

Content

- Definition of “Inappropriate Prescribing” and “Polypharmacy”
- Review on Drug Utilization Review Tools
- Review on interventions for inappropriate prescribing
- 10 steps to avoid inappropriate prescribing and polypharmacy with an case illustration

Polypharmacy

- “The administration of more medications than are clinically indicated, representing unnecessary drug use”
- The concomitant ingestion of 5 or more medications
- Common
- Increase risk of drug-drug, & drug-disease interactions
- Increase risk of adverse drug reactions (ADR), geriatric syndromes
- Decrease compliance with medications
- Increase costs
- Associated with use of inappropriate medications

Inappropriate Prescribing

“Medications or medication classes that should generally be avoided in person 65 years or older because they are either ineffective or they pose unnecessarily high risk for older persons and a safer alternative is available”

Beers. Arch Int Med 1991

Principles of
“Appropriateness” of
prescribing for older adults:

- Suitable indication
- Effective
- Dosage adjustments on the basis of PK and PD changes
- Duration
- Unnecessary duplication
- Low risk of adverse consequences

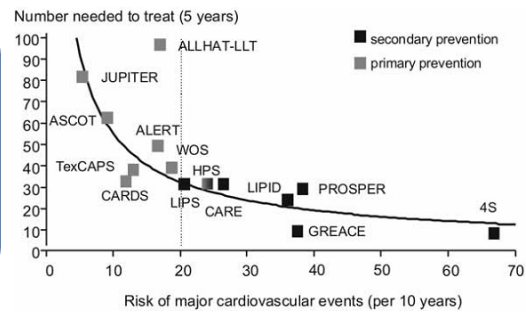
Talerico KA. J Am Geriatr Soc 2002

Will you prescribe statins to a man aged 75 y for primary prevention of CVD?

Review of 14 prospective studies:
Statin lowered the incidence rates of deaths from

- All cause (-17%)
- Heart attack (-28%)
- Stroke (-22%)

Taylor F, et al. The Cochrane Library. 2011; 1-72.



NCEP

0-1 risk factors,
aim LDL-C at <4.2 mmol/L

When the CVD risk is more than 20% in 10 years, the benefits of statins are probably greater than the potential short-term risks.


Grammer TB, Maerz W. Int Journal of Clinical Pharmacology and Therapeutics. 2011; 49: 293-6

Is it appropriate to prescribe statin to a 70-year-old man with LDL-C 5 mmol/L and inoperable lung cancer?

Probably not.

The patient may not survive 10 years later.

Is it appropriate to prescribe statin to a 70-year-old man with LDL-C 5 mmol/L and early prostate cancer?



**65% of patients in the Specialist Out-patient clinic had polypharmacy.
10.8% were taking 10 or more medications.
30.3% patients were taking at least 1 PIM.**
Lam PY, et al. JAGS 2010; 58: 203-4

Perhaps you should not ask “when to avoid polypharmacy and inappropriate prescription?”

But “How to avoid?”

Drug Utilization Review Tools – Explicit tools

Authors	Year	Patient age	Criteria	Limits
Beers et al.	1989	NHR ≥ 65 y	Avoid 19 drugs Not to exceed 11 drug doses, frequencies or durations	-Drugs NA in other countries -Did not address: underuse, duplicate, dd interactions
Beers	1997	All elderly ≥ 65 y	28 drugs or classes of drugs (independent dx) 35 drugs or classes of drugs (15 diseases)	~
Fick et al.	2002	All elderly ≥ 65 y	48 drugs or classes of drugs (20 diseases or conditions)	~
Naugler et al.	1997	All elderly ≥ 70 y	Improving Prescribing in the Elderly Tool (IPET) 14 drug-disease Interactions	-Obsolete criteria (for example: β-blockers in patients with CHF -to be evaluated
Gallagher et al.	2006	All elderly ≥ 65 y	65 criteria STOPP list 22 criteria START list	To be evaluated in clinical studies

Drug Utilization Review Tools – Implicit tool

Table 1. Medication Appropriateness Index*

To assess the appropriateness of the drug, please answer the following questions and circle the applicable score:

1. Is there an indication for the drug? Comments:	1 Indicated	2	3 Not Indicated	9 DK†	
2. Is the medication effective for the condition? Comments:	1 Effective	2	3 Ineffective	9 DK	-Indication
3. Is the dosage correct? Comments:	1 Correct	2	3 Incorrect	9 DK	-Effectiveness -Geri dosing
4. Are the directions correct? Comments:	1 Correct	2	3 Incorrect	9 DK	-Tx duration -Duplication
5. Are the directions practical? Comments:	1 Practical	2	3 Impractical	9 DK	-Risk
6. Are there clinically significant drug-drug interactions? Comments:	1 Insignificant	2	3 Significant	9 DK	Clinical judgment
7. Are there clinically significant drug-disease/condition interactions? Comments:	1 Insignificant	2	3 Significant	9 DK	10 min / drug ax
8. Is there unnecessary duplication with other drug(s)? Comments:	1 Necessary	2	3 Unnecessary	9 DK	Evaluation on ADR
9. Is the duration of therapy acceptable? Comments:	1 Acceptable	2	3 Unacceptable	9 DK	Hanlon JT J Clin Epidemiol 1992
10. Is this drug the least expensive alternative compared to others of equal utility? Comments:	1 Least expensive	2	3 Most expensive	9 DK	

Potentially Inappropriate Medication Use in Older Adults (Regardless of diseases)

Drug class	Drug examples	Recommendation	Quality of Evidence	Strength of Recommendation
1 st G antihistamine	Hydroxyzine Promethazine	Avoid	high	Strong
Antiparkinson	Benzotropine	Avoid	Moderate	Strong
Antispasmodics	Hyoscyamine	Avoid except in palliative care	Moderate	Strong
Antithrombotics	Dipyridamole (short acting), Ticlopidine	Avoid	Moderate	Strong
Anti-infective	Nitrofurantoin	Avoid	Moderate	Strong
Alpha1 blockers	Prazosin, Doxazosin Terazosin	Avoid use as an antihypertensive	Moderate	Strong
Antiarrhythmics	Digoxin >0.125 mg/d	Avoid	Moderate	Strong

The AGS 2012 Beers Criteria Update Expert Panel

Potentially Inappropriate Medication Use in Older Adults Due to Drug-Dis or Drug-Sx Interactions (Exacerbate Dis or Sx)			
Dis or Sx	Drug examples	Recommendation	Strength of Recommendation
Heart failure	NSAIDs & COX-2 inh CCBs Pioglitazone, rosiglitazone Cilostazol Dronedarone	Avoid	Strong
Delirium	All TCAs Anticholinergics BZDs Corticosteroids H2-receptor antagonist Thioridazine	Avoid	Strong
Hx of falls or fractures	Anticonvulsants Antipsychotics BZDs / non-BZDs analogs TCAs & SSRIs	Avoid	Strong
The AGS 2012 Beers Criteria Update Expert Panel			

Potentially Inappropriate Medications to Be Used with Caution in Older Adults			
Drug	Rationale	Recommendation	Strength of Recommendation
Aspirin for primary prevention of cardiac events	Lack of evidence of benefit versus risk in individuals aged 80	Use with caution in adults aged 80	Weak
Dabigatran	Greater risk of bleeding than with warfarin in adults aged 75; lack of evidence for efficacy and safety in individuals with CrCl < 30 mL/min	Use with caution in adults aged 75 or if CrCl < 30 mL/min	Weak
Antipsychotics 3C SSRI, SNRI TCA Vincristine	May exacerbate hypoNa or SIADH	Use with caution	Strong
The AGS 2012 Beers Criteria Update Expert Panel			

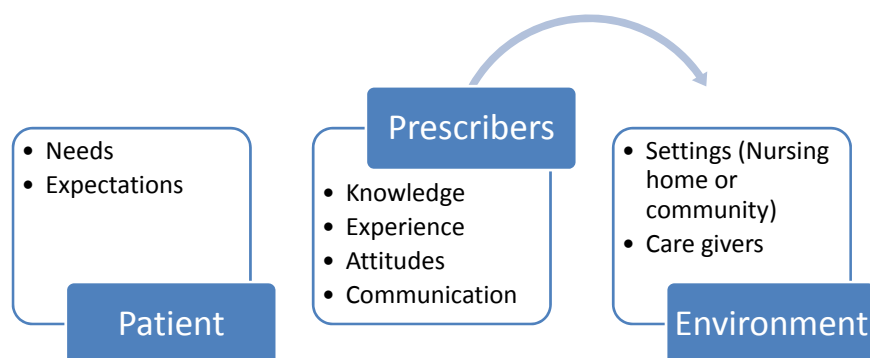
An ideal tool for detecting Potentially Inappropriate Medications

- Simple application, not time consuming
- Applicable in different settings, or countries
- Address over-, under-, mis-prescribing, drug-drug interactions, drug-dis interactions
- Associate with adverse outcomes
- Integrate into the electronic health record
- Feedback on a lists of drugs to avoid based on the patient's conditions, or suggest on alternative medications
- Updatable database

Fick DM, Semla TP. J Am Geriatr Soc 2012

Approach to avoid inappropriate prescribing and polypharmacy

Prescribing = patient x prescribers x environment



Spinewine A, et al. Lancet 2007; 370: 173-84

Settings	No.	Interventions	Results
Educational approaches			
Pimlott et al. Ambulatory care	372 family doctors	Mailed prescribing feedback and educational materials on prescription of bzd	Absolute reduction of 0.7% in prescribing of long-acting bzd intervention group
Computerised decision support systems			
Tamblyn et al. ambulatory care	107 family doctors	Computerised decision support system	Lower prescription of new PIM in the intervention group (RR 0.82)
Clinical pharmacy			
Hanlon et al. Medicine clinic	208 patients	Drug review and written drug therapy recommendations for drs	Decrease in PIM in intervention group at 3 month (24% vs 6%) and 12 months (28% vs 5%)
Geriatric medicine services			
Coleman et al. 9 primary care physician practices	169 patients	Chronic care visit with geriatrician, nurse, and pharmacist	No significant difference in PIM at 12 mon or 24 mon No difference in geriatric sx
Multidisciplinary approaches			
Allard et al. Ambulatory care	266 patients	Drug review by an interdisciplinary team	Decrease no. of PIM by 0.24 in intervention group, and by 0.15 in control group

A Case Example

- 81 yr lady, admitted to hospital with an exacerbation of CHF attributed to non-adherence with diuretic medications
- HT, IHD, old MI, CHF, chronic AF, Parkinson's disease, osteoporosis, Colles' fracture, osteoarthritis, T2DM with past episodes of hypoglycaemia, mild renal impairment, cognitive impairment, and GERD
- Walked with frame, BADL independent, frequent falls. She lived with her daughter.
- BP 110/60 mmHg, pulse rate 60/min
- Cr = 130 $\mu\text{mol/L}$, eGFR = 35 mL/min/m², HbA1c = 6.7%, EF = 30%, BMD (z score) = -1

Scott IA, et al. The American Journal of Medicine 2012; 125: 529-37

A Case Example

- Carvediolol 12.5 mg bd
- Perindopril 5 mg om
- Frusemide 80 mg om
- Spironolactone 12.5 mg om
- Amlodipine 5 mg om
- Isosorbide dinitrate 60 mg om
- Digoxin 62.5 µg om
- Warfarin 3 mg om
- Pravastatin 40 mg nocte
- Gliclazide 80 mg bd
- Carbidopa/benserazide 100/25 mg tds
- Donepezil 10 mg nocte
- Sertraline 150 mg om
- Alendronate 75 mg weekly
- Cholecalciferol 1000 units om
- Calcium carbonate 600 mg om
- Omeprazole 20 mg bd
- Paracetamol-codeine 1 tab tds
- Lactulose 10 ml bd

Scott IA, et al. The American Journal of Medicine 2012; 125: 529-37

Minimising Inappropriate Medications in Older Adults: A 10-step Conceptual Framework

Framework Step

1. Ascertain current drug use

Operational Strategies

- Ask the patient to disclose all medications she is taking
- Apply the “brown paper bag” method of ascertainment
- Seek collateral information on adherence, side effects, out-of-pocket expenses, and administration burden from family, caregivers and prescribing primary care doctors

Scott IA, et al. The American Journal of Medicine 2012; 125: 529-37

Minimising Inappropriate Medications in Older Adults: A 10-step Conceptual Framework

Framework Step

2. Identify patients at high risk of or experiencing ADRs

Her risk of a major ADR over the next 6 months ~ 30%

Operational Strategies

Table 2. Variables Included in the Score^a

Variable	OR (95% CI)	Points
≥4 Comorbid conditions	1.31 (1.04-1.64)	1
Heart failure	1.79 (1.39-2.30)	1
Liver disease	1.36 (1.06-1.74)	1
No. of drugs		
≤5	1 [Reference]	0
5-7	1.90 (1.35-2.68)	1
≥8	4.07 (2.93-5.65)	4
Previous ADR	2.41 (1.79-3.23)	2
Renal failure ^b	1.21 (0.96-1.51)	1

Onder GO, et al. Development and validation of a score to assess risk of ADR among in-hospital patients 65 years or older. Arch Intern Med 2010; 170:1142-8

Minimising Inappropriate Medications in Older Adults: A 10-step Conceptual Framework

Framework Step

3. Estimate life expectancy

The median survival for this patient is 2 years 4 months.

Operational Strategies

Table 3. Risk Factors Associated with Mortality in Multivariable Analysis and Associated Point Scores

Risk Factor	Hazard Ratio (95% Confidence Interval)	Estimated Points
Male	1.4 (1.2-1.6)	2
Age		
75-79	1.3 (1.1-1.7)	2
80-84	1.6 (1.3-1.9)	2
≥85	1.8 (1.5-2.1)	3
Dependence in toileting	1.3 (1.1-1.5)	1
Dressing		
Partially dependent	1.2 (1.0-1.4)	1
Fully dependent	1.6 (1.3-2.1)	3
Malignant neoplasm	1.6 (1.3-1.9)	2
Congestive heart failure	1.7 (1.5-2.0)	3
Chronic obstructive pulmonary disease	1.3 (1.1-1.6)	1
Renal failure or insufficiency	1.6 (1.3-2.1)	3

Carey EC, et al. Prediction of mortality in community-living frail elderly people with LTC needs. J Am Geriatr Soc 2008; 56:68-75

Minimising Inappropriate Medications in Older Adults: A 10-step Conceptual Framework

Framework Step

4. Define care goals in reference to life expectancy , level of fx incapacity and QOL, and patient/caregiver priorities

Operational Strategies

- Both the patient and her daughter demanded for pain relief and the continued ability to perform BADL as priorities of mx
- Both agreed a reduction of the no. of drugs and the burden of monitoring of INR

Minimising Inappropriate Medications in Older Adults: A 10-step Conceptual Framework

Framework Step

5. Define and confirm existent indications for ongoing tx with reference to defined care goals

Operational Strategies

- Ascertain the disease diagnoses
- Assess the disease severities
- The diagnoses of depression, Parkinson's disease, osteoporosis were in doubt.
- She did not have angina.
- She had depression during the death of her husband in the past.

Minimising Inappropriate Medications in Older Adults: A 10-step Conceptual Framework

Framework Step

6. Determine time until benefit for preventive disease-specific medications

Operational Strategies

- Event prevention is not regarded as a care goal in this case.
- Based on investigation results, the risks of developing osteoporosis, recurrent MI, and ESRF in 2 years are low.

Minimising Inappropriate Medications in Older Adults: A 10-step Conceptual Framework

Framework Step

7. Determine disease-specific benefit-harm thresholds that may support treatment discontinuation

Operational Strategies

- Benefit > harm:
 - CHF tx (ACEI, β -blocker)
- Benefit < harm:
- Indication not exist:
 - CHF tx (spironolactone, digoxin)
 - HT tx (amlodipine)
 - Anticoagulation (warfarin)
 - DM tx (gliclazide)
 - Dementia tx (donepezil)

Minimising Inappropriate Medications in Older Adults: A 10-step Conceptual Framework

Framework Step

8. Review the relative utility of individual drugs

Operational Strategies

Table 3 Proposed Classification of Drug Utility*

Class	Description
A	Clear-cut benefit with large absolute effect size with no or minimal toxicity for a given indication and few drug-drug and drug-disease interactions. Mortality and morbidity data for older populations consistent and favorable.
B	Proven efficacy in older patients but limited or inconsistent data on absolute effects or safety concerns relating to side effects or drug-drug and drug-disease interactions. Could be omitted in case of side effects or under pressure of > 5 class A drugs.
C	Questionable efficacy and safety profiles in older patients. Should be omitted if indications are in doubt, any side effects or clinically significant potential for interactions, or under pressure of > 5 class A drugs.
D	Avoid in older patients because likelihood of side effects or interactions outweighs realizable benefit in virtually all cases; delete first.

A: ACEI, β -blockers, vit D, omeprazole, paracetamol

B: Frusemide, warfarin

C: Spironolactone, pravastatin, gliclazide

D: Carbidopa-benserazide, isosorbide dinitrate, digoxin, alendronate, sertraline, donepezil

Wehling M. *J Am Geriatric Soc.* 2009; 57: 560-1

Minimising Inappropriate Medications in Older Adults: A 10-step Conceptual Framework

Framework Step

9. Identify drugs that may be discontinued or have their dosing modified

Operational Strategies

- Discontinue drugs of limited benefit or with significant potential for harm
 - spironolactone, digoxin, amlodipine, donepezil, carbidopa-benserazide, isosorbide dinitrate, alendronate, sertraline
- Discuss with the patient and/or care giver for drugs associated with both significant potential for benefit and harm, and set the treatment targets
 - Warfarin, gliclazide, ACEI, β -blocker, frusemide

Minimising Inappropriate Medications in Older Adults: A 10-step Conceptual Framework

Framework Step

10. Implement and monitor revised therapeutic plan with ongoing reappraisal of drug utility and patient adherence

Operational Strategies

- Stop immediately
 - digoxin, alendronate, pravastatin immediately
- Gradual weaning
 - spironolactone, isosorbide dinitrate, gliclazide, sertraline, donepezil, carbidopa-benserazide, codiene
- Drug regime adjustment
 - Change carvediolol to bisoprolol daily
 - Advise to put on frusemide in the mid day
- Liaise with care giver on working on medication adherence

Take Home Message

When Prescribing:

- Take into account the patient as a whole, including his or her life expectancy and quality of life within a social and economical context
- Select essential medications
- Avoid drugs with a poorer-benefit-to-risk ratio

Talerico KA. J Am Geriatr Soc 2002

The end

Thank you