yrs and funx = I in ADLs
6. ACE-I w/CHF w/o contraindication
7. B-block w/chronic stable angina w/o contraindication
Stopping Medications: More Gray Zones

Duration of OP tx, if/when to d/c?

- Concerns re: long duration bisphosphonate rx
  - ONJ
  - Atypical femur fractures
  - Atrial Fibrillation
  - Esophageal CA

- How long is long enough in the elderly?
Stopping Drugs in the Elderly Gray Zone: Time to loss of benefit

FLEX Trial: RCT alendronate x 5 yr then 5 yr f/u w/continued rx vs placebo: Bone Density Δs

Bone density slowly ↓ off rx in average risk pts

*JAMA.* 2006;296(24):2927
Stopping Drugs in the Elderly
Gray Zones: Time to loss of benefit

FLEX Trial: Fx rate Δs in *average* risk pts

Non-vert fx unchanged

Vert fx rate ↓ by 55%

*JAMA.* 2006;296(24):2927
Stopping Medications: More Grey Zones
Duration of OP tx, if/when to d/c?

- Tx 3-5 yrs *low-average* risk pts before consider d/c
- Higher risk pts (eg hx fx, very low T-score < -3.5, falls, steroids, ↑ age) may benefit from continued tx
- Extension trials not powered for fx Δs, post-hoc analyses, lower risk pts, other limitations
- Consider d/c if on rx 5+ yrs and expected survival < 5 yrs? (age ~ 90 W, age ~ 85 M)

*N Engl J Med* 2012;366(22):2048
Osteoporosis Tx Addendum

• Undertreatment also a problem in elderly

• Fragility fx = osteoporosis dx → tx indicated

• 60K Medicare pts w/fragility fx (2006-10)
  ➢ Mean age 81, 90% white women
  ➢ 40% hip fx, remainder humeral & wrist fx’s
  ➢ At 6 m < 20% received tx
  ➢ We appear to be substantially undertreating

Initiating Tx Grey Zones: Time to benefit

- 92 yo healthy robust F, falls w/hip fx → THA
  - Fully recovers, asks about OP tx
  - FRAX 10 yr risk: 31% major fx, 16% hip fx

- Bisphosphonates (or Prolia) ↓ risk by 50%

- Would you treat this pt with rx beyond Ca/Vit D and fall prevention strategies?
Initiating Tx: Time to Benefit Issue

Time Horizon to Benefit

% event-free

What is the benefit?

TIME

Is there a wide variation in time to benefit, or by subgroups?

Is the effect statistically and/or clinically significant?
Osteoporosis Tx: Time to benefit
10 yr Hip Fx risk 16%, 5 yr risk 8%

Time to benefit
9 - 18 months

Exptected survival 5 yrs

50% RR: 8% → 4%
ARR 4%/5yrs
## Life Expectancy at Selected Ages

U.S. Census Bureau, Statistical Abstract of U.S. 2012

<table>
<thead>
<tr>
<th>Age</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>65</td>
<td>17.2</td>
<td>19.9</td>
</tr>
<tr>
<td>70</td>
<td>13.7</td>
<td>16.0</td>
</tr>
<tr>
<td>75</td>
<td>10.6</td>
<td>12.5</td>
</tr>
<tr>
<td>80</td>
<td>7.8</td>
<td>9.4</td>
</tr>
<tr>
<td>85</td>
<td>5.8</td>
<td>6.8</td>
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<tr>
<td>90</td>
<td>4.1</td>
<td>4.8</td>
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<tr>
<td>95</td>
<td>2.9</td>
<td>3.3</td>
</tr>
<tr>
<td>100</td>
<td>2.1</td>
<td>2.3</td>
</tr>
</tbody>
</table>
Welcome to ePrognosis.org!

Estimating Prognosis for Elders

Home

1. Where is the patient

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Time to benefit: What does UK do w/this data?

- “Tx is recommended in the majority of older women w/prior fx even if fx probability lies below tx threshold \( \bar{p} \) BMD measure”
- “These thresholds are for guidance only & the final decision to initiate therapeutic intervention lies w/the individual clinician”

National Osteoporosis Guideline Group
<table>
<thead>
<tr>
<th>Table 2: AVOID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spironolactone &gt; 25mg/d</td>
</tr>
<tr>
<td>Antipsychotics (all)</td>
</tr>
<tr>
<td>Benzodiazepines (all)</td>
</tr>
</tbody>
</table>

# Medications and Risk of Delirium

<table>
<thead>
<tr>
<th>Drug Class</th>
<th>Relative Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticholinergic drugs</td>
<td>4.5-11.7</td>
</tr>
<tr>
<td>Sedative-hypnotics</td>
<td>3.0-11.7</td>
</tr>
<tr>
<td>Any antipsychotic</td>
<td>3.9</td>
</tr>
<tr>
<td>Narcotics</td>
<td>2.6</td>
</tr>
</tbody>
</table>

**Number Drugs**

- 2-3 rx	extsuperscript{es}  | 2.7           |
- 4-5 rx	extsuperscript{es}  | 9.3           |
- 6+ rx	extsuperscript{es}   | 13.7          |

*Am J Med 1999;106:565*
<table>
<thead>
<tr>
<th>Medication</th>
<th>Anti-Ach activity (ng/ml atropine eq)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Furosemide</td>
<td>0.22</td>
</tr>
<tr>
<td>Digoxin</td>
<td>0.25</td>
</tr>
<tr>
<td>Theophylline</td>
<td>0.44</td>
</tr>
<tr>
<td>Warfarin</td>
<td>0.12</td>
</tr>
<tr>
<td>Prednisolone</td>
<td>0.55</td>
</tr>
<tr>
<td>Nifedipine</td>
<td>0.22</td>
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<tr>
<td>Isosorbide</td>
<td>0.15</td>
</tr>
<tr>
<td>Codeine</td>
<td>0.11</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>0.22</td>
</tr>
</tbody>
</table>

Am J Psych 1992;149:1393
Before Prescribing New Med Consider:

• Is this medication necessary/non-pharm options?
• What are the therapeutic end points?
• Do the benefits outweigh the risks?
• Is it used to treat effects of another drug?
• Could it interact with diseases, other drugs?
• Consider compliance and cost challenges
• Does patient know what it’s for, how to take it, and what ADEs to look for?
Osteoporosis

50% reduction in risk of fracture over a 3 year period
1.2% absolute risk reduction for fractures in 3 years

Median life expectancy: 2.7 - 4.7 years

Time to benefit: 9 to 18 mos

*Benefits possibly similar in men, but data is extrapolated from studies of women

Prevention of osteoporotic fracture

National Osteoporosis Foundation. Clinician’s guide to prevention and treatment of osteoporosis, 2009