polypharmacy



Dr.Chit Thet Aung

"As older patients move through time, often from physician to physician, they are at increasing risk of accumulating layer upon layer of drug therapy, as a reef accumulates layer upon layer of coral."

Jerry Avorn, MD

From Gurwitz J. Arch Intern Med Oct 11, 2004

Definition

- Strictly defined as the use of multiple medications
 - Threshold for the total number qualifying varies in the literature (2-10)

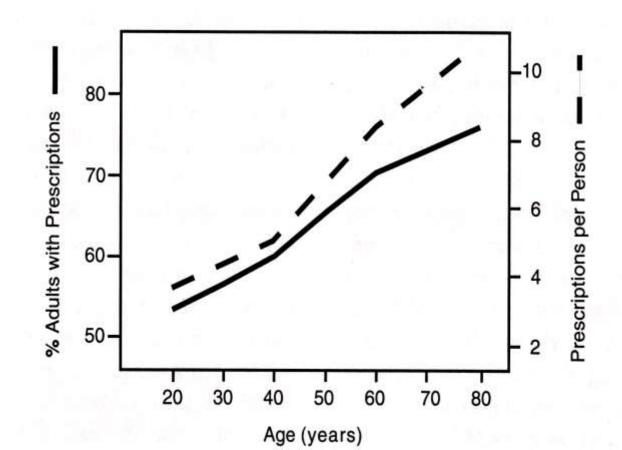


Definition

- ≥ 5 daily medications = 'Polypharmacy'
- ≥ 10 daily medications = 'Major Polypharmacy'



The percentage of population with prescriptions, and the number of medications per individual, increase with age.



Definition

 Comprehensively defined as the use of medications with duplicative indications, drug-drug interactions, diseasedrug interactions, in adequate attention to pharmacokinetic/ pharmacodynamic principles, and/or no indication

> Lee RD. *J Am Board Fam Pract*. 1998;11(2):140-144. Monane M, et al. *West J Med*. 1997;167:233-237.

Types of Polypharmacy

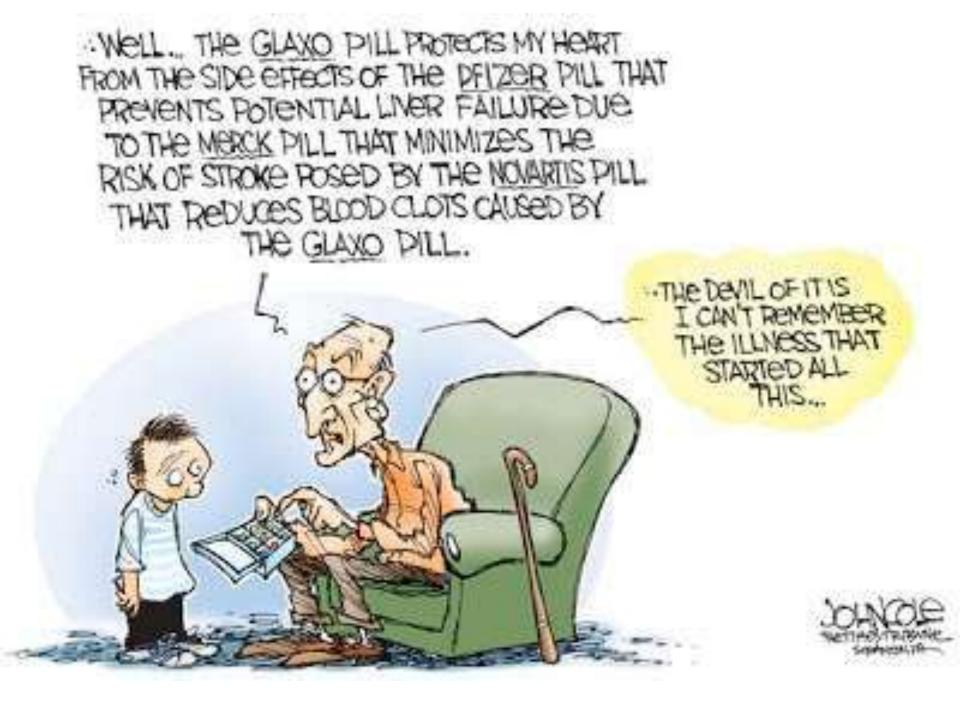
- 1. Same-Class Poly-pharmacy- Use of more than one medication from the same class (2 SSRI's).
- 2. **Multi-Class Poly-pharmacy** Use of more than one medication from different classes for the same symptom cluster (ACEI + CCBs).
- 3. Adjunctive Poly-pharmacy- Use of one medication to treat the side effects of another medication from a different class (Antibiotics+ Probiotics+Multivitamins).
- 4. Augmentation Poly-pharmacy- Use of one medication at a lower dose along with another medication from a different class in full therapeutic dose for the same symptom cluster.

Factors Contributing to Polypharmacy

- Increasing age
- Multiple symptoms
- Multiple medical problems
- Copious prescribing
- Multiple providers

Factors Contributing to Polypharmacy

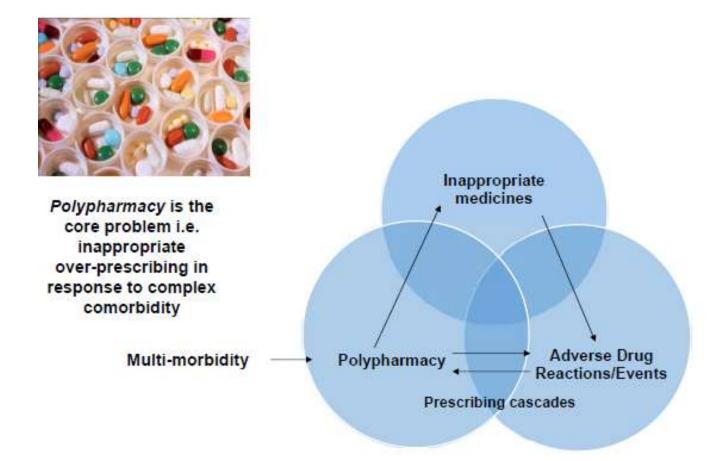
- Lack of primary care provider to coordinate
- Use of multiple pharmacies
- Drug regimen changes
- Hoarding of medications
- Self-treatment



Indicators of Polypharmacy

- Prescribing medications with no apparent indication
- Use of medications in same drug category
- Concurrent use of interacting medications
- Prescribing drugs contraindicated in the elderly
- Ordering inappropriate dosages
- Using a drug to treat an ADR
- Clinical improvement following discontinuation of medications

Unifying Theory/Concept



Consequences of Polypharmacy

- Increased healthcare costs
- Adverse drug events
- Drug interactions
- Medication Non-adherence
- Decreased functional status
- Geriatric Syndromes: Delirium, Falls, Urinary Incontinence

Age-Related Changes in the Elderly

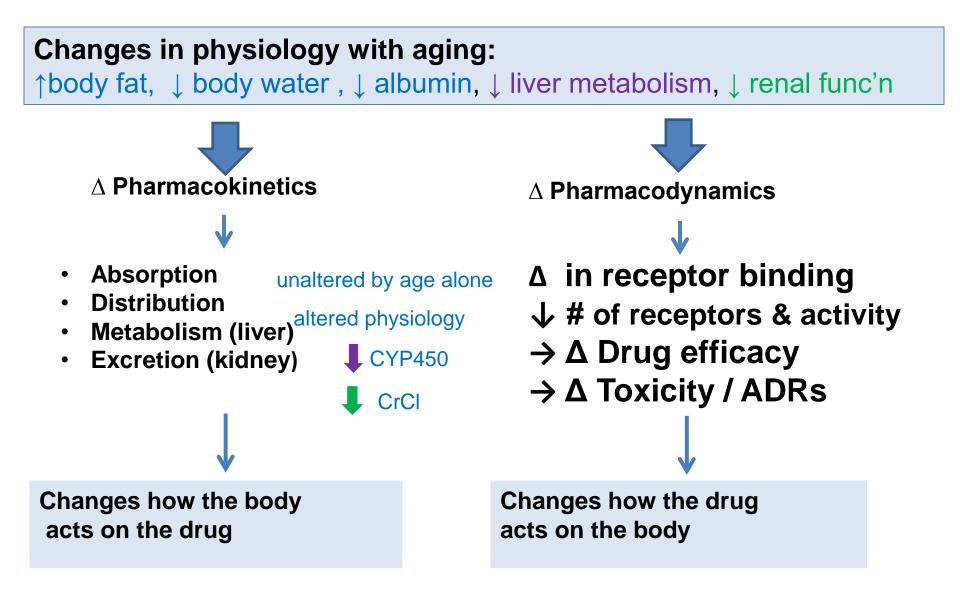
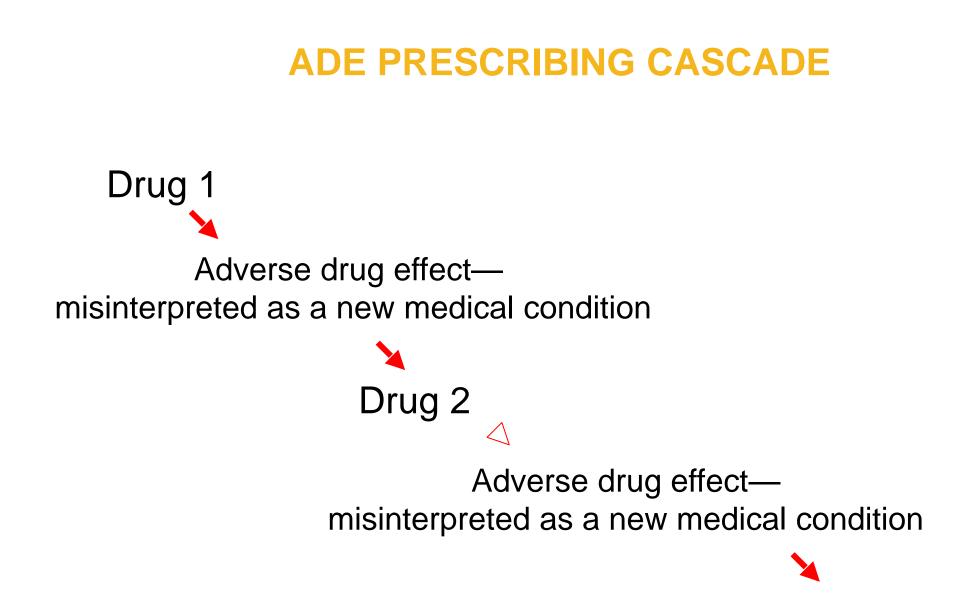
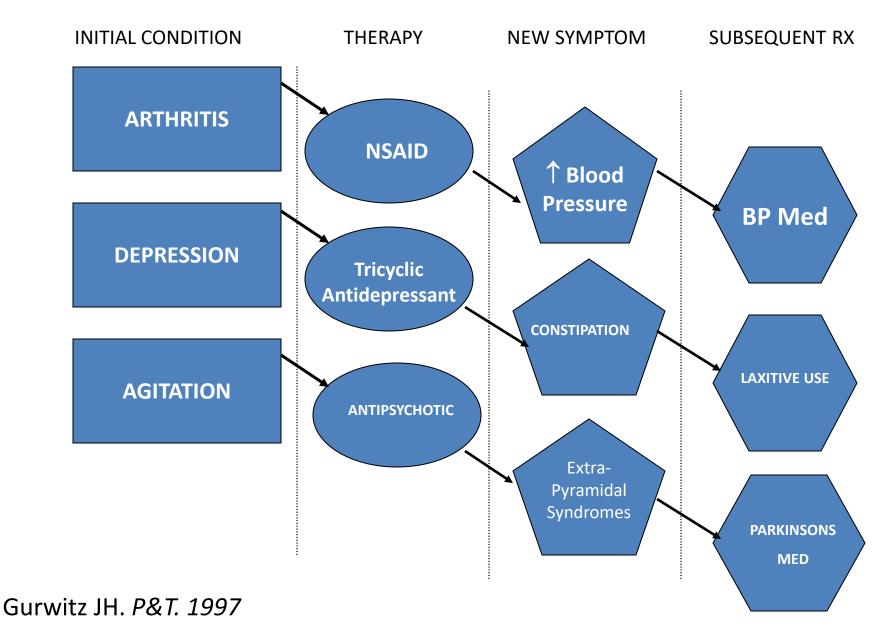


Table 2 : Age related pharmacokinetic changes in the elderly.4

Pharmacokinetic parameter	Age related changes Nil		
Absorption			
Distribution of			
Lipid soluble drugs	Increased		
Water soluble drugs	Decreased		
Acidic drugs	Increased		
Basic drugs	Decreased		
Metabolism			
Phase I	Decreased		
Phase II	Nil		
Excretion	Decreased		



The Prescribing Cascade





green are for the effects of the blue."

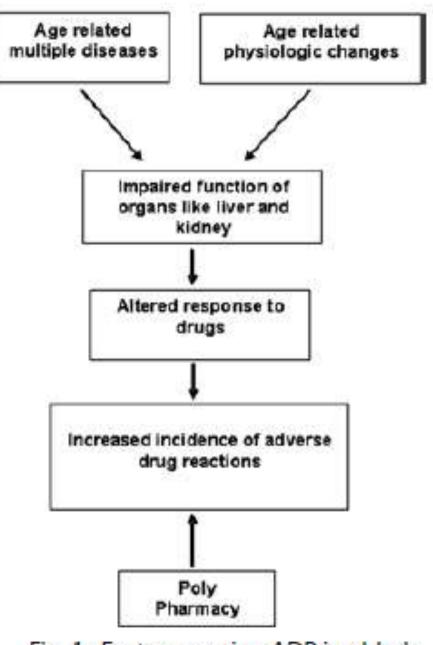


Fig. 1 : Factors causing ADR in elderly.



Identifying Polypharmacy

Tools

- Comprehensive Geriatric Assessment(CGA)
- Medication Appropriateness Index (MAI)
- •Assessing Care of Vulnerable Elders (ACOVE)

CGA

- •Holistic Approach
- •Uses mutliple disciplines to evaluate:
- Clinical
- Functional
- Cognitive
- Nutritional
- Social Parameters
- •Nurses, OT, PT, social workers, general practictioners, geriatricians and pharmacists

MAI

- 10 component assessment tool
- Evaluates the appropriateness of medications in elderly patients
- Efficacy
- Drug dosage
- Interactions
- Cost
- Duplications

Medication Appropriateness Index

Each question is answered using a three-point Likert scale. The first two questions receive a weighting of (3), the next four a weighting of (2), and the last four a weighting of (1).

- 1. Is there an indication for the drug?
- 2. Is the medication effective for the condition?
- 3. Is the dosage correct?
- 4. Are the directions correct?
- 5. Aare the directions practical?
- 6. Are there clinically significant drug–drug inter-actions?
- 7. Are there clinically significant drug–disease/condition interactions?
- 8. Is there unnecessary duplication with other drugs?
- 9. Is the duration of therapy acceptable?
- 10. Is the drug the least expensive alternative compared to others of equal utility?

ACOVE

- Vulnerable elderly
- Most likely to die or become severely disabled in the next two years
- Comprehensively evaluate the medical care given to elderly patients
- Increased risk of decline
- Covers all four domains of care:
- Screening and prevention
- Diagnosis
- Treatment
- Follow-up continuity

Guidelines for Medication Use in Older Adults

- Three tools provide limited guidance in prescribing in the elderly
- Beers Criteria (American Geriatrics Society Update Expert Panel, 2019)
- Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP)
- Screening Tool to Alert doctors to the Right Treatment (START)

BEERS CRITERIA



Data from "Updating the Beers Criteria for Potentially Inappropriate Medication Use in Older Adults: Results of a US Consensus Panel of Experts." Donna M. Fick, PhD, RN, et al. Arch Intern Med. 2003;163(22):2716-2724.

BEERS CRITERIA

- Originally developed in 2003 and updated in 2012,2015,2019 by the American Geriatrics Society
- Intend to improve drug selection and reduce exposure to potentially inappropriate medications in older adults
- Recommendations are evidence-based and in 3 categories:
 - Drugs to avoid
 - Drugs to avoid in patients with specific diseases or syndromes
 - Drugs to use with caution
- Available at AGS web site: www.americangeriatrics.org

From THE AMERICAN GERIATRICS SOCIETY A POCKET GUIDE TO THE AGS 2015 BEERS CRITERIA

This guide has been developed as a tool to assist healthcare providers in improving medication safety in older adults. The role of this guide is to *Inform* clinical decision-making, research, training, quality measures and regulations concerning the prescribing of medications for older adults to improve safety and quality of care. It is based on *The AGS* 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults.

Originally conceived of in 1991 by the late Mark Beers, MD, a geriatrician, the Beers Criteria catalogues medications that cause side effects in the elderly due to the physiologic changes of aging. In 2011, the AGS sponsored its first update of the criteria, assembling a team of experts and using an enhanced, evidence-based methodology. In 2015, the AGS again funded the development of the Updated Criteria using an evidencebased methodology and rating each Criterion (quality of evidence and strength of evidence) using the American College of Physicians' Guideline Grading System, which is based on the GRADE scheme developed by Guyatt et al.

The full document, along with accompanying resources can be viewed in their entirety online at geriatricscareonline.org.

INTENDED USE

The goal of this guide is to improve care of older adults by reducing their exposure to Potentially Inappropriate Medications (PIMS).

- This should be viewed as a guideline for identifying medications for which the risks of their use in older adults outweigh the benefits.
- These criteria are not meant to be applied in a punitive manner.
- This list is not meant to supersede clinical judgment or an individual patient's values and needs. Prescribing and managing disease conditions should be individualized and involve shared decision-making.
- These criteria also underscore the importance of using a team approach to prescribing and the use of non-pharmacological approaches and of having economic and organizational incentives for this type of model.
- Two companion pieces were developed for the 2015 update. The first addresses the best way for patients, providers, and health systems to use (and not use) the 2015 AGS Beers Criteria. The second is a list of alternative medications included in the current use of High-Risk Medications in the Elderly and Potentially Harmful Drug-Disease Interactions in the Elderly quality measures. Both pieces can be found on geriatricscareonline.org.

The criteria are not applicable in all circumstances (i.e. patient's receiving palliative and hospice care). If a provider is not able to find an alternative and chooses to continue to use a drug on this list in an individual patient, designation of the medication as potentially inappropriate can serve as a reminder for close monitoring so that adverse drug effects can be incorporated into the electronic health record and prevented or detected early.



TABLE 1. 2015 American Geriatrics Society Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

Organ System, Therapeutic Category, Drug(s)	Recommendation, Rationale, Quality of Evidence (QB, Strength of Recommendation (SR)
Anticholinergics	·····, ······
First-generation antihistamines: Brompheniramine Carbinoxamine Chlorpheniramine Clemastine Dexbrompheniramine Dexchlorpheniramine Dimenhydrinate Diphenhydramine (oral) Doxylamine Hydroxyzine Meclizine Promethazine Triprolidine	Avoid Highly anticholinergic; clearance reduced with advanced age, and tolerance develops when used as hypnotic; risk of confusion dry mouth, constipation, and other anticholinergic effects or toxicity Use of diphenhydramine in situations such as acute treatment of severe allergic reaction may be appropriate QE = Moderate; SR = Strong
Antiparkinsonian agents Benztropine (oral) Trihexyphenidyl	Avoid Not recommended for prevention of extrapyramidal symptoms with antipsychotics; more-effective agents available for treatment of Parkinson disease QE = Moderate; SR = Strong
Antispasmodics: Atropine (excludes ophthalmic) Belladonna alkaloids Clidinium- Chlordiazepoxide Dicyclomine Hyoscyamine Propantheline Scopolamine	<i>Avoid</i> Highly anticholinergic, uncertain effectiveness ΩE = Moderate; SR = Strong
Antithrombotics	
 Dipyridamole, oral short-acting (does not apply to the extended- release combination with aspirin) 	Avoid May cause orthostatic hypotension; more effective alternatives available; IV form acceptable for use in cardiac stress testing QE = Moderate; SR = Strong
■Ticlopidine	Avoid Safer, effective alternatives available ΩE = Moderate; SR = Strong

CNS=central nervous system; NSAIDs=nonsteroidal anti-inflammatory drugs; SIADH, syndrome of inappropriate antidiuretic hormone.

Beers Criteria example

Drug class or disease	Rationale	Recommendation	Quality of Evidence	Strength of recommendation			
PIMs							
Antispasmodics	Highly anticholinergic, uncertain effectiveness	Avoid	Moderate	Strong			
PIMs due to concomitant diseases/conditions							
Syncope & alpha blockers	Increases risk of orthostatic hypotension or bradycardia	Avoid	High	Weak			
PIMs to be used with caution							
Aspirin for primary prevention of CVD	Lack of evidence of benefit vs. risk in ≥ 80yrs	Use with caution in adults aged ≥ 80 yrs	Low	Weak			

		ABLE 1. 2015 American Geriatrics Society Beers Criteria for Potentially Inappropriate Iedication Use in Older Adults		
From THE AMERICAN GERIATRICS SOCIETY	Organ System, Therapeutic Category, Drug(s)	Recommendation, Rationale, O (OB, Strength of Recommendat		
A POCKET GUIDE TO THE	Anticholinergics			
AGS 2015 BEERS CRITERIA	First-generation	Avoid		
AUS ZUIS DEEKS CRITERIA	antihistamines:		arance reduced with advanced age, en used as hypnotic; risk of confusion,	
Thisgi Avoid in most			d other anticholinergic effects or	
• 1 st generation antihistamines			situations such as acute treatment of ay be appropriate	
^{2015U} • Antispasmodics			g	
Origin				
Criteri physic • Peripheral alpha-1 blockers (pl	razosin)			
assem • Digoxin				
based • TC Avoid in those with renal failu	re			
based • Snironolactone			ion of extrapyramidal symptoms ctive agents available for	
The fu			8	
• Be • Gabapentin				
Important Drug-Drug inter	ractions to avoid	k	less	
Potent Marfarin _amiodaror				
Opioids- other CNS a	acting drugs			
This list is not meant to superand needs. Prescribing and Storaide_ NSAIDe				
and involve shared decision Avoid drugs with stron	g anticholinergi	c effects	<u> </u>	
prescribing and the use of n Dimenhydrinate			3	
 Two companion pieces were devel the best way for patients, provider Diphenyhdramine 				
2015 AGS Beers Criteria. The second				
in the current use of High-Risk Mee • Amitriptyline				
on geriatricscareonline.org. • Oxybutynin				
The criteria are not applicable in all circ hospice care). If a provider is not able to				
use a drug on this list in an individual patient, designation of the medication as potentially inappropriate can serve as a reminder for close monitoring so that adverse drug effects	inappropriate antidiuretic ho		iniatory uruga, arAbri, aynuronie or	
can be incorporated into the electronic health record and prevented or detected early.	 			

Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP)

STOPP: <u>Screening Tool of Older People's</u> potentially inappropriate <u>Prescriptions</u>

The following drug prescriptions are potentially inappropriate in persons aged \geq 65 years of age.

Cardiovascular System

- Digoxin at a long-term dose > 125µg/day with impaired renal function*
- 2. Loop diuretic for dependent ankle oedema only i.e. no clinical signs of heart failure
- 3. Loop diuretic as first-line monotherapy for hypertension
- 4. Thiazide diuretic with a history of gout.
- 5. Non-cardioselective beta-blocker with Chronic Obstructive Pulmonary Disease (COPD).
- 6. Beta-blocker in combination with verapamil
- 7. Use of diltiazem or verapamil with NYHA Class III or IV heart failure
- 8. Calcium channel blockers with chronic constipation
- 9. Use of aspirin and warfarin in combination without histamine H2 receptor antagonist (except cimetidine because of interaction with warfarin) or PPI
- 10. Dipyridamole as monotherapy for cardiovascular secondary prevention
- Aspirin with a past history of peptic ulcer disease without histamine H2 receptor antagonist or proton pump inhibitor
- 12. Aspirin at dose > 150mg day
- Aspirin with no history of coronary, cerebral or peripheral vascular symptoms or occlusive event
- 14. Aspirin to treat dizziness not clearly attributable to cerebrovascular disease
- 15. Warfarin for first, uncomplicated deep venous thrombosis for > 6 months
- 16. Warfarin for first uncomplicated pulmonary embolus for > 12 months
- Aspirin, clopidogrel, dipyridamole or warfarin with concurrent bleeding disorder

 eGFR <50ml/min.

Central Nervous System and Psychotropic Drugs

- 1. Tricyclic antidepressants (TCA's) with dementia
- 2. TCA's with glaucoma
- 3. TCA's with cardiac conductive abnormalities
- 4. TCA's with constipation
- 5. TCA's with an opiate or calcium channel blocker
- 6. TCA's with prostatism or prior history of urinary retention
- Long-term (i.e. > 1 month), long-acting benzodiazepines e.g. chlordiazepoxide, fluazepam, nitrazepam, chlorazepate and benzodiazepines with long-acting metabolites e.g. diazepam
- 8. Long-term (i.e. > 1 month) neuroleptics as long-term hypnotics
- 9. Long-term neuroleptics in those with parkinsonism
- 10. Phenothiazines in patients with epilepsy
- 11. Anticholinergics to treat extra-pyramidal side-effects of neuroleptic medications
- Selective serotonin re-uptake inhibitors (SSRI's) with a history of clinically significant hyponatraemia
- Prolonged use (> 1 week) of first generation antihistamines i.e. diphenydramine, cyclizine, chlorpheniramine, promethazine

Gastrointestinal System

- Diphenoxylate, loperamide or codeine phosphate for treatment of diarrhoea of unknown cause
- Diphenoxylate, loperamide or codeine phosphate for treatment of severe infective gastroenteritis i.e. bloody diarrhoea, high fever or severe systemic toxicity
- 3. Prochlorperazine (Stemetil) or metoclopramide with Parkinsonism
- 4. PPI for peptic ulcer disease at full therapeutic dosage for > 8 weeks
- 5. Anticholinergic antispasmodic drugs with chronic constipation

Respiratory System

- 1. Theophylline as monotherapy for COPD
- Systemic corticosteroids instead of inhaled corticosteroids for maintenance therapy in moderate-severe COPD
- 3. Nebulised ipratropium with glaucoma

Musculoskeletal System

- 1. Non-steroidal anti-inflammatory drug (NSAID) with history of peptic ulcer disease or GI bleeding, unless with concurrent H2 receptor antagonist, PPI or misoprostol
- 2. NSAID with moderate-severe hypertension
- 3. NSAID with heart failure
- Long-term use of NSAID (>3 months) for symptom relief of mild osteoarthtitis
- 5. Warfarin and NSAID together
- 6. NSAID with chronic renal failure*
- Long-term corticosteroids (>3 months) as monotherapy for rheumatoid arthrtitis or osterarthritis.
- 8. Long-term NSAID or colchicine for chronic treatment of gout where no contraindication to allopurinol

Urogenital System

- 1. Bladder antimuscarinic drugs with dementia
- 2. Antimuscarinic drugs with chronic glaucoma
- 3. Antimuscarinic drugs with chronic constipation
- 4. Antimuscarinic drugs with chronic prostatism
- Alpha-blockers in males with frequent incontinence
- 6. Alpha-blockers with long-term urinary catheter

Endocrine System

- 1. Glibenclamide or chlorpropamide with type 2 DM
- 2. Beta-blockers in those with DM and frequent hypoglycaemic episodes
- 3. Oestrogens with a history of breast cancer or venous thromboembolism
- 4. Oestrogens without progestogen in patients with intact uterus

Drugs that adversely affect those prone to falls

- 1. Benzodiazepines
- 2. Neuroleptic drugs
- 3. First generation antihistamines
- 4. Vasodilator drugs with persistent postural hypotension
- 5. Long-term opiates

Analgesic Drugs

- 1. Use of long-term powerful opiates e.g. morphine or fentanyl as first line therapy for mild-moderate pain
- 2. Regular opiates for >2 weeks in those with chronic constipation without concurrent laxative
- 3. Long-term opiates in those with dementia unless indicted for palliative care or management of moderate/severe chronic pain syndrome

Duplicate Drug Classes

1. Any duplicate drug class prescription e.g. concurrent opiates, NSAID's, SSRI's, loop diuretics, ACE inhibitors

Screening Tool to Alert doctors to the Right Treatment (START)

START: <u>Screening Tool to Alert doctors to Right i.e.</u> appropriate, indicated <u>Treatment</u>.

These medications should be considered for people **2** 65 years of age with the following conditions, where no contraindication to prescription exists.

Cardiovascular System

- 1. Warfarin in the presence of chronic atrial fibrillation
- 2. Aspirin in the presence of chronic atrial fibrillation, where warfarin is contraindicated, but not aspirin
- Aspirin or clopidogrel with a history of atherosclerotic coronary, cerebral or peripheral vascular disease in patients with sinus rhythm
- Antihypertensive therapy where systolic BP consistently >160 mmHg
- Statin therapy with a history of coronary, cerebral or peripheral vascular disease, where functional status remains independent for activities of daily living and life expectancy is > 5 years
- 6. Angiotensin Converting Enzyme (ACE) inhibitor with chronic heart failure
- 7. ACE inhibitor following acute myocardial infarction
- 8. Beta-blocker with chronic stable angina

Respiratory System

- 1. Regular inhaled beta 2 agonist or anticholinergic for mild to moderate asthma or COPD
- 2. Regular inhaled corticosteroid for moderate-severe asthma or COPD, where predicted FEV1 <50%
- 3. Home continuous oxygen with documented chronic type 1 respiratory failure or type 2 respiratory failure

Central Nervous System

- 1. L-DOPA in idiopathic Parkinson's disease with functional impairment and disability
- 2. Antidepressant with moderate-severe depressive symptoms

Gastrointestinal System

- 1. Proton Pump Inhibitor with severe GORD or peptic stricture requiring dilatation
- 2. Fibre supplement for chronic, symptomatic diverticular disease with constipation

Musculoskeletal System

- Disease-modifying anti-rheumatic drug (DMARD) with active rheumatoid disease lasting > 12 weeks
- Bisphosphonates in patients taking maintenance corticosteroid therapy
- Calcium/Vitamin D supplement in patients with osteoporosis (fragility fracture, dorsal kyphosis)

Endocrine System

- Metformin with type 2 diabetes +/- metabolic syndrome (in the absence of renal impairment*)
- ACE inhibitor or ARB in diabetes with nephropathy i.e. proteinuria or micoralbuminuria +/- renal impairment*
- Antiplatelet therapy in diabetes mellitus with co-existing cardiovascular risk factors
- 4. Statin therapy in diabetes mellitus if co-existing major cardiovascular risk factors present

eGFR <50ml/min.</p>

Medications Accounting for Most ADEs in Older Adults

- Cardiovascular medications
- Psychotropic medications
- Anticoagulants
- Antibiotics
- NSAIDS
- Anti-seizure medications

(JAGS 2004;52:1349-1354 and NEJM 2003;348:1556-64)

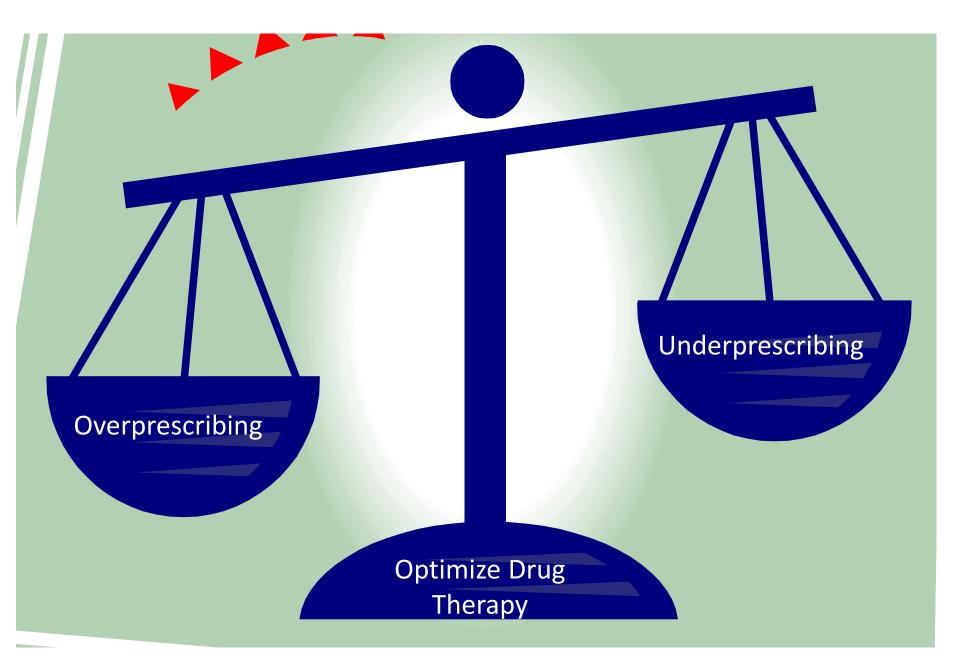
COMMONLY OVERPRESCRIBED AND INAPPROPRIATELY USED DRUGS

- Anti-infective agents
- Anticholinergic agents
- Urinary & GI antispasmodics
- Antipsychotics
- Benzodiazepines
- Digoxin for diastolic dysfunction
- Dipyridamole

- H₂ receptor antagonists
- Laxatives & fecal softeners
- NSAIDs
- Proton-pump inhibitors
- Sedating antihistamines
- Tricyclic antidepressants
- Vitamins and minerals

COMMONLY UNDERPRESCRIBED DRUGS

- ACE inhibitors for patients with diabetes and proteinuria
- Angiotensin-receptor blockers
- Anticoagulants
- Antihypertensives and diuretics for uncontrolled hypertension
- β-blockers for patients after MI or with heart failure
- Bronchodilators
- Proton-pump inhibitors or misoprostol for GI protection from NSAIDs
- Statins
- Vitamin D and calcium for patients with or at risk of osteoporosis



Steps to Reducing Poly-pharmacy

- "Brown Bag" all medications at each office visit. Keep accurate records
- Identify all medications by brand/generic name and drug class
- All drugs prescribed should have a clinical indication
- Stop any drug without known benefit
- Consider what effect drug therapy has on quality of life

Steps to Reducing Poly-pharmacy

- Know the side effects of the drugs prescribed and what to expect from them
- Understand the PK and pharmacodynamics of drugs prescribed
- Substituting drugs within classes can eliminate DI's and ADR's
- Be aware for the prescribing cascade
- "ONE DISEASE, ONE DRUG, ONCE DAILY"
- "START LOW, GO SLOW, BUT GO"

Principles of Drug Prescribing

- Make diagnosis before drug therapy is initiated
- Non-pharmacologic therapy is always initiated first whenever appropriated
- Carefully weigh the risks versus benefits
- Inquire about the use of over-the-counter and alternative medications

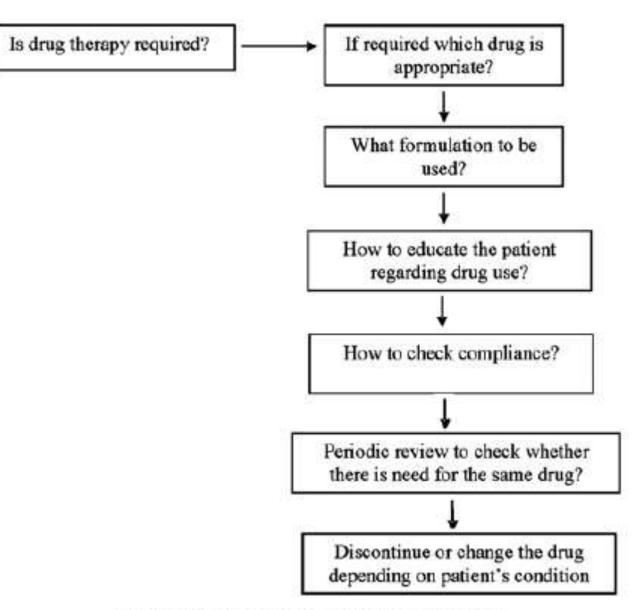


Fig. 3 : Principles of prescribing in elderly.^{4,16}

- Discontinuing unnecessary medications is one of the most important aspects of decreasing polypharmacy
- Drugs without indications should be stopped
- Avoid treating adverse reactions/side effects of drugs with more drugs

Example - Dizziness from anti-hypertensive treated with meclizine

- Edema from a calcium-channel blocker treated with furosemide

Combined intervention programme reduces inappropriate prescribing in elderly patients exposed to polypharmacy in primary care

L. Bregnhøj • S. Thirstrup • M. B. Kristensen • L. Bjerrum • J. Sonne

> Conclusions A combined intervention consisting of an interactive educational meeting plus recommendations given by clinical pharmacologists/pharmacists concerning specific patients can improve the appropriateness of prescribing among elderly patients exposed to polypharmacy. This study adds to the limited number of well-

Key messages

- Clinicians identify medicines for review
- supported by evidence based tools

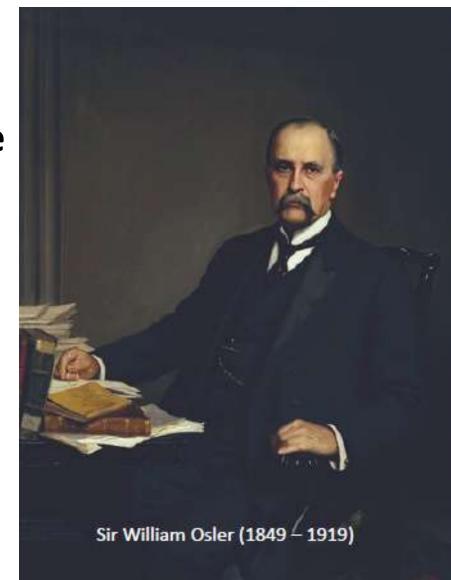




- Patient identifies what they want
 - from their medicines for their
 - health and well being.
- Working together is the route to medicines optimisation

- Aim to understand the patient's experience
- Evidence based choice of medicines
- Ensure medicines use is as safe as possible
- Make medicines optimisation part of routine practice

"One of the first duties of the physician is to educate the masses *not to take medicine.*"



Thank You

"To care for those who once cared for us is one of the highest honours."

