Prevention of drug related problems in geriatrics – New approaches in research and clinical practice

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ESCP
European Society of Clinical Pharmacy

Drug-related problems in elderly patients

- Prevalence ADEs : up to 35% in community-dwelling older people
- 10 to 30% of hospital admissions in older people are directly linked to drug related problems (DRPs)
- A substantial percentage of ADEs (32-69%) are possibly preventable.

Inappropriate prescribing → adverse drug events (ADEs) → increase in utilization of healthcare services and costs

Gallagher 2007; Hanlon 2004 ; Klarin 2005 ; Kongkaew 2008 ; Mannesse 2000 ; Col 1990 ; Franceschi 2008 ; Sorensen 2004 ; Page II 2006

Clinical pharmacy / pharmaceutical care model

- Medication review
- Medication reconciliation
- Follow-up phone calls
- Visits
- Consultations
- Therapeutic Education
- Seamless care
- Interdisciplinary collaboration
- Deprescribing
- Prescribing pharmacists

- Inappropriate prescribing
- Adverse effects
- Falls
- Hospital admission
- Mortality

- Outcomes that matter to the patient

Appropriate prescribing

- SR &MA
- Four trials (n = 1,164 patients), inpatients

- *Three trials reported statistically significant reductions in the Medication Appropriateness Index score in the intervention group (mean difference from admission to discharge = -7.45, 95% CI: -11.14, -3.76) and other PIP tools such as Beers Criteria.*

Effectiveness of medication review: a systematic review and meta-analysis of randomized controlled trials

- to assess the effectiveness of medication review as an isolated short-term intervention, irrespective of the patient population and the outcome measures used.

- **an effect was found on most drug-related problems**: decrease in the number of drug-related problems, more changes in medication, more drugs with dosage decrease and a greater decrease or smaller increase of the number of drugs.

- No effect on clinical outcomes
  - mortality, hospital admissions/healthcare use, the number of patients falling, physical and cognitive functioning, except a decrease in the number of falls per patient.
- No effect on quality of life / inconclusive about economical outcome measures.

Interventions to improve the appropriate use of polypharmacy for older people

- 32 studies
  - 18 randomised trials, 10 cluster randomised trials, two non-randomised trials and two controlled before-after studies.
  - 1 computerised decision support (CDS); 31 were complex, multi-faceted pharmaceutical-care based approaches
  - variety of settings

Cochrane Library

- Pharmaceutical care may make little or no difference in hospital admissions / quality of life (low-certainty evidence).
- No consistent intervention effect on medication-related problems was noted across studies.

The OPERAM trial

Optimizing Therapy to Prevent Avoidable Hospital Admissions in Multimorbid Older Adults (OPERAM): cluster randomised controlled trial

- Design : cluster RCT (EU; 4 hospitals: CH, B, NL, IR)
- Patients ≥70 y, multimorbidity & polypharmacy (n=2.000)
- Intervention : medication review (Med Rev)
- Control: standard care
- Outcome: Drug-Related hospital Admissions (DRAs) at 1 year

This project has received funding from the European Union's Horizon 2020 research and innovation programme under the grant agreement No 634238, and is supported by the Swiss State Secretariat for Education, Research and Innovation (SERI) under contract number 15.0137

Recommendations

- In the intervention group (n=916 older multi-morbid inpatients) :
  - 83 % of inappropriate prescribing (IP)
  - 86 % of patients with ≥ 1 recommendation
    - ~ 2.300 recommendations regarding IP : STOPP (~ 1800) > START (~ 500)
  - Rather low proportion (62 %) of patients with ≥ 1 implemented recommendation (n= 491 / 789)
    - ~ 730 recommendations implemented at 2 months : 33% of STOPP & 25% of START

Specific recommendations (intervention group, n = 916)

STOPP/START	Description	No (%) Count in intervention group	Implemented*	Not implemented
STOPP				
STOPP A1†	Any drug prescribed without an evidence based clinical indication	828 (35.5)	428 (51.7)	400 (48.3)
STOPP A3	Any duplicate drug class prescription	147 (6.3)	95 (64.6)	52 (35.4)
STOPP D5	Benzodiazepines for ≥4 weeks	115 (4.9)	45 (39.1)	70 (60.9)
START				
START E3	Vitamin D supplement in patients with known osteoporosis and with previous fragility fracture or BMD T scores >−2.0 in multiple sites, or both	96 (4.1)	22 (22.9)	74 (77.1)
START H2	Laxatives in patients receiving opioids regularly	82 (3.5)	12 (14.6)	70 (85.4)
START A6	Angiotensin converting enzyme inhibitor with systolic heart failure or documented coronary artery disease, or both	80 (3.4)	19 (23.8)	61 (76.3)
START E5	Vitamin D supplement in older people who are housebound, experiencing falls, or with osteopenia (BMD T score >−1.0 but <−2.5 in multiple sites)	80 (3.4)	31 (38.8)	49 (61.3)

10 most commonly identified drug classes with no evidence-based indication were in descending order of frequency: antacids, mineral supplements, psycho-analeptics, lipid modifying agents, psychotropics, anti-thrombotics, vitamin, analgesics including opioids, drugs for constipation, and drugs for COPD

UCLouvain

LDRI

OPERAM Intervention

- Structured medication history taking “SHIM”
- Medication review “STRIP” Systemic Tool to Reduce Inappropriate Prescribing
  - CDSS using STRIP-A (STOPP/START, DDI…)
  - Evaluation by research team (pharmacist+physician)
  - Discussion with hospital physician
  - Shared decision making with the patient
  - Written Med Rev plan sent to GP

UCLouvain (Crowley, Sallevelt et al. 2020) (Sallevelt, Huibers et al. 2022) DDI drug drug interaction GP general practitionner

LDRI

Discussion : from research to practice

- Single timepoint pharmacotherapy optimization may not persist over a 1-year follow-up?
- Recommendations often involved drugs that are unlikely to DRA?

- Effect negated by new IP after the index hospital stay ?
- Effect attenuated by the 20% one-year mortality rate ?
- Effect hampered by the low recommendation implementation rate ?
- Effect hampered by implementations postponed to a GP visit ?
- Effect lowered by little (written) collaboration with GPs
- Effect lowered by the limited shared decision making ? Limited interest in and comprehension of prescribing recommendations made during hospital stay – while patients were dealing with acute illness

- Focus on implementation of recommendation
- Focus on specific drugs
- Communication with GP
- Written communication for the patient
- Improve SDM process
- Adjust follow-up to timing of the intervention

Research and practice

- Selection of patients does not fit the aim of the intervention.
  - Other risk factors
  - Need to adapt the population to the objectives (adherence vs admission)

- The interventions. No golden standard exists for medication review
  - Implicit vs explicit methods
  - Multidisciplinarity

- The outcome measures and follow-up time
  - Large, impacted by other factors (admissions, falls)
  - Adapt the objective (safety, costs, focused on a pathology)
  - Positive and negative

Research and practice

- The right timing?
- Cross-sectional, arbitrary moment
  - Start, stop of a medication
  - Integrated approach, longitudinal assessment
  - Consider general interventions vs individual

Impact of Medication Reviews Delivered by Community Pharmacist to Elderly Patients on Polypharmacy: A Meta-analysis of Randomized Controlled Trials

- Community Pharmacist to Elderly Patients on Polypharmacy
- Meta-analysis of Randomized Controlled Trials
- 4 studies with a total of 4633 participants were included.

- compared with usual care
- medication reviews reduced risk of ED visits (risk ratio = 0.68; 95% confidence interval = 0.48–0.96).

- tendency that pharmacist interventions decreased risk of hospitalizations (risk ratio = 0.88; 95% CI = 0.78–1.00).

International core outcome set for clinical trials of medication review in multi-morbid older patients with polypharmacy

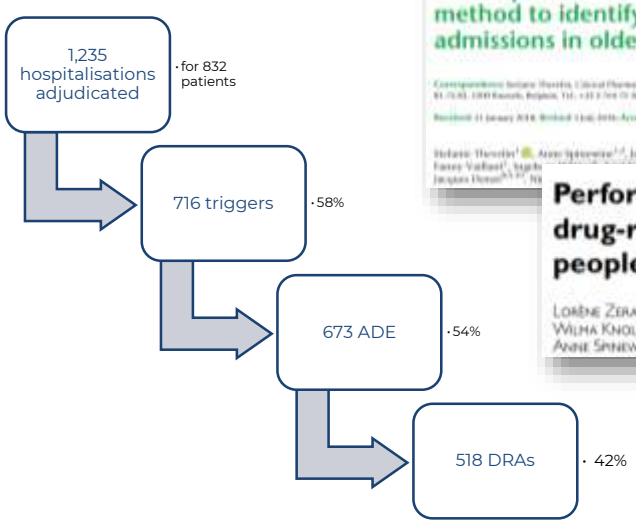
Jean-Baptiste Beuscart[1,2*], Wilma Knol[3], Shane Cullinan[4,5], Claudio Schneider[6], Olivia Dalleur[1,7], Benoit Boland[8], Stefanie Thevelin[1], Paul A. F. Jansen[3], Denis O'Mahony[9], Nicolas Rodondi[6,10] and Anne Spinewine[1,11]

Domain	Outcome	Definition
Adverse events	Drug-related hospital admissions	Hospitalization due to an adverse drug event: harm due to an adverse drug reaction or a medical error related to overuse, underuse, or misuse of prescription and non-prescription medications and which is the main reason for or contributes to hospital admission of a patient
Medication use	Overuse	The use or prescription of more drugs than clinically needed, including (1) any drug prescribed or used without an evidence-based clinical indication; (2) therapeutic duplication; (3) medication prescribed or used beyond the recommended duration
	Underuse	A failure to prescribe drugs that are indicated, including (1) omission of an evidence-based drug; (2) too short a duration
	Potentially inappropriate medications	Drugs with risk of adverse drug reactions exceeding their expected clinical benefit to patients, particularly when safer therapeutic alternatives are available to treat the same condition [40]
	Clinically significant DDI	A clinically significant DDI is defined as having a significant severity rating according to the drug interaction compendia used in the study (e.g. *Drug Interaction Facts* or *Micromedex*) [41]
Patient-reported outcomes	Health-related quality of life	Personal health status: HRQoL usually refers to aspects of our lives that are dominated or significantly influenced by our mental or physical well-being
	Pain relief	Whether pain has improved over the course of the trial

Abbreviations: *HRQoL* Health-related quality of life, *DDI* drug-drug interaction

Prague 2022

Structuring medication review



Development of a standardized chart review method to identify drug-related hospital admissions in older people

Performance of a trigger tool for detecting drug-related hospital admissions in older people: analysis from the OPERAM trial

Lorène Zerah[1], Séverine Henrard[1,2], Stefanie Thevelin[1], Martin Feller[3,4], Carla Meyer-Masetti[4], Wilma Knol[5], Ingeborg Wilting[6], Denis O'Mahony[7], Erin Crowley[8], Olivia Dalleur[1,9], Anne Spinewine[1,10]

The overall PPV of the trigger tool for detecting DRAs was 0.66 [0.62–0.69]

Table 3. The proposed revised version of the trigger tool for identifying drug-related hospital admissions in older patients

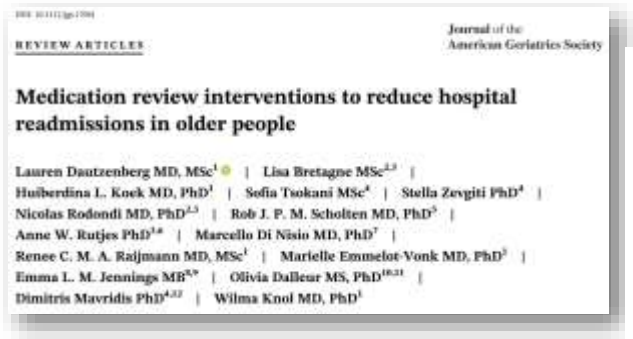
TRIGGER TOOL FOR SCREENING FOR DRUG-RELATED HOSPITAL ADMISSIONS IN OLDER PERSONS	
Trigger on admission or up to 48 hours of admission (Diagnoses)	Suspected causative drugs or causes for undertow
Fall and/or fracture and/or orthostatic hypotension	**Use** of any of the following drugs? - Benzodiazepines - Non-benzodiazepine hypnotics e.g. zopiclone, zolpidem - Antipsychotics - Antidepressants - Sedating antihistamines - Opioids - Anticholinergics - Other (Please specify)
	Use of any drugs that cause orthostatic hypotension? - Direct renin inhibitors (e.g. aliskiren) - Anti-Parkinson drugs - Antidepressants (mainly tricyclic) - Antipsychotics - Calcium channel blockers - Diuretics - β blockers - ACE inhibitors - Angiotensin receptor blockers - Nitrates - Dihydropyridine (SCICI)-inhibitors) - α1-receptor blockers - Other (Please specify)
	If a fall is caused by hypoglycaemia, look for **use** of drugs that contribute to hypoglycaemia
	Underuse of any of the following drugs in patients with known osteoporosis and/or history of fragility fracture(s) and/or Bone Mineral Density T-scores of -2.5 or lower in multiple sites? - 800 IU Vitamin D/d (+ 1000-1200 mg calcium/day if dietary intake is <1200-1000mg/day) - Bone anti-resorptive therapy (e.g. bisphosphonates, strontium, raloxifen, teriparatide, or denosumab)
	Underuse of any of the following drugs in patients on corticosteroid therapy > 3 months? - 800 IU Vitamin D/d (+ 1000-1200 mg calcium/day if dietary intake is <1200-1000mg/day) - Bisphosphonates **Underuse** of vitamin D in patients who are housebound and/or have experienced falls or with osteopenia with Bone Mineral Density T-score between -1 and -2.5 in multiple sites?
Confusion/delirium	**Use** of any of the following drugs? - Benzodiazepines - Non-benzodiazepine hypnotics e.g. zopiclone, zolpidem - Antipsychotics - Antiepileptics - Antihistamines (H1- and H2-receptor blockers) - Antidepressants - Opioids - Dopaminergic agonists - Acetylcholinesterase-inhibitors (new-onset confusion in patients with dementia) - Digoxin - Fluoroquinolones (dose-adjustment in case of impairment renal) - Other anticholinergics
	Abrupt discontinuation/rapid dose reduction of any of the following drugs? - Benzodiazepines - Non-benzodiazepine hypnotics e.g. zopiclone, zolpidem - Antipsychotics - Dopaminergic agonists - Antidepressants - Lithium - Opioids - Corticosteroids - Other (Please specify)

SCREENING QUESTIONS FOR NON-TRIGGERED, SPONTANEOUSLY DETECTED EVENTS	
1. Could the main or contributory reason for admission be related to a drug or recent change in medications?	
☐ Adverse drug reaction (non-preventable side effect, first allergic reaction)	☐ Wrong drug
☐ Overuse of medication(s) (drug without an indication, too long duration of therapy, therapeutic duplication)	☐ Wrong dose (supratherapeutic or subtherapeutic)
☐ Inappropriate discontinuation (removal or dosage decrease) leading to physiological withdrawal signs/symptoms or return of the underlying disease signs/symptoms	☐ Clinically significant drug-drug or drug-food interactions ☐ Inappropriate monitoring ☐ Other (e.g. drug not correctly dispensed/prepared/administered)
2. Could the main or contributory reason for admission be related to underuse?	
☐ Omission of an indicated drug	☐ Suspected adherence concerns
☐ Too short duration of medication therapy	

Medication Counselling in Older Patients Prior to Hospital Discharge

- 29 studies
- 15 different components of medication counselling
  - Discussing the dose and dosage of patients' medications (19/29; 65.5%)
  - providing a paper-based medication list (19/29; 65.5%)
  - explaining the indications of the prescribed medications (17/29; 58.6%)
- Evidence remains inconclusive regarding clinical benefit

Prevention of hospital readmissions



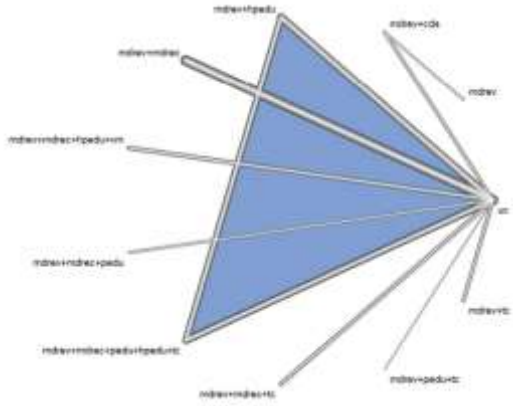
REVIEW ARTICLES

Journal of the American Geriatrics Society

Medication review interventions to reduce hospital readmissions in older people

Lauren Dautzenberg MD, MSc[1] | Lisa Bretagne MSc[2,3] | Huiberdina L. Koek MD, PhD[1] | Sofia Tsokani MSc[4] | Stella Zevgiti PhD[4] | Nicolas Rodondi MD, PhD[2,3] | Rob J. P. M. Scholten MD, PhD[5] | Anne W. Rutjes PhD[1,6] | Marcello Di Nisio MD, PhD[7] | Renee C. M. A. Raijmann MD, MSc[1] | Marielle Emmelot-Vonk MD, PhD[5] | Emma L. M. Jennings MB[8,9] | Olivia Dalleur MS, PhD[10,11] | Dimitris Mavridis PhD[4,12] | Wilma Knol MD, PhD[1]

- Network Meta-Analysis



30-d hospital readmission

All-cause 30-d hospital readmission vs usual care

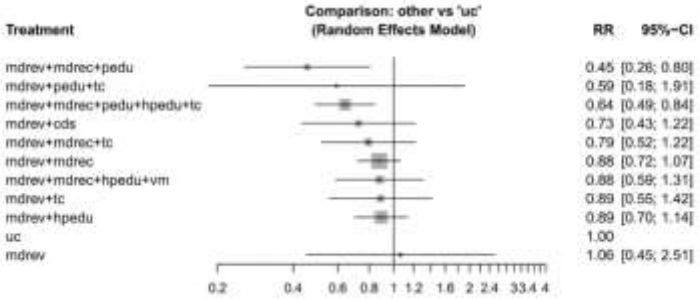


TABLE 1 Intervention components to prevent hospital readmissions

Intervention component	Abbreviation
Medication review	Mdrev
Medication reconciliation	Mdrec
Shared decision making	Sdm
Patient education/medication counseling	Pedu
Health professional education	Hpedu
Use of validated methods	Vm
Use of Computerized Decision Support	Cds
Compliance aid	Ca
Transitional care	Tc

Medication review *in combination with* ***medication reconciliation, patient education, professional education and transitional care****, was associated with a lower risk of hospital readmissions compared to usual care.*

Preventing Adverse Drug Reactions After Hospital Discharge (PADR-AD)

- Following discharge, nominated general practitioners and community pharmacists will receive the risk score and related medication management advice to guide their ongoing care of the patient.
- The primary outcome is moderate-severe ADRs at 12 months post-discharge

(58.0%). The risk of patients having an ADR-related hospitalization was more than three times higher in those who scored ≥6 compared to those who scored <6 (OR 3.59 [95% CI 2.32–5.55]).

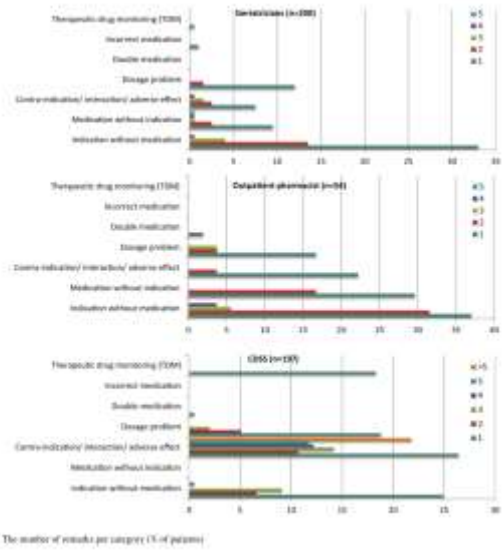
Table 4. Variables included in the risk score.

Variable	OR (95% CI)	Points
Drug changes in the preceding 3 months	1.54 (1.00–2.37)	2
Renal failure	1.97 (1.22–3.17)	2
Dementia	2.44 (1.17–5.10)	2
Number of antihypertensives		
1–2	3.00 (1.22–7.38)	3
≥3	4.75 (1.89–11.93)	5
Anticholinergics	2.09 (1.16–3.75)	2

Frequency and Acceptance of Clinical Decision Support System-Generated STOPP/START Signals for Hospitalised Older Patients with Polypharmacy and Multimorbidity

- In 819/826 (99%) of the patients => at least one STOPP/START signal
- Overall, 39% of the 5080 signals accepted by the pharmacotherapy team.

Complementarity



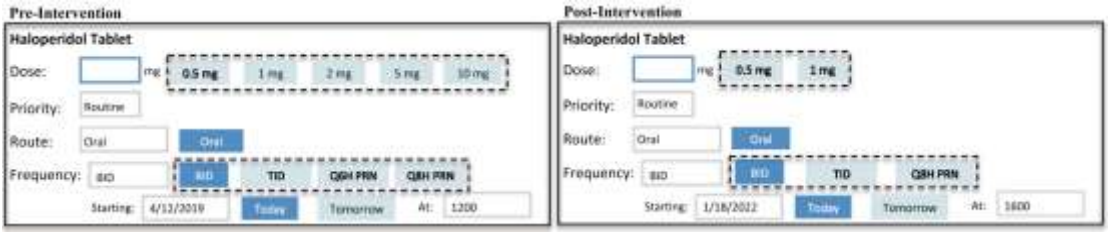
(Zwietering, Westra et al. 2019)

Decision-support systems for managing polypharmacy in the elderly : Ideal system

(Mouazer, Tsopra et al. 2022)

Tailoring

- Post-intervention, the proportion of orders with IP for the targeted medications decreased significantly, 42%–35% (p = 0.003), with interrupted time series analysis showing an immediate and sustained decrease



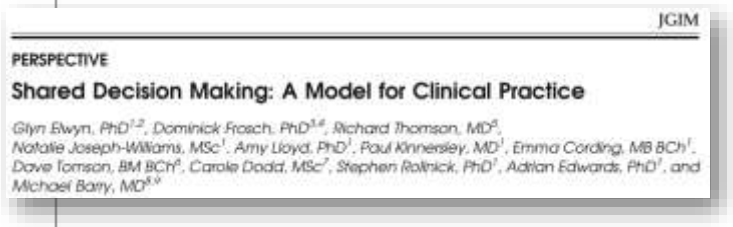
Shared decision making

Box 4. Summary of the model: choice talk, option talk and preference talk

Choice talk
- Step back
- Offer choice
- Justify choice - preferences matter
- Check reaction
- Defer closure

Option talk
- Check knowledge
- List options
- Describe options – explore preferences
- Harms and benefits
- Provide patient decision support
- Summarize

Decision talk
- Focus on preferences
- Elicit preferences
- Move to a decision
- Offer review


JGIM

PERSPECTIVE

Shared Decision Making: A Model for Clinical Practice

Glyn Elwyn, PhD[1,2], Dominick Frosch, PhD[3,4], Richard Thomson, MD[5], Natalie Joseph-Williams, MSc[1], Amy Lloyd, PhD[1], Paul Kinnersley, MD[1], Emma Cording, MB BCh[1], Dave Tomson, BM BCh[6], Carole Dodd, MSc[7], Stephen Rollnick, PhD[7], Adrian Edwards, PhD[1], and Michael Barry, MD[8,9]

"an approach where healthcare professionals and patients share the best available evidence when faced with making decisions regarding healthcare,
and where patients are supported to consider options to achieve informed preferences"

(Elwyn, Laitner et al. 2010)
(Elwyn, Frosch et al. 2012)

what matters to you?

- *Most decisions about stopping, starting, continuing, modifying or selecting medications in MedRev in older people with multiple comorbidities are preference-sensitive.*
- *SDM results in better-informed patients who tend to choose more conservative options (e.g. more medication stops, more dosage decreases, fewer medication switches, and fewer medication starts); this facilitates deprescribing and potentially reduces the treatment burden*

Patients' experience


Experience of hospital-initiated medication changes in older people with multimorbidity: a multicentre mixed-methods study embedded in the OPtimising thERapy to prevent Avoidable hospital admissions in Multimorbid older people (OPERAM) trial

Aim

To explore older multi-morbid persons' experience of hospital-initiated medication changes to underpin our understanding of contextual factors and mechanisms affecting OPERAM intervention effectiveness

Method

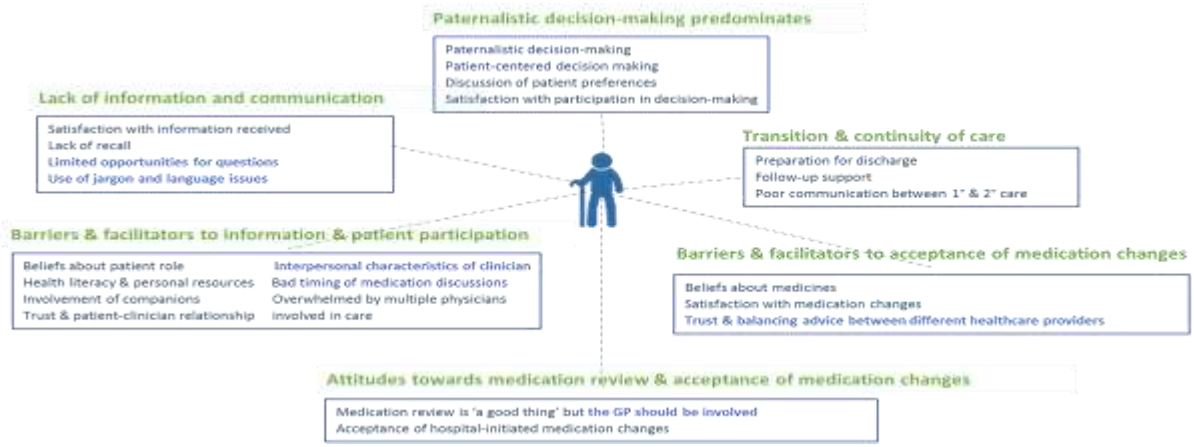
Mixed-method study

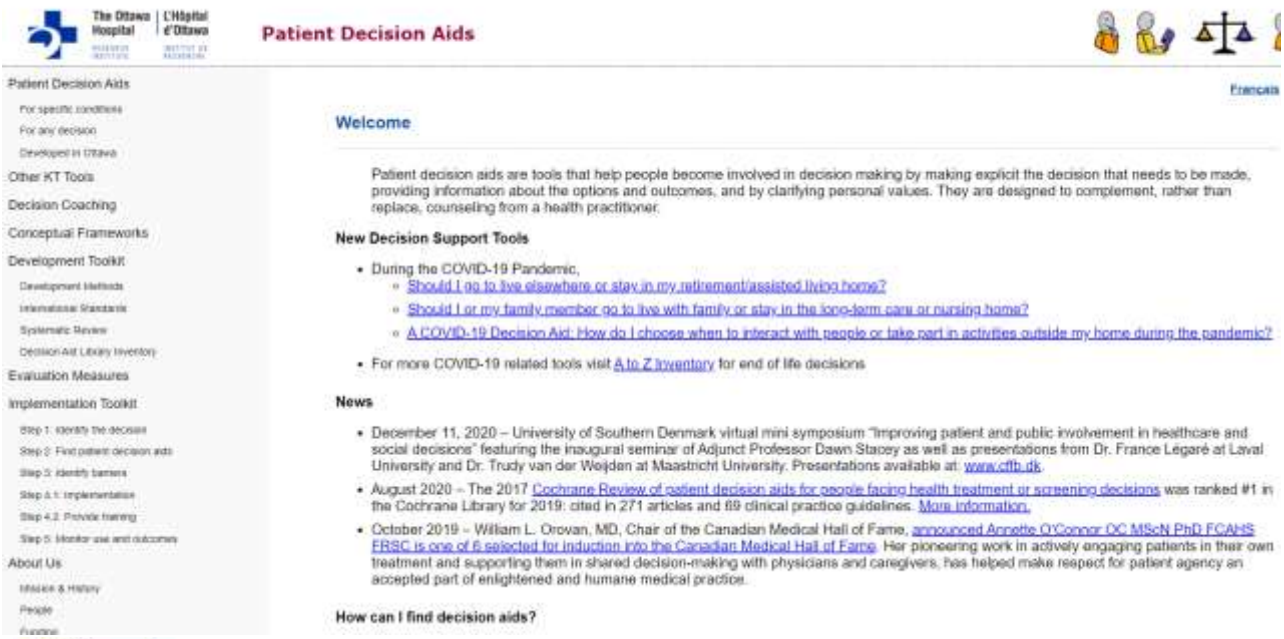
Semi-structured interviews (n=48)

Multi-Morbid Older Persons' Experience of Hospital-Initiated Medication Changes:A Multi-Centre Mixed Methods Study Embedded in The OPERAM trial

- Patients generally display positive **attitudes** towards medication review and hospital-initiated medication changes…
- … yet an interplay of factors related to unmet information needs, patients' beliefs, clinicians' attitudes, trust and doctor-patient relationships highlight the complexity of medication review and shared decision-making and may affect its effectiveness

- **Decisions shared** with patients? Patients' views differed from prescribers' views





Patient-reported experience measure

Developing CollaboRATE: A fast and frugal patient-reported measure of shared decision making in clinical encounters

Glyn Elwyn [a,b,c,*], Paul James Barr [a], Stuart W. Grande [a], Rachel Thompson [a], Thom Walsh [a,c], Elissa M. Ozanne [d]

- *How much effort was made to help you understand your health issues?*
- *How much effort was made to listen to the things that matter most to you about your health issues?*
- *How much effort was made to include what matters most to you in choosing what to do next?*

Effects of a clinical medication review focused on personal goals, quality of life, and health problems in older persons with polypharmacy: A randomised controlled trial (DREAMeR-study).

- RCT in 35 community pharmacies and cooperating general practices in the Netherlands
- 629 participants
- Over 6 months, in the intervention group,
  - HR-QoL measured with **EQ-VAS increased by 3.4 points** (95% confidence interval [CI] 0.94 to 5.8; p = 0.006),
  - **number of health problems** with impact on daily life **decreased by 12%** (difference at 6 months -0.34; 95% CI -0.62 to -0.044; p = 0.024)

- *The main study limitations include the risk of bias due to the lack of blinding and difficulties in demonstrating which part of this complex intervention (for example, goal setting, extra attention to patients, reducing health problems, drug changes) contributed to the effects that we observed.*

UCLouvain (Verdoorn, Kwint et al. 2019) 35 LDRI

UCLouvain LDRI

BE-SAFE

Implementing a patient-centred and evidence-based intervention to reduce BEnzodiazepine and sedative-hypnotic use to improve patient SAFEty and quality of care

BE-SAFE

funded by the European Union (Horizon Europe research and innovation programme, Grant Agreement 101057123) and by the Swiss State Secretariat for Education, Research and Innovation (SERI) (contract No **22.00116**)

BE-SAFE

09/2022 – 08/2027

+ 2 network partners:
- W Levinson (UTOR)
- J Grimshaw (OHRI)

BE-SAFE

BE-SAFE

- Goal: to improve patient safety by addressing knowledge and practice gaps related to the reduction of BSHs used for sleep difficulties

- Perspective: to provide resources for patients, HCPs, healthcare systems and policymakers throughout the diverse European healthcare landscape **to reduce BSH use**, and **serve as a model to address the reduction of other harmful medications**

HORIZON- 101057123

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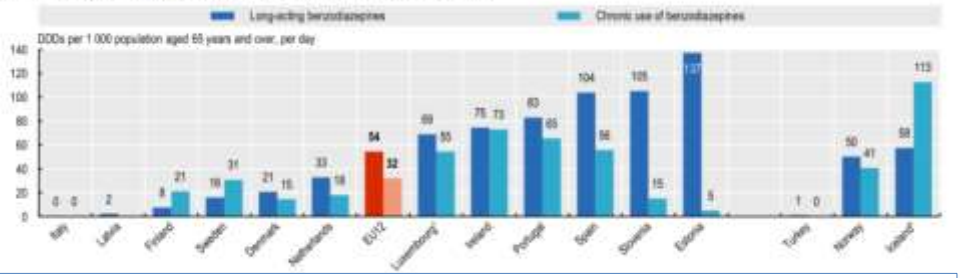
BE-SAFE

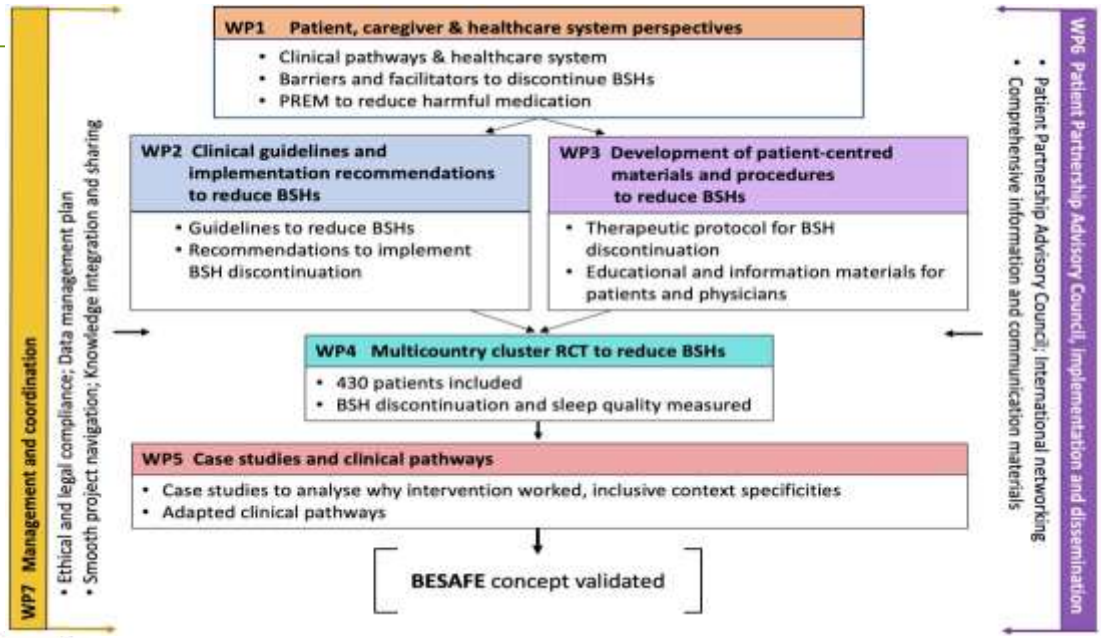
Figure 1.2.2a Benzodiazepine use in adults aged ≥65 years.



The costs of inappropriate prescribing—beyond harms—are likely underestimated

Beyond medication-related harms, the extent and cost of inappropriate prescribing is more difficult to measure, but may dwarf the costs of medication-related adverse events alone (safe prescribing is further discussed in Section 2). In Canada, it has been estimated that in 2013 $419 million ($75 per older Canadian) was spent on potentially inappropriate medications outside the hospital setting. Benzodiazepines and other hypnotics were the leading contributors to both frequency and cost of potentially inappropriate prescriptions. In the United States, a study of the extent and cost of potentially

OECD Health Working papers No. 147. The economics of medication safety.



BE-SAFE

ongoing

WP 1

Clinical pathways, barriers and enablers

To identify and describe the current clinical pathways in relation to BSHs discontinuation in the 6 countries participating in the BE-SAFE trial.

HCPs :
- To identify barriers and enablers to discontinuing BSHs, for physicians and other HCPs.

Patients:
- To identify patients' attitudes, barriers and enablers to discontinuing BSHs

BE-SAFE

Thank you very much!

@BESAFE_HORIZONEU

Conclusions

- Positive impact on prescribing quality
- Uncertain impact on admissions, mortality, likely reduction in emergency room visits
- Need for standardisation of MedRev and outcomes measured
- Target patients /molecules
- Integrate understanding of setting and behaviours in design of intervention
- Address implementation of recommendations
- Combination of tools and techniques
- Consider integrated, longitudinal, patient-centred practice

Tools

Tool	reference
SHIM Structured medication history taking	BMC Health Serv Res. 2020 Mar 17;20(1):220
STRIP Structures medication review	J Eval Clin Pract. 2018;24(2):317–22 BMC Health Serv Res. 2020 Mar 17;20(1):220
STOPP/STARTv2	Anglais : Age Ageing. 2015;44(2):213–8
Eliciting patient preference **SDM model** **Collaborate PREM**	J Gen Intern Med. 2012;27(10):1361–7
Ohri Shared decision making tutorials	decisionaid.ohri.ca
Deprescribing canadian network	https://www.reseaudeprescription.ca/ Deprescribing.org
DRA adjudication guide	Br J Clin Pharmacol 2018;84:2600-14 Age Ageing. 2022 Jan 6;51(1):afab196 Int J Clin Pharm. 2019;41(1):198–206.
COS medication review older patients (multimorbidity and polypharmacy)	BMC Med. 2018 Feb 13;16(1):21
International consensus **list of potentially clinically significant drug-drug interactions** in older people	J Am Med Dir Assoc. 2022 Mar;23(3):522
Prescribing cascade ThinkCascades	Drugs Aging 2022 Vol. 39 Issue 10 Pages 829-840
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