

Polypharmacy @Age



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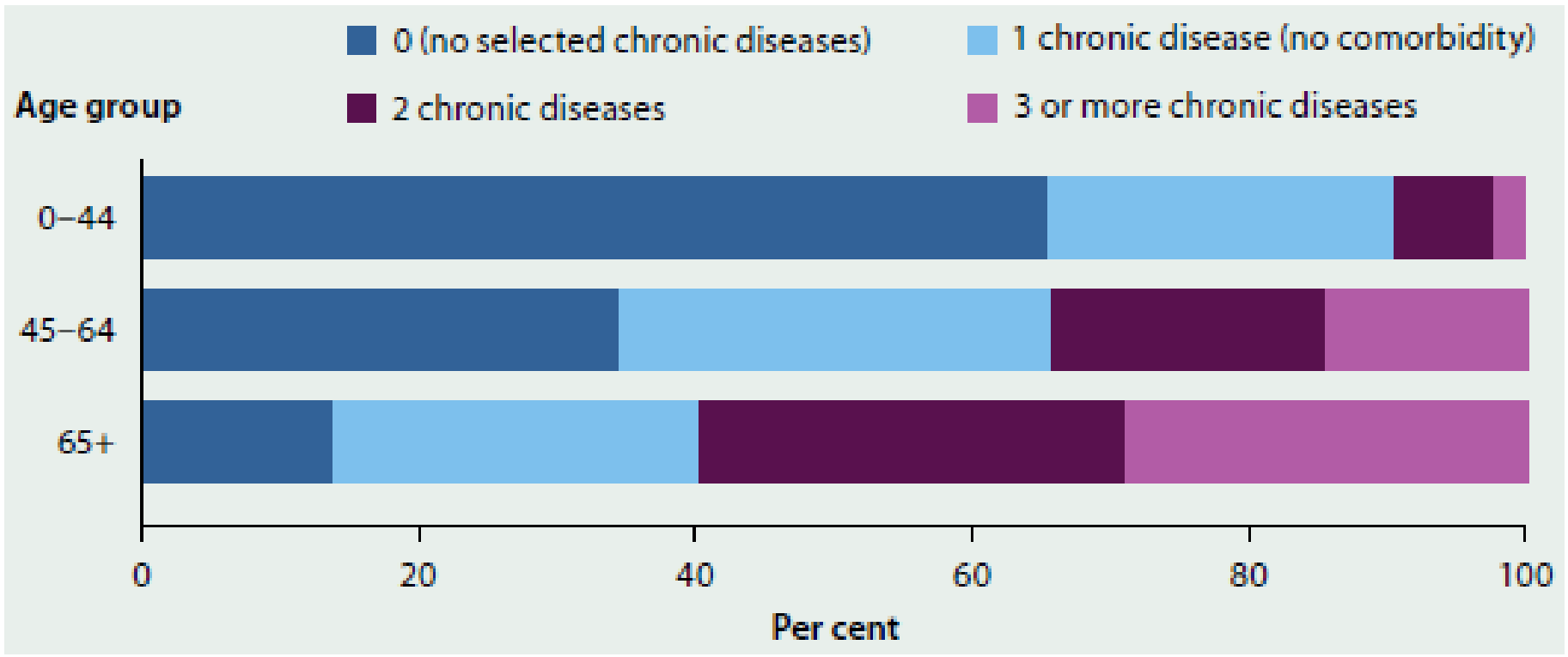


THE UNIVERSITY OF
MELBOURNE



The Royal
Melbourne Hospital

Comorbidity by age 2014-15 (AUS)



ABS 2015 (Table 18.3); Table S3.3.2

Usual patient – guideline

diabetes

HT

COPD

arthrosis

osteoporosis



-19 pills

-12 medications

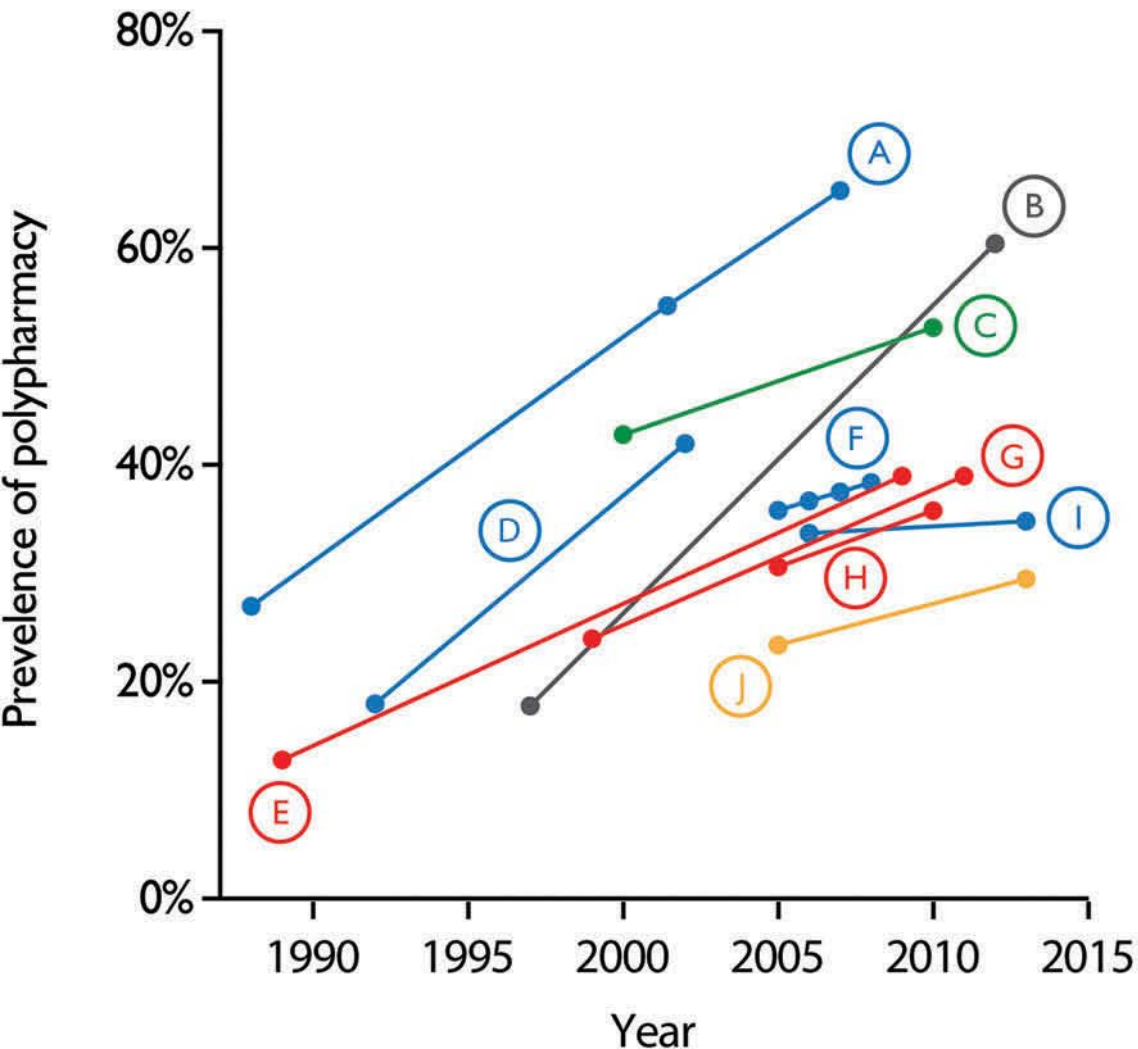
at 5 different time points a day

- 22 lifestyle interventions

- 5 visits per year

- 22 additional actions

International trends in the prevalence of polypharmacy (5+) in older adults



- (A) Craftman et al., Sweden
- (B) Moriarty et al., Ireland
- (C) Franchi et al., Italy
- (D) Haider et al., Sweden
- (E) Charlesworth et al., United States
- (F) Hovstadius et al., Sweden
- (G) Kantor et al., United States
- (H) Qato et al., United States
- (I) Wastesson et al., Sweden
- (J) Nishtala et al., New Zealand



National strategic plan – inappropriate polypharmacy

Key facts and figures²⁻⁸



2 out of 3 Australians aged over
75 take 5 or more medicines



Approximately HALF of all older adults are
taking a medicine that is harmful or unnecessary



9 out of 10 older adults are willing to stop one or more of
their medicines if their doctor said it was possible

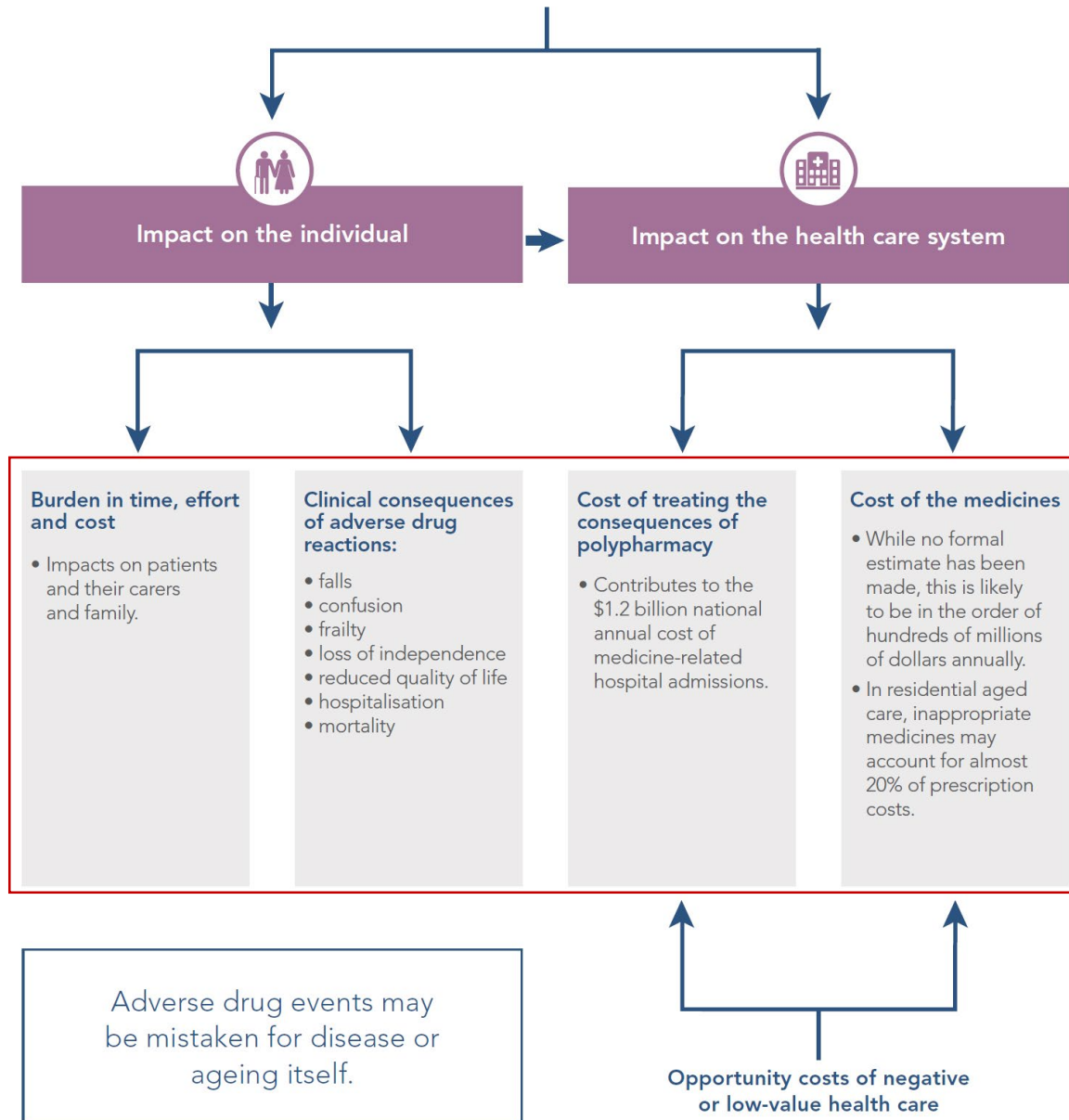


National strategic plan – inappropriate polypharmacy

There is emerging evidence that supervised withdrawal of harmful or unnecessary medicines (deprescribing) is safe and may improve quality of life in older people.^{5,9}

Deprescribing is not about denying effective treatment. It is about improving the overall harm versus benefit balance of medicine use for individuals.

POLYPHARMACY AND UNNECESSARY OR HARMFUL MEDICINES

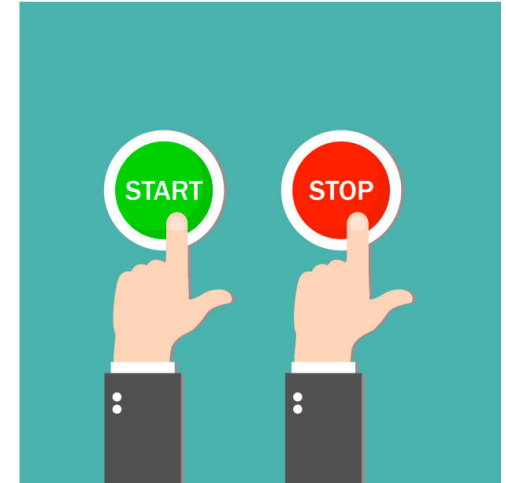


STOPP/START criteria (version 2)



STOPP = Screening Tool of Older Persons Prescriptions ¹

START = Screening Tool to Alert to Right Treatment ¹



- explicit, **evidence based rules** of **avoidance** of potentially inappropriate prescribing and potential prescribing omissions
- improve medication appropriateness
- prevent adverse drug events
- reduce drug costs

Potentially Inappropriate Medication – PIM

Potential Prescribing Omissions - PPO



Potentially inappropriate prescribing defined

Risk > Benefit

- **Over-prescribing**: excessive doses/duration of medicines → polypharmacy
- **Misprescribing**: unfavourable choice of medicine, dose, or duration
- **Under-prescribing**: not prescribing a clinically indicated medicine, despite the patient not having any contra-indication to that medicine



Contents of STOPP

START

Physiological System	Number of criteria	Number of criteria
Cardiovascular system	17	8
Central nervous system	13	2
Gastro-intestinal system	5	2
Musculoskeletal system	8	3
Respiratory system	3	3
Urogenital system	6	
Endocrine system	4	4
Drugs that adversely affect fallers	5	
Analgesics	3	
Duplicate drug classes	1	

STOPP: Screening Tool of Older People's Potentially Inappropriate Prescriptions

The following drug prescriptions are potentially inappropriate in persons aged ≥ 65 years of age

Cardiovascular System

1. Digoxin at a long-term dose $> 125\mu\text{g}/\text{day}$ with impaired renal function
- X 2. Loop diuretic for dependent ankle oedema only i.e. no clinical signs of heart failure
- X 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
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 H_2 receptor antagonist
10. Dipyridamole as monotherapy for cardiovascular secondary prevention
- X 11. Aspirin with a past history of peptic ulcer disease without histamine H_2 receptor antagonist or Proton Pump Inhibitor
12. Aspirin at dose $> 150\text{mg}$ day
13. 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 longer than 6 months duration
- X 16. Warfarin for first uncomplicated pulmonary embolus for longer than 12 months duration
17. Aspirin, clopidogrel, dipyridamole or warfarin with concurrent bleeding disorder

START: Screening Tool to Alert doctors to Right Treatments

These medications should be considered for people ≥ 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
3. Aspirin or clopidogrel with a documented history of atherosclerotic coronary, cerebral or peripheral vascular disease in patients with sinus rhythm.
- X 4. Antihypertensive therapy where systolic blood pressure consistently >160 mmHg
5. Statin therapy with a documented history of coronary, cerebral or peripheral vascular disease, where the patient's functional status remains independent for activities of daily living and life expectancy is greater than 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 β_2 agonist or anticholinergic agent for mild to moderate asthma or COPD
- X 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 definite functional impairment and resultant disability
2. Antidepressant drug in the presence of moderate-severe depressive symptoms lasting at least three months.



Prevalence of PIM/PPO in hospitalized older patients at admission

Most prevalent PIMs

- Lack of Clinical Indication
- Benzodiazepines
- Nonsteroidal anti-inflammatory drugs
- Spironolactone

Most prevalent PPOs

- Lack of Vitamin D Supplementation
- Pneumococcal Vaccination

Comparison of current and previous systematic review
identification of PIMs and PPOs⁴

	Current Systematic Review		Previous Systematic Review	
	Range (%)	Prevalence (%)	Range (%)	Prevalence (%)
PIMs	27.0-95.0	53.4	21.4-79.0	50
PPOs	47.6-100	56.5	22.7-74.0	49

Version 2

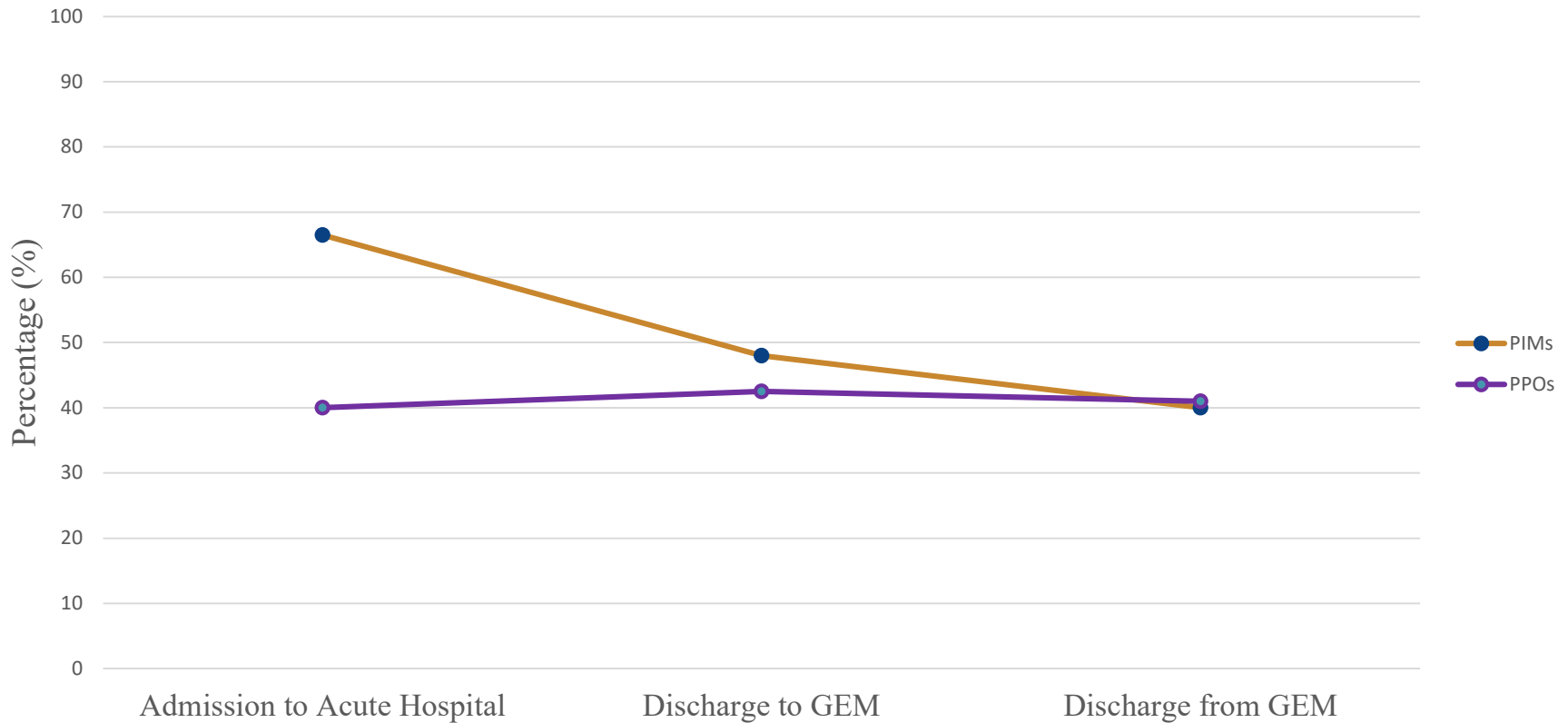
Version 1



PIM/PPO defined by STOPP/ START v2 - transitions of hospital care



Prevalence of older inpatients with at least one PIM and PPO identified by STOPP/START version 2

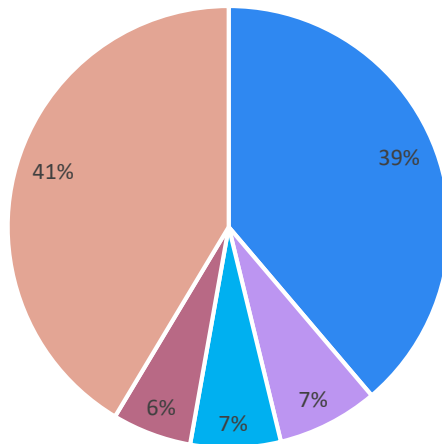


N= 200 Mean Age= 81.9±8.09
% Female = 56.2 Av. Medications/Patient = 11.4±4.83



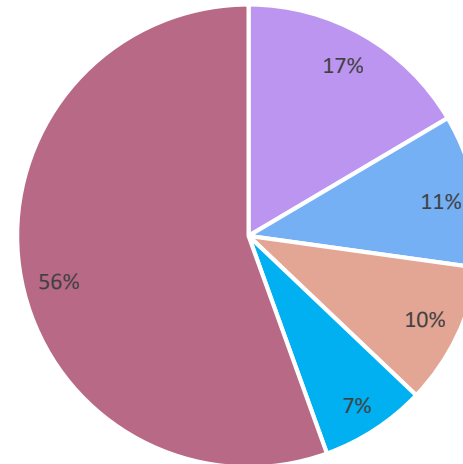
Most prevalent PIMs and PPOs

PIMs



- Lack of Clinical Indication
- Benzodiazepines
- Neuroleptics
- Opioids w/o Laxatives
- Other

PPOs



- Anti-resorptive/anabolic therapy for osteoporosis
- Beta-Blocker with IHD
- Vitamin D and Calcium supplementation
- Vit. K antagonist, direct thrombin inhibitor or factor Xa inhibitor w/ AF
- Vitamin D Supplementation in people with falls
- Other



PIM/PPO in GEM and 3 months outcome



Yes

		Mortality		Re-Admission to Hospital	
		HR (95% CI)	P-Value	OR (95% CI)	P-Value
PIM, with	Crude	1.88 (0.78-4.56)	0.16	2.70 (1.41-5.17)	0.00
	Age + Sex	2.15 (0.87-5.30)	0.10	2.83 (1.44-5.56)	0.00
	Fully	3.43 (1.18-10.0)	0.02	2.40 (1.17-4.94)	0.02
PPO, with	Crude	1.48 (0.62-3.56)	0.38	1.07 (0.56-2.03)	0.84
	Age + Sex	1.41 (0.58-3.40)	0.45	1.10 (0.57-2.11)	0.78
	Fully	1.62 (0.63-4.15)	0.32	0.98 (0.49-1.93)	0.95

Fully Adjusted for: Age, Sex, Number of Comorbidities, Total number of Medications at Discharge from GEM, Cohabitation Status.

Number

		Re-Admission to Hospital	
		Count (95% CI)	P-Value
PIM, n	Crude	1.73 (1.21-2.47)	0.00
	Age + Sex	1.70 (1.19-2.43)	0.00
	Fully	1.48 (1.01-2.16)	0.04
PPO, n	Crude	1.04 (0.69-1.58)	0.84
	Age + Sex	1.06 (0.70-1.61)	0.77
	Fully	0.97 (0.63-1.50)	0.90

Fully Adjusted for: Age, Sex, Number of Comorbidities, Total number of Medications at Discharge from GEM, Cohabitation Status.

Interventions





Deprescribing medications in primary care – methods / setting

Success of Deprescription Interventions Based on Methods of Deprescription

Deprescription Methods to Improve Medication Burden		
Type of Intervention	No. of Successful Studies	Results
Educational interventions	2/2	+
Patient-specific interventions (inpatient setting)	0/2	-
Patient-specific interventions (outpatient setting)	2/5	+ / -
Patient-specific interventions (long-term care setting)	4/5	+
Mixed (education and patient-specific) method to improve overall medication burden	4/6	+ / -

Instruction of nurses in an assisted living,¹¹ and education with on-demand support of doctors primarily practicing in nursing homes¹² resulted in a small, but statistically significant, reduction in PIM per person (0.4 to 0.5).^{11,12} The IG did not have any increase in measured adverse outcomes compared to CG.

Use of the STOPP criteria demonstrated decline in overall PIM usage though the proportion of patients taking at least 1 PIM at discharge was similar among the 2 groups.¹⁸ Use of the FORTA tool (Fit for the Aged) did not demonstrate a reduction in polypharmacy, but there may have been a higher prescribing quality and a lower rate of falls in the IG.

Two studies^{14,17} demonstrate feasibility of deprescribing via an intense pharmacist-physician collaboration. The CGA¹⁵ resulted in medications both added to and removed from the intervention group. The team of physicians, nurse, and pharmacist sending recommendations to the physician did not result in deprescription.¹⁶ The 2 patient drug-specific studies in the inpatient setting used PIM screening tools to reduce PIMs.

Three of the 4 successful studies^{21,22,24} required strong pharmacist-physician collaboration. The fourth successful study²⁰ followed an algorithm in a population with high baseline polypharmacy (mean number of medications more than 9 per person) and reduced medication burden by 2 medications per person. Medications withdrawn included bisphosphonates, aspirin, angiotensin receptor blockers (ARB), vitamins/minerals, and statins; medications with the lowest success rate in withdrawal included psychotropic medications and proton pump inhibitors (PPIs).

These studies^{25,28-30} were all multidisciplinary in nature. Of the 2 negative studies, one was an intense added value intervention in elders hospitalized in acute geriatric units to address readmissions by educating patients and families about their medications and condition, and helping patients and families identify patient-specific goals of care.²⁶ Results may have been attenuated because of the high level of care already offered in the French geriatric care units. The second negative study randomized pharmacists to educate nursing staff in Australian nursing homes as well as make patient-specific drug recommendations to the attending physicians,²⁷ essentially mirroring the role of the consulting pharmacist in most US nursing homes. However, when adjusted



Deprescribing medications in primary care – psychotropic drugs

Success of Deprescribing Psychotropic Drugs

Deprescription of Psychotropic Drugs

Medication Type	No. of Successful Studies	Results
Antipsychotics for behavior	5/9	<p>Although antipsychotics were successfully withdrawn without need for resumption in 50% of the participants in 5^{31,32,35,36,39} of the 9 studies, 2 of the studies^{35,36} had a duration of only 4 wk. Actigraphy was measured in Ruths et al,³⁵ and it revealed that the average sleep efficacy was less (by 54 minutes) in IG. There was notably more physical aggression in the withdrawal group in a study,³⁷ and preintervention antipsychotic dose was predictive of worsening of behaviors. In the DART-AD,³¹ which followed patients for over a year, only 9% of those in IG had to resume an antipsychotic, and there was reduced mortality in the withdrawal group.</p> <p>Only one-third of subjects with intellectual and developmental disabilities (IDD) taking antipsychotics for behavior problems were successfully weaned from the antipsychotic, but another fifth tolerated a 50% dose reduction.³⁸ Overall, the withdrawal group did better in terms of higher activity engagement, without increase in maladaptive behavior. Individuals with IDD living in hospitals or settings with a specialist mental health orientation or lower staff-to-resident ratios, and those receiving neuroleptic medication for more than 5 y were more likely to be successful in withdrawal of the medication. Greater restrictiveness of the setting, absence of written policy, and poorer staff training on use of physical restraints were associated with higher rates of drug reinstatement.</p>
Benzodiazepines	1/6	<p>Successful withdrawal of benzodiazepines was achieved in a small group of nursing home residents who completed the study (though one-third drop out in both arms) with improved functional scores at 6 mo and 1 y, but there was a decline in sleep quality in IG.⁴⁰ Four community-based trials^{41–44} used self-tapering protocols in deprescribing benzodiazepines among chronic users who were cognitively intact. Although none met the definition of feasibility, 1 came close, with 45% discontinuation in the intervention group.⁴⁴ In all 4 of these trials, there were substantial dose reductions in many who were unable to discontinue the drug. The sixth trial⁴⁵ studied “academic detailing.” This process involved a 20-min primary care visit with a specially trained general practitioner who advised the physician on management of chronic benzodiazepine users. The prescribing rates dropped in both the intervention group and the control group, but the intervention did not result in a difference in prescribing between 2 groups by the end of the study.</p>
Antidepressants	1/3	<p>Deprescribing in nursing home residents <u>without a diagnosis of major depression or dementia was feasible in 80% of the residents.</u>⁴⁶ However, in community-dwellers with major depression or general anxiety disorder, deprescribing is associated with a high risk of relapse.^{47,48}</p>

+/-

IG: less mortality, but less sleep, physical aggression

NH: better functional outcome
GP practice: no different prescribing by end of study



Deprescribing medications in primary care – medical indication

Success of Deprescribing Drugs With Medical Indications

Medications for Chronic Medical Conditions		
Disease/Medication Class	No. of Successful Studies	Results
Oral hypoglycemic in diabetes	0/1	Postintervention A1c higher by 1%-1.5%, but less hypoglycemia in the IG. ⁴⁹
Inhaled corticosteroids in asthma	0/1	Withdrawal of long-acting beta-agonist is associated with more moderate exacerbations when weaning off inhaled corticosteroids. ⁵⁰
Inhaled corticosteroids in COPD	0/1	Withdrawal of ICS resulted in sustained and statistically significant decline in PFTs, and increase in mild exacerbations requiring rescue inhalers. ⁵¹
PPI for gastric issues (GERD, dyspepsia, prevention)	1/5	The one successful PPI deprescription required intense efforts directed at both the patient and prescriber. ³⁰
Bisphosphonates in osteoporosis	0/1	A drug holiday may be considered for some postmenopausal women while understanding the increased risk for clinical vertebral fractures. ⁵⁶
Antihypertensives/diuretics	5/5	Antihypertensives and diuretics may be withdrawn while following BP closely. BP may rise above 160 mm Hg (in 15% of the patients). In some (approximately 20%), withdrawal of a diuretic can unmask edema or heart failure, requiring the drug to be restarted.
Nitrates	2/2	Most (approximately 90%) of the persons with chronic stable angina will tolerate withdrawal of long-acting nitrate
Dopaminergic agents for Parkinson's disease	1/1	Frail, dependent elders may tolerate dopaminergic withdrawal to reduce polypharmacy and medication-related adverse effects.
Multiple drug withdrawal	4/4	Beer et al ⁶⁵ demonstrated gradual withdrawal of 1 target medication related to a stable chronic disease with a negative symptom, with successful discontinuation of the target medicine in 73% of participants in the IG. Among the 3 studies related to psychotropic medicines, a pharmacist-led intervention in nursing homes ⁶⁸ led to a 0.4 reduction in psychotropic prescriptions and the total number of residents taking psychotropics in IG nursing homes compared to the CG. Attempt at a withdrawal of psychotropics was successful in nursing home residents without diagnoses of major depression or schizophrenia, ⁶⁷ without any statistically significant increase in agitation or behaviors. Deprescribing of psychotropic medications in outpatient setting ⁶⁶ demonstrated fall reduction but there was high dropout (45%) and drug resumption by the end of the study (47%) in the IG; insomnia was a frequent complaint.



Interventions to improve appropriate use of polypharmacy

Uncertain whether pharmaceutical care:

- improves medication appropriateness
- Reduces n of potentially inappropriate medications (PIMs)
- Reduces the proportion of patients with one or more PIMs
- No/little difference in hospital admissions
- No/little difference in quality of life

Pharmaceutical care:

- may slightly reduce n of potential prescribing omissions (PPOs) (NB 2 studies), uncertain if proportion of patients with one or more PPOs changes



Summary



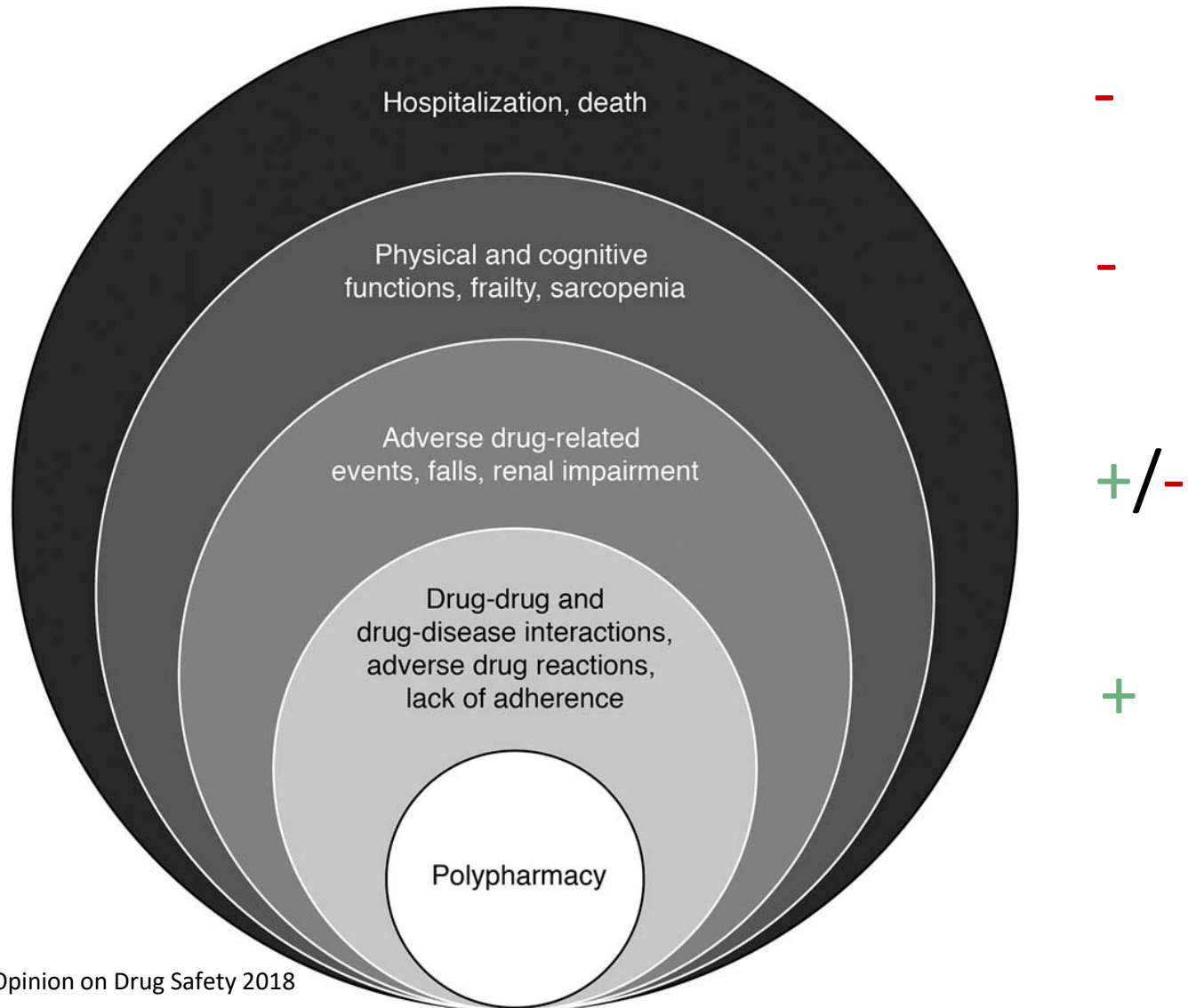
Polypharmacy is highly prevalent.

Inappropriate polypharmacy is highly prevalent.

Potentially inappropriate medication is associated with worse outcome.

Results of interventions have the potential to reduce PIMs and PPOs, but relation with meaningful outcomes is unclear.

Framework for polypharmacy and conceptual classification of outcomes



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Series 2; Episode2: Ageing Well