Le politerapie complesse: l'arte del deprescribing

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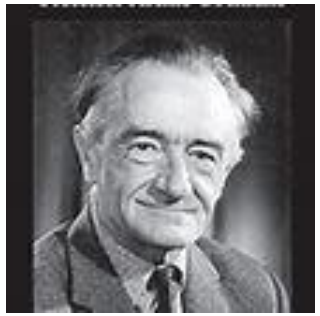
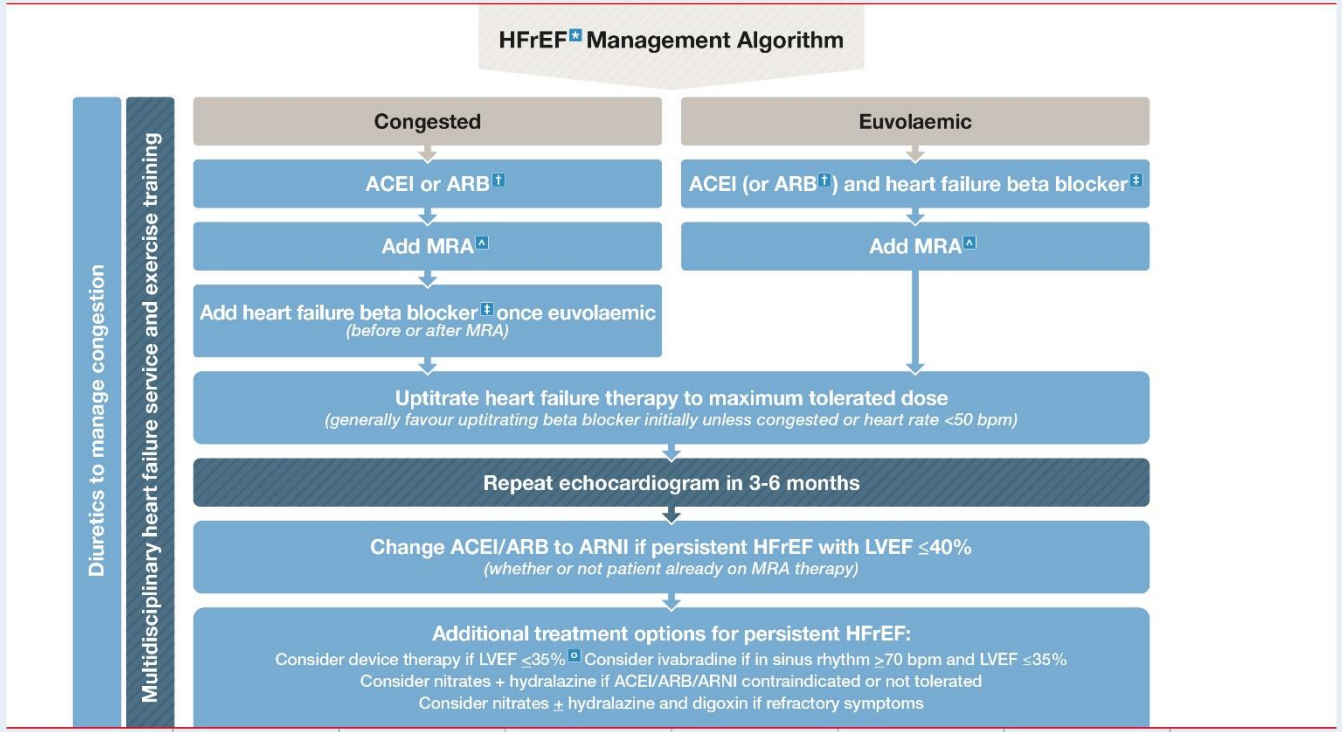


Archibald Leman Cochrane (12 January 1909 – 18 June 1988) was a Scottish doctor noted for his book *Effectiveness and Efficiency: Random Reflections on Health Services*.[1] This book advocated for the use of randomized control trials to make medicine more effective and efficient.[2] His advocacy of randomized controlled trials eventually led to the development of the Cochrane Library database of systematic reviews, the establishment of the UK Cochrane Centre in Oxford and the international Cochrane Collaboration.[3] He is known as one of the fathers of modern clinical epidemiology and Evidence-Based Medicine and is considered to be the originator of the idea of Evidence-Based Medicine in the current era.

CSANZ Cardiac Society of Australia and New Zealand | Heart Foundation

Figure 3: Management of patients with heart failure with reduced ejection fraction



HFrEF	ACEI	ARB	MRA	ARNI	LVEF	ICD	CRT
heart failure with reduced ejection fraction	angiotensin converting enzyme inhibitor	angiotensin receptor blocker	mineralocorticoid receptor antagonist	angiotensin receptor neprilysin inhibitor	left ventricular ejection fraction	implantable cardioverter defibrillator	cardiac resynchronisation therapy

* HFrEF refers to patients with symptoms ± signs of heart failure associated with an LVEF less than 50% (unless otherwise specified)
† ARB should only be used if ACEI is contraindicated or not tolerated
‡ carvedilol, bisoprolol, metoprolol succinate, nebivolol
^ Commencing MRA usually avoided if serum K >5 mmol/L or CrCl <30 mL/minute
o ICD and/ or CRT

Adapted from Tomlinson S, Atherton JJ. Heart failure - The crucial role of the GP. MedicineToday 2018;19:19-27 with permission.

Antihyperglycemic Therapy in Adults with Type 2 Diabetes

At diagnosis, initiate lifestyle management, set A1C target, and initiate pharmacologic therapy based on A1C:

- A1C is less than 9%, **consider Monotherapy.**
- A1C is greater than or equal to 9%, **consider Dual Therapy.**
- A1C is greater than or equal to 10%, blood glucose is greater than or equal to 300 mg/dL, or patient is markedly symptomatic, **consider Combination Injectable Therapy** (See Figure 3).

Monotherapy — Lifestyle Management + Metformin

Initiate metformin therapy if no contraindications* (See Table 7)

A1C at target after 3 months of monotherapy?
- **Yes:** - Monitor A1C every 3–6 months
- **No:** - Assess medication-taking behavior
  - Consider Dual Therapy

Dual Therapy — Lifestyle Management + Metformin + Additional Agent

ASCVD?
- **Yes:** - Add agent proven to reduce major adverse cardiovascular events and/or cardiovascular mortality (see recommendations with * on p. 24 and **Table 7**)
- **No:** - Add second agent after consideration of drug-specific effects and patient factors (See Table 7)

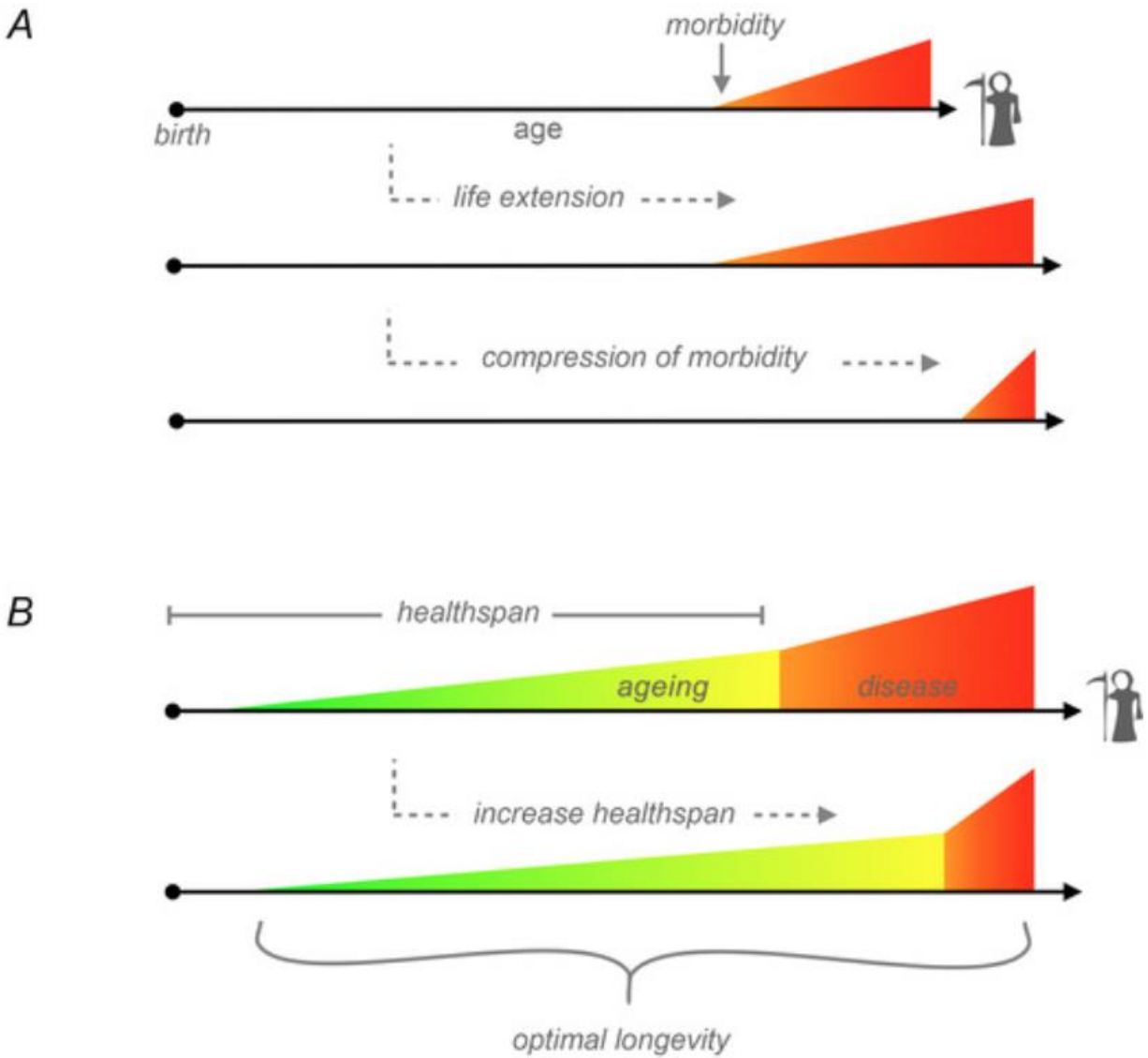
A1C at target after 3 months of dual therapy?
- **Yes:** - Monitor A1C every 3–6 months
- **No:** - Assess medication-taking behavior
  - Consider Triple Therapy

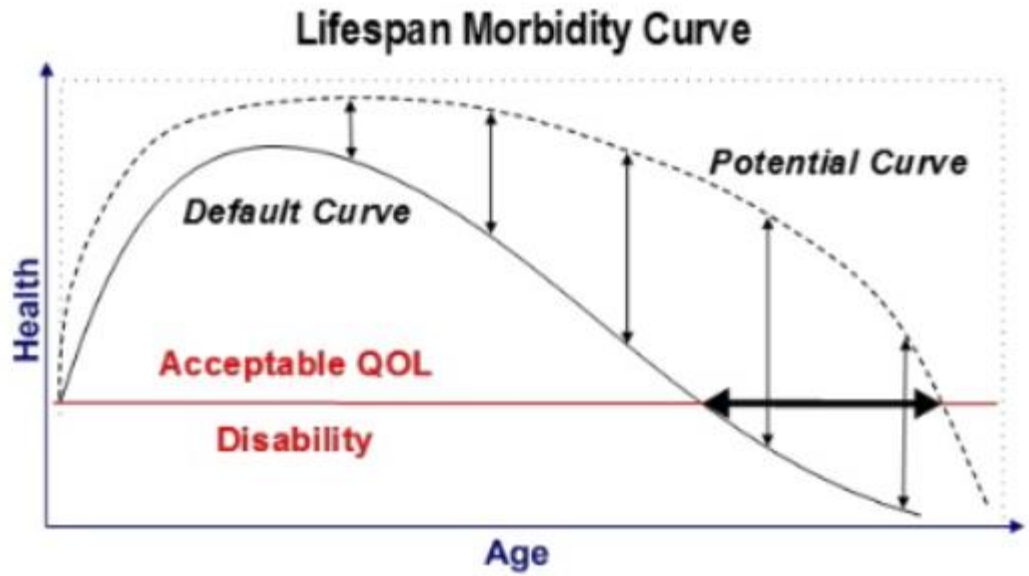
Triple Therapy — Lifestyle Management + Metformin + Two Additional Agents

Add third agent based on drug-specific effects and patient factors# (See Table 7)

A1C at target after 3 months of triple therapy?
- **Yes:** - Monitor A1C every 3–6 months
- **No:** - Assess medication-taking behavior
  - Consider Combination Injectable Therapy (See Figure 3).

Combination Injectable Therapy **(See Figure 3)**


A
morbidity
birth
age
life extension
compression of morbidity
B
healthspan
ageing
disease
increase healthspan
optimal longevity


Lifespan Morbidity Curve
Potential Curve
Default Curve
Health
Acceptable QOL
Disability
Age

Clinical Practice Guidelines and Quality of Care for Older Patients With Multiple Comorbid Diseases

Implications for Pay for Performance

JAMA, August 10, 2005—Vol 294, No. 6

Table 3. Treatment Regimen Based on Clinical Practice Guidelines for a Hypothetical 79-Year-Old Woman With Hypertension, Diabetes Mellitus, Osteoporosis, Osteoarthritis, and COPD*

Time	Medications†	Other
7:00 AM	Ipratropium metered dose inhaler 70 mg/wk of alendronate	Check feet Sit upright for 30 min on day when alendronate is taken Check blood sugar
8:00 AM	500 mg of calcium and 200 IU of vitamin D 12.5 mg of hydrochlorothiazide 40 mg of lisinopril 10 mg of glyburide 81 mg of aspirin 850 mg of metformin 250 mg of naproxen 20 mg of omeprazole	Eat breakfast 2.4 g/d of sodium 90 mmol/d of potassium Low intake of dietary saturated fat and cholesterol Adequate intake of magnesium and calcium Medical nutrition therapy for diabetes‡ DASH‡
12:00 PM		Eat lunch 2.4 g/d of sodium 90 mmol/d of potassium Low intake of dietary saturated fat and cholesterol Adequate intake of magnesium and calcium Medical nutrition therapy for diabetes‡ DASH‡
1:00 PM	Ipratropium metered dose inhaler 500 mg of calcium and 200 IU of vitamin D	
7:00 PM	Ipratropium metered dose inhaler 850 mg of metformin 500 mg of calcium and 200 IU of vitamin D 40 mg of lovastatin 250 mg of naproxen	Eat dinner 2.4 g/d of sodium 90 mmol/d of potassium Low intake of dietary saturated fat and cholesterol Adequate intake of magnesium and calcium Medical nutrition therapy for diabetes‡ DASH‡
11:00 PM	Ipratropium metered dose inhaler	
As needed	Albuterol metered dose inhaler	

SOUNDING BOARD

Potential Pitfalls of Disease-Specific Guidelines for Patients with Multiple Conditions

N ENGL J MED 351;27 WWW.NEJM.ORG DECEMBER 30, 2004

DISEASE GUIDELINES AND PRESCRIPTION DECISIONS

Making decisions about medications for patients with multiple conditions requires an optimal tradeoff between benefit and harm within the context of patients' health priorities. Such decision making depends on an accurate and complete presentation of the evidence — of the absolute benefit and harm over time with respect to a spectrum of outcomes — along with a discussion of preferences and tradeoffs. The successful translation of disease guidelines into prescriptions that meet the needs of individual patients hinges on the use of information technology to collect, analyze, and present complex data. Success also depends on effective communication between physicians and patients.[13]

Teachable Moment

Polypharmacy in the Elderly—When Good Drugs Lead to Bad Outcomes
A Teachable Moment

Casey Carroll, MD; Ahmed Hassanin, MD

JAMA Internal Medicine June 2017 Volume 177, Number 6

Story From the Front Lines

An 83-year-old woman with a history of atrial fibrillation and congestive heart failure was admitted to the hospital after presenting with lightheadedness and palpitations secondary to atrial fibrillation with rapid ventricular response. This was her third admission for atrial fibrillation with uncontrolled heart rate in the past 6 months. Pharmacy records indicated she had not refilled either of her prescribed nodal blocking agents for several months. She was restarted on her reported home dose of metoprolol succinate at 50 mg daily and diltiazem 180 mg daily with prompt normalization of heart rate. She was discharged the following day.

Two days after returning home, the patient presented to the emergency department with a presyncopal episode caused by bradycardia and hypotension after an unintentional metoprolol overdose. She was admitted to the intensive care unit and initiated on a glucagon drip. Her symptoms resolved after 24 hours, and she was transferred to the floor. At discharge, the patient expressed frustration with her home medication regimen, stating that it was confusing, burdensome, and expensive. Her pill regimen at home included 11 medications: metoprolol, diltiazem, digoxin, apixaban, atorvastatin, lisinopril, furosemide, ibandronate, loratadine, ranitidine, and a multivitamin. The patient and her family desired to simplify her medication regimen, preferring to continue only those that would help preserve function and keep the patient out of the hospital. At discharge digoxin and atorvastatin were discontinued.

Epidemiology of multimorbidity and polypharmacy

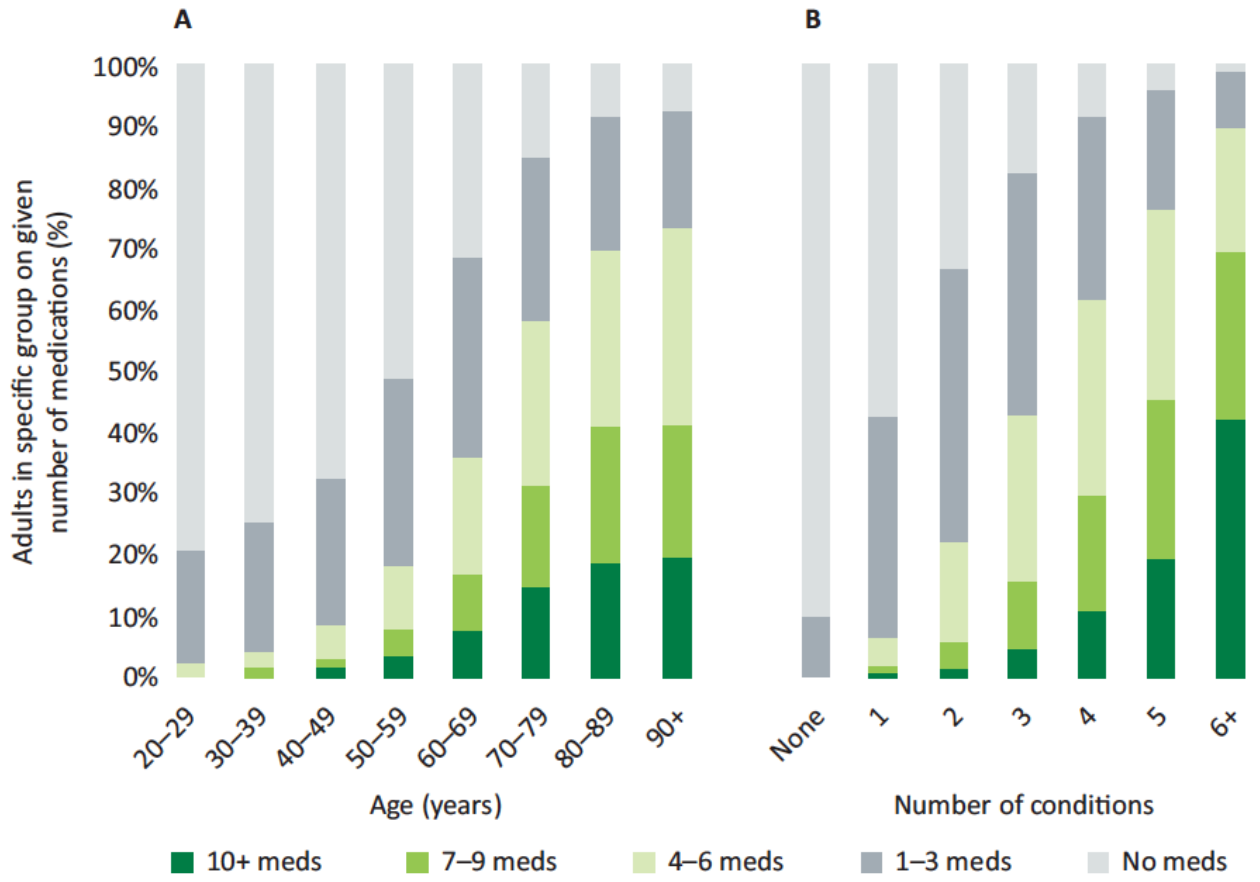
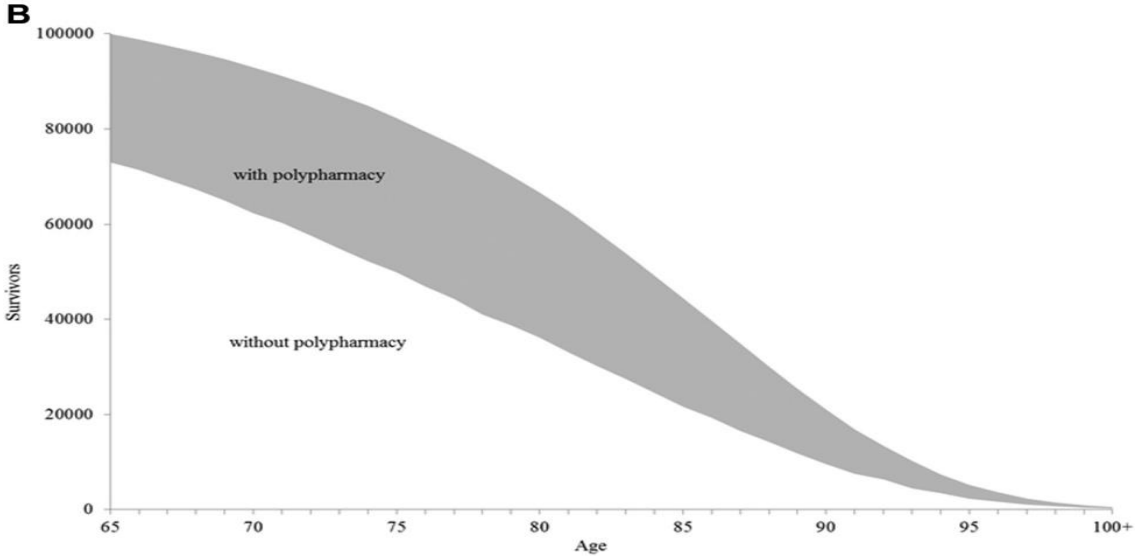


Fig 2. Percentage of Scottish adults on given number of medications by age (A) and number of conditions (B). Adapted with permission from Payne *et al.*[15]

Clinical Medicine 2016 Vol 16, No 5: 465–9

Older people spend most of their remaining life expectancy with polypharmacy

Males



Females

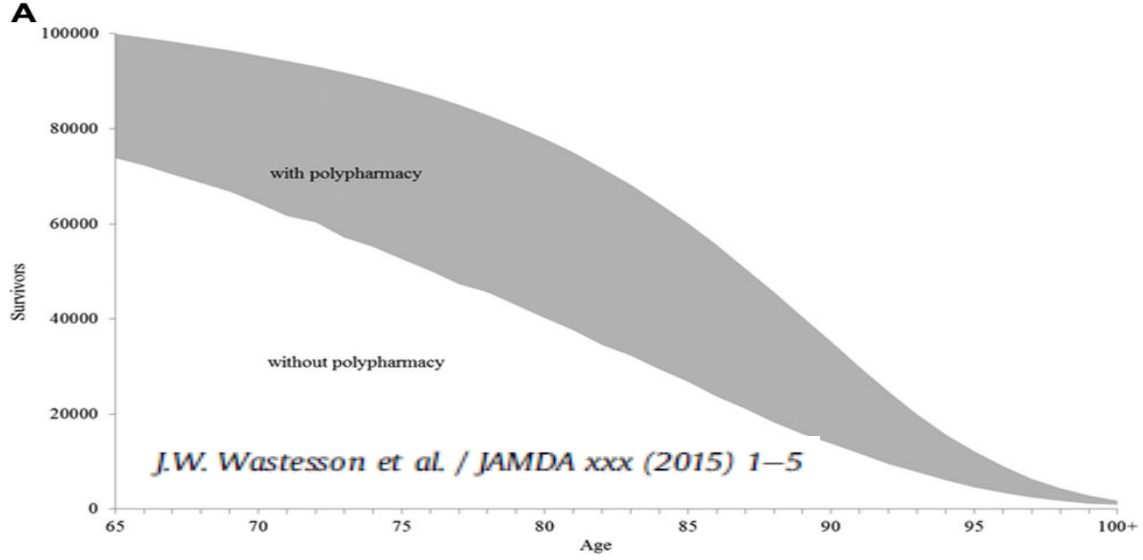
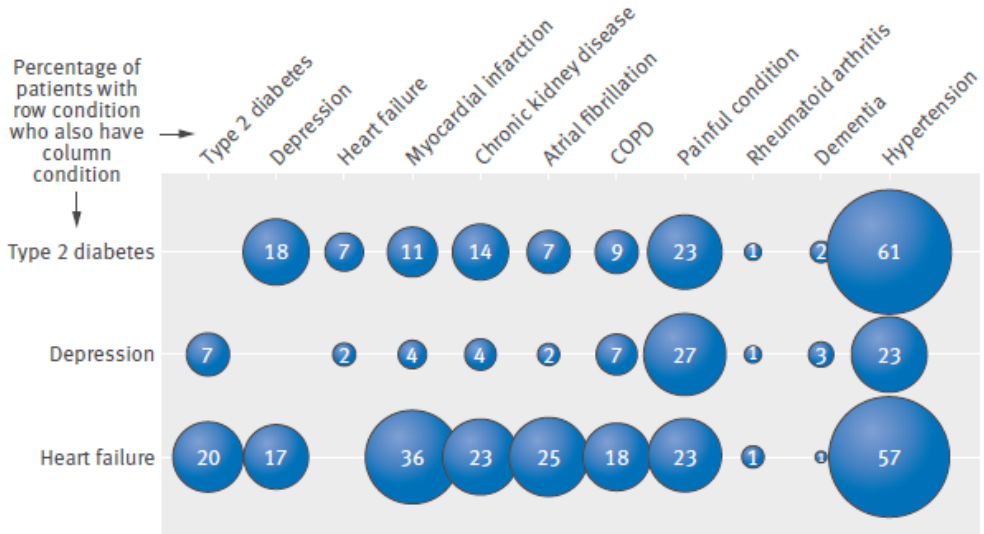


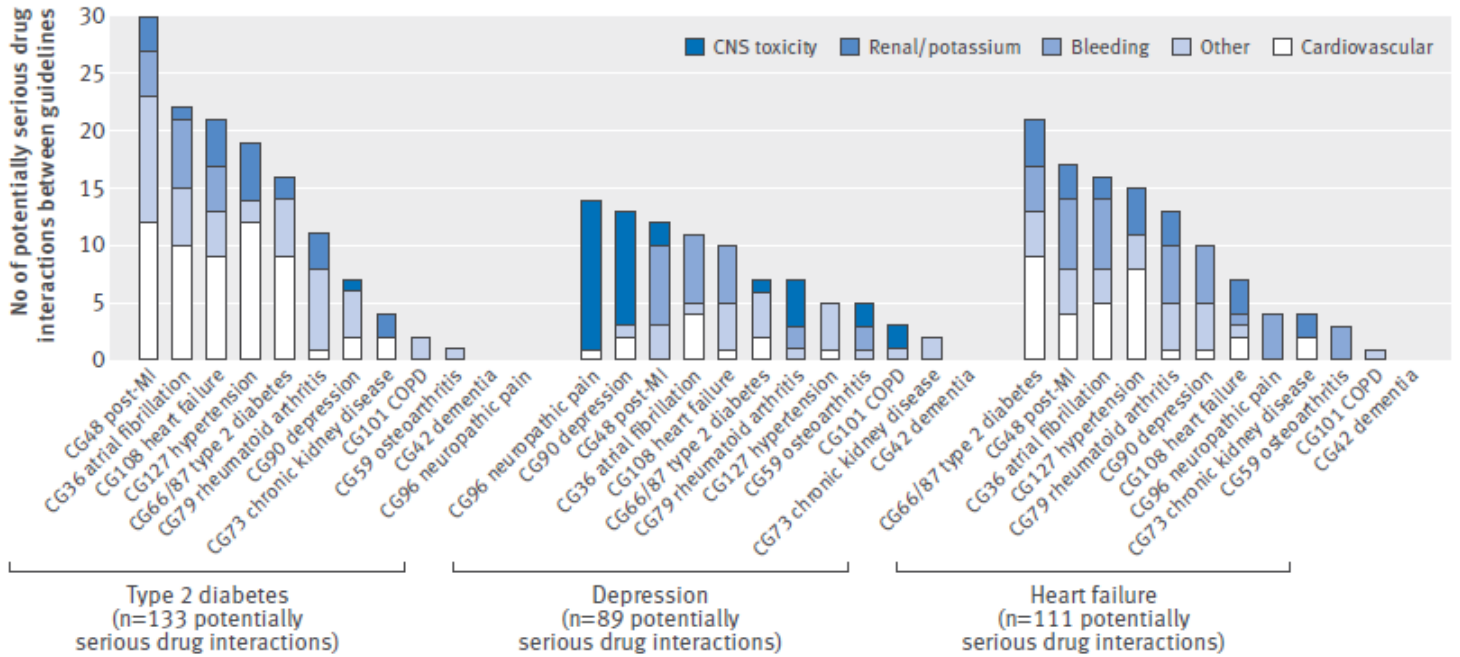
Table 1
Prevalence of Polypharmacy (PP) and Life Expectancy (LE) for Selected Ages Above 65 Total LE and divided into years with and without polypharmacy of the total remaining LE. Swedish total, female and male population 2008.

Age	Total Population				Female Population				Male Population			
	Polypharmacy, %	LE, y			Polypharmacy, %	LE, y			Polypharmacy, %	LE, y		
		Total	Without PP	With PP		Total	Without PP	With PP		Total	Without PP	With PP
65	26.6	19.7	11.6	8.1	26.2	21.0	12.1	8.9	27.0	18.1	11.0	7.1
70	32.8	15.7	8.6	7.1	32.6	16.9	9.0	7.9	33.0	14.3	8.1	6.2
75	40.1	12.0	6.1	6.0	40.8	13.0	6.3	6.6	39.4	10.8	5.8	5.1
80	47.3	8.7	4.1	4.7	48.4	9.4	4.2	5.2	45.8	7.7	3.9	3.9
85	53.9	6.0	2.6	3.4	55.4	6.4	2.6	3.8	51.3	5.3	2.5	2.8
90	58.9	3.9	1.6	2.3	60.9	4.1	1.6	2.5	54.6	3.5	1.6	1.9
95	60.7	2.5	1.0	1.5	62.2	2.6	1.0	1.6	55.9	2.4	1.1	1.3
100+	52.4	1.1	0.5	0.6	48.1	0.7	0.4	0.4	48.1	2.4	1.2	1.1

Drug-disease and drug-drug interactions: systematic examination of recommendations in 12 UK national clinical guidelines

thebmj | *BMJ* 2015;350:h949 | doi: 10.1136/bmj.h949





More research is needed to make guidelines effective and safe for patients with multimorbidity. In the meantime, new electronic tools, better use of old ones, and comprehensive assessments of patients will help doctors to optimise drug treatments by processing all the available information about each patient's diseases, drugs, and characteristics. For this group of vulnerable patients, doing the right thing could be better than doing the thing right.

Guidelines, polypharmacy, and drug-drug interactions in patients with multimorbidity

A cascade of failure

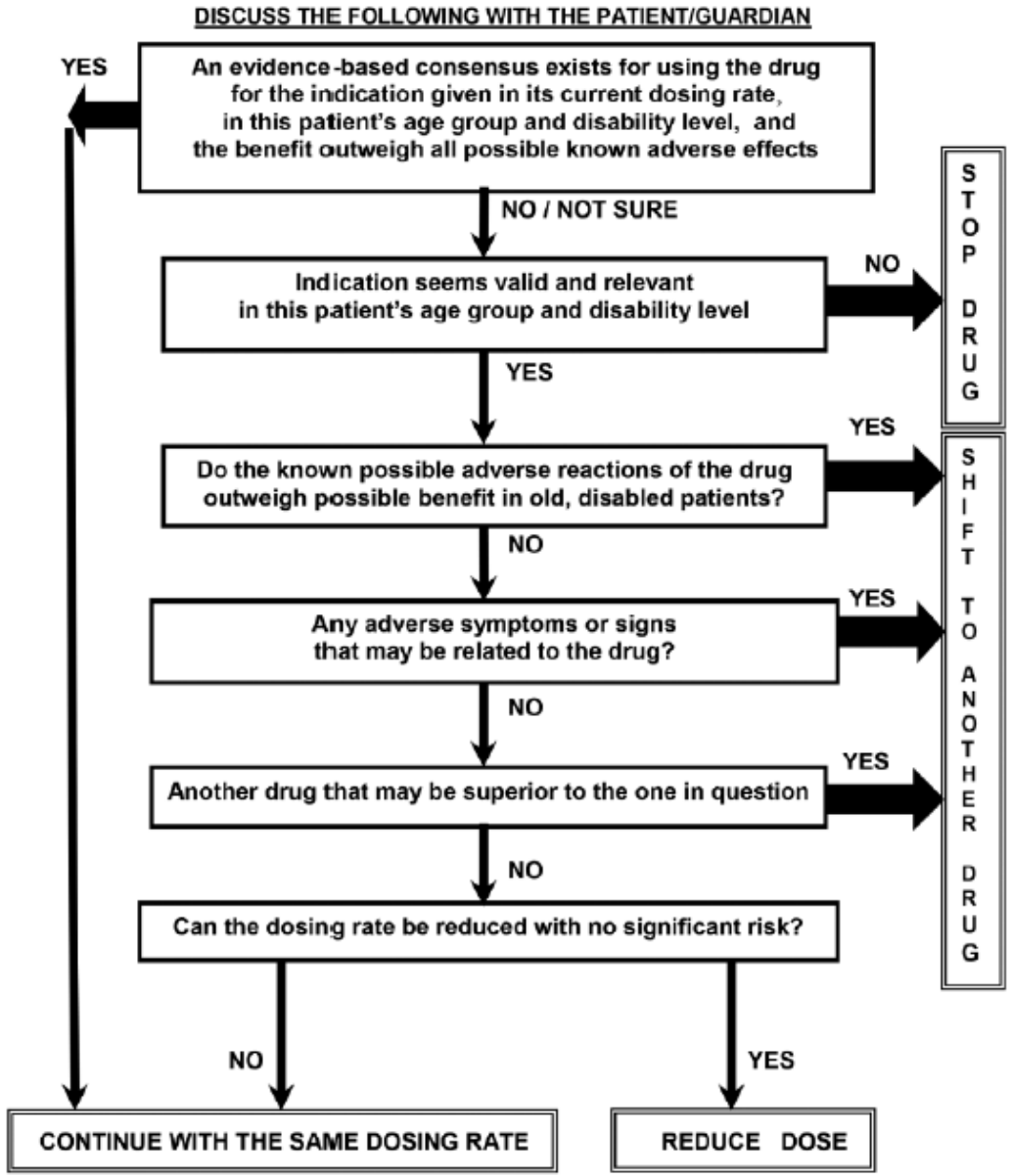
Alessandra Marengoni *assistant professor*[1 2], Graziano Onder *assistant professor*[2 3]

Deprescribing?

- The word “deprescribing” first appeared in the literature in 2003 [2,3]. With growing concern worldwide about the negative effects of overuse of certain medications, increasing attention is being paid to approaches to minimize harm. The focus is shifting from prescribing, which has traditionally been thought of as starting or renewing medications, to that of deprescribing - especially as people age.
- Deprescribing has been defined as “**the process of withdrawal of an inappropriate medication, supervised by a health care professional with the goal of managing polypharmacy and improving outcomes**” based on a systematic review of articles using this term between 2003 and 2014 [3]. Dose reduction and switching to safer medications are also considered deprescribing strategies that maintain effectiveness while minimizing harm.

E. Reeve et al. / European Journal of Internal Medicine 38 (2017) 3–11

Improving Drug Therapy in Elderly Patients – The Garfinkel Algorithm



Ref: Garfinkel D, Mangin D. Feasibility study of a systematic approach for discontinuation of multiple medications in older adults – Addressing Polypharmacy. ARCH INT MED 170: 1648-54, 2010.

Timeline of PIMs explicit criteria

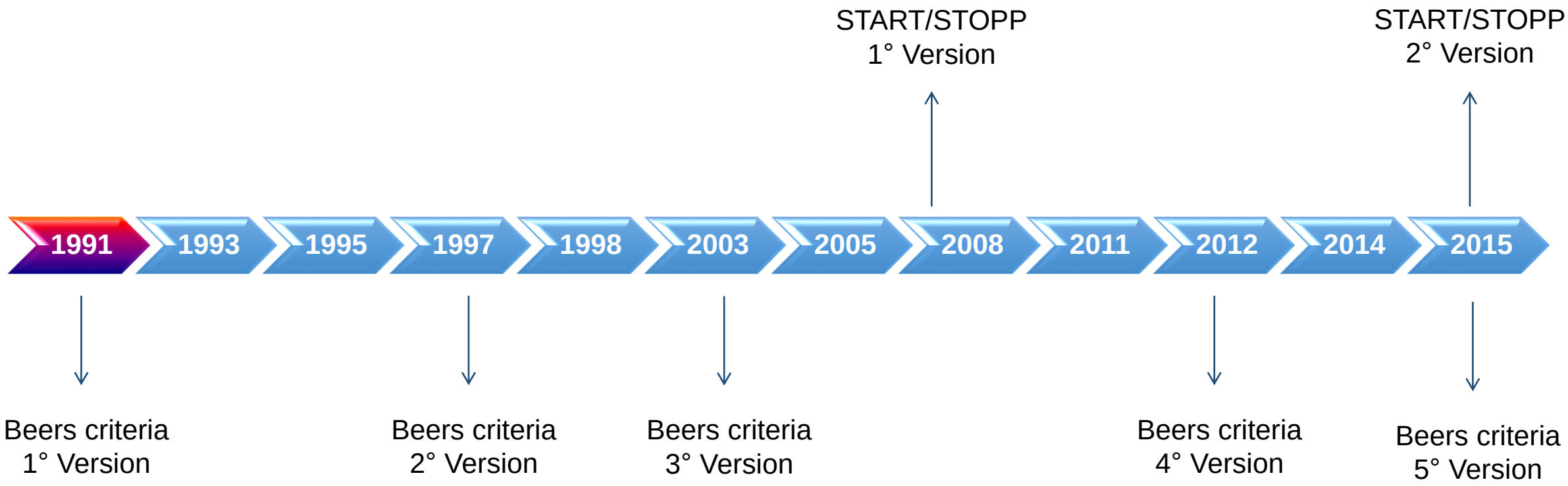
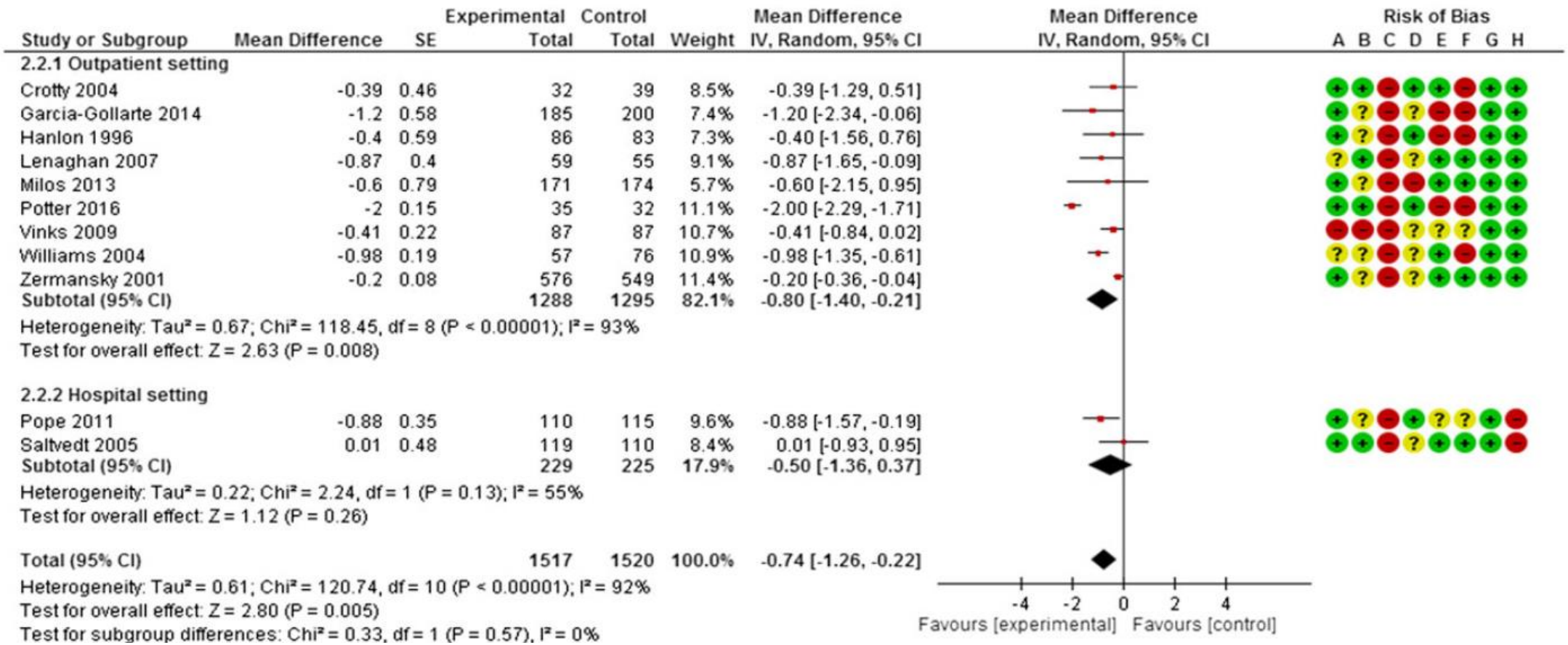


Figure 4

Mean difference in the change in number of drugs comparing experimental (intervention) group and control group. Subgroup analysis on intervention setting (outpatient setting versus hospital setting)



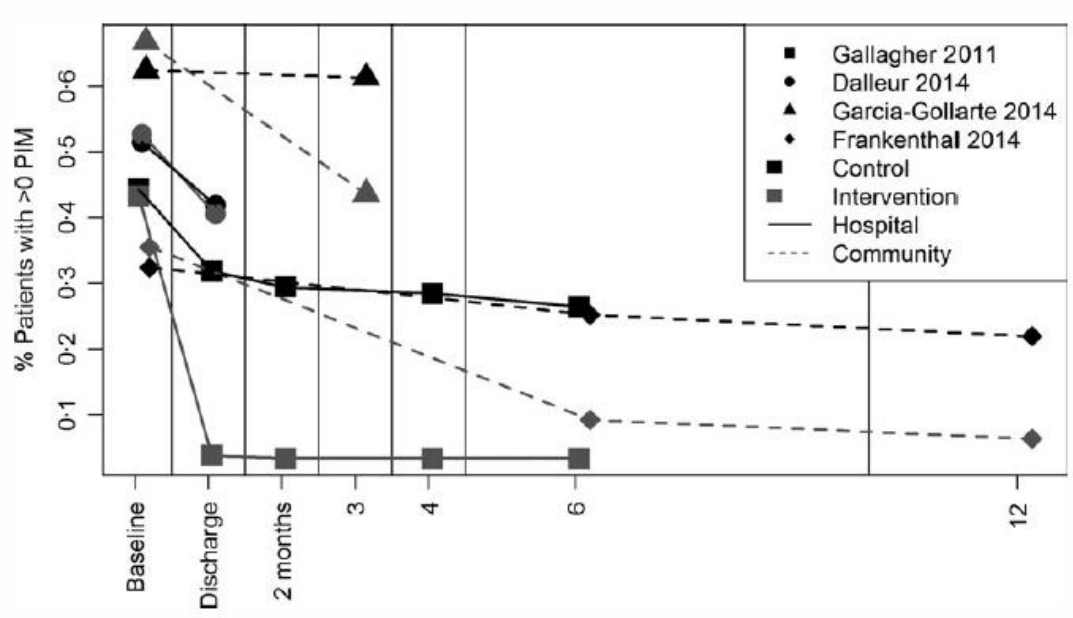
Br J Clin Pharmacol (2018)

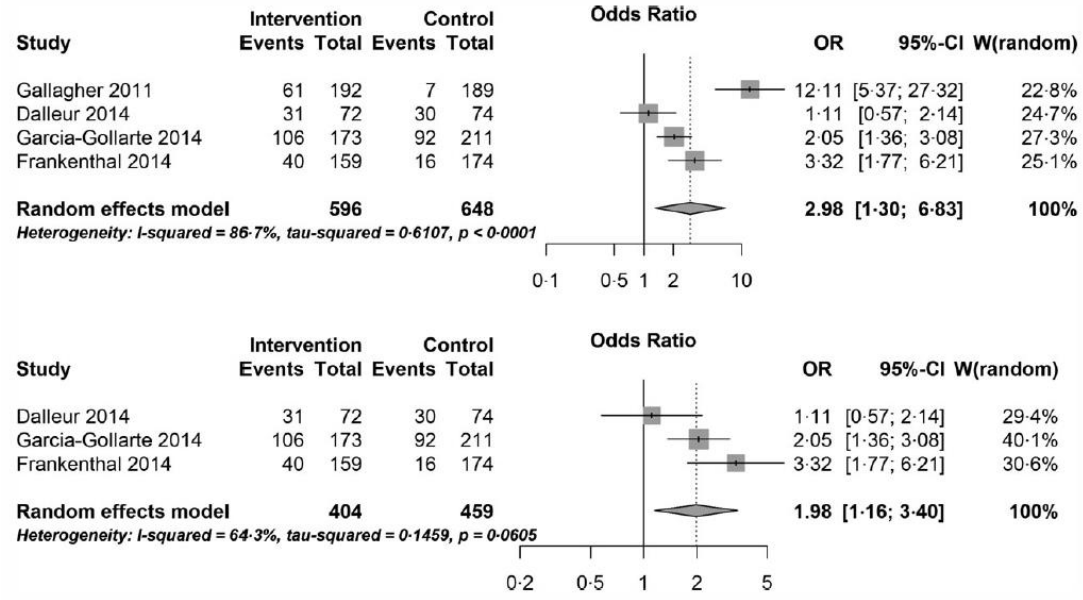
Journal of
Clinical Pharmacy and Therapeutics

Journal of Clinical Pharmacy and Therapeutics, 2016, **41**, 158–169 doi: 10.1111/jcpt.12372

Review Article

Effectiveness of the STOPP/START (Screening Tool of Older Persons' potentially inappropriate Prescriptions/Screening Tool to Alert doctors to the Right Treatment) criteria: systematic review and meta-analysis of randomized controlled studies





Current evidence

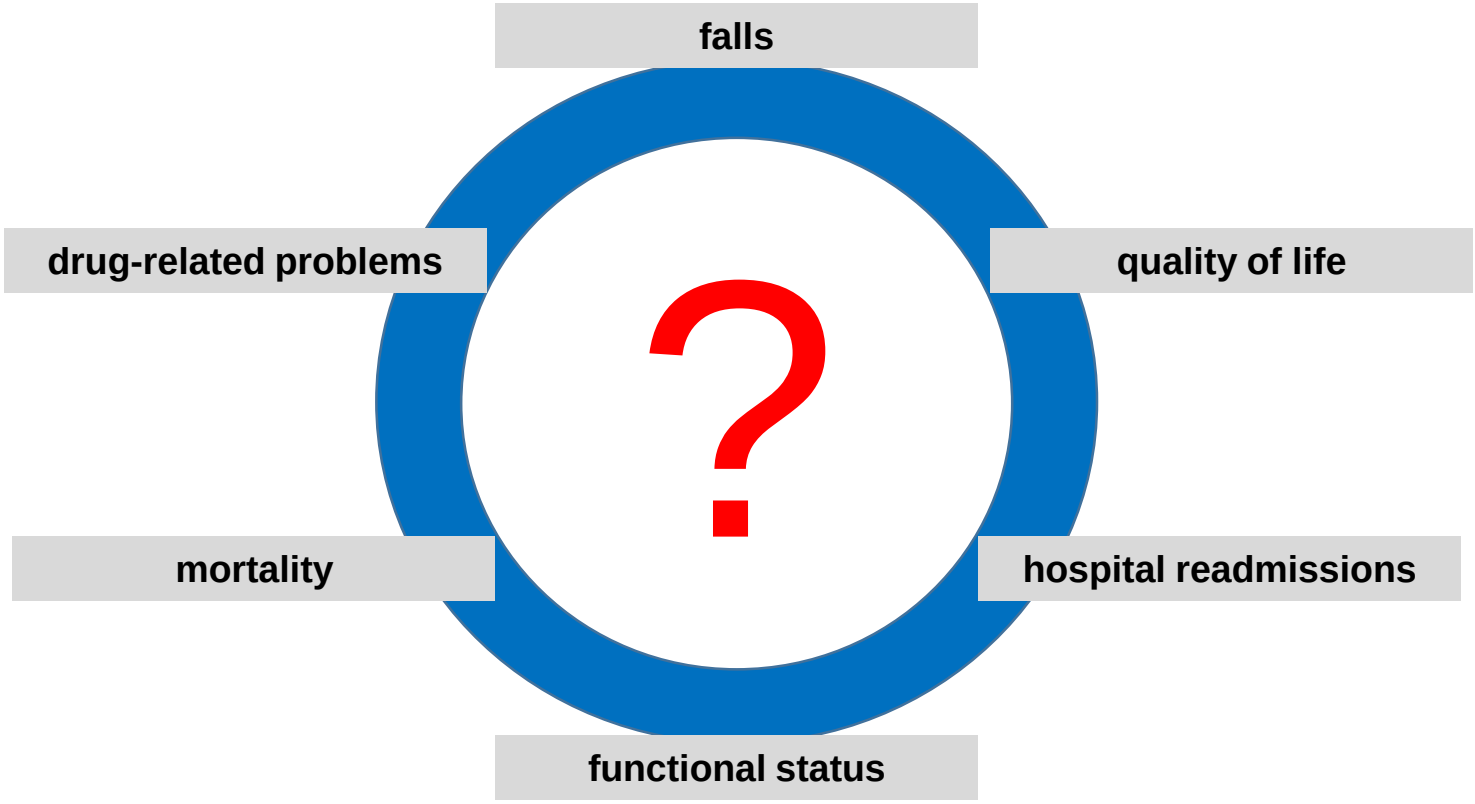
- Effects of deprescribing
  - A variety of interventions successfully reduced the number of medications taken by participants.
  - There was, however, minimal and conflicting data on clinical outcomes.
  - Only half out of 30 reviewed studies measured any type of clinical outcome. Six studies reported some benefit on clinical outcomes (e.g. reduction in serious ADRs), however the remaining nine found no positive effect of the intervention [Systematic Review, Gnjidic D et al, Clin Geriatr Med 2012].
  - Interventions to reduce polypharmacy generally lead to a reduction in inappropriate medication use [Cooper JA et al, BMJ Open 2015; Declercq T et al, Cochrane Database Syst Rev 2013].
  - **Currently we can not confirm that deprescribing leads to clinically important end-points such as improved mortality or reduced hospital admissions**.

E. Reeve et al. / European Journal of Internal Medicine 38 (2017) 3–11

Impact of Deprescribing Interventions in Older Hospitalised Patients on Prescribing and Clinical Outcomes: A Systematic Review of Randomised Trials.

Thillainadesan J, Gnjidic D, Green S, Hilmer SN.

Drugs Aging. 2018 Apr;35(4):303-319



Deprescribing in Frail Older People: A Randomised Controlled Trial

Kathleen Potter[1,3]*, Leon Flicker[1,2,3], Amy Page[1], Christopher Etherton-Beer[1,2,3]

PLOS ONE | DOI:10.1371/journal.pone.0149984 March 4, 2016

Table 3. Cognitive function, independence in ADLS, sleep quality, self-assessed quality of life, self-assessed general health.

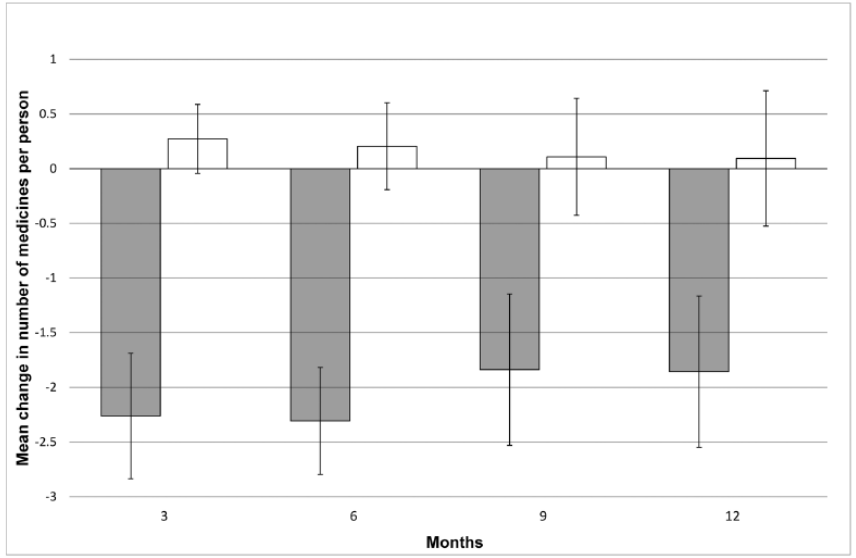
Outcome	6 months				12 months					
	Intervention		Control		Intervention		Control		p (raw)	p (adj)
	Change	n	Change	n	Change	n	Change	n		
MMSE	-2 (5)	39	-1 (5)	39	-3 (5)	34	-2 (4)	30	0.54	0.60
MBI	-8 (19)	39	-7 (14)	38	-10 (17)	34	-11 (15)	30	0.76	0.76
QOLAD	-0.7 (4.4)	23	-0.2 (4.8)	22	-1.0 (4.3)	22	-1.0 (4.7)	15	0.94	0.91
EQ-5D	-11 (24)	20	1(29)	17	-11 (17)	20	7 (15)	12	0.25	0.35
NPI-NH	-0.4 (4.9)	34	-0.1 (2.7)	39	-0.1 (4.7)	28	-0.2(2.3)	30	0.98	0.95
PSQI	-1 (3)	13	0 (1)	4	0 (3)	9	-1 (2)	3	0.78	0.76

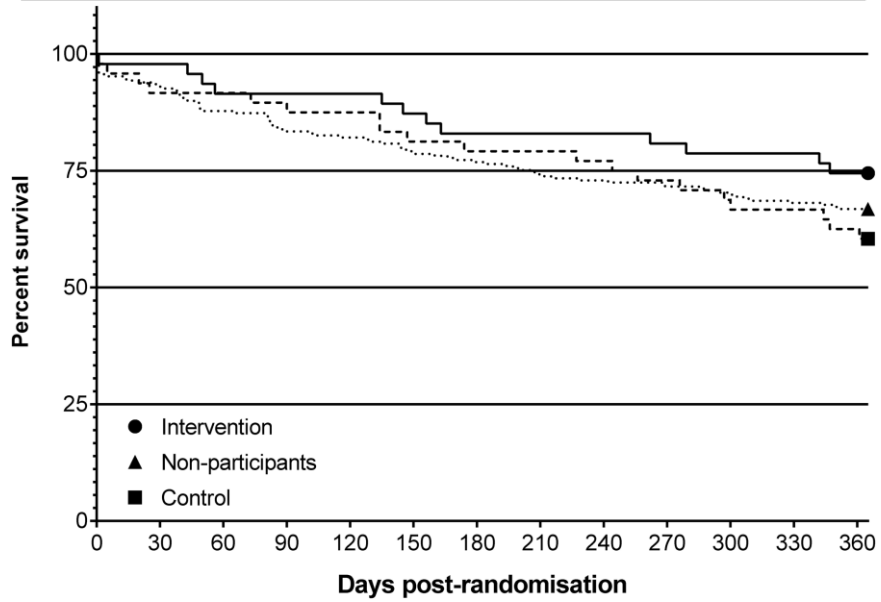
Table 4. Change in bowel function following deprescribing.

Bowel function*	6 months		p	12 months		p
	Intervention n = 39	Control n = 39		Intervention n = 34	Control n = 32	
Bowel motions	1.7 (7.0)	0.8 (3.8)	0.51	0.9 (3.7)	2.4 (6.3)	0.94
Any episode of faecal incontinence (n, %)	18 (46)	21 (54)	0.65	15 (44)	20 (63)	0.15
Episodes of faecal incontinence	3.9 (8.9)	2.9 (6.6)	0.65	3.6 (7.6)	2.8 (10.4)	0.77
Days with no bowel motion	-1.0 (3.7)	-0.4 (2.7)	0.53	-1.6 (3.9)	-1.4 (3.2)	0.86

Table 5. Adverse outcomes.

Outcome	Intervention (n = 45)		Control (n = 48)		p
	Proportion (95% CI)	Number of participants (number of events)	Proportion (95% CI)	Number of participants (number of events)	
Fall	0.56 (0.42, 0.69)	25 (221)	0.65 (0.50, 0.77)	31 (142)	0.40
Fracture	0.07 (0.02, 0.19)	3 (3)	0.04 (0.004, 0.15)	2 (2)	0.67
GP attendance	0.22 (0.12, 0.36)	10 (18)	0.10 (0.04, 0.23)	5 (10)	0.16
Call to GP	0.53 (0.39, 0.67)	24 (83)	0.60 (0.46, 0.67)	29 (71)	0.53
Hospital admission	0.51 (0.37, 0.61)	23 (43)	0.50 (0.36, 0.63)	24 (44)	0.99





JAMDA 19 (2018) 919–922

JAMDA

journal homepage: www.jamda.com

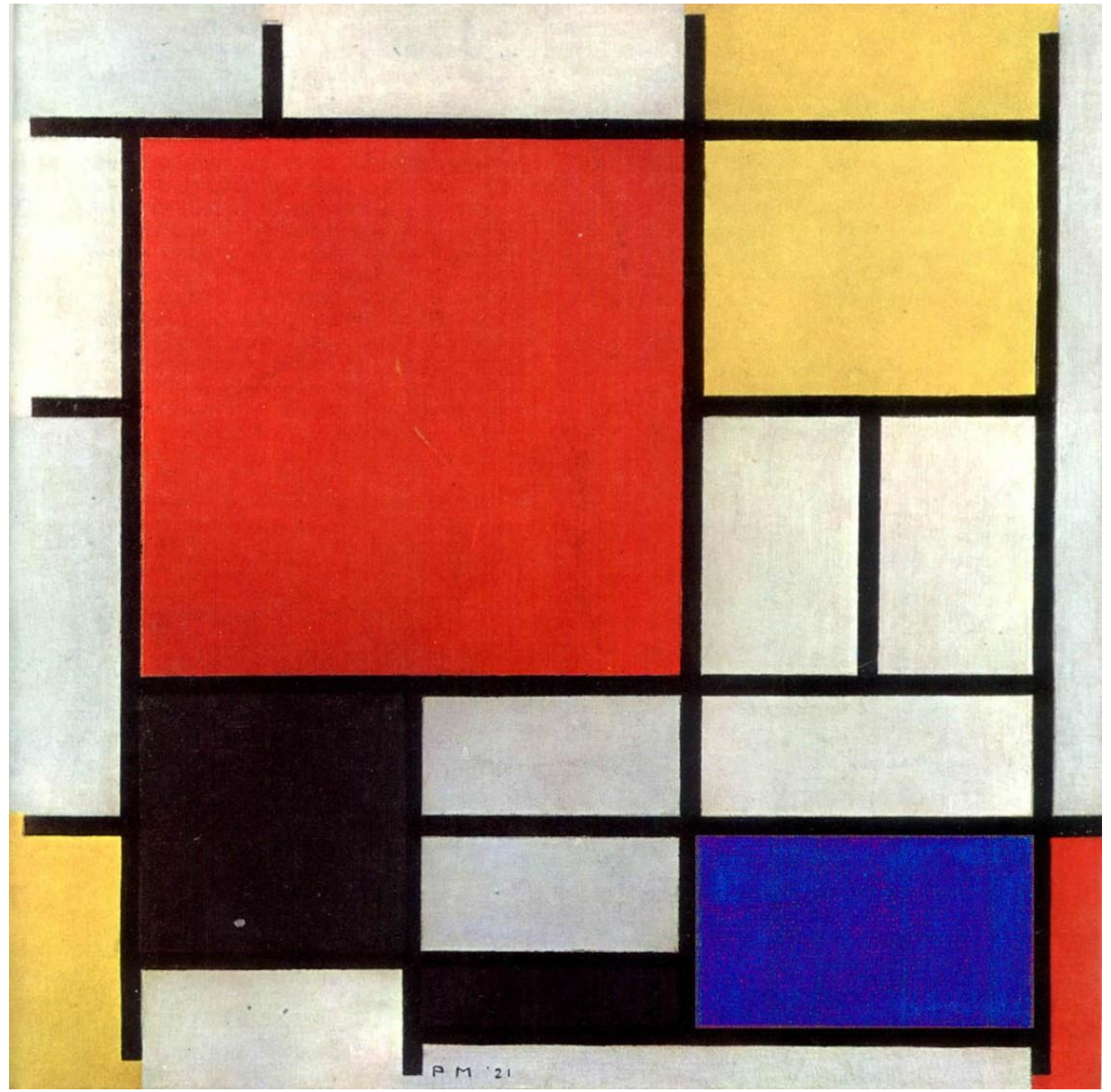
Editorial

Deprescribing in Geriatric Medicine: Challenges and Opportunities

Philip D. Sloane MD, MPH [a,*], Sheryl Zimmerman PhD [b]

Table 1
Barriers to Deprescribing in Clinical Practice

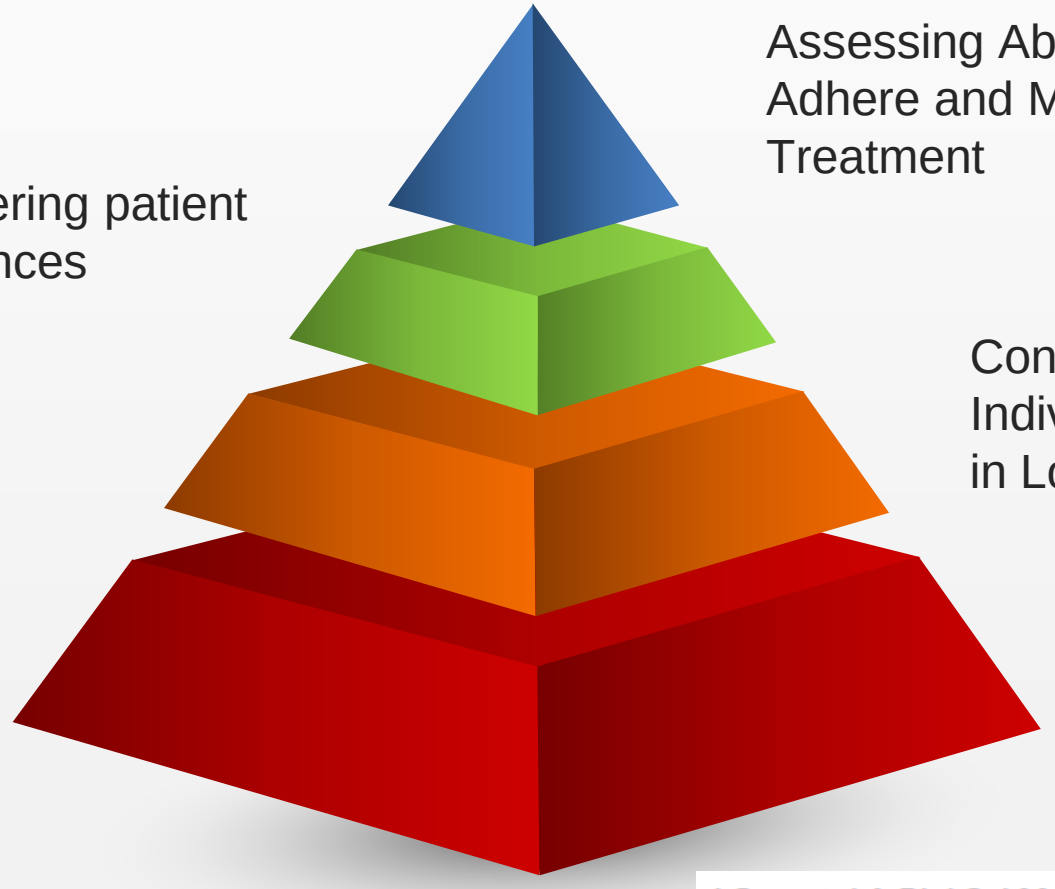
Barrier	Examples
Increasing numbers and effectiveness of medications for chronic diseases	Drug management of chronic congestive heart failure, chronic obstructive pulmonary disease, and rheumatoid arthritis
Pharmaceutical advertising	Aggressive media promotion of testosterone and of all classes of anticoagulants, despite conflicting research evidence
Organization of hospital and long-term care services around medication administration	Nurse role in nursing homes focuses largely on medication administration and monitoring
Medicalization and "pharmaceuticalization" of many ordinary problems	Promotion of pills to treat insomnia, constipation, anxiety, menopause, and gastroesophageal reflux
Ease of pill administration in comparison to changing personal behavior	Lifestyle modifications required to adopt a regular exercise routine or change longstanding dietary patterns
Ease and cost-efficiency of pill administration in residential long-term care settings	Lack of staff time and expertise to implement behavioral interventions; insurance pays for pills but not for behavioral interventions
Belief in the magical power of the pill	Consumers have unrealistic impressions that "there has to be a pill" for virtually any condition and that pills work; placebo effect
Patient resistance to stopping medications that relieve chronic symptoms, despite concern over long-term toxicity	Deprescribing interventions have particular difficulty getting patients to agree to stop taking opioid analgesics, proton pump inhibitors, sleeping pills, and antianxiety medications


P M '21

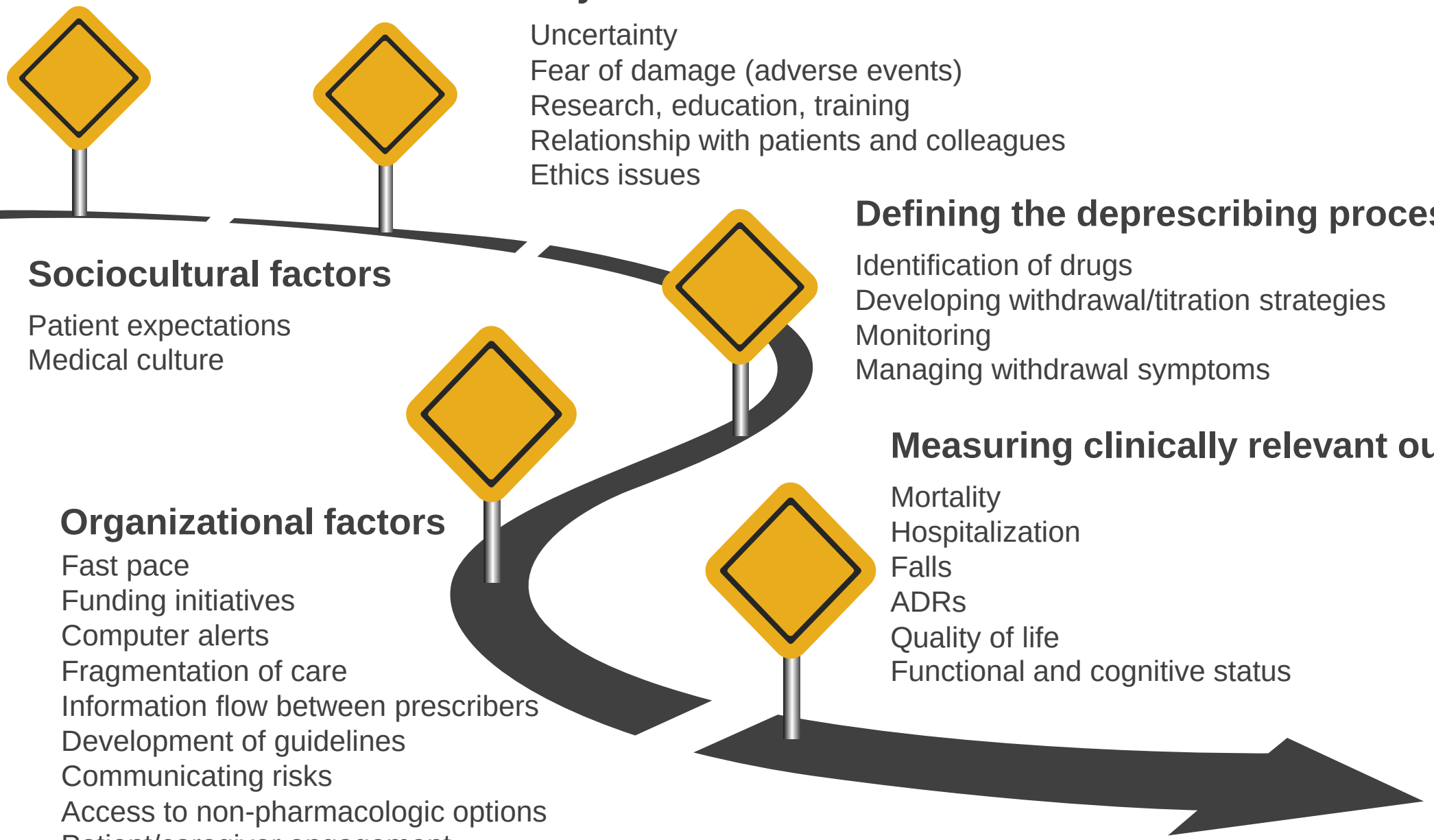
Potentially Inappropriate Drug Prescribing and the "Never Change a Winning Team" Principle

Graziano Onder,[1] Alessandro Nobili,[2] and Alessandra Marengoni[3]

Safe and effective evidence based deprescribing



J Gerontol A Biol Sci Med Sci, 2016, Vol. 71, No. 11, 1531–1532



Physician relational factors

Uncertainty
Fear of damage (adverse events)
Research, education, training
Relationship with patients and colleagues
Ethics issues

Sociocultural factors

Patient expectations
Medical culture

Defining the deprescribing process

Identification of drugs
Developing withdrawal/titration strategies
Monitoring
Managing withdrawal symptoms

Measuring clinically relevant outcomes

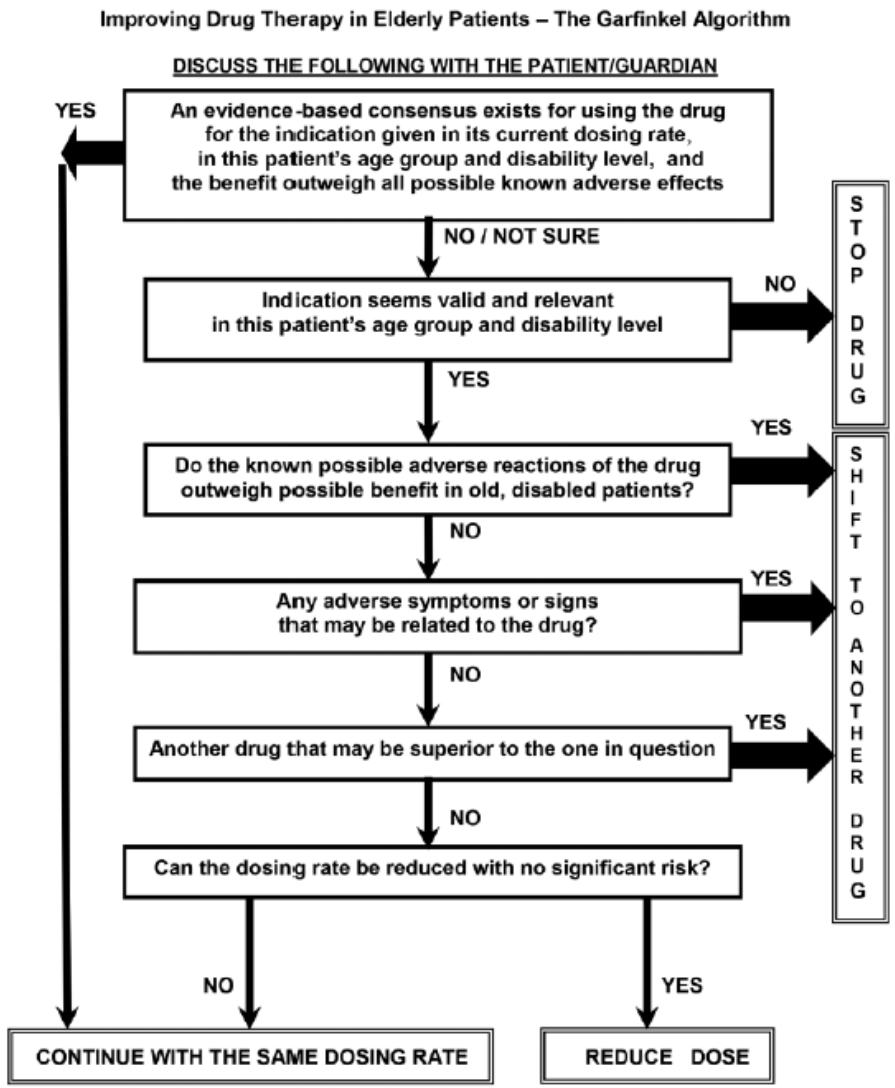
Mortality
Hospitalization
Falls
ADRs
Quality of life
Functional and cognitive status

Organizational factors

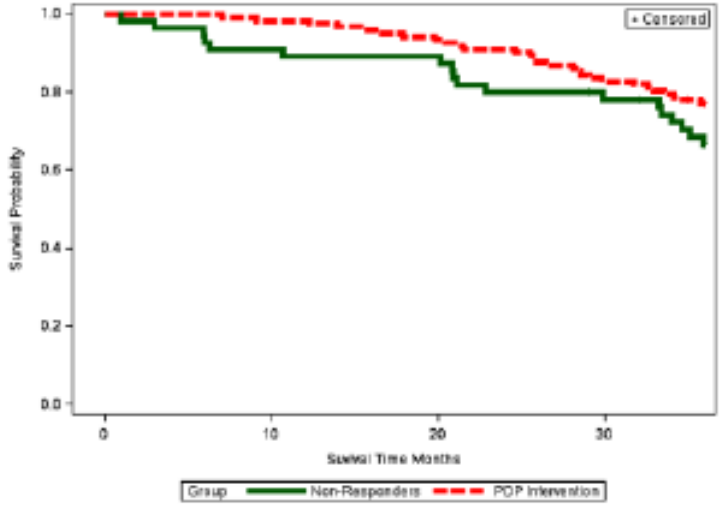
Fast pace
Funding initiatives
Computer alerts
Fragmentation of care
Information flow between prescribers
Development of guidelines
Communicating risks
Access to non-pharmacologic options
Patient/caregiver engagement

Safe and effective evidence-based deprescribing practice

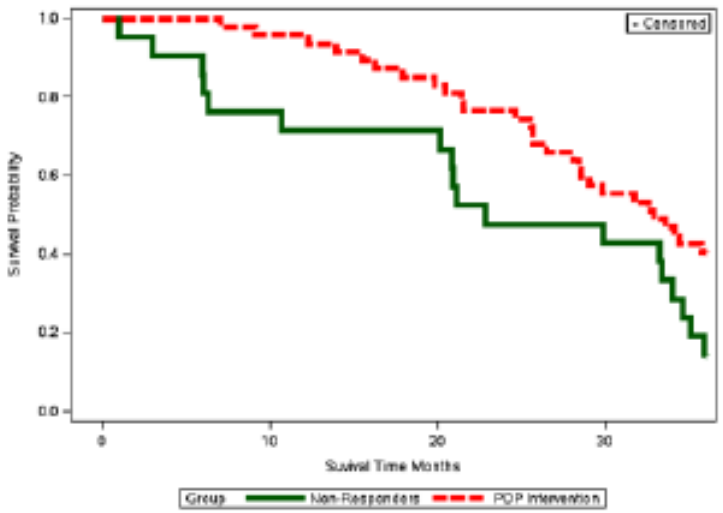
Backup



Ref: Garfinkel D, Mangin D. Feasibility study of a systematic approach for discontinuation of multiple medications in older adults – Addressing Polypharmacy. ARCH INT MED 170: 1648-54, 2010.



A. All Patients



B. Patients who Died (p=0.026)

Ther Adv Drug Saf

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Reducing Inappropriate Polypharmacy
The Process of Deprescribing

JAMA Intern Med. 2015;175(5):827-834. doi:10.1001/jamainternmed.2015.0324
Published online March 23, 2015.

Figure. Algorithm for Deciding Order and Mode in Which Drug Use Could Be Discontinued