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Co-inventor/author of STOPP/START criteria, Have received funding from the HRB and EU-FP7, H2020 to investigate the impact of STOPP/START v2 in optimising prescribing in older patients

SENATOR: https://pubmed.ncbi.nlm.nih.gov/32484850/ OPERAM: https://pubmed.ncbi.nlm.nih.gov/34257088/ TRUST https://pubmed.ncbi.nlm.nih.gov/28402245/ iKASCADE project: Identifying Key Prescribing CASCADes in the Elderly: A Transnational Initiative on Drug Safety















Royal Cork Yacht Club, 1720



Titanic 1912

Queen's College, Cork. Founded 1845



#### ESCP Symposium Prague 2022



ESCP SIG- Deprescribing Members Meeting Thursday 20 October 2022, 12.30 CET Room: Ostrava



# Potentially Inappropriate Prescribing (PIP)

- Prevalence of patients with PIP in secondary care: ~ 50%.
- Computerised interventions suggested as an effective strategy to reduce this.



#### AGEING AND MULTIMORBIDITY

- By the year 2050 in Europe the number of citizens older than 65 years will be higher than those younger than 10 years
- More than two thirds of older people have two or more apparently unrelated diseases
- Older people with multimorbidity will be around 75 millions in 2060 in Europe (nearly 10% of the whole population)
- Multimorbidity is inevitably associated with **polypharmacy**

Marengoni A et al. Aging Research Review 2011;10:430

- It is not possible to have evidence-based guidelines for every possible combination of multiple concomitant diseases
- We need to be able to provide advice regarding medicines least likely to harm





## Polypharmacy is associated with an increased risk of inappropriate prescribing, which in turn leads to different <u>negative outcomes</u>:



Despite this there is limited evidence on interventions to improve medication appropriateness and lower the risk of adverse clinical outcomes

**UCC** 

Sources: Davies et al. Journal of the American Medical Directors Association. 2020. | Liew et al. Annals of Family Medicine. 2019. | Mekonnen et al. Br J Clin Pharmacol. 2021. | Rochon et al. The Lancet. Health Longevity. 2021. | Xing et al. Ann Pharmacotherapy. 2019.

#### STRATEGIES TO HELP DEPRESCRIBING

- <u>Clinical guidelines</u> e.g. NICE guideline for the management of type 2 diabetes (2015): relaxation of HbA1c level for older or frail people with reduced life expectancy, risk of falling or those with significant comorbidities.
- Deprescribing guidelines
   and algorithms. e.g. Deprescribing
   of proton-pump inhibitors (Thompson
   2016); Deprescribing protocol (Scott
   2015).
- <u>Lists or criteria for</u> inappropriate precriptions or potentially inappropriate

<u>medications</u>. E.g. Beers Criteria, STOPP/START criteria, EU(7)-PIM list, etc.

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#### Systematic reviews on deprescribing in older people

 Thillainadesan et al. → older hospitalized patients (i.e. ≥65 years)

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

• Dills et al.  $\rightarrow$  adult patients (aged  $\geq \! 18$  years) in outpatient, assisted living, nursing home and acute care settings

J Am Med Dir Assoc. 2018;19(11):923-935

 Shrestha et al. → older patients (i.e. ≥65 years) with life-limiting illnesses and reduced life expectancy

Br J Clin Pharmacol. 2019;10.1111/bcp.14113

- Deprescribing can reduce polypharmacy and IP
- Unclear if tangible benefits for ADRs, falls, rehospitalization, quality of life and mortality



#### Multi-centre RCTs of Deprescribing

 SENATOR RCT (2012 – 2018): 6 European centres, 1,537 patients (primary endpoint: hospital-acquired ADRs within 14 days/discharge)
 O'Mahony D et al., Age & Ageing 2020; 49: 605-614

 OPERAM RCT (2015 – 2020): 4 European centres, 2,008 patients (primary endpoint: drug-related readmissions within 12 months) Blum M et al., BMJ 2021 Jul 13;374:n1585. doi: 10.1136/bmj.n1585

VALFORTA RCT (2013 – 2014): 2 German centres, 409 patients
 (primary endpoint: sum of medication errors i.e. over-, under- or mis-treatment)
 Wehling M et al. Age Ageing 2016; 45: 262-267

 OPTIMIST RCT (2013 – 2015): 4 Danish centres, 1,467 patients (primary composite endpoint: readmission or ED visits within 180 days) Ravn-Nielsen LV et al., JAMA Intern Med 2018; 178(3): 375-382

 MedSafer RCT (2017 – 2020): 11 Canadian centres, 5,698 patients (primary endpoint: ADEs within 30 days of hospital discharge) McDonald EG et al. JAMA Intern Med 2022; 182(3):265-273.



#### Available deprescribing tools

Tools for Deprescribing in Frail Older Persons and Those with Limited Life Expectancy: A Systematic Review

Wade Thompson, PharmD, MSc,\* Carina Lundby, MScPhm,<sup>14</sup> Trine Graabæk, MScPhm, PhD,<sup>24</sup> Dorthe S. Nielsen, RN, MHS, PhD,<sup>41</sup> Jesper Ryg, MD, PhD,<sup>\*\*†</sup> Jens Sondergaard, MD, PhD,<sup>\*</sup> and Anton Pottegård, MScPhm, PhD<sup>11</sup>

Thompson W., et al. JAGS 2019; 67:172-180



### Available deprescribing tools

Tool name	Population	Description
Geriatric- Palliative algorithm	Nursing home resident with incurable disease	Identifies if a drug can be deprescribed based on indication, safety, and alternative therapies.
STOPPFrail	Frail older persons (end-stage irreversible pathology, poor 1-year survival prognosis, severe functional impairment, goal of symptom control)	List of criteria for specific medications and health conditions for which deprescribing can be considered; provides suggested monitoring parameters
LESS-CHRON	Older persons with multiple comorbidities, specifically frail older persons (criteria are medication specific)	List of drugs/conditions to consider for deprescribing; provides monitoring/follow- up guidance
Holmes et al.	Individuals with advanced dementia	List of medications to guide deprescribing; medications considered never appropriate, rarely appropriate, sometimes appropriate, always appropriate.



#### Available deprescribing tools contd'

Tool name	Population	Description
Pruskowski and Handler.	Individuals with limited life expectancy (with comfort-focused treatment plan), particularly older nursing home residents	List of medications to consider deprescribing
Frank and Weir.		Algorithm to guide deprescribing process for entire medication list
Scott et al. (a)	Older persons, specific discussion of frail individuals and those with limited life expectancy (no specific criteria described)	Ten-step framework to approach deprescribing process for entire medication list
Scott et al. (b)		Five-step approach and algorithm to guide deprescribing process for entire medication list







#### SENATOR RCT

- Phase 1: Observational data in 800 patients (in order to estimate ADR rates in medical specialties in the 6 participating hospitals)
- Phase 2: Cluster-randomization of 1872 patients to 'normal' pharmaceutical care (n= 936) or SENATOR-guided pharmaceutical care (n= 936)
- Primary outcome measure:
- % of patients adjudicated as having at least one likely or definite, non-trivial hospital acquired ADR within 14 days of enrolment during index hospitalization.





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#### ICD-10 codes in the software

ICD-10 coding	Name of condition with this ICD-10 code	Disease severity	Cause of admission
K57	Diverticular disease of intestine	🛛 Hild 🗋 Hoderate 🗋 Severe	🗋 Yes 🗹 🌆
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295.5	Presence of coronary angioplasty implant and graft	🖉 Hild 🔲 Moderate 🛄 Severe	🗆 Yes 🗹 No
195.1	Orthostatic hypotension	🕑 Hild 🛄 Moderate 🛄 Severe	🔲 Yus 🕑 Abo
M81.9	Osteoporosis, unspecified	😰 Hild 🔲 Hoderate 🖂 Severa	Yes 🗹 No
112	Unspectfied acute lower respiratory infection	🗋 Hild 🕑 Hoderate 🗋 Severe	Yes 🗋 No



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## Uptake of SENATOR software medication advice points in each of the six participating centres.



#### Problems encountered in SENATOR

- Couldn't take into account all patient parameters - e.g. reason for admission >Suggested to start antithrombotic in a patient who may have presented with a bleed
- Some recommendations were falsely triggered - extra information would be required to prevent such false triggers in future applications
- Doesn't always consider route of e.q. IV vs PO administration corticosteroids SENATOR

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

Blum MR; Sallevelt BTGM; Spinewine A; O'Mahony D; Moutzouri E; Feller M; Baumgartner C; Roumet M; Jungo KT; Schwab N; Bretagne L; Beglinger S; Aubert CE; Wilting I; Thevelin S; Murphy K; Huibers CJA; Drenth-van Maanen AC; Boland B; Crowley E; Eichenberger A; Meulendijk M; Jennings E; Adam L; Roos MJ; Gleeson L; Shen Z; Marien S; Meinders AJ; Baretella O; Netzer S; de Montmollin M; Fournier A; Mouzon A; O'Mahony C; Aujesky D; Mavridis D; Byrne S; Jansen PAF; Schwenkglenks M; Spruit M; Knol W; Dalleur O; Trelle S; Rodondi N



Blum et al. BMJ.



PFRAM

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#### OPERAM – Across 4 Clinical Sites





Countries participating in the OPERAM trial Source: https://www.operam-2020.eu/index.php?id=1502, accessed 26.08.2022



#### **OPERAM study participants**

#### **Participants**

- Adults aged ≥ 70 years
- Admitted to a participating hospital ward
- Multimorbidity (≥ 3 chronic conditions)
- **Polypharmacy** (≥ 5 daily drugs)
- Few exclusion criteria to maximize generalizability

#### **Intervention**

- Cluster-randomisation at the level of attending hospital physicians
- 1:1 randomisation to the intervention or control arm
- Intervention performed by team of a doctor and a pharmacist
- Structured assessment of preadmission medication list



#### **OPERAM Intervention** (contd')

- Web-based evidence-based structured medication review using STRIP assistant
  - Based on the STOPP/START criteria
- Generation of patient specific prescribing recommendations
- Final report sent to general practitioners with all prescribing recommendations



#### Excerpt from the 'Systematic Tool to Reduce Inappropriate Prescribing' (STRIP) assistant

Sources: (1) O'Mahony et al. Age Ageing. 2015. | Drenth-van Maanen et al. J Eval Clin Pract. 2018. | Crowley et al. BMC Health Serv Res. 2020. | Adam et al. BMJ Open. 2019



#### **OPERAM - Study Flow Chart**



#### **OPERAM - Clinical Outcome**

	Even	ts (%)	Hazard ratio
	Control	Intervention	interval)
First drug related hospital admission	234 (22.4)	211 (21.9)	0.95 (0.77 to 1.17)
Death	203 (19.4)	172 (17.9)	0.90 (0.71 to 1.13)
First fall	263 (25.2)	237 (24.6)	0.96 (0.79 to 1.15)
First preventable DRA	100 (9.6)	84 (8.7)	0.89 (0.63 to 1.25)
First DRA in patients with ≥1 STOPP recommendation implemented at 2-month follow-up	156/875 (17.8)	64/398 (16.1)	0.88 (0.65 <b>to</b> 1,19) <sub>AM</sub>

DRA = drug-related hospital admission

#### Lessons learnt from OPERAM

#### Strengths:

- Enrolment of >2000 patients with multimorbidity with minimal exclusion criteria
- Few patients lost to followup
- Addressing limitations of previous trials through
  - Cluster randomisation
  - Maximized blinding
  - Adjudication of hospital readmissions

#### Limitations

- Perhaps some medication changes in the control arm were similar to the intervention, potential bias
- Single timepoint intervention
- Cluster randomisation at the level of the doctor (not hospital), ? potential for contamination in control clusters





#### Frequency and acceptance of CDSSgenerated STOPP/START signals

An expert team's involvement in ing happing an and the second -----商 translating population-based Frequency and Acceptance of Clinical Decision Support System-Generated STOPM/START Signals for Hospitalised Older CDSS signals to individual don'ts with Polyphannecy and Maltimorbidity patients is essential, as more nd" - Lodina I. S. Helson" - Son H. I. Op Hal - Darger Harr Harris Lands - Baker than half of the signals for potential overuse, underuse and misuse were not deemed <u>clinically appropriate in a</u> hospital setting. al. Drugs Aging. 2022 Patient-cente



Lisa M. McCarthy<sup>1,2,3</sup> © Rachel Savage<sup>4,2</sup> O · Kleran Dalton<sup>6</sup> O · Robin Mason<sup>4,4</sup> O · Joyce Li<sup>4</sup> · Andrea Lawson<sup>4</sup> Wei Wu<sup>4</sup> O · Shelley A. Sternberg<sup>6</sup> O · Stephen Byrne<sup>6</sup> · Mirko Petrovic<sup>6</sup> O · Graziano Onder<sup>10</sup> O · Antonio Cherubini<sup>11</sup> O · Denis O'Mahony<sup>12</sup> O · Jerry H. Gurwitz<sup>13</sup> O · Francesco Pegreff<sup>14</sup> O · Paula A. Rochon<sup>4,5,15,16</sup> O

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OPERAM

#### ThinkCascade

• 'Clinically important' prescribing cascades in older adults.

Drug A	Side effect	Drug B
Cardiovascular System (n=2		
Calcium Channel Blocker	Peripheral edema	Diuretic
Diuretic 💼	Urinary Incontinence	Overactive bladder medication
Central Nervous System (n=	4)	
Antipsychotic m	Extrapyramidal symptoms	Antiparkinsonian agent
Benzodiazepine	Cognitive impairment	Cholinesterase inhibitor or memantine
Benzodiazepine	<ul> <li>Paradoxical agitation or agitation secondary to withdrawa</li> </ul>	Antipsychotic
SSRI / SNRI	insomnia	Sleep agent
Musculoskeletal System (n=	1)	
NSAID .	Hypertension	Antihypertensive
Urogenital System (n=2)	- 0	
Urinary anticholinergics for overactive bladder	Cognitive impairment	Cholinesterase inhibitor or memantine
Alpha-1 receptor blocker	Orthostatic hypotension, dizziness	Vestibular sedatives

#### **Challenges with deprescribing**

#### **Knowledge**

- Identification of opportunities
- Knowing how to deprescribe



#### Fear of adverse drug withdrawal effects (ADWEs)

These occur much less frequently than adverse drug effects

#### **Responsibility**

• Whose job is it anyway?



#### **Time constraints**

#### Overcoming challenges to deprescribing

#### Equip teams to become better deprescribers

- Geriatric pharmacotherapy education
- Explicit deprescribing criteria > Potential for software
- Deprescribing algorithms

#### **Regular medication reviews**

• Improving communication between levels of care

#### Patient involvement

- Education and empowerment
- Shared decision-making

#### Deprescribing Guideline Algorithms and Protocols









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