Using Medications in the Elderly

A Rational, Evidence-Informed Approach with a Touch of Common Sense

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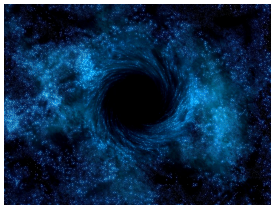
No approach is wrong,but few are likely right

AGE 40 50 60 70 80 90

RISKS (Heart attacks/strokes/fractures) go up

THEORETICAL BENEFIT GOES UP

THE EVIDENCE GOES INTO A BLACK HOLE



SYMPTOMS (pain, cognition, disability etc) INCREASE

BENEFITS FROM TREATMENTS STAY THE SAME?

ABILITY TO ELIMINATE MEDICATIONS GOES DOWN

SIDE EFFECTS FROM MULTIPLE MEDICATIONS GOES UP

PATIENT AND FAMILY VALUES

THE INEVITABLE

POLYPHARMACY

does NOT= >5 meds

It means taking medications/supplements which

For symptoms

are not providing a complete or clinically important effect or are given at doses larger than is required to achieve that effect

For prevention

if one was fully informed by the best available evidence about benefits and harms one would not take them

Poly-Problems

Problem: Age ≥65 = mean 6 chronic conditions[2]

Chronic pain, osteoarthritis, diabetes, hypertension, insomnia, constipation, COPD, incontinence, etc

And we have medicines for them all!

2) *Ann Fam Med* 2005;3:223-228. MJA 2008; 189 (2): 72-77

Two opposite & effective solutions

Studies promoting adherence in elderly

- Systematic Review of 8 studies, 4 found benefit[1]
- RCT: Pharmacists telephone to age 71 to ≥5 drugs
  - Reduced mortality (NNT 16)[2]

Studies promoting medication withdrawal[3-5]

- Stopped 3-4 drugs: BP meds, benzo, antipsychotics, statin, antidepressants, H2 blocker, etc.
- Death 21% (vs 45%) & hospitalization 12% (vs 30%)[3]

1).Drugs Aging 2008; 25(4): 307-324. 2) BMJ. 2006 Sep 9;333(7567):522. 3) Isr Med Assoc J. 2007;9(6): 430-4. 4) Lancet Neurology; 8(2): 151-7. 5) Arch Intern Med. 2010;170(18):1648-54

Cooks in the Kitchen

Each additional prescriber is associated with 29% increase in Adverse Drug Reactions

If your patient sees someone else, Take a good drug history.

Am J Geriatr Pharmacother. 2007 Mar;5(1):31-9.

Criteria for Drug Use in Elderly

Beers: 12 experts.[1] Updated in 2003.

>10 types[2]: Beers, STOPP, START, Canadian Criteria, IPET, French Consensus, Australian Prescribing indicator, Japanese Beers, NORGEP, & Italian, + Drug Burden Index (DBI)[3], + PRISCUS[4]

All are consensus based

Overlap as little as 30%

1) Arch Intern Med. 2003;163:2716-2724. 2) Pharmacother 2010;44:1968-75. 3) Arch Intern Med. 2007;167:781-787. 4) Dtsch Arztebl Int 2010; 107(31–32): 543–51

Guides to safe prescribing

Beers, the most popular: weak evidence[1]

- Assoc with hospitalization in community elderly
- No other consistent associations

Drug Burden Index (DBI)

- DBI assoc decreased physical function & falls[2]
- Beers not[3]

STOPP[5] may be better

- STOPP slightly better to predict ADE & hospitalization

1) Ann Pharmacother 2007;41:438-48. 2) Am J Med (2009) 122, 1142-1149. J Am Geriatr Soc. 2011 May; 59(5):875-80. 3) J Clin Pharmacol published online 2 February 2011 2) Ann Pharmacother 2010;44:1725-32. 5) *Age & Ageing* 2008; **37:** 673–79 *Arch Intern Med. 2011;171:1013-1019.*

Are these associations helpful?

Hospitalization for Drug-related Adverse Events

In people ≥65

- Half happened in ≥80
- 66% were unintentional overdoses

67% were:

warfarin (33%), insulins (14%), oral antiplatelet agents (13%), and oral hypoglycemic agents (11%)

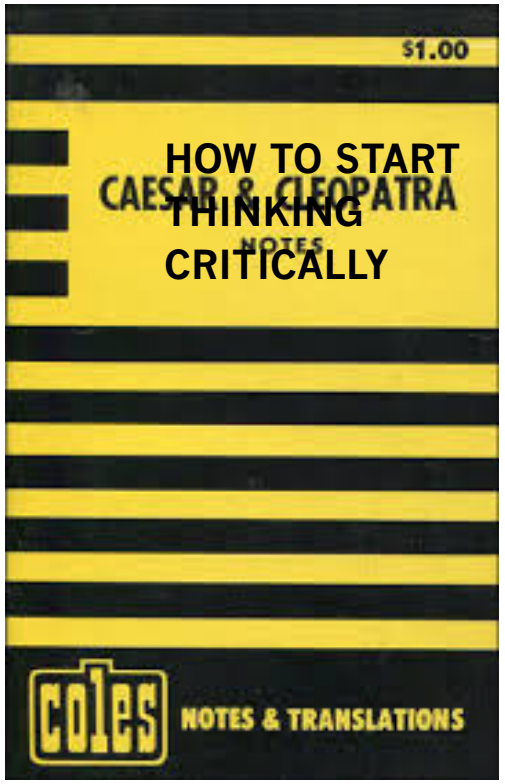
Prescribing rules (HEDIS, BEERS) would identify only 1-6% of the problems

N Engl J Med 2011;365:2002-12

When you do a Patient Medication History

UNTIL PROVEN OTHERWISE

The drug and the dose are wrong!!!!!!



Obtain a good drug history

Why are you on the “white one”?

It’s for my dizziness

How long have you been dizzy?

A while

How long’s a while?

Sometime now

Do you know when it started?

My sister’s birthday

When is your sister’s birthday?

Which sister?

Top Useless Meds in the Elderly

Any drug that was not started at the very lowest dose

- No hurry
- Most standard doses are excessive
- DON’T start with low doses
- Start with VERY low doses

Any drug you haven't re-eVALUated annually

"starting drugs is like the bliss of marriage, stopping them is like the agony of divorce"

Need

Dose

Duration

Guiltless choice

Any drug that doesn't make your patient, not you, feel better

primary prevention

1% benefit over 5 years - 99% do not

secondary prevention

5% benefit over 5 years - 95% do not

lab tests

false positives

witch hunt

evidence plus patient values - 1/3 not adherent

Studies of unsafe prescribing

- Mainly benzodiazepines, antidepressants, antipsychotics, anticholinergics, BP meds, etc.[1]
- Benzodiazepine in age ≥80 associated with falls
  - Perhaps 2.8% increase falls/yr (9% fatal)[2]
- Systematic Rev: 29 studies (28 cohort, 1 RCT)[3]
  - Mainly benzodiazepine, antidepressants, antipsychotics
  - Also BP meds & anti-epileptic (weaker association)
- Med associated with falls[4]
  - Consistent: Sedative/hypnotics, Benzodiazepines, & antidepressants
  - Less consistent: Neuroleptics/antipsychotics & anti-hypertension

1) Arch Intern Med. 2009;169(21):1952-1960. 2) Drugs Aging. 2008;25(1):61-70. 3) J Gerontol A Biol Sci Med Sci. 2007 Oct;62(10):1172-81. 4) Arch Intern Med. 2009;169(21):1952-1960

Studies of unsafe prescribing

Systematic review[1]: meds associated with fracture

1.34 (1.24, 1.45) for benzodiazepines (23 studies),

1.60 (1.38, 1.86) for antidepressants (16 studies),

1.54 (1.24,1.93) for antiepileptic drugs (13 studies)

1.59 (1.27, 1.98) for antipsychotics (12 studies)

1.38 (1.15, 1.66) for opioids (six studies).

NSAIDS may also be associated with falls.[2]

1) Drug Safety 2007; 30 (2): 171-184. 2) Drug Safety 2009; 32(6): 489-98.

Risk …

Risk markers - associated with a bad outcome

Risk factors - modifiable?

Risky behaviors - smoking, nutrition, activity

Risk of disease - CVD, MI, strokes, fractures

Risk of treatment - harms, costs

Risk of over diagnosis - inconvenience, labelling, worry

Risk Factors versus Clinical Endpoints

"a risk factor/marker is a variable associated with an increased risk of disease"

Not As Important	Very Important
blood pressure	symptoms/exacerbations
cholesterol	heart attacks
glucose/diabetes	strokes
bone density	heart failure
heart rate	death
CRP	dialysis
proteinuria	amputation
family history	fractures
age	blindness
gender	revascularization
race	angina
FEV1	TIAs

Evidence-based risk communication

"There is likely no single best method of communicating probabilities to patients but rather several good options with some better suited to certain risk scenarios."

Ann Intern Med 2014;161:270-80

Bone density/fractures

Testing for Osteoporosis

True. Study of risk factors to predict osteoporosis

An index on age and weight ≥ other published indices

4 systematic reviews from 2007-2010, with 36 studies & 72,315 women supported the findings[1-4]

Age - Weight (kg), If > -10, increased risk of osteoporosis and BMD is warranted

60 yrs – 60kg = 0 High Risk

60 yrs – 100kg = -40 Low Risk

#44. "Screening for Osteoporosis": http://www.acfp.ca/whatwedo/toolsforpractice.aspx

Does your patient have osteoporosis?

(Osteoporosis Self-assessment Tool)

Age – weight (kg) = ????

CHANCE OF OSTEOPOROSIS

> 20 – approx 50-60%

0-20 – approx 15-20%

<0 – less than 5%

An example
60 years old
130 lbs = 60 kg
Score = 0

Valid in men as well

Mayo Clin Proc 2003;78:723-7

Mayo Clin Proc. 2002;77:629-637
The Singapore Family Physician Jul-Sep 2003;29:12
MOH Osteoporosis clinical practice guidelines - Singapore Mar 2002

Simple is better

"Simple models based on age and BMD alone or age and fracture history alone predicted 10-year risk of hip, major osteoporotic, and clinical fracture as well as more complex FRAX models"

Arch Intern Med 2009;169:2087-94

10 year fracture risk %

Major osteoporotic fracture (clinical spine, forearm, hip or shoulder fracture)/Hip

RISK FACTORS	Zero				One				Two			
BMI	35	30	25	20	35	30	25	20	35	30	25	20
Female												
50	2	3	3	3	4	4	5	5	6	6	7	8/1
60	5	6	6	7/2	7	9	10/1	10/4	11/1	13/2	14/2	16/6
70	8/1	9/2	10/2	11/4	11/2	13/3	15/4	17/7	16/4	18/6	21/7	25/12
80	14/4	16/5	19/7	21/11	20/8	23/10	27/13	31/20	28/14	33/18	38/22	43/32
Male												
50	2	2	2	2	3	3	4	4	4	5	6	6
60	3	4	4	4	5	6	6	7/1	7	8	10/1	10/2
70	4	5/1	6/1	6/2	6	7	8/2	9/4	8	10	12/4	13/6
80	6/2	7/3	9/4	9/5	9/4	11/5	13/7	14/10	13/7	16/9	19/12	21/16

Risk factors - Previous fracture “atraumatic”, Parent hip fracture, Smoker, Rheumatoid arthritis, Glucocorticoids - now or more than 3 months, >3 drinks a day

FRAX® WHO Fracture Risk Assessment Tool

10 year fracture risk %

Major osteoporotic fracture (clinical spine, forearm, hip or shoulder fracture)/Hip

RISK FACTORS	Zero			One			Two		
t-score	-1.5	-2.5	-3.5	-1.5	-2.5	-3.5	-1.5	-2.5	-3.5
Female									
50	4	5/1	9/4	6	8/2	14/7	8	12/3	21/11
60	7	10/2	16/6	10/1	14/3	23/9	14/1	20/5	32/14
70	9/1	13/3	21/7	12/1	18/4	30/11	16/2	25/6	41/16
80	13/3	18/6	29/14	17/6	26/12	40/24	24/10	35/20	52/37
Male									
50	4	5/2	11/6	5	8/3	16/10	8/1	12/5	24/16
60	6/1	9/3	15/8	8/1	12/4	21/11	12/2	18/6	29/17
70	6/2	10/4	16/8	9/3	14/6	22/13	12/4	19/10	31/20
80	7/3	11/5	16/9	11/5	16/9	23/16	15/9	22/15	32/25

Risk factors - Previous fracture “atraumatic”, Parent hip fracture, Smoker, Rheumatoid arthritis, Glucocorticoids - now or more than 3 months, >3 drinks a day

FRAX® WHO Fracture Risk Assessment Tool

Absolute (and relative) benefits of Bisphosphonate therapy over 5 years

~30% reduction in risk

	Vertebral Fractures		Non-Vertebral		Hip Fracture	
	1º	2º	1º	2º	1º	2º
Alendronate[1]	2% (45%)	6% (45%)	ns	2% (23%)	ns	1% (53%)
Risedronate[2]	ns	5% (39%)	ns	2% (20%)	ns	1% (26%)
Etidronate[3]	ns	5% (47%)	ns	ns	ns	ns

1) Cochrane 2008; 1: CD001155. 2) Cochrane 2008; 1: CD004523. 3) *Cochrane Database Syst Rev. 2008(1):003376.*

• Osteoporosis Drugs Benefit - 2-3 years •

RELATIVE BENEFITS	FRACTURE RISK REDUCTION*		
	Vertebral	Non-vertebral	Hip
Bisphosphonates**	~ 50%	~ 20%	~40%
Raloxifene	~ 40%	NS	NS
Teriparatide	~ 70%	~ 40%	NS
Vitamin D usually with calcium	~15-25%	~15-25%	~15-30%
Denosumab	~ 70%	~ 20%	~40%
Strontium	~40%	~ 15%	NS
ALL DRUGS	~50%	~20%	~25%

ABSOLUTE BENEFITS	FRACTURE RISK REDUCTION*		
	Vertebral	Non-vertebral	Hip
Bisphosphonates**	~4-8%	~2%	~0.5-1%
Raloxifene	~4%	NS	NS
Teriparatide	~10%	~4%	NS
Vitamin D usually with calcium	1-2%	1-2%	~1%
Denosumab	~5%	~2%	~0.5%
Strontium	~8%	~2%	NS
ALL DRUGS	~5%	~2%	~0.5%

*~ 90% of the studies enrolled patients with a history of fractures with the exception of the VitaminD/calcium studies where this was ~ 50%
** etidronate has only been shown to reduce vertebral fractures in secondary prevention

Retesting BMD

When do you retest her BMD

We say: Not for at least 3 years

True,

- Alendronate yearly increase = variation in BMD
- Variation in BMD= 2.4% to 5% (over 2 weeks)
- Alendronate “sufficient” BMD for 97.5% after 3 yrs
- However, if no change[2] or even decreased BMD[3] still reduced fracture risk.

Can Fam Physician. 2010 Dec;56(12):1299.

Stopping therapy

A 65 year old woman on Alendronate 5 years is asking if any meds can be stopped?

We say: You can stop Alendronate

True: (FIT & Horizon Trials) Continue or Stop Alendronate (after 5 yrs) or Zoledronic (3yrs)

- No effect fractures1,2
- 2 Weaker studies show the same thing3

FDA requires label that duration unknown

1) JAMA 2006;296:2927-2938. 2) J Bone Min Res 2011; Oct 25. DOI 10.1002/jbmr.1494
3) NEJM 2004;350:1189-99 Osteoporos Int 2008;19:365-72. 4) NEJM 2012; 366:2048-51

What you should shoot for

Start with really low doses

No hurry

Surrogate markers

Is the benefit because of the effect on the surrogate?

Don't measure obsessively

The most benefit is getting them from really HIGH,
not getting to really low

Target Doses

If you can get them to the doses in the studies
GREAT but don't sweat it nor let your patients sweat it

75% of side effects are dose-related

Side effects are unacceptable

Guidelines and the Law

"As per the Canadian Medical Association Handbook on Clinical Practice Guidelines, guidelines should NOT be used as a legal resource in malpractice cases as "their more general nature renders them insensitive to the particular circumstances of the individual cases."

CJD
Canadian Journal of Diabetes
A Publication of the Professional Sections of the Canadian Diabetes Association
Une publication des sections professionnelles de l'Association canadienne du diabète
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It's a dose thing

"more than 80% of ADRs causing admission or occurring in hospital ... are dose related, an 'accentuation' of the known pharmacological effect of the drug, and thus predictable and potentially avoidable"

Br J Clin Pharmacol 2004; 57:121–6

Issues to Consider

Symptoms - many clinical trials show a placebo group response of 20-30%

Disease states fluctuate

Prevention - patients believe “prevention” drugs produce a 70% absolute benefit over 5 years Clin Med 2002;2:527-33 when at most only ~ 20% could benefit over a lifetime

The frequency and dose used for many drugs is often way too much

Practical issues/ suggestions for cutting doses

1) Start with half of the lowest marketed dose for older established products
2) For newly marketed medications start with a half or even a quarter of the lowest available dose
3) Need a discussion with the patient
4) Dosage forms - pill cutters, capsules, liquid
5) Increase interval if can't decrease dose