Amsterdam UMC
Universitair Medische Centra

- Deprescribing - Innovation and Implementation

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Geriatric Medicine Amsterdam UMC

WFG
World Falls Guidelines for Prevention and Management of Falls in Older Adults

EuGMS
European Geriatric Medicine Society
Fostering geriatric medicine across Europe

CONFLICT OF INTEREST DISCLOSURE

No commercial interest

Governmental and university funding of ongoing falls/deprescribing studies by:

ZonMW, NWO, VWS, Amsterdam Universityfund

Faculty: Geriatrics, Amsterdam UMC

Multimorbidity

- 2/3 ≥65 yrs multiple chronic conditions

- 65 yrs 50% ≥1 diseases
- 75 yrs 50% ≥3 diseases

Rochon PA et al, Lancet Healthy Longev 2021; Stuck AE, Age Ageing 2022

Polypharmacy

- **Chronic drug use** ≥65 yrs
- >90% ≥1 prescribed drug(s)
- 45% polypharmacy

Delara M et al, BMC Geriatrics 2022, Lavan AH et al, Ther Adv Drug Saf 2016

Polypharmacy

- Appropriate
  - ↓ Unfavorable outcomes
  - Prolonging life
- Inappropriate
  - No (EB) indication
  - Not effective
  - Risk of ADRs

Rochon PA et al, Lancet Healthy Longev 2021; Stuck AE, Age Ageing 2022

Potentially inappropriate medication (PIM)

- Highly prevalent
  - Instutional care ±50%
  - Community dwelling older adults ±25%

Fialova D et al, Ther Adv Drug Saf, 2019; Petrovic M et al, Age Ageing 2022; Mucalo I et al, Eur J Clin Pharm 2017

ADEs & ageing

Risk ADEs ↑ :

- Changes in pharmacodynamics & kinetics
- Problems following prescription
- Vision, memory, mobility

Delara M et al, BMC Geriatrics 2022, Lavan AH et al, Ther Adv Drug Saf 2016

Geriatric conditions & ADRs, putative mechanisms

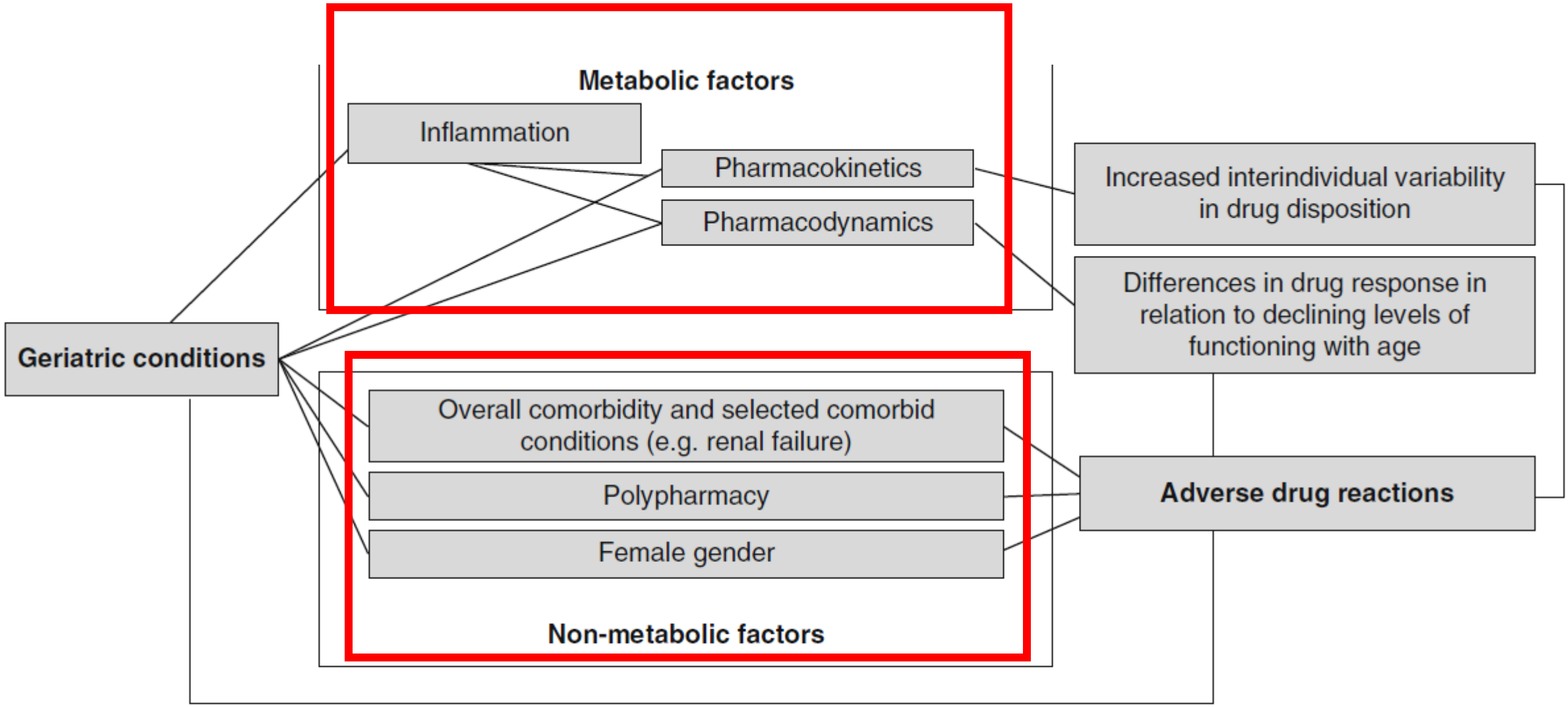

Fig. 1. Putative mechanisms linking geriatric conditions and adverse drug reactions.

F Lattanzio et al. Drug Saf 2012.(35)

Aging & ADRs

- Risk adverse drug reactions ↑2-3x
  Predominantly in polypharmacy
- Up to 25% hospital admissions due to ADR
- Serious ADRs:
  GE-bleeding, *fall related injury*

Lavan AH et al, Ther Adv Drug Saf 2016, Schmiedl S et al, Exp Opin Drug Saf 2019, Oscanoa TJ et al, Eur J Clin Pharmacol 2017

Adverse events & hospital admissions

8.6 million yearly in Europe

- 70%: older patients with polypharmacy
- 50% preventable

https://simpathy.eu/resources/publications/simpathy-project-reference-book

WHO: Medication Without Harm

Third international Global Patient Safety Challenge

Goals:

- Global awareness PIM and hazardous prescribing
- 50%↓ serious avoidable medication harm in 5 yrs time

"I've thrown in some prescription drugs that don't interact well."

https://www.who.int/patientsafety/medication-safety/en/2017

Facilitating optimal pharmacotherapy

- Regularly pro-actively re-evaluate polypharmacy appropriateness
  - At least yearly
  - Every 6 months if frail
  - Changed health conditions, acute setting

- Especially if frail, cognitively impaired, geriatric syndromes

https://www.nice.org.uk/guidance/qs85; Van Poelgeest et al, submitted

Medication review

- Systematic, structured approach

- Apply structured & validated tools
  - Evidence-based deprescribing guidelines eg. deprescribing.org
  - Supporting tools eg. Beers, STOPP/START and STOPPFrail, STOPPFall
  - Clinical decision support systems

American Geriatrics Society Beers Criteria® Update Expert Panel, JAGS 2019; O'Mahony D et all, Age Ageing 2015; Lavan AH, Age Ageing 2017

Medication review

- Individualized: patient characteristics, drug-drug and drug-disease interactions, efficacy & safety

- Special attention: high-risk medications, uneffective/ unnecessary medications, preventive drugs aimed at long-term benefit

- Be aware prescribing cascades

Mungin D et al, Drugs Aging 2018; Odden MC et al, JAMDA 2021; McCarthy L et al, Drugs Aging 2022; Van Poelgeest E et al, EGM, submitted

The challenge of deprescribing

- Drug prescriptions based on single-disease guidelines
- Context of multiple diseases and patient characteristics (frailty)
- Beliefs in positive health effects
- Few patients recognize & mention potential ADE

Van Poelgeest E et al, EGM, submitted

Patient empowerment

- Improving health literacy
  Inform adequately
  Educational materials

- Shared decision making
  Goals & values

How can the pharmacist help me?

Your pharmacist knows if your medications can be taken together or if there are combinations that increase your risk of falling

- Ask your pharmacist to educate you about your medication and possible side effects
- Report any concerns about your medication use to your pharmacist
- Tell your pharmacist if you are experiencing side effects. Perhaps you can use less of this medication or another drug is more suitable for you
- Ask your pharmacist whether you can take all your different medications together
- Ask your pharmacist how to properly take your medication and what the best time of the day is to take your medications

Always try to go to the same pharmacy. This allows your pharmacist to have a good and up-to-date overview of all medication that you use.

What can I do to decrease the risk of falling caused by medications?

Fill in the checklist!

- ☐ I ask my GP and pharmacist to check my medication yearly.
- ☐ I ask my pharmacy for an up-to-date medication list.
- ☐ I tell my GP, consultant and pharmacist which medications I bought over the counter or which I bought at a foreign pharmacy.
- ☐ I use only my own medication and I only use the prescribed amount of medication.
- ☐ I ask my doctor or pharmacist whether I use medication that might increase my fall risk.
- ☐ When I get a new prescription, I ask about the possible side effects and if this medication can be taken together with my other medications.
- ☐ I inform my GP when I have fallen, even if I didn't sustain (major) injuries.
- ☐ I ask my GP for a general leaflet about falls and fall prevention.

Useful website for more information

www.csp.org.uk/conditions/falls-fractures

www.nhs.uk/conditions/falls/

www.eugms.org/research-cooperation/task-finish-groups/frid-fall-risk-increasing-drugs

veiligheid nl
kenniscentrum letselpreventie

Amsterdam UMC
Universitair Medische Centra

KNMP

BGS

Jansen J et al, BMJ 2016

Values and goals: ranking health outcomes

Table. Proportion of Participants With Different Health Outcome Rankings, Organized by Health Outcome Ranked as Most Important

Health Outcome Ranking				
First (Most Important)	Second	Third	Fourth	No. (%)[a]
Independence				270 (76)[b]
	Pain relief	Symptom relief	Staying alive	104 (39)[c]
	Symptom relief	Pain relief	Staying alive	76 (28)[c]
	Staying alive	Pain relief	Symptom relief	38 (14)[c]
	Staying alive	Symptom relief	Pain relief	22 (8)[c]
	Pain relief	Staying alive	Symptom relief	19 (7)[c]
	Symptom relief	Staying alive	Pain relief	11 (4)[c]
Staying alive				40 (11)[b]
	Independence	Pain relief	Symptom relief	13 (33)[c]
	Independence	Symptom relief	Pain relief	13 (33)[c]
	Pain relief	Independence	Symptom relief	7 (18)[c]
	Pain relief	Symptom relief	Independence	5 (13)[c]
	Symptom relief	Independence	Pain relief	2 (5)[c]
Pain relief				26 (7)[b]
	Independence	Symptom relief	Staying alive	11 (42)[c]
	Symptom relief	Independence	Staying alive	7 (27)[c]
	Independence	Staying alive	Symptom relief	4 (15)[c]
	Symptom relief	Staying alive	Independence	3 (12)[c]
	Staying alive	Symptom relief	Independence	1 (4)[c]
Symptom relief				21 (6)[b]
	Independence	Pain relief	Staying alive	11 (52)[c]
	Staying alive	Independence	Pain relief	4 (19)[c]
	Independence	Staying alive	Pain relief	3 (14)[c]
	Pain relief	Independence	Staying alive	2 (10)[c]
	Pain relief	Staying alive	Independence	1 (5)[c]

76%

Fried TR, Arch Intern Med/Vol 171 (no. 20), Nov 14, 2011

Joint medication management

Goals

-values, goals in life

Treatment choices

-trade offs

Treatment options

-expected results

Decision making

Evaluation decision making process

European survey on deprescribing practices

- 964 participants, 21% geriatricians in training

- Generally willing to deprescribe (94%)
- Confident about deprescribing (85%)

- Medical training poorly prepared (25%: sufficient)

Van Poelgeest E et al, EGM 2022

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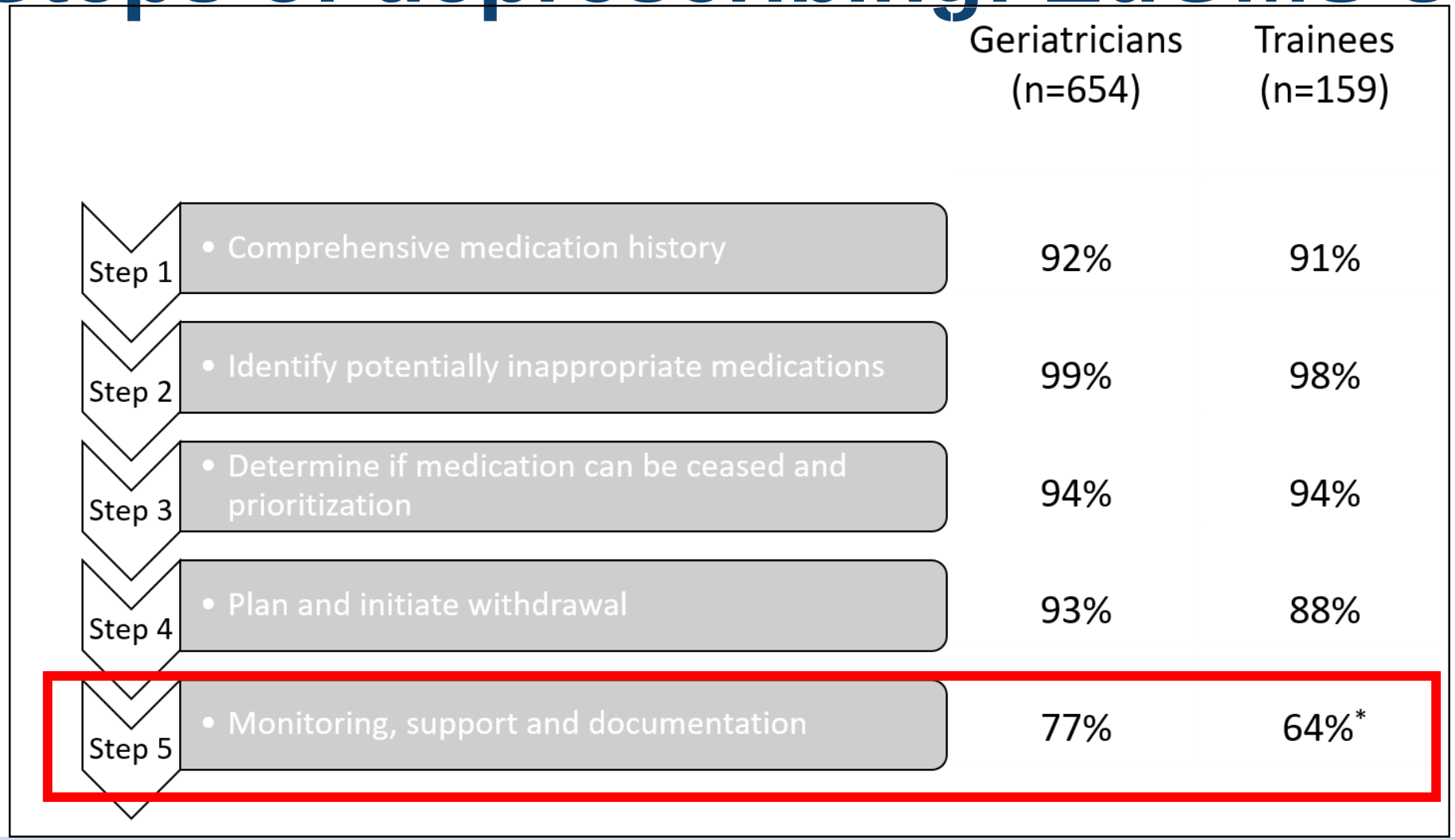
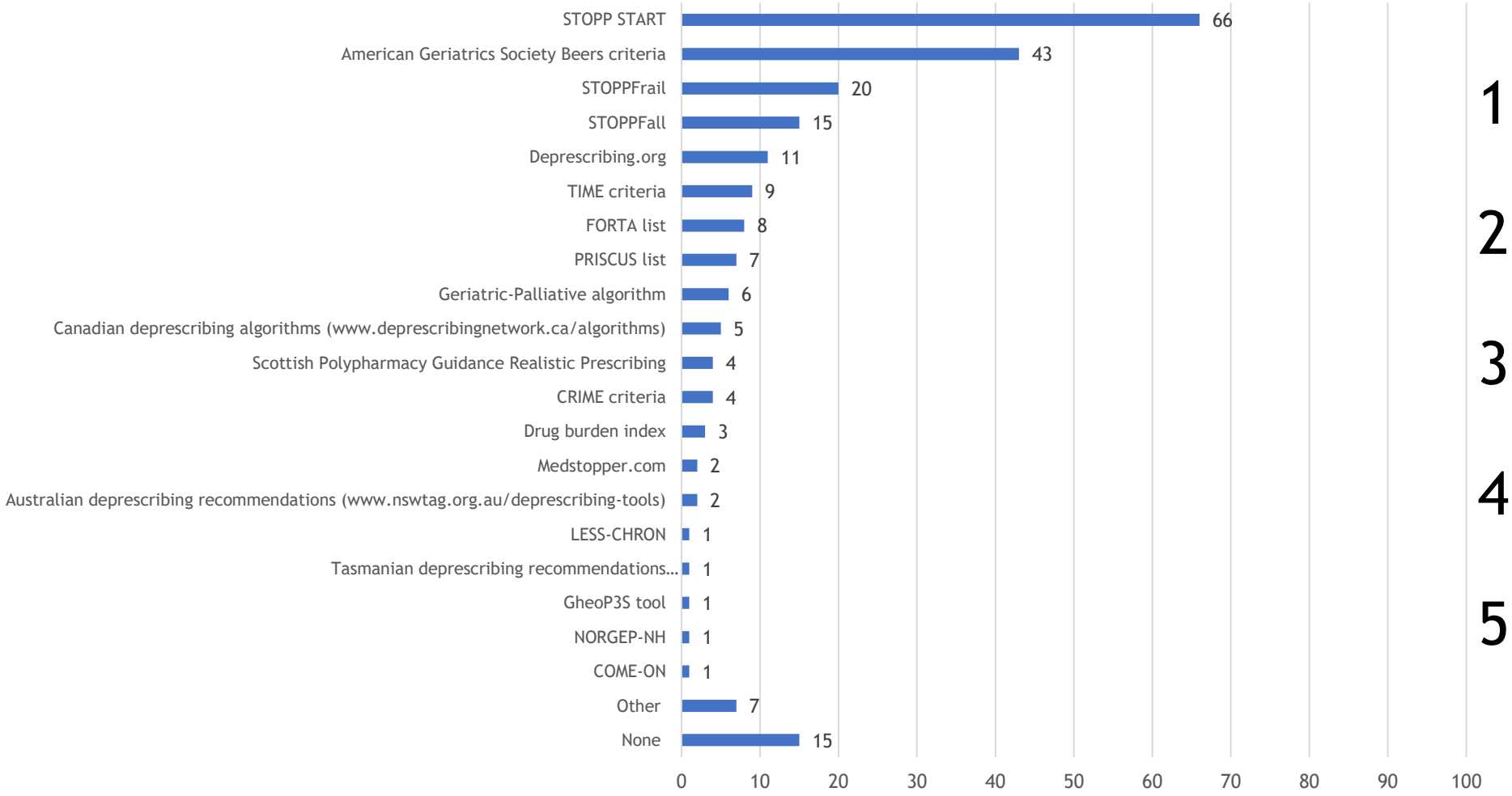
5 Steps of deprescribing: EuGMS survey



Van Poelgeest et al, EGM 2022; Reeve E, Br J Clin Pharm 2014

Frequently used tools: EuGMS survey

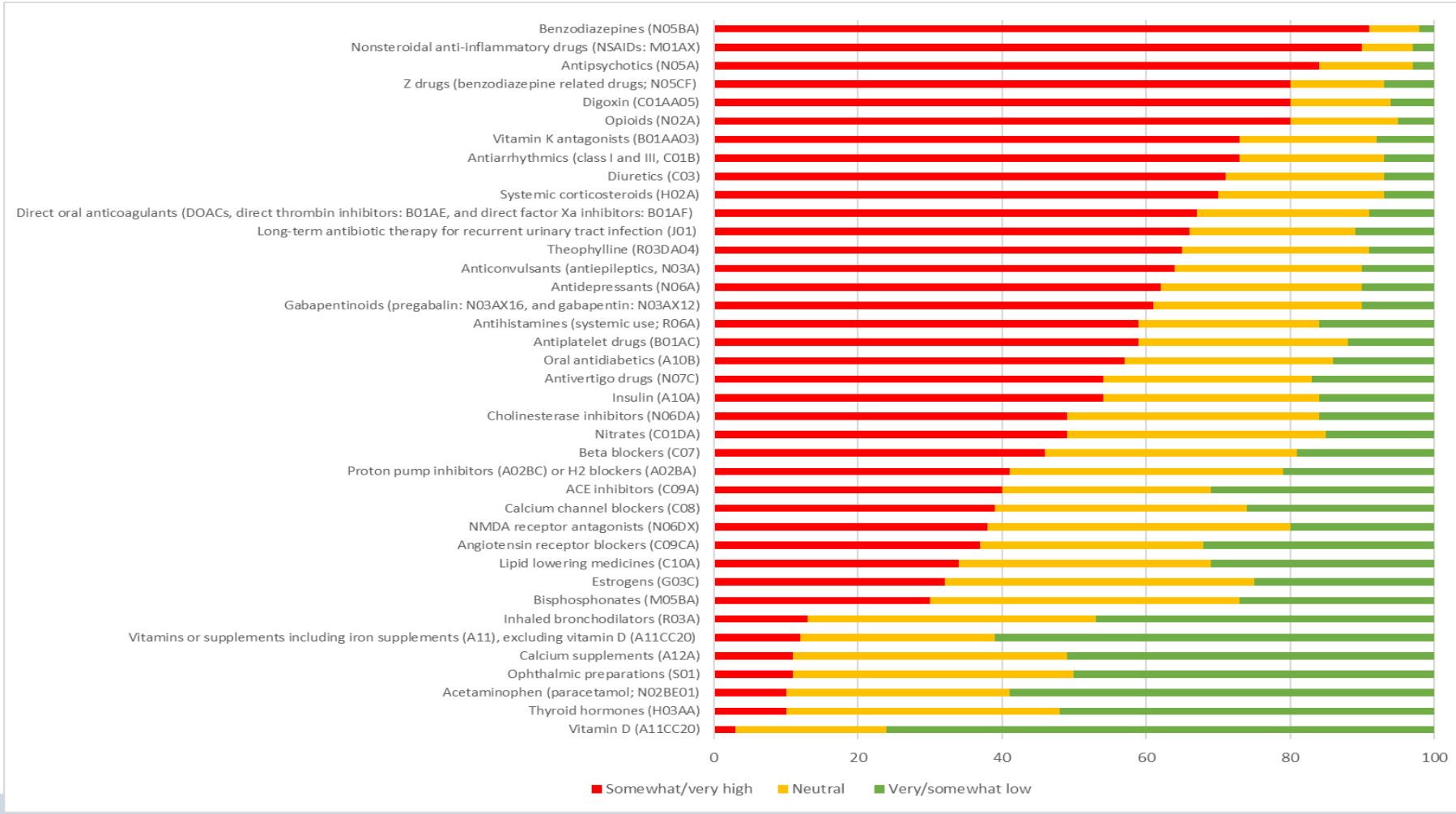


1. STOPP/START
2. Beers
3. STOPPFrail
4. STOPPFall
5. Deprescribing.org

Van Poelgeest et al, EGM 2022

Risk drugs according to EuGMS survey

1. Benzodiazepines
2. NSAIDs
3. Z-drugs
4. Digoxin
5. Opioids



Van Poelgeest et al, EGM 2022; Reeve E, Br J Clin Pharm 2014

STOPP/START vs 3

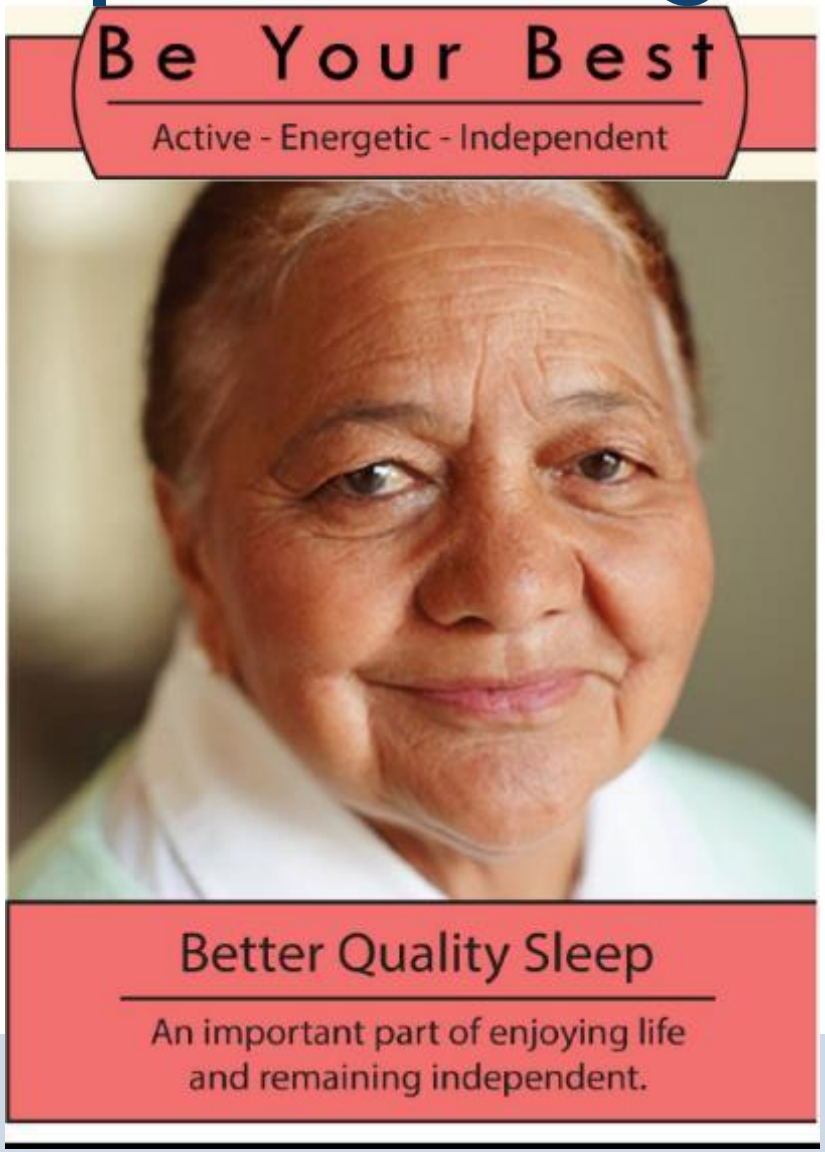
114→ 191 criteria

Category	STOPP criteria (% change)
Cardiovascular system	21 (61.5% increase)
Coagulation system	16 (23.1% increase)
Central nervous system	25 (78.6% increase)
Renal system	10 (66.7% increase)
Gastrointestinal system	8 (100.0% increase)
Respiratory system	4 (0% increase)
Musculoskeletal system	9 (0% increase)
Urogenital system	8 (400% increase)
Endocrine system	10 (66.7% increase)
Falls-risk increasing drugs	12 (300% increase)
Analgesic drugs	6 (100% increase)
Vaccines	Not applicable

O'Mahony et al, EGM 2023 *in press*

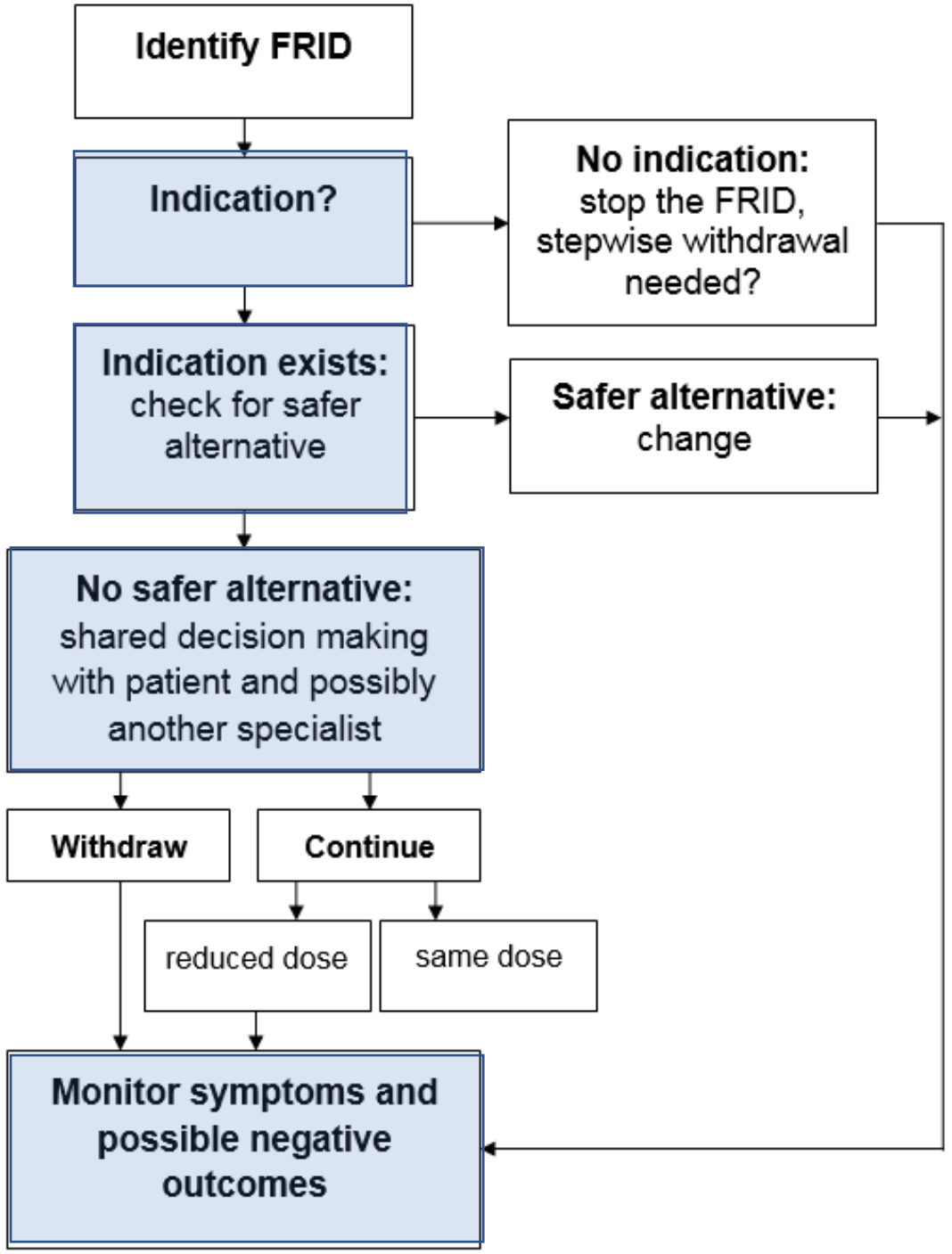
Deprescribing benzodiazepines/Z-drugs

- Shared decision making
  - Inform adequately
  - Educational materials
- Motivational interviewing
  - Behavioural intervention
- Withdrawal schedules
  - Close monitoring
  - Supporting



Barker A et al, Plos Med 2019; Reeve E et al; Eu J Clin Pharm 2017

Decision tree for medication management Fall-risk increasing drugs



Simplified from Seppala et al. Statement paper EUGMS T&F group FRID 2019 Drugs and Aging

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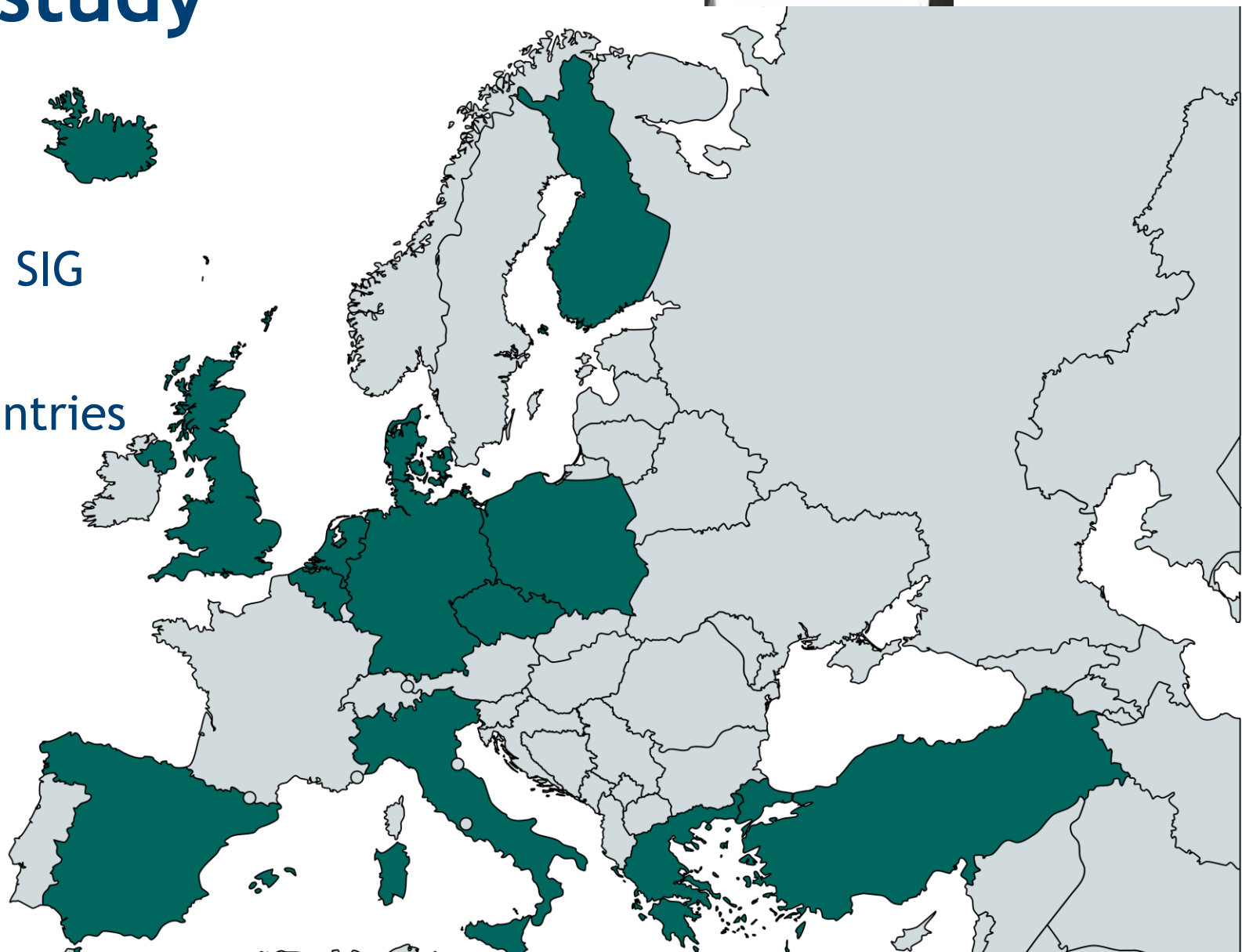
European Delphi study

STOPPFall

- Members of T & F on FRIDs and SIG pharmacology were invited.
- In total 24 experts from 13 countries
- International advisory board
- 4 Delphi rounds



STOPPFall tool EUGMS T&F group FRIDs;
Seppala et al, Age & Ageing 2020

Benzodiazepines

Benzodiazepine-related drugs

Antipsychotics

Antidepressants

Antiepileptics

Central antihypertensives

Vasodilators used in cardiac diseases

Alpha-blockers used as antihypertensives

Diuretics

Opioids

Antihistamines

Alpha-blockers for prostate hyperplasia

Urinary frequency and incontinence medication

Anticholinergics

Deprescribing when & how?

Follow-up?

Monitoring for symptoms?

Clinical dilemma: prescribe or deprescribe?

Cardiovascular disease

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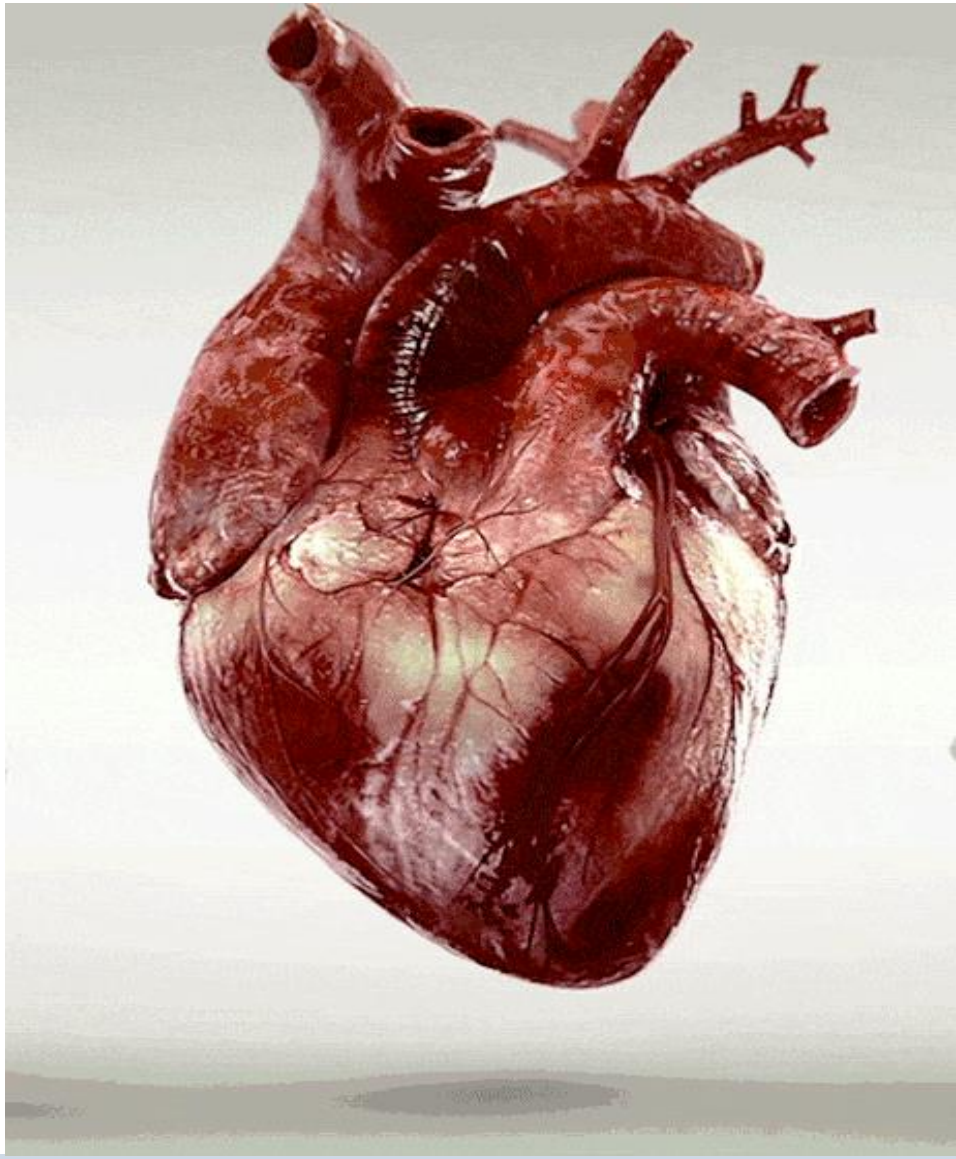
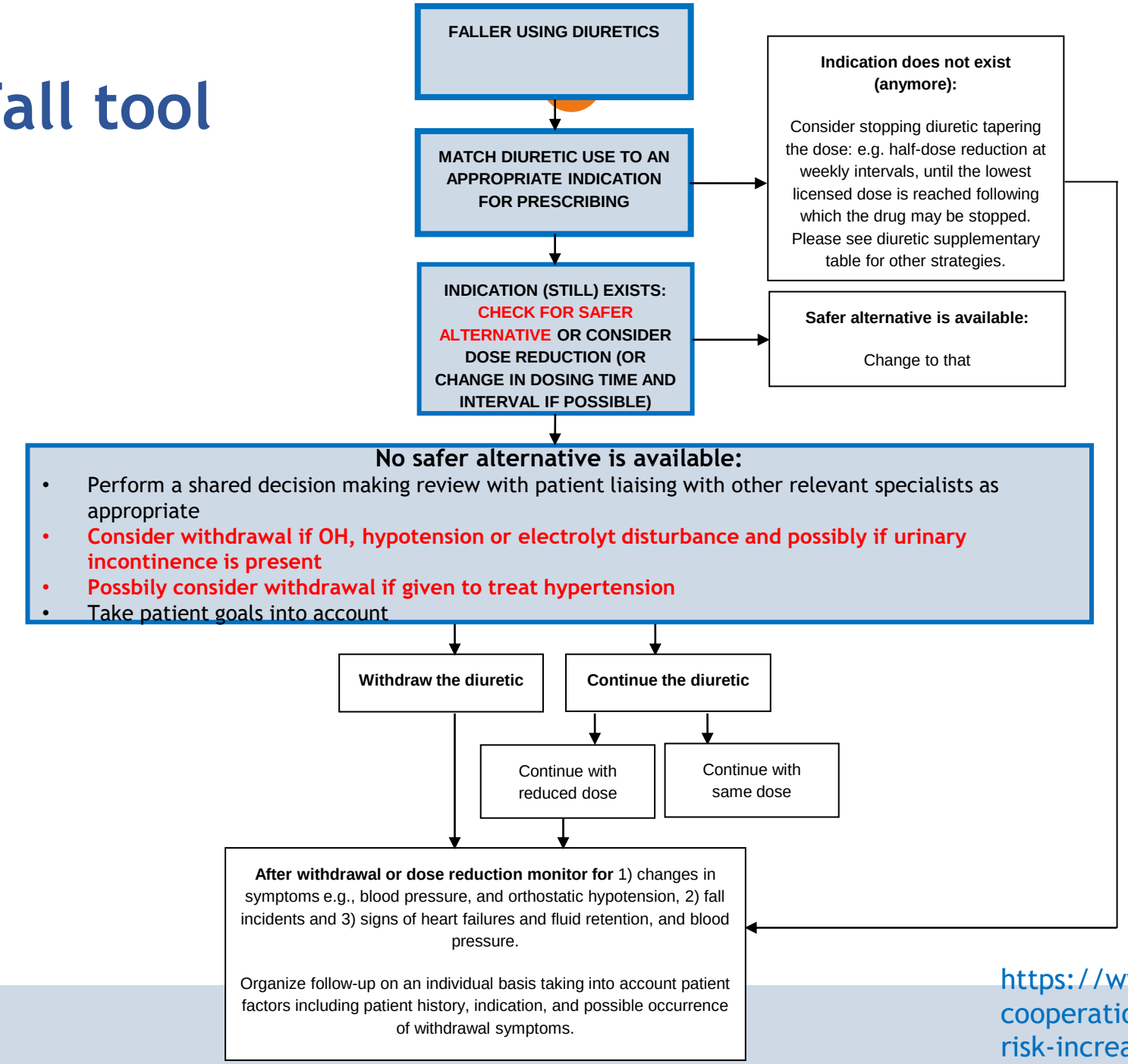
↑

Cardiovascular drugs

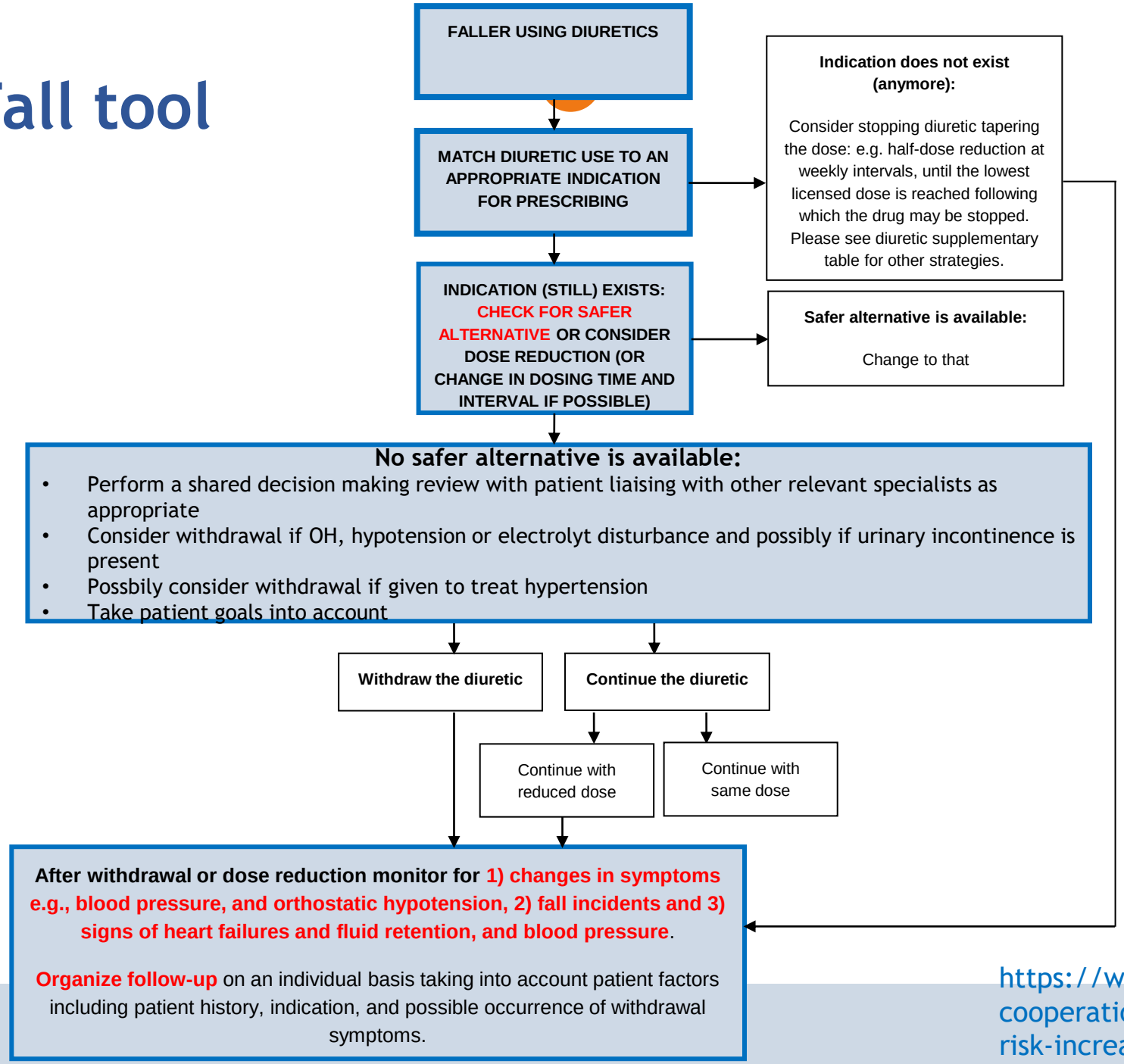


STOPPFall tool



https://www.eugms.org/research-cooperation/task-finish-groups/frid-fall-risk-increasing-drugs.html

STOPPFall tool



https://www.eugms.org/research-cooperation/task-finish-groups/frid-fall-risk-increasing-drugs.html

Clinical review series deprescribing dilemma's in older fallers by EuGMS T&F group on FRIDs

In depth reflection for important FRIDs groups:

- Antidepressants
- Opioids
- Benzodiazepines
- Diuretics
- *Antihypertensives*
- *Antipsychotics*
- *Cognitive enhancers*
- *BPH drugs*

Van Poelgeest E et al EGM 2021; Virnes RE et al Drugs Aging. 2022; Capiau A et al EGM 2022; Van Poelgeest E et al EGM 2023

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Estimation of fall-related ADE prevalence: diuretics

	(ORTHOSTATIC) HYPOTENSION	DIZZINESS	HYPOKALEMIA	HYPONATREMIA	VOLUME DEPLETION	SEDATION	SYNCOPE
LOOP DIURETICS							
Bumetanide (C03CA02)	++	+++	+++	+++	++	+++	++
Furosemide (C03CA01)	++	No data	No data	No data	++	No data	No data
THIAZIDE(LIKE) DIURETICS							
Hydrochlorothiazide (C03AA03)	+++	+	++++	++++	No data	No data	No data
Indapamide (C03BA11)	+	+	No data	No data	No data	No data	No data
ALDOSTERONE RECEPTOR ANTAGONISTS							
Eplerenone (C03DA04)	+++	++	No data	++	++	No data	++
Spironolactone (C03DA01)	No data	++	No data	No data	No data	++	No data
SGLT2 INHIBITORS							
Canagliflozine (A10BK02)	++	++	No data	No data	++	No data	++
Dapagliflozine (A10BK01)	+++	+++	No data	No data	++	No data	No data
Empagliflozine (A10BK03)	++	++	No data	No data	++	No data	++
Ertugliflozine (A10BK04)	+++	+++	No data	No data	+++	No data	+++

+: Seldom (<1/1000)

++: Sometimes (1/100-1/1000)

+++: Often (1/10-1/100)

++++: Very often (>1/10)

Van Poelgeest E et al EGM 2023

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ALDOSTERONE RECEPTOR ANTAGONISTS							
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Empagliflozine (A10BK03)	++	++	No data	No data	++	No data	++
Ertugliflozine (A10BK04)	+++	+++	No data	No data	+++	No data	+++

+: Seldom (<1/1000)

++: Sometimes (1/100-1/1000)

+++: Often (1/10-1/100)

++++: Very often (>1/10)

SGLT2 inhibitor may be safer alternative

	DIURETICS	SGLT2 INHIBITORS
Risk of electrolyte disorders	High	Low ✓
Risk of (orthostatic) hypotension	High	Low to moderate ✓
Heart failure modification	No	Yes ✓
Risk of insulin resistance	Yes	No ✓
Risk of hypoglycemia	No ✓	Low
Risk of gout	Yes	No (may reduce risk) ✓
RISK OF FALLS	Yes	Yes (probably lower) ✓
RISK OF LOSS OF INDEPENDENCE	Yes	Yes (probably lower) ✓

Clinical dilemma: prescribe or deprescribe?

Pain

↓

↑

Opioids

Virnes RE et al, Drugs Aging 2022

Pain & fall risk

- Pain related prospective (recurrent) fall risk:

  OR 1.79 (95% CI 1.44-2.12)

- Pathways
  - Psychomotor retardation
  - Deconditioning
  - Gait & balance abnormalities
  - Impaired sleep and impaired attention
  - Fear of falling

Stubbs B et al, Pain Med 2014, Virnes RE et al, Drugs Aging 2022

Opioids and fall risk

- Sedation
- Drowsiness, somnolence
- Dizziness, vertigo
- Orthostatic hypotension
- Confusion, delirium
- Eye disorders
- Muscle disorders (rigidity)

- Indications
- (Non-)pharmacological alternatives
- Subclass considerations

Virnes RE: clinical review opioids & falls; Drugs Aging. 2022 March

Estimation of fall-related ADE prevalence: Opioids

Table 1 Prevalence of fall-related side effects of opioids based on summaries of product characteristics (Finnish Medicine Agency)

Opioids	(Orthostatic) hypotension	Drowsiness or somnolence	Dizziness or vertigo	Sedation	Confusion	Delirium or confusional state	Eye disorders	Muscle problems (e.g. rigidity)
Codeine (tablet)	Unknown	Unknown	Unknown	No data	No data	No data	Unknown	No data
Dihydrocodeine (tablet)	No data	No data	No data	No data	No data	No data	No data	No data
Tramadol (capsule)	++	+++	++++	No data	+	+	+	+
Buprenorphine (sublingual tablet)	+++	+++	+++	No data	No data	No data	+++	+++
Buprenorphine (transdermal patch)	++	++++	++++	++	+++	No data	++	+++
Fentanyl (sublingual tablet)	++	+++	+++	No data	No data	++	++	No data
Fentanyl (transdermal patch)	++	++++	+++	+++	No data	+++	++	+++
Hydromorphone (capsule)	++	++++	++++	+	No data	+++	++	No data
Methadone (tablet)	+++	+++	+++	+++	++++	Unknown	Unknown	No data
Morphine (tablet)	++	+++	+++	No data	+++	No data	++	No data
Oxycodone (capsule)	+	++++	++++	+++	No data	+++	++	++
Pethidine (tablet)	Unknown	Unknown	Unknown	Unknown	No data	No data	Unknown	Unknown

+: *Seldom (<1/1000)*

++: *Sometimes (1/100-1/1000)*

+++: *Often (1/10-1/100)*

++++: *Very often (>1/10)*

Virnes RE: clinical review opioids & falls; Drugs Aging. 2022 March

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Clinical dilemma: prescribe or deprescribe?

Antidepressants

↓

↑

Depression

Depression & fall risk

- Depression related fall risk:

  OR 1.63 (95% CI 1.36-1.94)

- Pathways
  - Psychomotor retardation
  - Deconditioning
  - Gait & balance abnormalities
  - Impaired sleep and impaired attention
  - Concerns about falling

Poelgeest E et al, Eur Geriatr Med. 2021 Jun

Antidepressants and fall risk

- Sedation
- Sleep disturbance
- Delirium
- Orthostatic hypotension
- Dizziness
- Dehydration, deconditioning
- Anticholinergic effects
- Movement disorders
- Cardiac rhythm and conduction disorders
- Hyponatriemia

Medication related falls in older people, eds A.R. Huang, L. Mallet 2016
Van der Velde N 2007 Br J Clin Pharm Hartholt KA BMC Geriatr 2011

Deprescribing antidepressants

- Initial step only in severe depressive disorders
  - Both under- and overtreatment in older persons
  - Off-label use high, specifically in instutionalized older persons

- Consider withdrawal if
  - Hyponatriemia, OH, dizziness, sedative symptoms, tachycardia/arrhythmia
  - Indication sleeping disorder, neuropathic pain or anxiety disorder
  - Indication depression: take symptom free period and history of symptoms into acount
  - Dependend on patient goals

Estimation of fall-related ADE prevalence: antidepressants

	Orthostatic hypotension	Imbalance and/ or dizziness	Extrapyramidal symptoms	Sedation	Delirium or confusional state	Visual impairment	Hyponatremia
SSRIs							
Citalopram	No data	+ + +	No data	+ + + +	+ + +	No data	+
Escitalopram	No data	+ + +	No data	+ +	+ +	+ +	+
Paroxetine	+ +	+ + +	+ +	+ + +	+ +	+ + +	+
Fluvoxamine	+ +	+ + +	+ +	No data	+ +	No data	+
Fluoxetine	+ +	+ + +	No data	+ + +	No data	+ + +	+
Sertraline	No data	+ + + +	+ + +	+ + + +	+	+ + +	+
SNRIs							
Venlafaxine	+ +	+ + + +	No data	+ + + +	+	+ + +	+
Duloxetine	+ +	+ + +	+	+ + + +	+	+ + +	+
TCAs							
Amitriptyline	+ + + +	+ + + +	No data	+ + + +	+ + +	+ + + +	+ + +
Nortriptyline	+ + +	+ + + +	No data	No data	+	+ + + +	No data
Clomipramine	+ + +	+ + + +	No data	+ + + +	+ + +	+ + + +	No data
Doxepin	+ + +	+ + +	+ + +	+ +	+ +	+ +	+
Maprotiline	+ + +	+ + + +	No data	+ + +	+	+ + +	+
Dosulepin	+ + +	+ + +	+ +	+ + +	+ +	+ +	No data
Other							
Mirtazapine	+ + +	+ + +	No data	+ + + +	+ + +	No data	+
Bupropion	+	+ + +	+	No data	+ +	+ + +	No data
Trazodone	+ + +	+ + + +	No data	+ + +	+ + +	+ + +	No data
Agomelatine	No data	+ + +	No data	+ + +	+ +	+ +	No data
Vortioxetine	No data	+ + +	No data	No data	No data	+	+
Mianserin	+ + +	No data	+	+ + + +	No data	No data	+

Poelgeest E: clinical review antidepressants & falls Eur Geriatr Med. 2021 Jun

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Deprescribing trials

- SRs: effective in decreased prescribing of PIMs

- Consistent and sustainable changes in clinical outcomes lacking
  - Limitations with regard to study design
    - Small sample size
    - Short f-up time
    - Infrequent use QoL measures (PROMS)
    - Insufficient targeting high risk patients
    - Suboptimal intensity or duration
    - Limited use of CDSS

Thillainadesan J, drugs Aging 2018; Bloomfield HE, J Gen Internal Med 2020

SENATOR & OPERAM trials (STOPP/START)

- No effect primary clinical outcomes

- Both disapointing acceptance of deprescribing advice 15% & 62%
- Suboptimal implementation
- Low intervention intensity
- Timing of the intervention

O'Mahony D et al, Age Ageing 2020; Blum MR et al, BJM 2021

Clinical Decision Support Systems (CDSS)

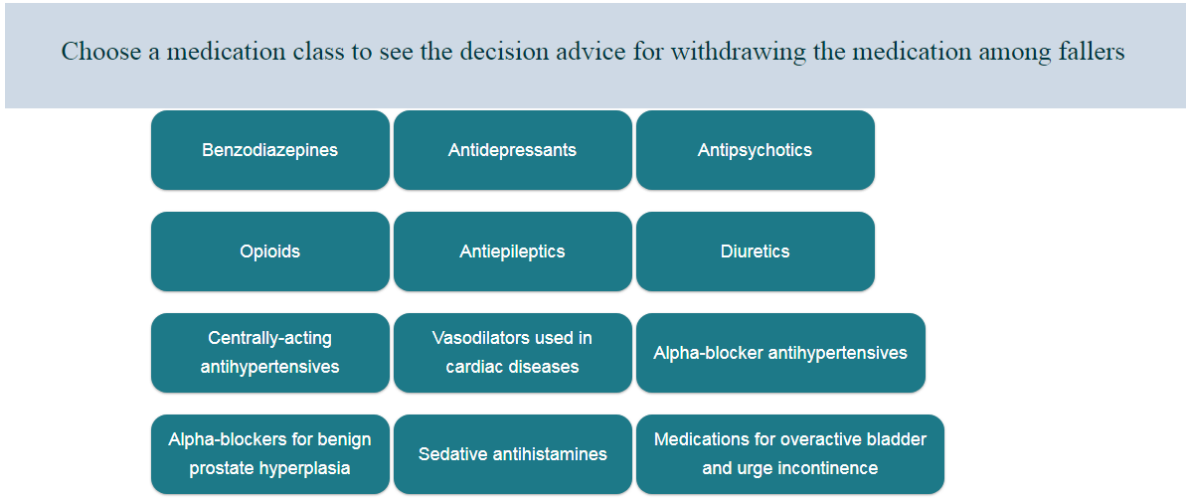
- EMR: opportunity
- Many potential barriers

- End-users need to be involved in each step of development process
- Incorporate CDSS at point of care
- User-friendly
- Avoidance of alert fatigue
- Responsive to patient contexts

Damoiseaux-Volman BE et al, JMIR Med Inform. 2021

Online version STOPPFall tool

- Link EuGMS website -> Task and Finish Group -> Fall-risk-increasing Drugs
- https://kik.amc.nl/falls/decision-tree/



Clinical decision support system:

1. personalized risk estimates &
2. personalized deprescribing advice

- Clinical Decision Support System (CDSS) & Patient portal
  - Personalized fall risk estimates
  - Information on medication and falls prevention

➢Prediction, causal and explanatory models

➢Recommendations of >50 Guidelines incorporated

- RCT in 10 Dutch falls (outpatient) clinics
- RCT in 20 Family care practices

Clinical Decision Support Systems FRIDs deprescribing

www.onderzoeknaarvallen.nl/adfice_it_en/

CDSS: personalized medication advice

Patiëntinformatie (uit Epic):

Patiënt: 143
Leeftijd: 81
Co-morbiditeit: hypertensie, hartfalen, diabetes
Lab-waarden: geen

Kans om te vallen binnen 12 maanden: **25%** (open het predictiemodel)

Medicijnen met aanbevolen maatregelen: Pantoprazol, MetFORMINE, METOPROLOL, Atorvastatine, TemaZEPAM
Medicijnen zonder aanbevolen maatregelen: Apixaban
Ga direct naar: Andere adviezen

Medicijnen met aanbevolen maatregelen

Pantoprazol FK

Advies:
Bij langdurige gebruik van PPI's is er een verhoogd risico op heup-, wervel- en polsfracturen. Overweeg stoppen. Als een PPI nodig is, heeft pantoprazol de voorkeur.

Richtlijnen: 32

Maatregelen (aangekruist indien aanbevolen):

Kies een maatregel...
- ☒ Stoppen (afbouwen niet nodig)
- ☐ Afbouwen waarna stoppen. Afbouwschema: *Specificeer hier…*
- ☐ Afbouwen tot minimaal effectieve dosis bereikt is. Afbouwschema: *Specificeer hier…*
- ☐ Continueren
- ☐ Vervolgafspraak: *Specificeer hier…*
- ☐ Overig: *Specificeer hier…*

Overview risk medication with advices based on patient characteristics

Future developments

- Integrating knowledge implementation and behavioral sciences
- Computational modelling (simulation models)
- Applying Machine Learning to identify complex interactions
- Take novel biomarkers into account (genetic variance ao)

Personalized deprescribing

Take into account:

- Valid indication, dosages
- Interactions
- Symptoms/ADEs

Personalized deprescribing

Take into account:

- Patient goals
- Values and preferences
- Disease severity
- Comorbidity
- Level of functioning, frailty
- Life expectancy
- Patient adherence

Take home messages

- If possible withhold from prescribing risk drugs
- Consider safer (non)pharmacological alternatives
- Regular medication review: (half)yearly
- Personal treatment effects
- Potential drug-disease interactions
- Invest in education & patient empowerment
- CDSS: potential aid in complex decision making
- Future: Implementation, biomarkers and AI

Collaborators

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