Optimising the Use of Medicines in Clinical Practice – Why and How?

Anne SPINEWINE

TFAR - Clinical Pharmacy and Pharmacoepidemiology Research Group (CLIP)

CHU UCL Namur, Pharmacy Department, Godinne

Group Leader Seminar Series, Louvain Drug Research Institute, 02.12.2024

Where and how it all started

be
be.brussels

Montréal

- Willingness to develop clinical pharmacy practice
- Need to provide evidence on the added value

Appropriate Use of Medicines in Older Adults
Impact of the Clinical Pharmacist

Measure
Improve
Spread

Appropriateness of use of medicines in elderly inpatients: qualitative study

Anne Spinewine, Christian Swine, Soraya Dhillon, Bryony Dean Franklin, Paul M Tulkens, Léon Wilmotte, Vincent Lorant

BMJ 2005

Effect of a Collaborative Approach on the Quality of Prescribing for Geriatric Inpatients: A Randomized, Controlled Trial

Anne Spinewine, PhD, Christian Swine, MD,*§ Soraya Dhillon, PhD,‖ Philippe Lambert, PhD,¶ Jean B. Nachega, MD, MPH, DTM&H,#** Léon Wilmotte, MPharm,*† and Paul M. Tulkens, MD, PhD*‡*

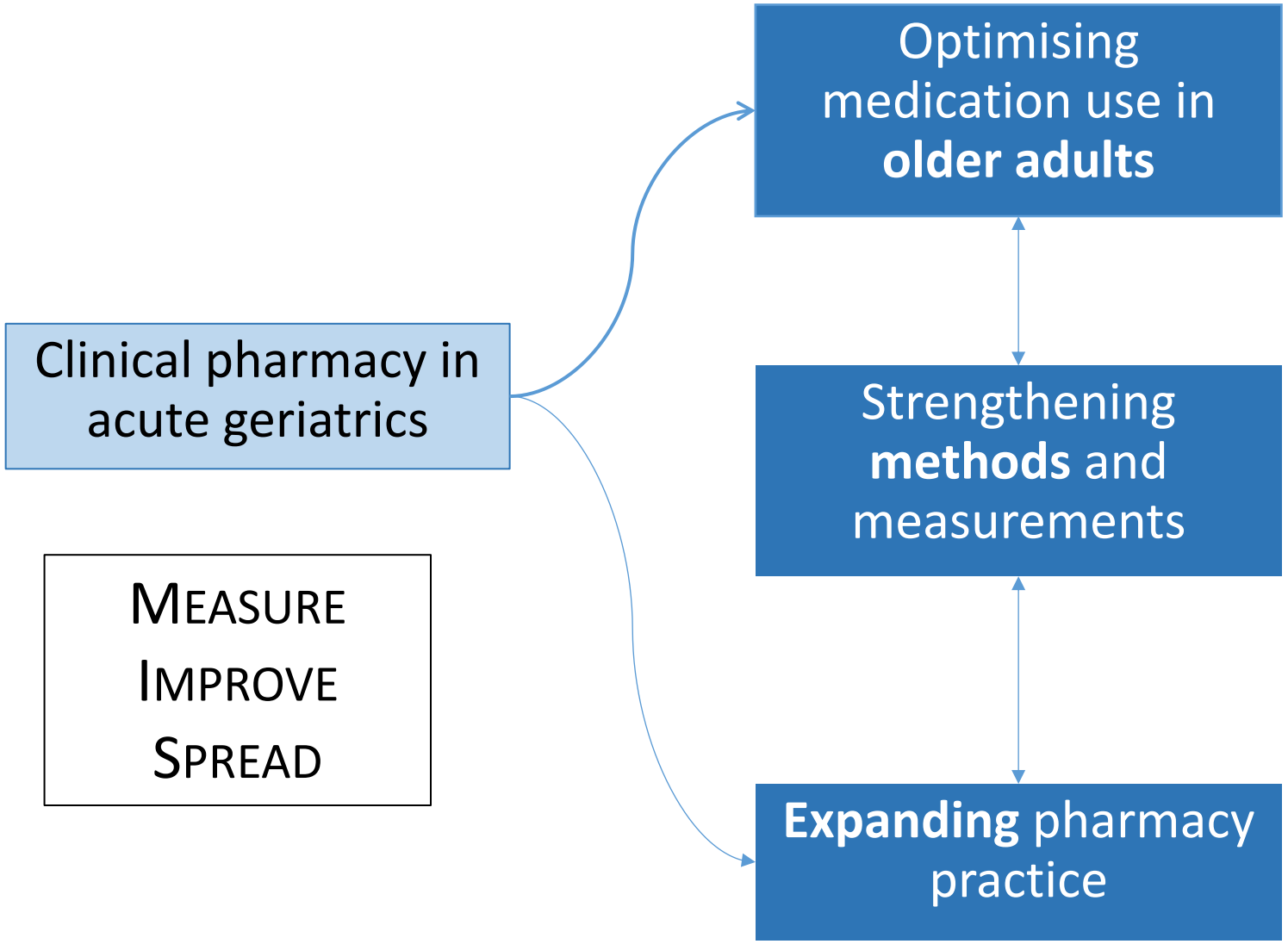
JAGS 2007

Implementation of Ward-Based Clinical Pharmacy Services in Belgium—Description of the Impact on a Geriatric Unit

Anne Spinewine, Soraya Dhillon, Louise Mallet, Paul M Tulkens, Léon Wilmotte, and Christian Swine

- Appropriateness of prescribing at discharge OR=9.1 (95% CI 4.2-21.6)

- 9 interventions / patient (5 moderate, 2 major)
- 5% rejected


Clinical pharmacy in acute geriatrics
Optimising medication use in **older adults**
Strengthening **methods** and measurements
Expanding pharmacy practice
MEASURE
IMPROVE
SPREAD

1.1. Optimising medication use in older adults: focus on **prescribing** and **medication review**

Prescribing in Elderly People 1

Appropriate prescribing in elderly people: how well can it be measured and optimised?

Anne Spinewine, Kenneth E Schmader, Nick Barber, Carmel Hughes, Kate L Lapane, Christian Swine, Joseph T Hanlon

Lancet 2007; 370:173-84

APPROPRIATE

INAPPROPRIATE

Over- prescribing

Mis- prescribing

Under- prescribing

Explicit or Implicit measurement

SCREENING TOOLS FOR THE ASSESSMENT OF PRESCRIBING IN OLDER PATIENTS: SHOULD WE STOPP&START?

- Measuring using STOPP & START: 2 Belgian cohort studies
  - ≥1 STOPP: 40-50% of patients ≥1 START: 60% of patients
  - 27% of hospital admissions potentially related to STOPP&START

- Benzodiazepines
- Duplication
- NSAIDS
- CV prevention
- CV prevention
- Osteoporosis
- Atrial fibrillation

Dalleur et al. Inappropriate prescribing and related hospital admissions in frail older persons according to the STOPP and START criteria. Drugs Aging 2012;29:829-37.
Dalleur et al. Detection of potentially inappropriate prescribing in the very old: cross-sectional analysis of the data from the BELFRAIL observational cohort study. BMC Geriatr 2020;15:156.

SCREENING TOOLS FOR THE ASSESSMENT OF PRESCRIBING IN OLDER PATIENTS: SHOULD WE STOPP&START?

- Measuring using STOPP & START
- Improving: geriatric liaison teams – RCT
  - Systematic screening with STOPP + recommendations
  - STOPP discontinuation rate at discharge: 40% intervention group vs 19% control group (p=0.013)

- Spreading
  - Opportunity for integration in computerised systems - improvements needed
  - Integrating STOPP-START in the education of pharmacists, doctors, geriatricians/GPs

Dalleur et al. Reduction of potentially inappropriate medications using the STOPP criteria in frail older inpatients: a randomised controlled study. Drugs Aging 2014;31:291-8

Louvain Médical

TIRÉ À PART

Revue du Secteur des Sciences de la Santé de l'Université catholique de Louvain

STOPP/START, VERSION.2

UN OUTIL À JOUR POUR LA QUALITÉ DE LA PRESCRIPTION MÉDICAMENTEUSE CHEZ LES PATIENTS ÂGÉS DE 65 ANS ET PLUS

O. Dalleur [1,2], A. Mouton [1], S. Marien [2,3], B. Boland [3,4]

Liste courte. Exemples fréquents de prescription potentiellement inappropriée observés chez les patients de 65 ans et plus, par excès (STOPP.v2) ou par défaut (START.v2)

STOPP	si
Benzodiazépines ou Z-Drugs	> 4 semaines
AINS	Insuffisance rénale et/ou cardiaque
Aspirine	Prévention cardiovasculaire primaire
Vasodilatateur (nitré, α_1-bloquant, anti-calcique)	Hypotension orthostatique
Anticholinergique	Troubles cognitifs
si	**START**
Chutes, ostéoporose	Vitamine D et Calcium
Fibrillation auriculaire	Anticoagulation
Prévention cardiovasculaire secondaire	Aspirine
Anxio-dépression importante	Antidépresseur ISRS
Douleur intense	Opiacé (et laxatif)

Table 1a. Liste complète des critères STOPP.v2 (Screening Tool of Older Person's Prescriptions, version 2), regroupés par médicaments

	STOPP.v2 : médicament	& situation suivante → potentiellement inapproprié (> 65 ans) : envisager son arrêt
	médicament sans indication, de durée trop longue, dupliqué (2 de même classe)	Dans tous les cas
NEURO PSYCHIATR	**benzodiazépine**	Dans tous les cas *a fortiori* si > 4 semaines pour insomnies ou anxiété [à diminuer progressivement] si insuffisance respiratoire
	Z-drug (somnifère)	Dans tous les cas (zolpidem, zopiclone)
	neuroleptique	Dans tous les cas *a fortiori* si prostatisme/ globe vésical & effet anticholinergique modéré à marqué syndrome parkinsonien ou démence à corps de Lewy (sauf pour clozapine et quétiapine) symptômes psycho-comportementaux (sauf si sévères et échec non-pharmacologique) insomnies (sauf si dues à psychose ou démence) phénothiazine comme neuroleptique de 1ère ligne
	antidépresseur tricyclique vu effet anticholinergique	& dépression, en 1ère ligne & démence, glaucome angle aigu, trouble de conduction, ou prostatisme/globe vésical

H2020-634238

THE **OPERAM** TRIAL

Objective

To assess the impact of a complex intervention on drug-related hospital admission

Design

International multicenter, cluster-controlled trial

Complex intervention

Medication review

CDSS using STOPP/START

→ evaluation by physician + pharmacist

→ discussion with hospital physician; patient/family

→ plan sent to GP

4 hospitals

Cliniques universitaires SAINT-LUC UCL BRUXELLES

2017-2019

Patients N=2008

≥ 70 years

Multimorbidity and polypharmacy

Admitted to hospital, various wards

Hospital physicians

Adam et al. Rationale and design of OPtimising thERapy to prevent Avoidable hospital admissions in Multimorbid older people: a cluster randomised controlled trial. BMJ Open 2021.
Crowley et al. Intervention protocol OPERAM: a structured medication review with support of a computerised decision support system. BMC Health Serv Res 2020.

Optimizing Therapy to Prevent Avoidable Hospital Admissions in Multimorbid Older Adults (OPERAM): cluster randomised controlled trial.
Blum M, Sallevelt B, Spinewine A et al. BMJ 2021: 374: n1585.

- Primary outcome: Drug-related hospital admissions (DRAs) at 1yr
  - 22.4% in control group; 21.9% in intervention group – HR 0.95 [0.77-1.17]
    - First preventable DRA HR 0.89 [0.63-1.25]
- Secondary outcomes: NSS differences between groups
- Subgroup analyses: NSS differences, except for site

- Potential explanations
  - Intervention design: Single timepoint pharmacotherapy optimization not persisting over a 1-year f/up ? Limited collaboration with GPs, shared decision making with patients?
  - Recommendations often involved drugs that are unlikely leading to DRA ?

THE COME-ON STUDY

COME · ON
Collaborative approach to Optimise MEdication use for Older people in Nursing homes


P Anrys

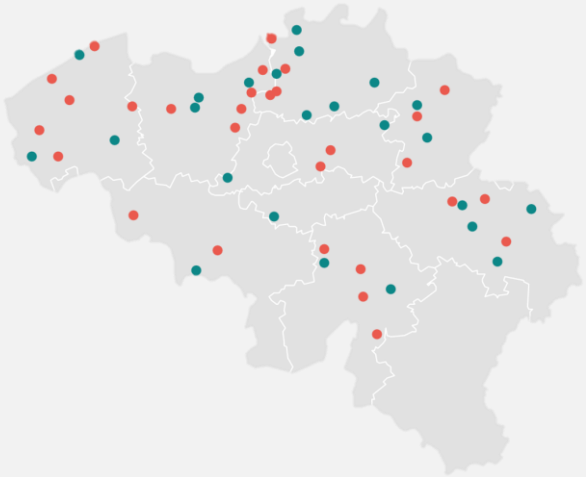
Objective

To assess the impact of a complex intervention on the appropriateness of prescribing in NHs

Design

National multicenter, cluster-controlled trial

54 nursing homes



Control : 30 NHs
Intervention : 24 NHs

From March 2015 to June 2016

Nursing home Residents (N=1804)

Median 87 years,
9 medications

Health care professionals

- Coordinating physician
- General practitioners
- Nurses
- Delivering pharmacist

Complex intervention

INAMI

Anrys et al. Collaborative approach to Optimise MEdication use for Older people in Nursing homes (COME-ON): study protocol of a cluster controlled trial. Impl Sci 2016;11:35.

THE COME-ON STUDY


P Anrys

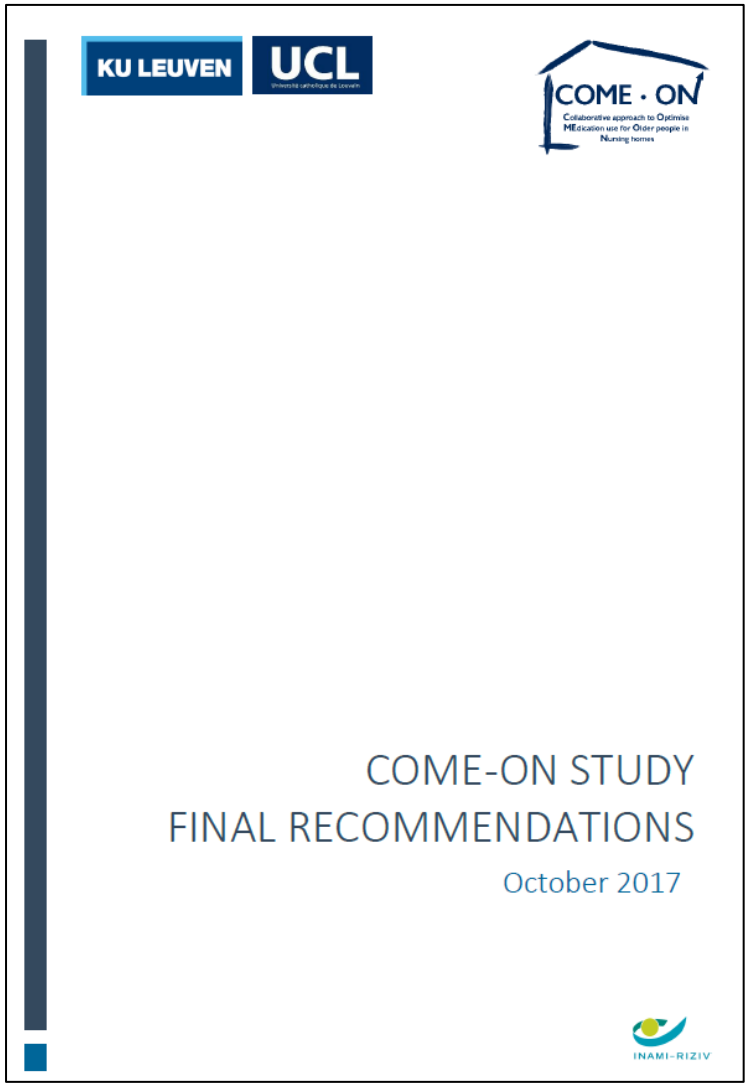
- Measure
  - STOPP: 88% of NHRs, median 2 [1-4]
  - START: 85% of NHRs, median 2 [1-3]

! Psychotropic medications; PPIs
Osteoporosis and CV prevention

- Improve
  - Improvement in appropriateness of prescribing: OR 1.479 (95%CI 1.062 – 2.059)
  - No significant difference for most clinical outcomes; median number of medications
  - *Process* evaluation
    - Implementation and satisfaction: good
    - Perceived positive impact for most HCPs
    - Key factors for success: interdisciplinary and face-to-face approach
    - Importance of: GP's attitude; pharmacist's competency; leadership

Anrys et al. Potentially Inappropriate Prescribing in Belgian Nursing Homes: Prevalence and Associated Factors. JAMDA 2018;19:884-90.
Strauven et al. Cluster-Controlled Trial of an Intervention to Improve Prescribing in Nursing Homes Study. JAMDA 2019;20:1404-11.
Anrys et al. Process evaluation of a complex intervention to optimize quality of prescribing in nursing homes (COME-ON study). Impl Sci 2019;14:104.

THE COME-ON STUDY: SPREAD?



1.2. Optimising medication use in older adults : Focusing on **deprescribing** and leveraging **implementation science**

The New York Times

Taking Multiple Medications?
You May Need to Scale Back.

Mikyung Lee

April 22, 2024

Medication overuse

The use of a medication which is not (or no longer) clinically indicated, not effective for the targeted indication, or not aligned with the patient's treatment goals and preferences,
and which has an unfavorable benefits-to-risks ratio.

Frequent – Harmful – Societal and environmental costs

Medication overuse in Belgium

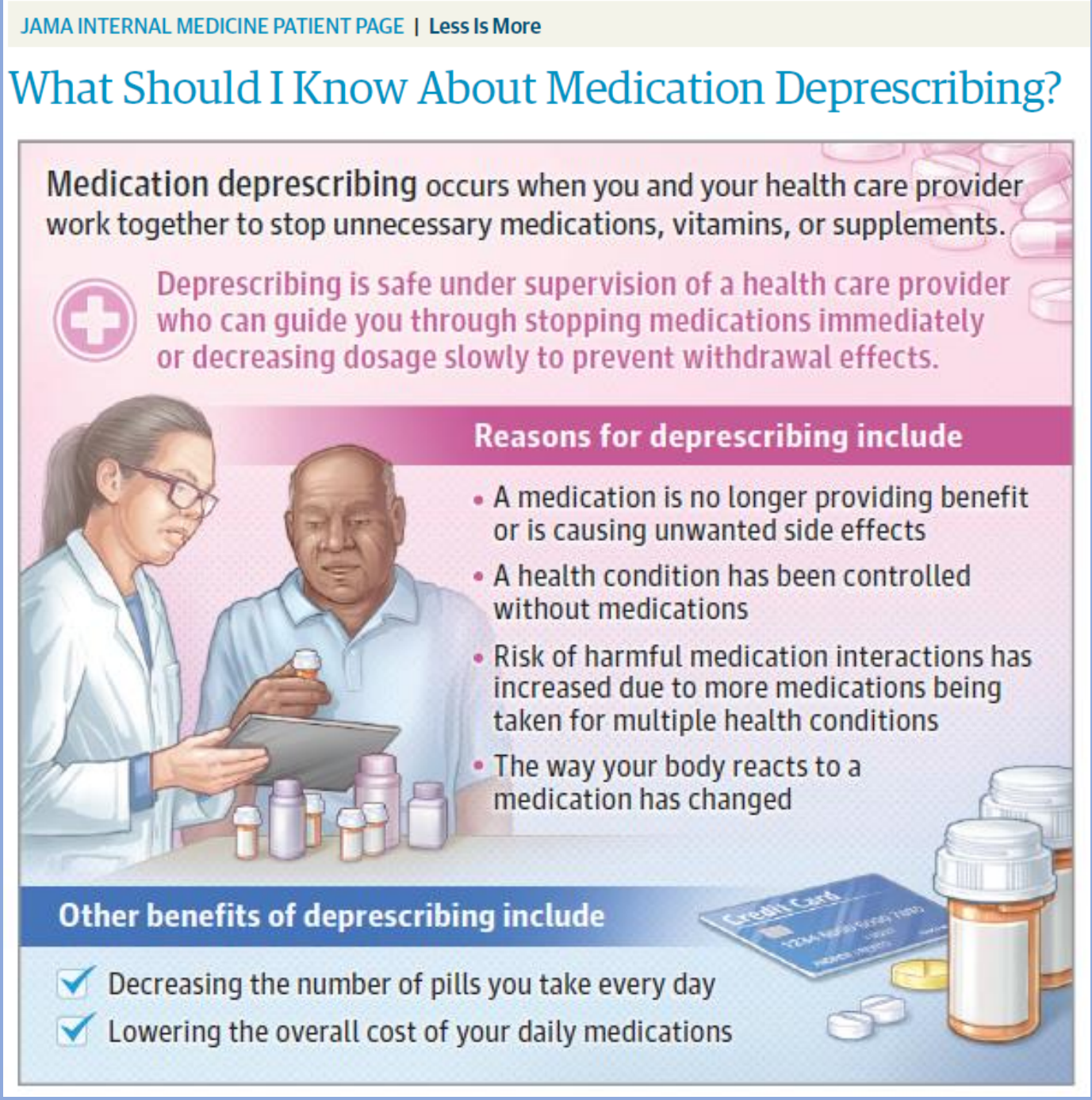
- **11% of medications** taken by older people admitted on acute geriatric wards have no valid indication (Spinewine et al., JAGS 2007)
- Overuse of glucose-lowering therapies in **34-57%** of older patients with **type 2 diabetes**; associated with higher mortality (Christiaens et al., BMC Geriatr 2020; Age Ageing 2023)
- Overprescription of intravenous fluids (IVF) in **57% of patients receiving IVF** (Sneyers et al., Int J Clin Pharm 2024)
- **59% of schizophrenic patients** discharged from hospital with antipsychotic polytherapy (Lagreula et al., Ther Adv Psychopharmacol 2022)

Deprescribing

The process of identifying and reducing or discontinuing medications in which existing or potential harms outweigh potential benefits within the context of an individual patient's care goals, function, values, and preferences.

(Scott IA et al., JAMA Intern Med 2015)

Limited implementation in routine practice



JAMA Intern Med 2023; 183:891

Implementation science: “The study of methods to promote the adoption and integration of evidence-based practices, interventions, and policies into routine health care and public health settings to improve the impact on population health”
(NIH, National Cancer Institute)

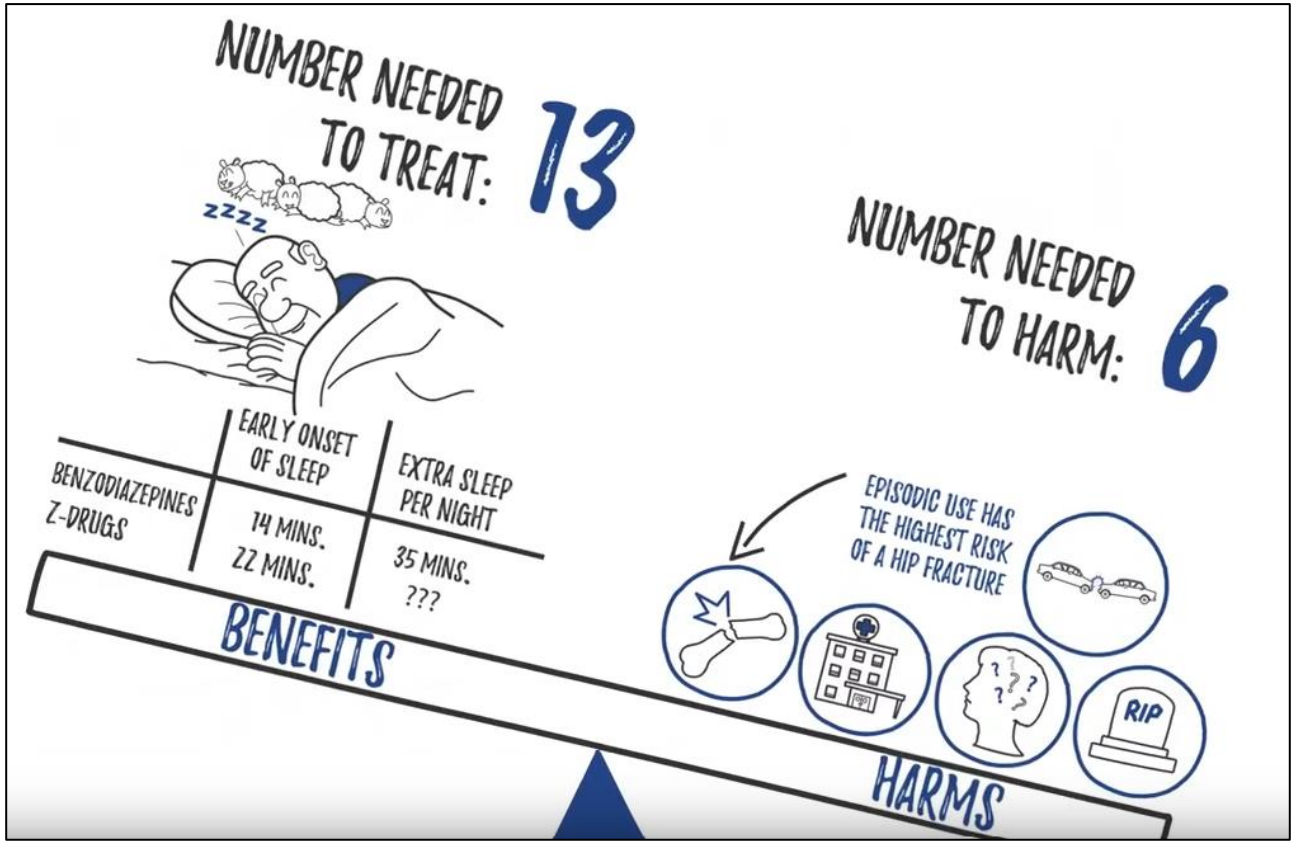
World Health Organization

Health Topics | Countries | Newsroom | Emergencies | Data | About WHO

Home / Initiatives / Behavioural Sciences for Better Health / Behavioural sciences global agenda

Behavioural Sciences for Better Health resolution on 29 May 2023 (WHA76.7)

Benzodiazepine Receptor Agonists (BZRAs)



Canadian Deprescribing Network

- One of the most frequently prescribed classes of harmful medications
  (Ma Sleep 2023; Borrelli 2024)
- One of the 3 overuse practices measured by OECD
- Incur significant adverse effects and costs, especially in older adults.

DEPRESCRIBING BZRAS

AMBULATORY

Perrine EVRARD

NURSING HOME

Catherine PETEIN

HOSPITAL

FX SIBILLE

DI PRESCRIBE

Deprescribing in older adults
through an **I**mplementation Science approach
Actions de Recherche Concertées (ARC) - 2022-2027

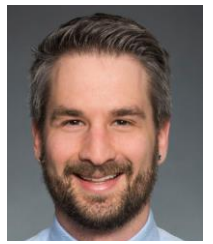


T Chevallereau, M Jaeken, S Van den Broucke (IPSY)

BE-SAFE

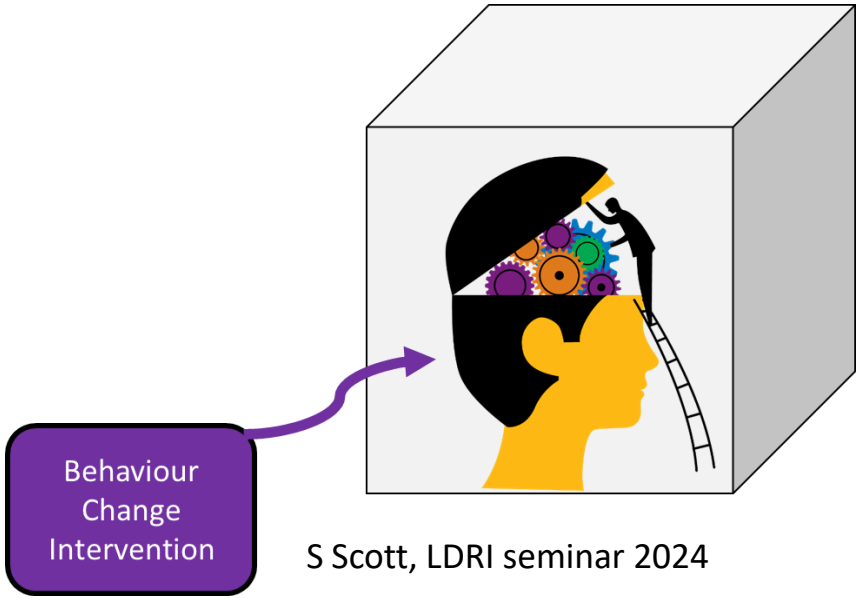
Implementing a patient-centred and evidence-based intervention to reduce BZRA use to improve patient SAFEty - **Horizon Europe -** 2022-2027

IMPLEMENTATION SCIENTISTS


J Grimshaw, J Presseau, A Patey (OHRI, Ottawa)

DEPRESCRIBING BZRAS & IMPLEMENTATION SCIENCE



S Scott, LDRI seminar 2024

Theories
Models
Frameworks
(TMFs)

52,4% of NHRs are BZRA users

Identifying barriers → Intervention development → Evaluation → Dissemination

Perrine EVRARD

General practitioners

Other Healthcare professionals

- Knowledge and skills gaps
- BZRA refilling happens automatically
- Competing priorities
- Social pressure to prescribe
- Environmental issues

9 Behaviour Change Techniques (BCTS) operationalised in a 6-component intervention

1. Steps and goals

Definition at the NH level

How ?

Tool 1: proposition of steps to adapt at the NH level (definition or responsible person, timeline for each step)

Who ?

Multidisciplinary team, in agreement with NH direction

2. Healthcare professionals education

How ?

Tool 2: PowerPoint presentation for an educational session for HCPs

Who ?

Presentator free of choice (suggestion to ask the coordinating physician)

Educational session for GPs and NH HCPs

3. Environmental adaptations

How ?

Tool 3: List of propositions of adaptations to choose upon. NHs are also asked to define goals for adaptation implementation

Who ?

NH direction, in agreement with HCPs

4. Audit and Feedback on BZRA use at the NH level

How ?

The research team sends a feedback every three months (**Tool 4**)

Who ?

The pharmacist provide us with BZRA use data

5. Residents and families raising awareness

How ?

Tool 5: educational leaflet

Who ?

Leaflet distribution by any HCPs

6. Multidisciplinary discussion about BZRA

How ?

Discussion on BZRAs indication, and potential alternatives and deprescribing

Communication with GP through the multidisciplinary opinion document (**Tool 6**)

Who ?

Multidisciplinary team

Evrard P. et al. Benzodiazepine Use and Deprescribing in Belgian Nursing Homes: Results from the COME-ON Study. J Am Geriatr Soc 2020

Evrard et al. Barriers and enablers towards benzodiazepine-receptor agonists deprescribing in nursing homes: A qualitative study of stakeholder groups. Exploratory Research in Clinical and Social Pharmacy 2023.

Evrard P et al. Development of a behavior-change intervention toward benzodiazepine deprescribing in older adults living in nursing homes. JAMDA 2024

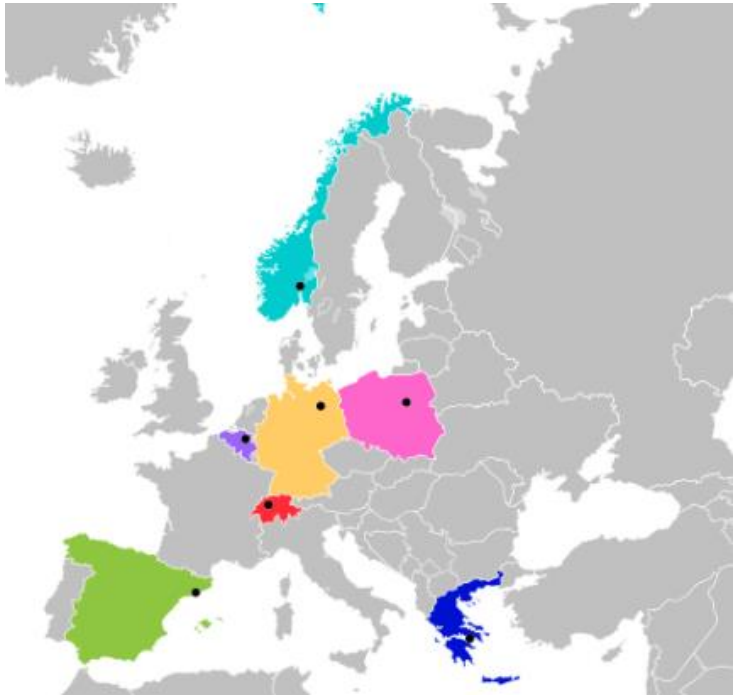
Testimony of an intervention NH quality coordinator

Evrard et al. Feasibility of a theory-based intervention towards benzodiazepine deprescribing in Belgian nursing homes: protocol of the END-IT NH cluster-randomised controlled trial. BMJ Open 2024;14:e085435.

BE-SAFE

Vladyslav SHAPOVAL

Implementing a patient-centred and evidence-based intervention to reduce **BE**nzodiazepine and sedative-hypnotic (BSH) use to improve patient **SAFE**ty and quality of care.



Survey: 183 patients, ≥65 years, from 6 European countries

BZRA essential to sleep well - low perception on the risks

- 72% feel they have no other choice but to take their BSH to feel or sleep well;
- 22% believe that their BZRA is giving them side effects.

Yet, opportunities for physicians to initiate discussion

- 60% would be willing to reduce the dose of their BSH if recommended by their doctor.

And need to offer resources / support

- 35% already read/heard information how to stop their BSH.

Horizon Europe – 101057123 – 09/2022-08/2027

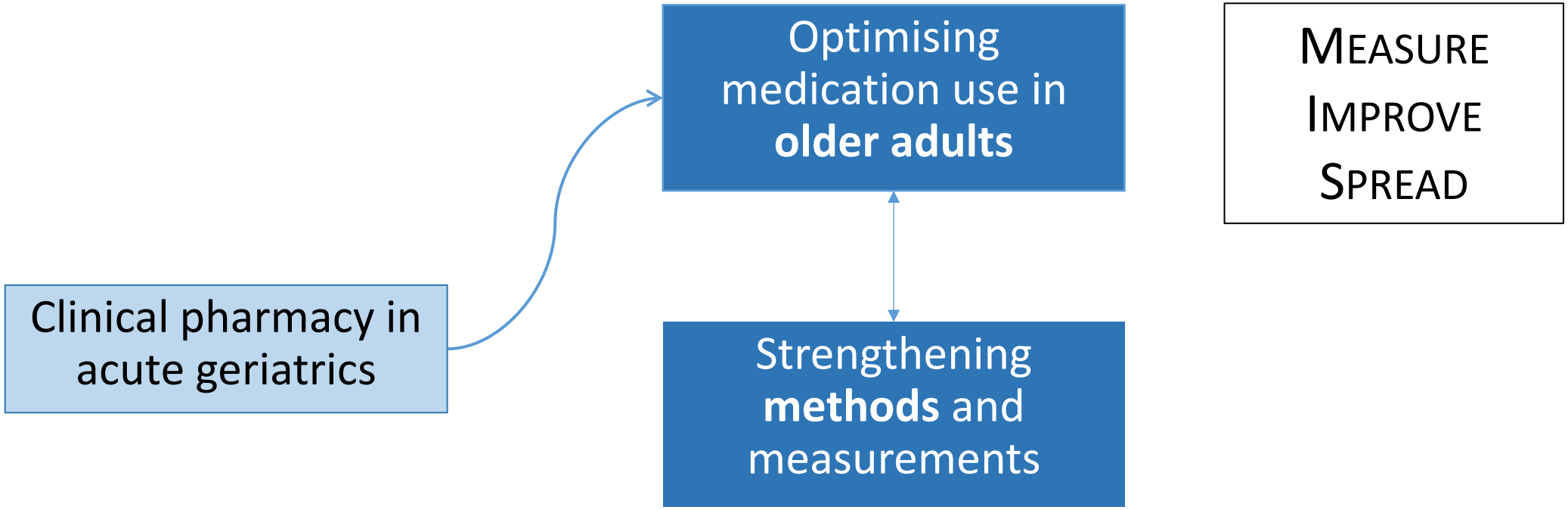
DI PRESCRIBE

Deprescribing in older adults through an **I**mplementation Science approach.
ARC - 2022-2027

Laudine ACKERMANS

DEPRESCRIBING: « CATCH THEM YOUNG »

- Survey: 1787 students in medicine, pharmacy and nursing in Belgium
  - Self-perceived knowledge and skills in deprescribing
- Survey and focus groups with Faculty members (UCLouvain)
- Revisiting existing curricula; interprofessional training


Clinical pharmacy in acute geriatrics
Optimising medication use in **older adults**
Strengthening **methods** and measurements
MEASURE
IMPROVE
SPREAD

Optimising methods and measurements

- Inappropriate prescribing – Clinical Outcomes – Deprescribing – …
- Patient and Public Involvement (PPI) in research

MEASURING – ↑ VALIDITY & RELEVANCE

JB Beuscart, L Zerah, V Shapoval

Topic, Problem	Our contribution towards better measurement, and impact
Trial **outcomes**: heterogenous, not always relevant to patients	Core Outcome Set (COS) for clinical trials of medication review in multi-morbid older adults with polypharmacy (Beuscart et al. BMC Medicine 2018)
Drug-related Admissions (DRA)	Standardized chart review method (Thevelin Br J Clin Pharmacol 2018); Positive Predictive Value: 0.66 [0.62-0.69] (Zerah et al. Age Ageing 2022)
Drug-drug interactions (DDIs)	International consensus list of potentially clinically significant DDIs in older people (Anrys et al. JAMDA 2021)
Attitudes towards deprescribing	Physicians' attitudes: TDF-based questionnaire (Shapoval et al.) Patients' attitudes (C Pétein; S Alves Jorge)

Other innovative methods developed at CLIP (e.g. emulation of target trials, A Christiaens, S Henrard)

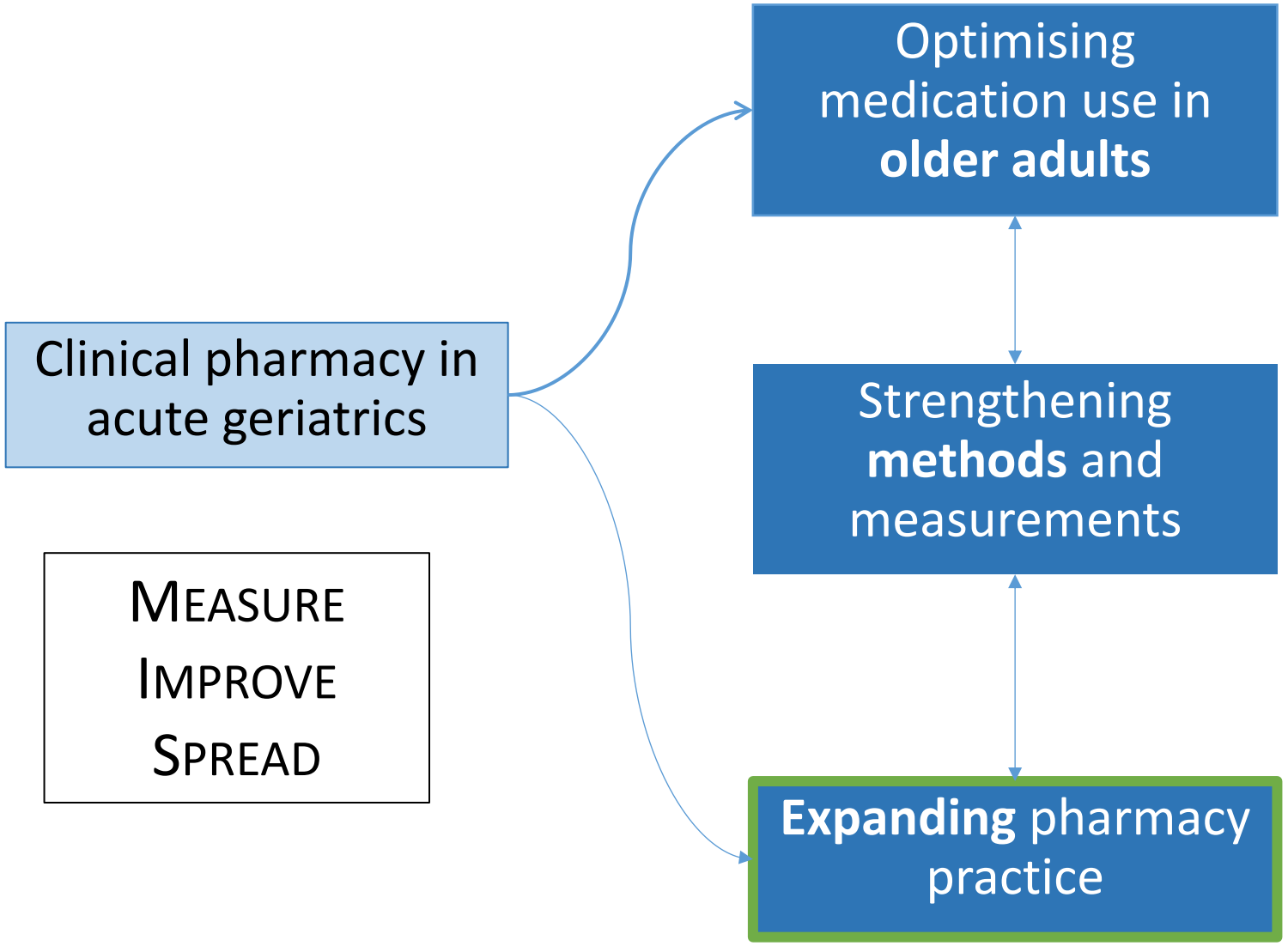
TDF: Theoretical Domains Framework

PATIENT AND PUBLIC INVOLVEMENT (PPI)

- Researchers consulting or working with members of the public, patients, service users, and carers in any or all part(s) of the research process, including the choice of research topic, design, planning, conduct or dissemination of research."
- Objective: To maximise relevance and impact of research
- Survey of pragmatic trials (2014-2019): 47.0% reported conducting PPI; e.g. codesign of interventions, recruitment/retention strategies (Vanderhout et al., CMAJ Open 2023)

BE-SAFE

Local and international PAC (Patient Partnership Advisory Council)
Dedicated tasks; milestones and deliverables; budget


Optimising medication use in **older adults**
Clinical pharmacy in acute geriatrics
Strengthening **methods** and measurements
MEASURE
IMPROVE
SPREAD
Expanding pharmacy practice

Expanding pharmacy practice

Other medications & clinical situations

Other research groups & collaborators

Optimizing Medication Use in Intensive Care

Barbara SNEYERS

"Use of guidelines by healthcare professionals in the intensive care : easier said than done ? The example of analgesia and sedation"

Sneyers, Barbara

Sneyers et al. What stops us from following sedation recommendations in intensive care units? A multicentric qualitative study. J Crit Care 2014.
Sneyers et al. Current practices and barriers impairing physicians' and nurses' adherence to analgo-sedation recommendations in the intensive care unit--a national survey. Crit Care 2014.

Optimizing the Use of Direct Oral Anticoagulants

Anne-Laure
SENNESAEL

Pradaxa® dabigatran etexilate

once-daily Lixiana® edoxaban

Eliquis® apixaban

Xarelto® rivaroxaban

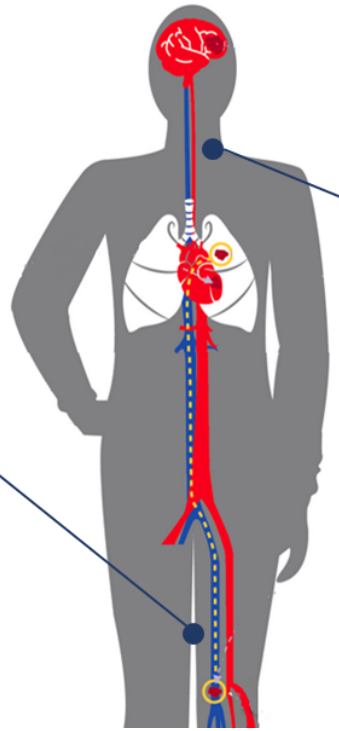
THROMBOTIC RISK

BLEEDING RISK

FOR WHICH INDICATIONS?

Prevention and treatment of venous thromboembolism

Stroke prevention in atrial fibrillation

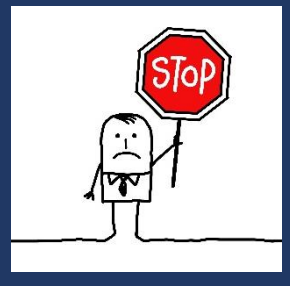


Optimizing the Use of Direct Oral Anticoagulants

Jeanne – 86 years old
Admitted to the hospital for severe nose bleeds

Xarelto® (rivaroxaban) 20mg once daily
Stroke prevention in atrial fibrillation

CHOICE



DOSE

ADHERENCE

"I'VE BEEN HALVING MY XARELTO® TABLET INTAKE FOR 2 MONTHS."

ENSURING APPROPRIATE AND SAFE USE OF DOAC REMAINS A CHALLENGE.

Sennesael et al. Optimizing the Safe Use of Direct Oral Anticoagulants in Older Patients: A Teachable Moment. JAMA Intern Med. 2015;175:1608-9
Larock et al. Appropriateness of prescribing dabigatran etexilate and rivaroxaban in patients with nonvalvular atrial fibrillation: a prospective study. Ann Pharmacother 2014;48:1258-68.

MON PATIENT EST SOUS AOD – COMMENT AMÉLIORER SA SÉCURITÉ ?

Outil développé dans le cadre d'une étude évaluant les événements indésirables (EIM) sous anticoagulants oraux directs (AOD)

Résultats principaux de l'étude*

46 patients sous **AOD,** admis au service des urgences pour **SAIGNEMENT** ou **THROMBOSE**
Age médian 80 ans – 52% ♂

53 % des EIM graves sous AOD ont été évalués **POTENTIELLEMENT ÉVITABLES**:

- Choix du médicament
- Adhérence du patient
- Dose inadéquate
- Interaction médicament

= ***80%*** *des évaluations potentiellement évitables*

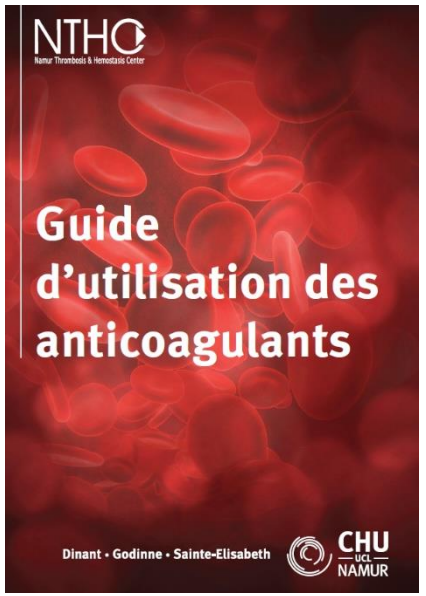
ENTRETIENS avec 21 médecins généralistes pour identifier les **FACTEURS CONTRIBUANT AUX EIM:**

- Oublis de prise, crainte d'effets secondaires
  EIM ou médicaments concomitants non signalés
- Manque de connaissance des AOD
  Choix du traitement non individualisé
  Interactions médicamenteuses non considérées
  Pas de suivi spécifique réalisé
- Manque de communication 1ère-2ème lignes
  Rapports d'hospitalisation erronés

Liste non exhaustive

* Br J Clin Pharmacol 2018. doi: 10.1111/bcp.13580.

CHU UCL NAMUR



Sennesael et al. Preventability of serious thromboembolic and bleeding events related to the use of oral anticoagulants: a prospective study; Br J Clin Pharmacol 2018; 84:1544-1556

Effect of *ABCB1* genetic polymorphisms on the transport of rivaroxaban in HEK293 recombinant cell lines

Anne-Laure Sennesael[1,2], Nadtha Panin[3], Christelle Vancraeynest[2], Lionel Pochet[2], Anne Spinewine[1,4], Vincent Haufroid[3,5] & Laure Elens[3,6]

Sci Rep 2018;8:10514.

In vitro assessment of the risk of ABCB1-mediated drug–drug interaction between rivaroxaban and tacrolimus in human embryonic kidney 293 recombinant cell lines

Gwenaëlle Mahieu[1,2] | Anne-Laure Sennesael[3] | Lionel Pochet[4] | Vincent Haufroid[5,6] | Françoise Van Bambeke[1] | Anne Spinewine[7,8] | Laure Elens[2,5]

Res Pract Thromb Haemost. 2024;8:e102521

The Impact of Strong Inducers on Direct Oral Anticoagulant Levels

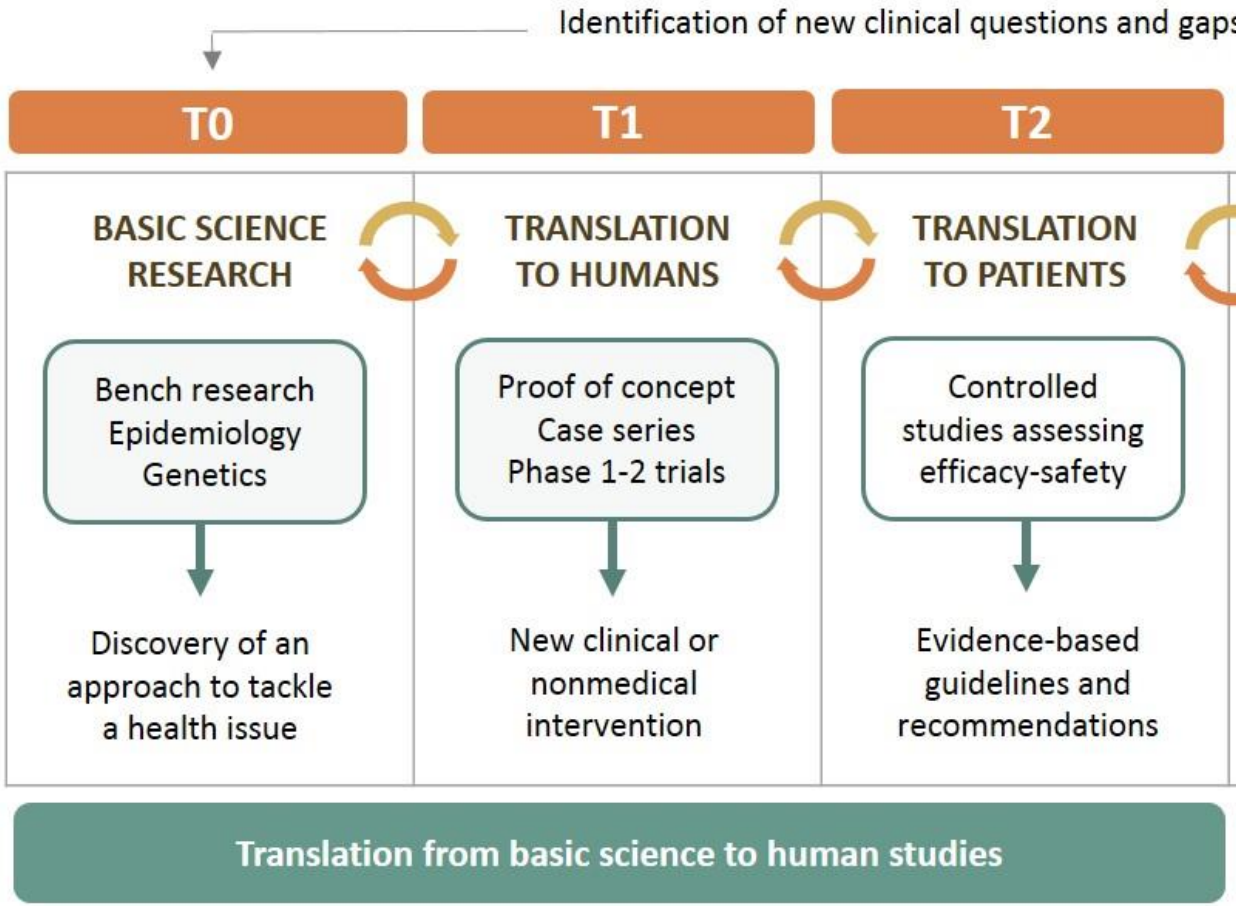
Anne-Laure Sennesael, MPharm, MSc, PhD,[a,b] Anne-Sophie Larock, MPharm, MSc,[a] Philippe Hainaut, MD, PhD,[c] Sarah Lessire, MD, PhD,[d] Michael Hardy, MD,[d,e] Jonathan Douxfils, MPharm, PhD,[f,g] Anne Spinewine, MPharm, MSc, PhD,[a,b] François Mullier, MPharm, MSc, PhD[e]

Am J Med 2021; 134: 1295-99.

Pharmacocinétique et pharmacodynamique des anticoagulants oraux directs chez les patients greffés pulmonaires

ATRAP-trial

Conclusion: CLIP within the LDRI



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