25 October 2023

Starting with the end in mind

Polypharmacy deprescribing and in research and practice

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RCSI
UNIVERSITY OF MEDICINE AND HEALTH SCIENCES

Outline

EPIDEMIOLOGY OF POLYPHARMACY

OPPORTUNITIES FOR DEPRESCRIBING

DEPRESCRIBING IN PRACTICE

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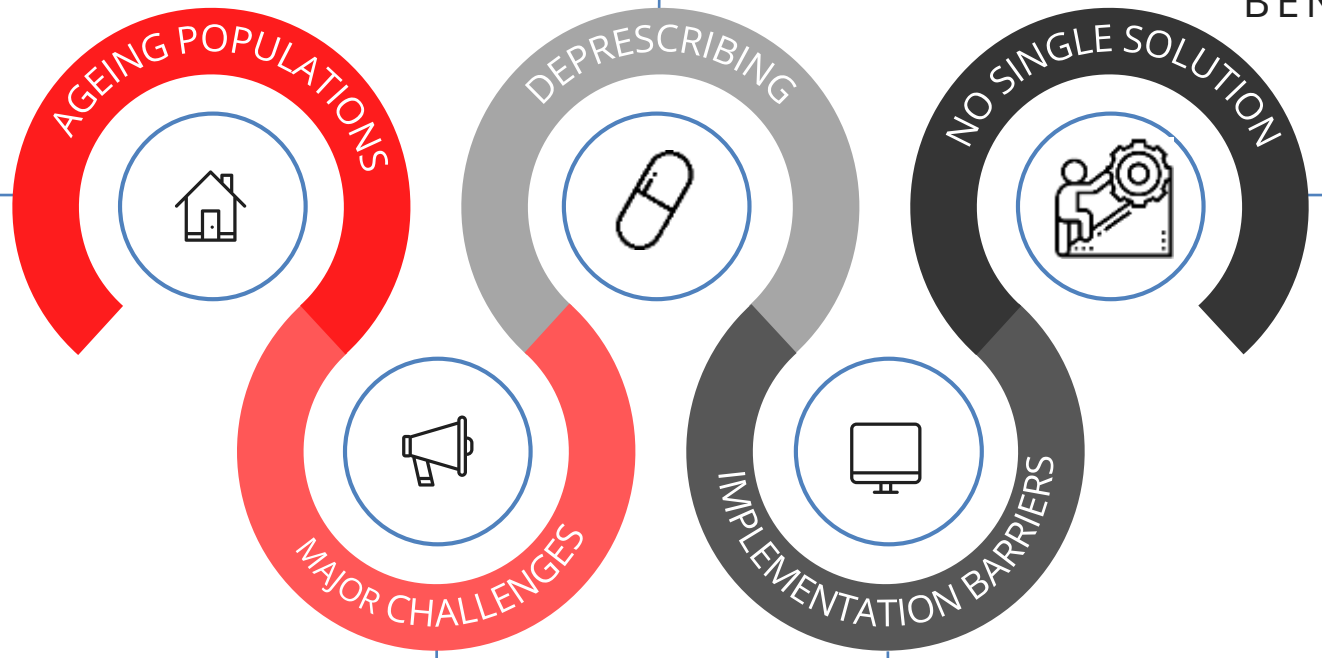
IMPORTANCE

STOP OR REDUCE MEDICINES NOT PROVIDING NET BENEFIT

GROWING BURDEN OF DISEASES AND MEDICATIONS



VARIETY OF INTERVENTIONS NEEDED TO ADDRESS THESE

MEDICATION HARM

IMPEDED BY A VARIETY OF BARRIERS

5.5 mins

World Health Organization

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POLYPHARMACY

- “Multiple medicines” – definition varies
- Number itself not important
- Someone on more than 5 medicines may be treated completely appropriately
- Someone on fewer than 5 medicines may have multiple medication problems

→ More important to consider whether the medicines are appropriate or not for that individual patient

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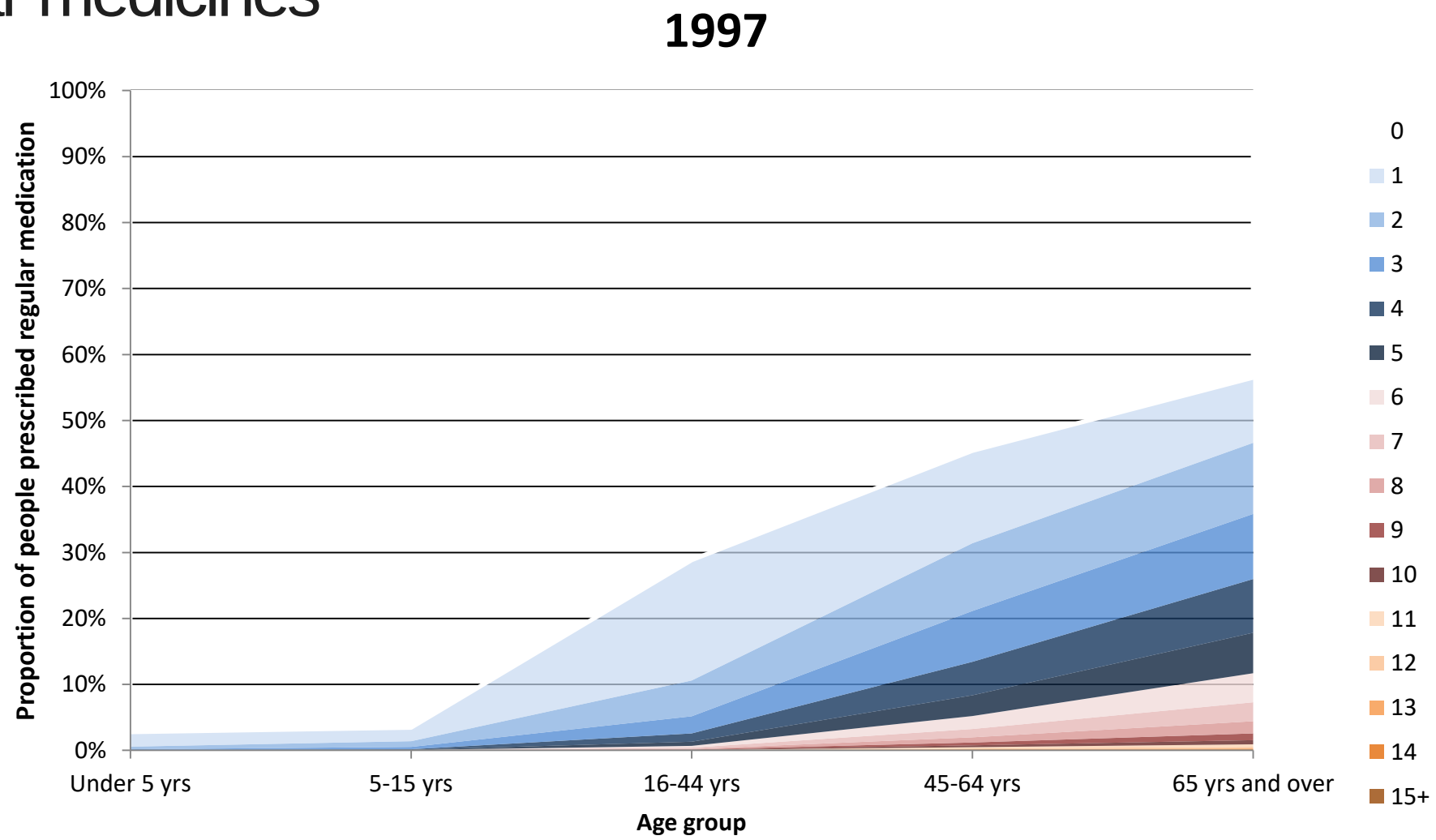
Open Access Research

BMJ Open

Trends and interaction of polypharmacy and potentially inappropriate prescribing in primary care over 15 years in Ireland: a repeated cross-sectional study

Frank Moriarty,[1] Colin Hardy,[1] Kathleen Bennett,[1,2] Susan M Smith,[1] Tom Fahey[1]

Proportion of GMS population by number of regular medicines



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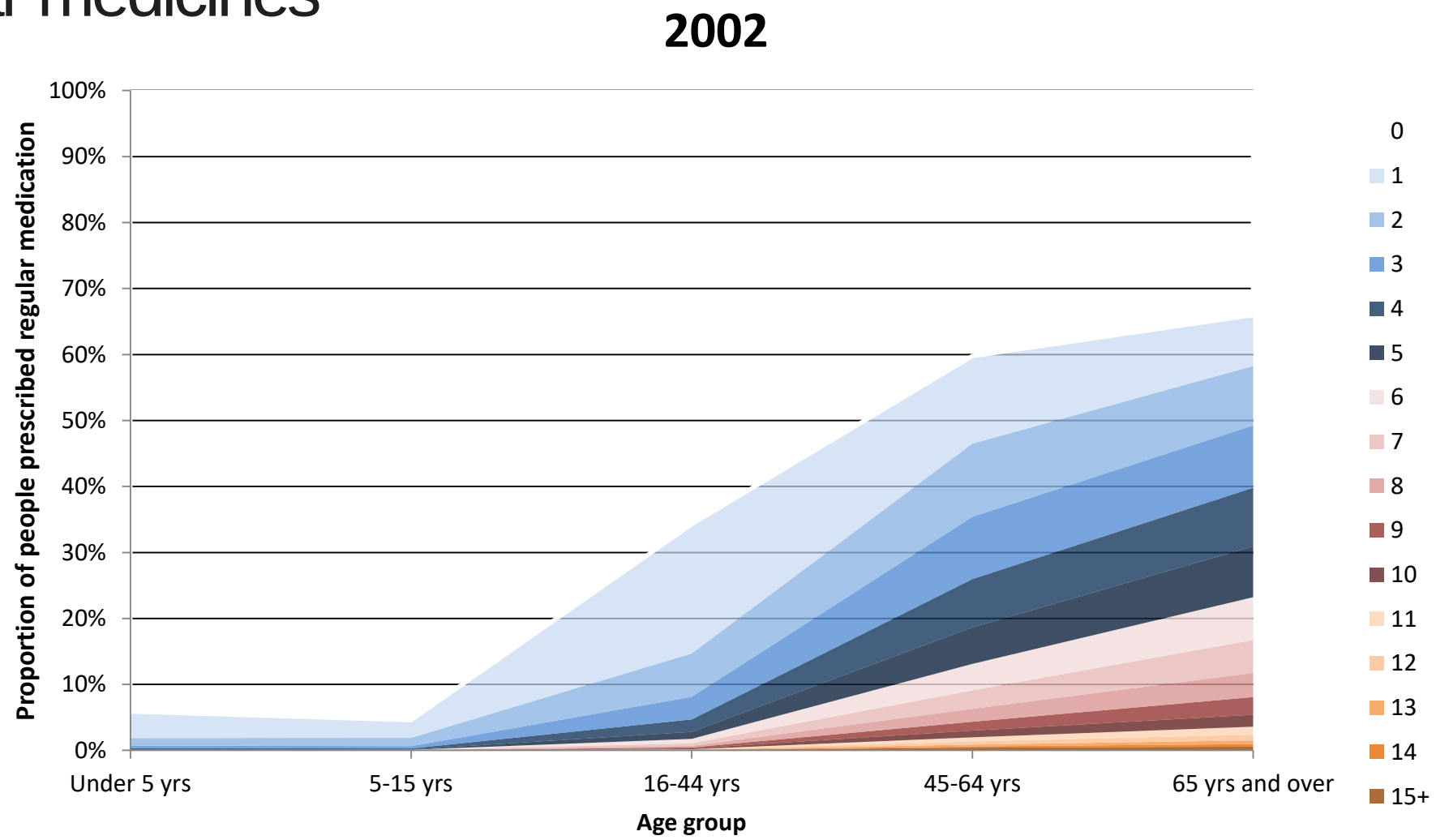
Proportion of GMS population by number of regular medicines



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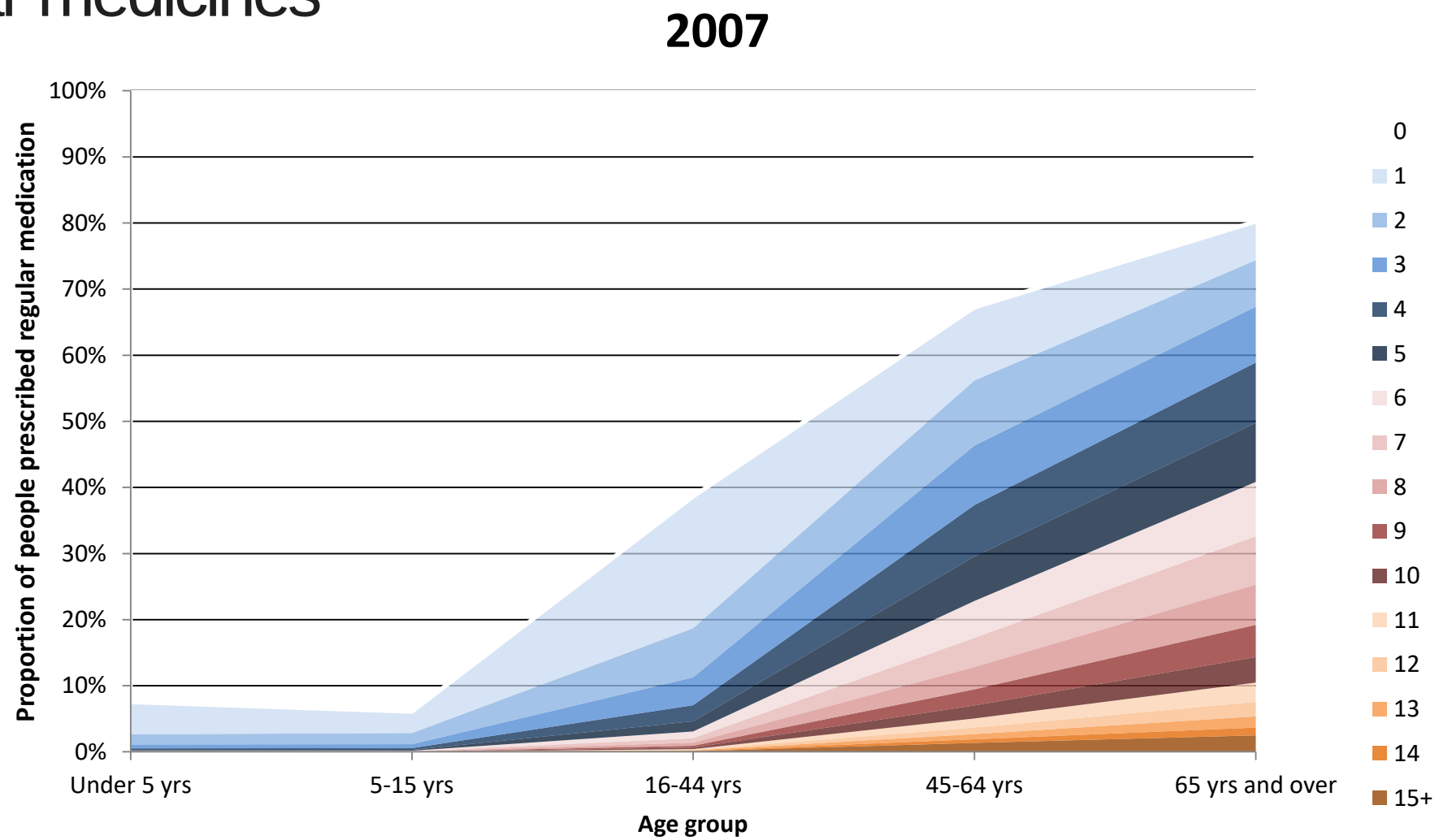
Proportion of GMS population by number of regular medicines



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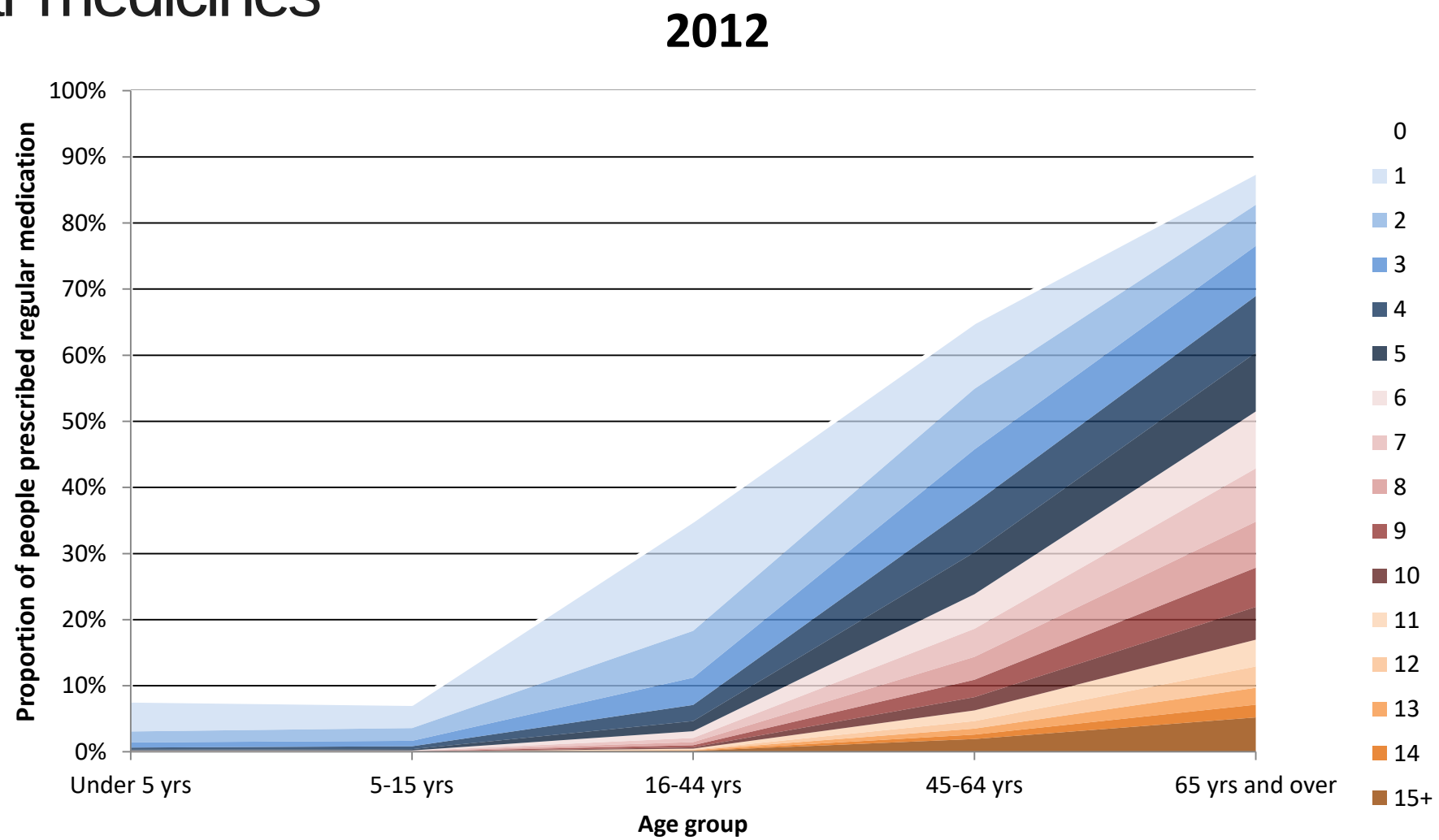
Proportion of GMS population by number of regular medicines



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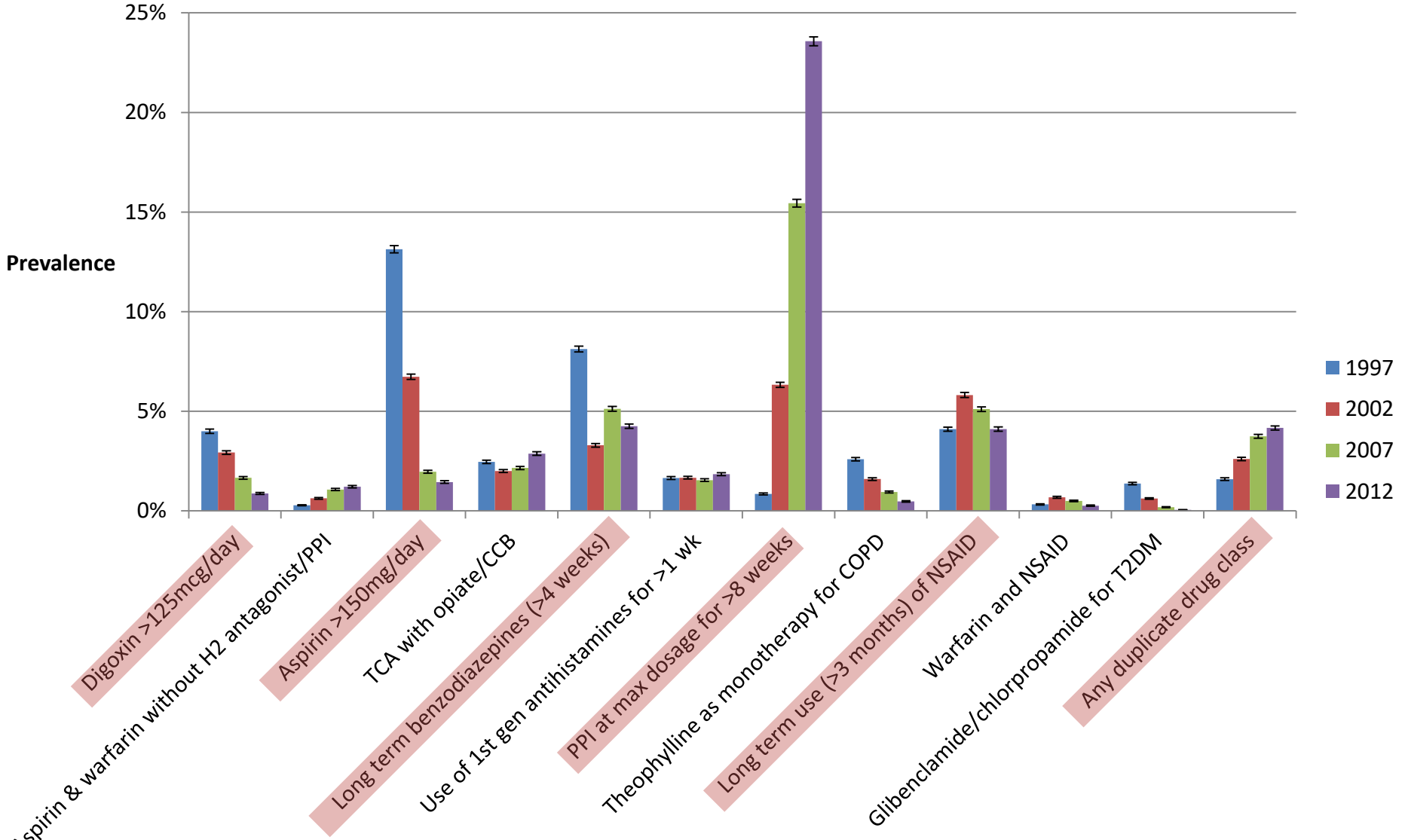
Prevalence of potentially inappropriate prescribing



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GP COHORT STUDY

Secondary analysis of a GP cohort

Patients aged 65+ from 44 GP practices, drawing on GP record and hospital discharge data, 2011-2018

Number of regular medications

For all time points, the number of unique medications prescribed per person over the previous 12 months

Analysis by health cover status

Determined trends in number of regular medicines and polypharmacy, and multilevel linear regression

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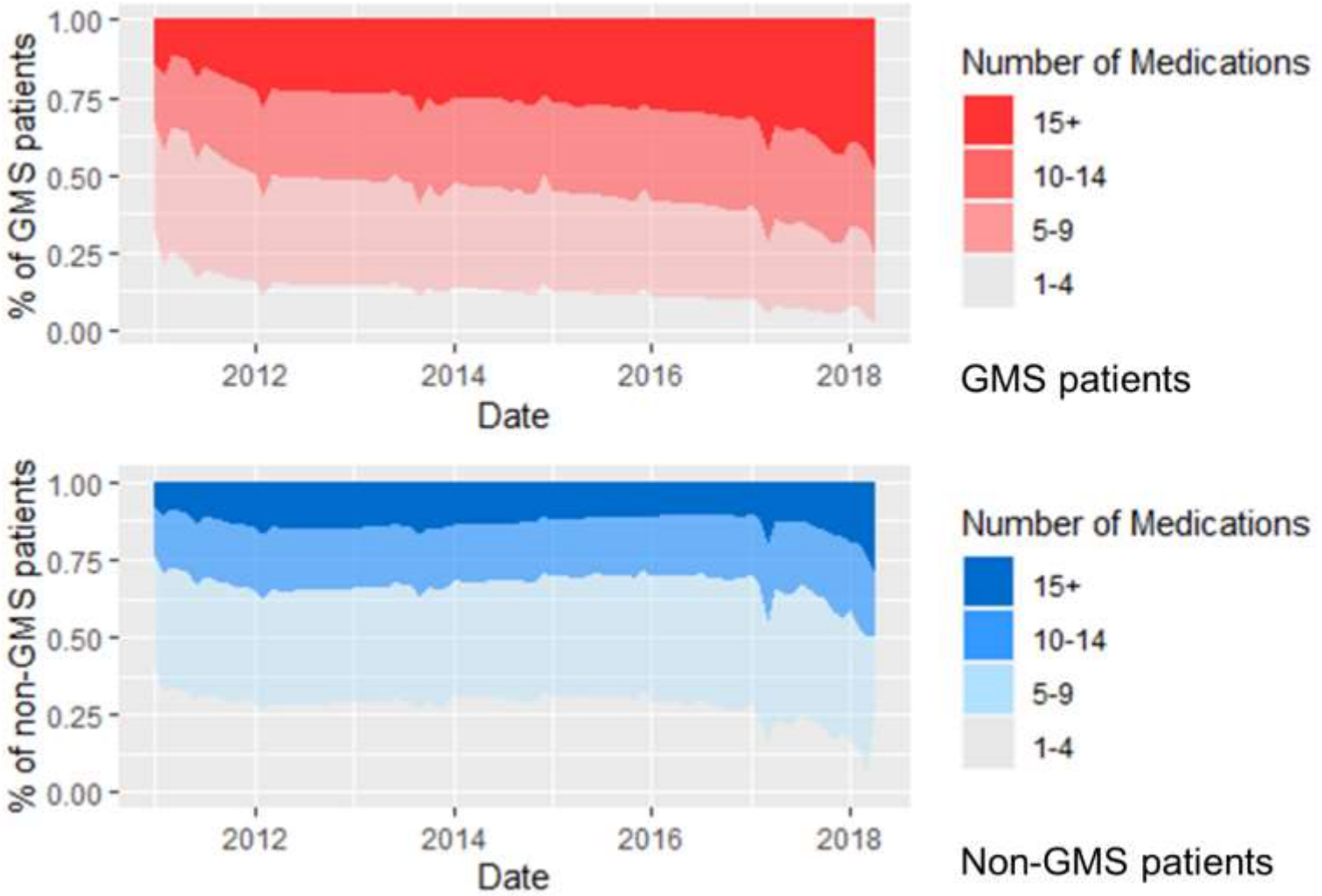
Prendergast C, Flood M, Murry LT, Clyne B, Fahey T, Moriarty F. Prescribing differences among older adults with differing health cover and socioeconomic status: a cohort study. medRxiv. 2023.

POLYPHARMACY

- 42,456 individuals
- 62% with GMS cover
- 56% female (slightly overrepresented in GMS cohort)
- 58.4% aged 65-79 years



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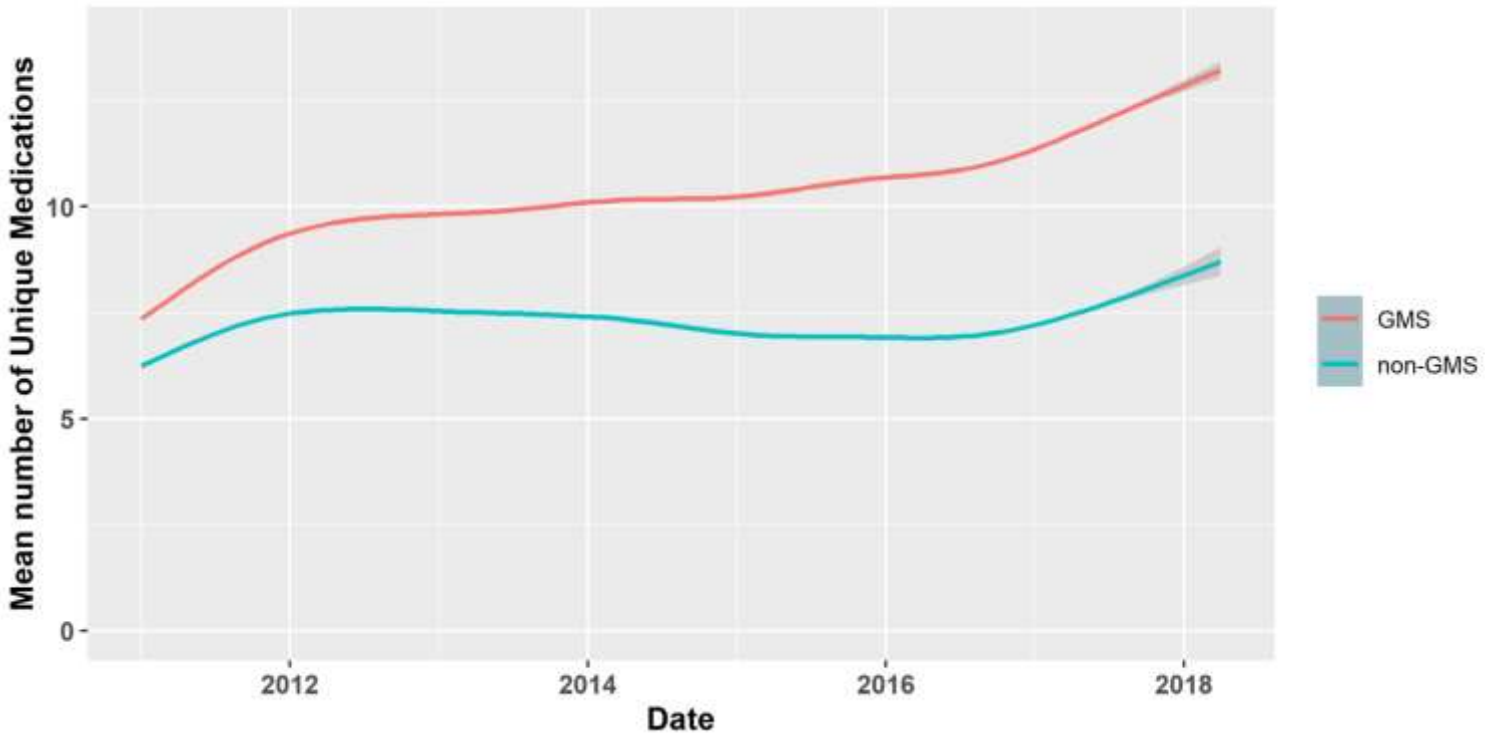
NUMBER OF MEDICINES



+0.67 medicines per year

(-0.13 per year less for non-GMS)

+0.54 medicines per year

(-0.10 per year less for non-GMS)

+0.48 per hospitalisation

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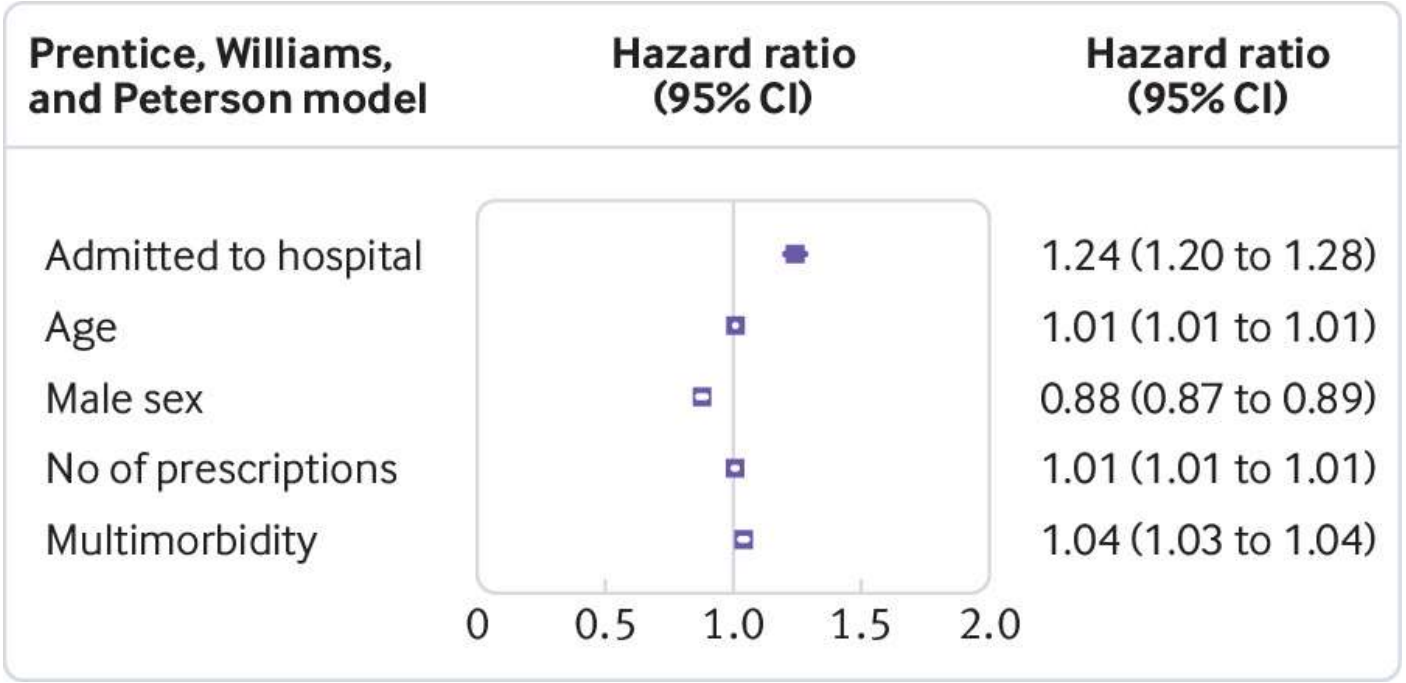
POTENTIALLY INAPPROPRIATE PRESCRIBING

- Applied STOPP criteria version 2
- Prevalence of potentially inappropriate prescribing ranged from 45.3% (2012) to 51.0% (2015)



Pérez T, et al. Prevalence of potentially inappropriate prescribing in older people in primary care and its association with hospital admission: longitudinal study. BMJ. 2018; 363:k4524.

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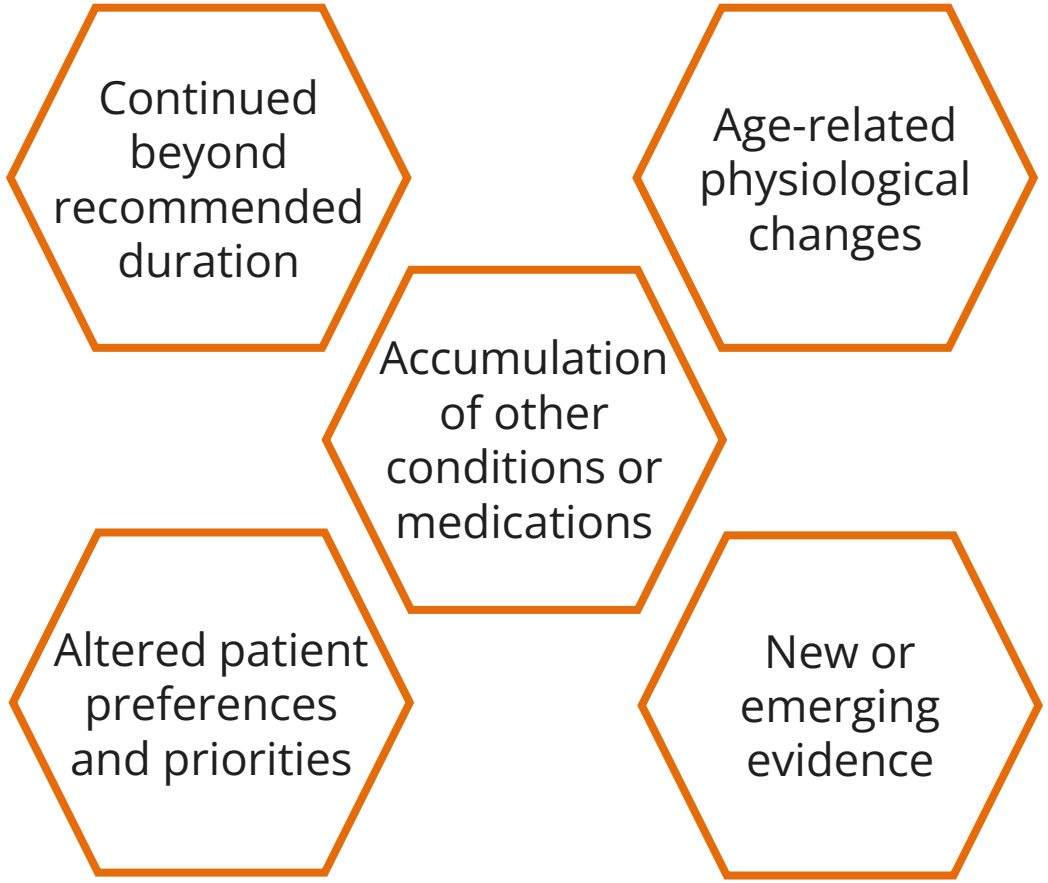
MEDICATION ISSUES

Over-prescribing
Unnecessary medications

Under-prescribing
Necessary medications omitted

Mis-prescribing
Necessary medications but with unfavourable risk-benefit

DRIVERS



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ASPIRIN

Preventive Medicine 147 (2021) 106504

Contents lists available at ScienceDirect

Preventive Medicine

journal homepage: www.elsevier.com/locate/ypmed

Aspirin prescribing for cardiovascular disease in middle-aged and older adults in Ireland: Findings from The Irish Longitudinal Study on Ageing

Frank Moriarty[a,b,c,*], Alan Barry[a], Rose Anne Kenny[c], Tom Fahey[a]

[a] HRB Centre for Primary Care Research, Department of General Practice, Royal College of Surgeons in Ireland, Ireland
[b] School of Pharmacy and Biomolecular Sciences, Royal College of Surgeons in Ireland, Ireland
[c] The Irish Longitudinal Study on Ageing, Trinity College Dublin, Ireland

TILDA: Study Design

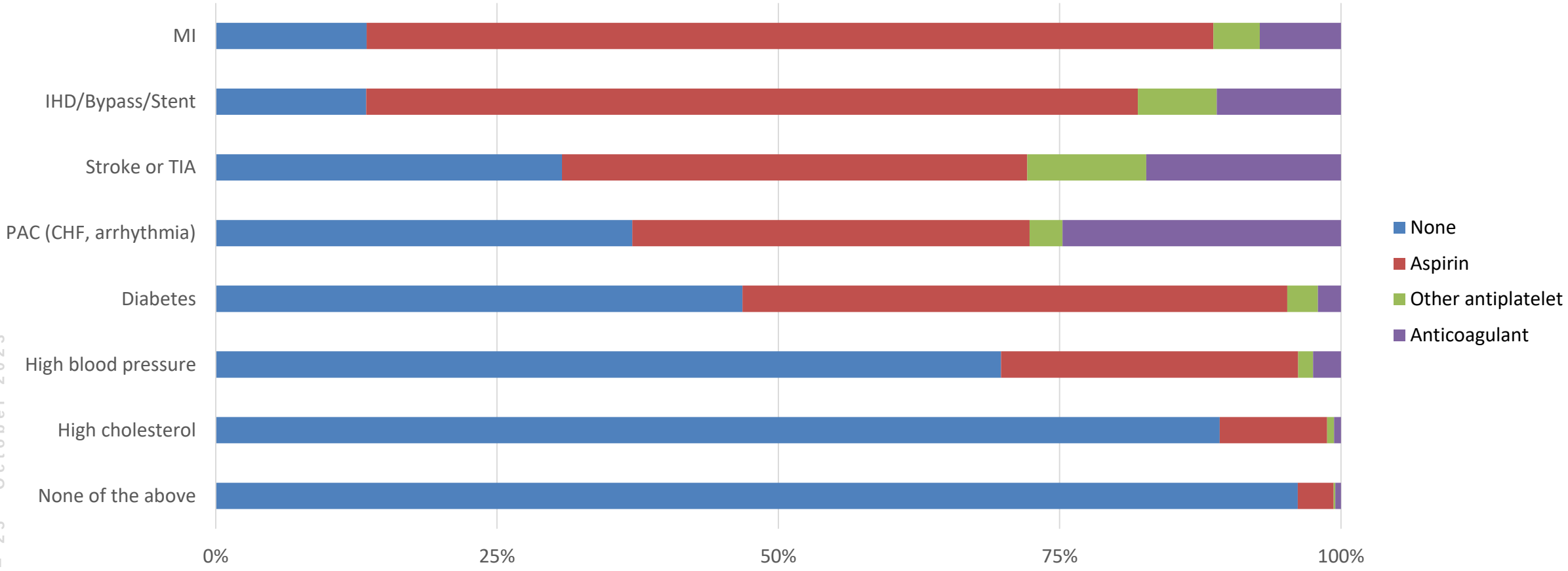
tilda
Staidéar Fadaimseartha na hÉireann um Dhul in Aois
The Irish Longitudinal Study on Ageing

The Irish Longitudinal Study on Ageing (TILDA)

Population representative prospective cohort study of the community dwelling older population aged 50 years or over

Sample:	*Sampling from Geo-directory of households in ROI with residents 50+ years*
Response rate:	62%
Baseline Sample size:	8,175.
Excluded:	< 50 years, nursing home or institutional care
Data: Collected	health, economic and social circumstances
Data collection:	every 2 years health assessment, alternate waves, every 4 years

Aspirin use by cardiovascular morbidity



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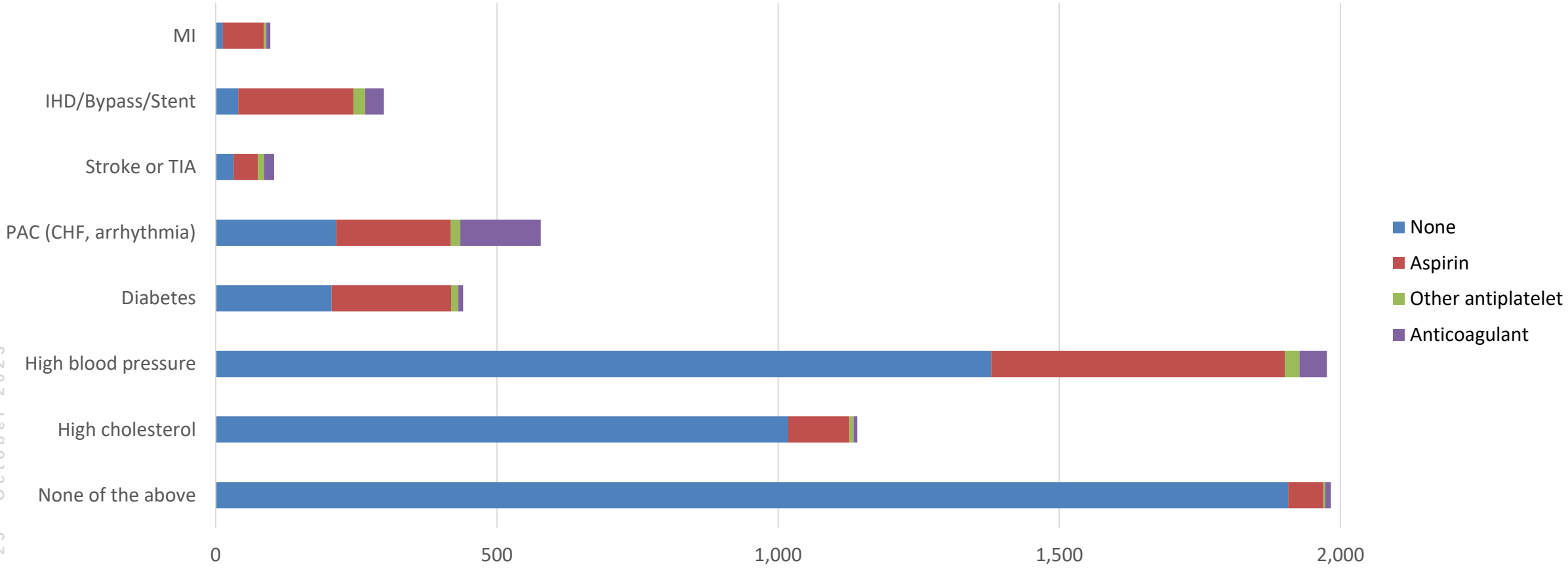
Aspirin use by cardiovascular morbidity



77.6% of aspirin users had no previous CVD → 201,000

17% with previous CVD were not prescribed aspirin or another antithrombotic → 16,000

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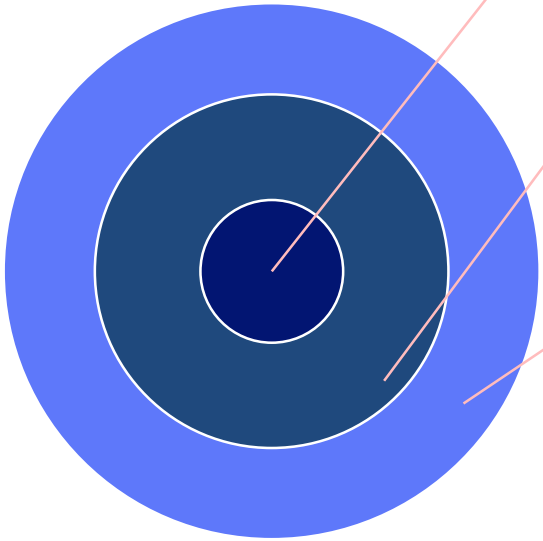
MEDICATION ISSUES



Can we prevent inappropriate prescribing arising?

Or increase chances of review and deprescribing?

Or if not, implement extra interventions to address

Previous research suggests reluctance to stop medications where:

- initiated by another prescriber,
- original intention unknown, or
- indication unclear

Empirically linked to long-term use of PPIs

- True of other medications with potential for inappropriate duration of use?

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BENZODIAZEPINES

Contents lists available at ScienceDirect

Research in Social and Administrative Pharmacy

journal homepage: www.elsevier.com/locate/rsap

Hospital initiation of benzodiazepines and Z-drugs in older adults and discontinuation in primary care

Seán Coll [a,b], Mary E. Walsh [a], Tom Fahey [a], Frank Moriarty [a,b,*]

Retrospective cohort study	Secondary analysis of anonymised data from 44 GP practices (2011-2016)
Initiation of benzodiazepine, Z-drug	Rx to patient with no Rx in previous 12 months
Continuation in primary care	Rx within 90 days of discharge
Time to discontinuation	BZRA-free period of ≥135 days after latest Rx
Covariates	Presence of instructions about BZRA in hospital discharge summary, age, gender, LOS, health cover, number of medicines, type of BZRA.
Regression analysis	Multivariate Poisson and Cox regression models.

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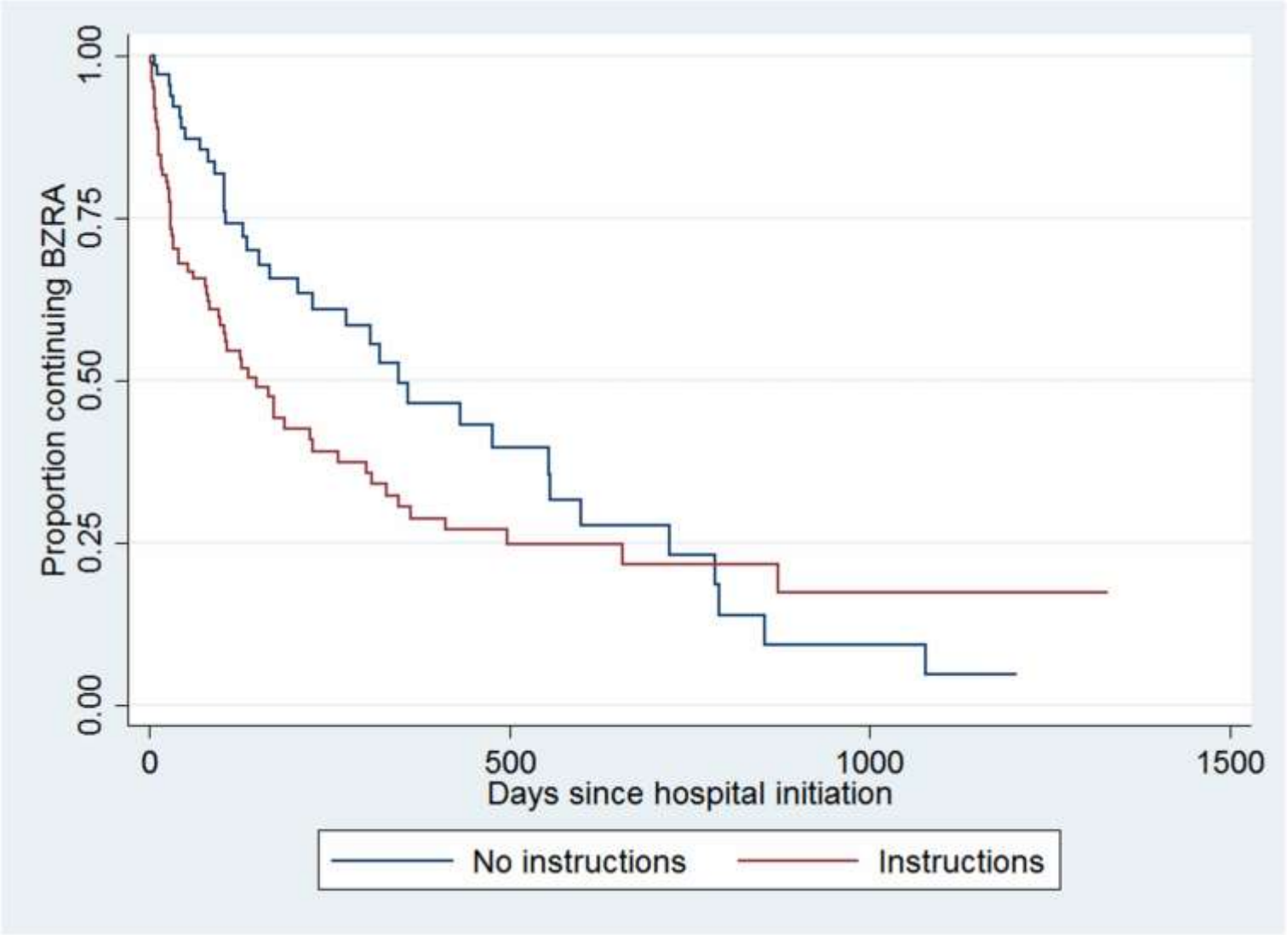
Time to discontinuation

- Of 171 hospital-initiated BZRA continued in primary care, for 102 (59.6%) the BZRA was discontinued during follow-up
- Presence of instructions had a discontinuation hazard ratio of 1.63 (95% CI: 1.08 – 2.45)



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OPIOIDS

Daunt A, Mc Mahon E, Mattsson M, Fahey T, Walsh ME, Moriarty F. Hospital initiation of opioids and long-term prescribing among older adults in primary care - a cohort study. *In preparation*

Initiation

Rx to patient with no Rx in previous 12 months

Continuation in primary care

Rx within 90 days of discharge

Time to discontinuation

Opioid-free period of ≥135 days after latest Rx

Covariates

Initial agent, duration, dosage, patient characteristics

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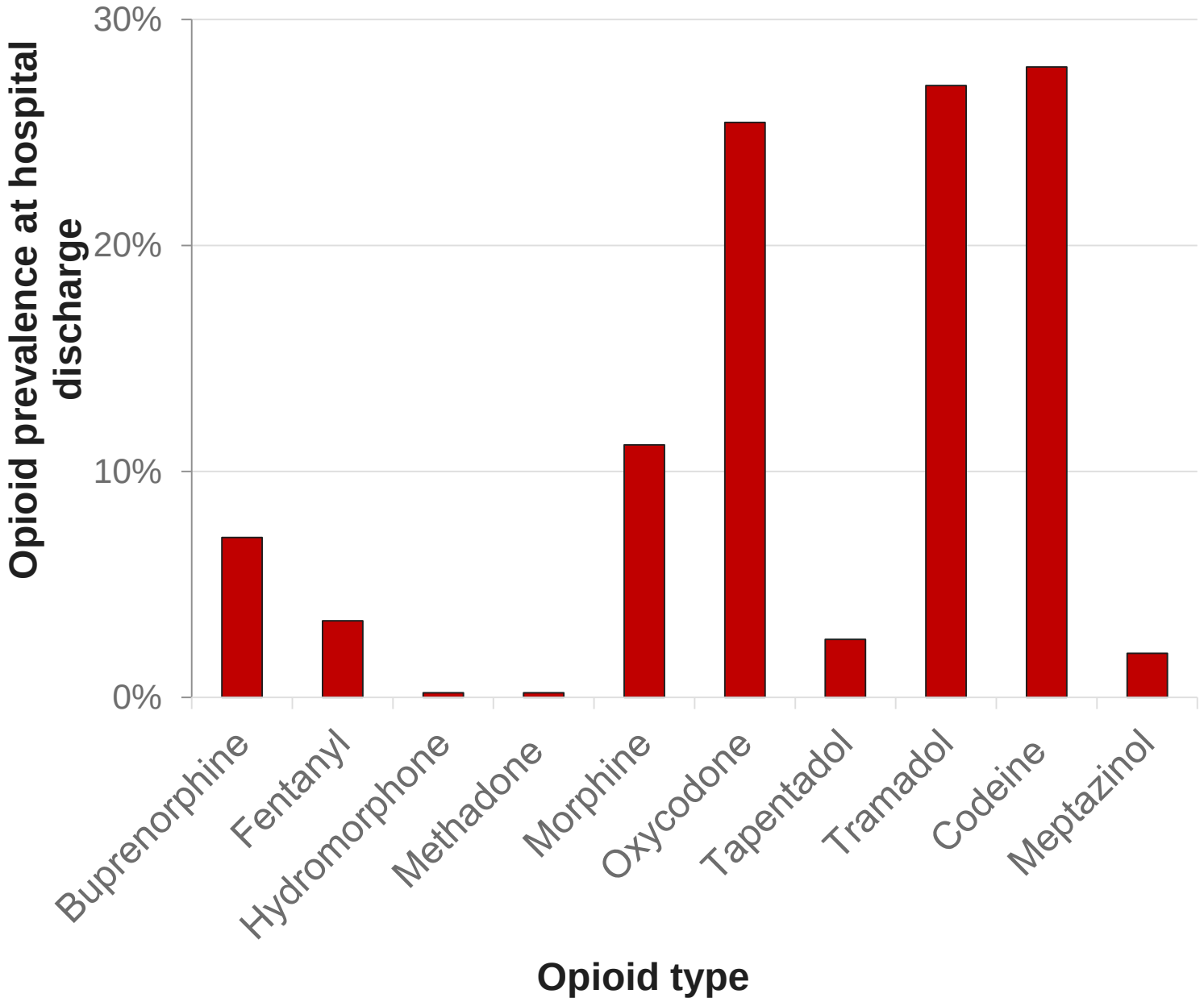
Opioid initiations

- 1,069 patients initiated an opioid at discharge, 975 with no cancer-related ICD-10 code.
- 14.5% prescribed >1



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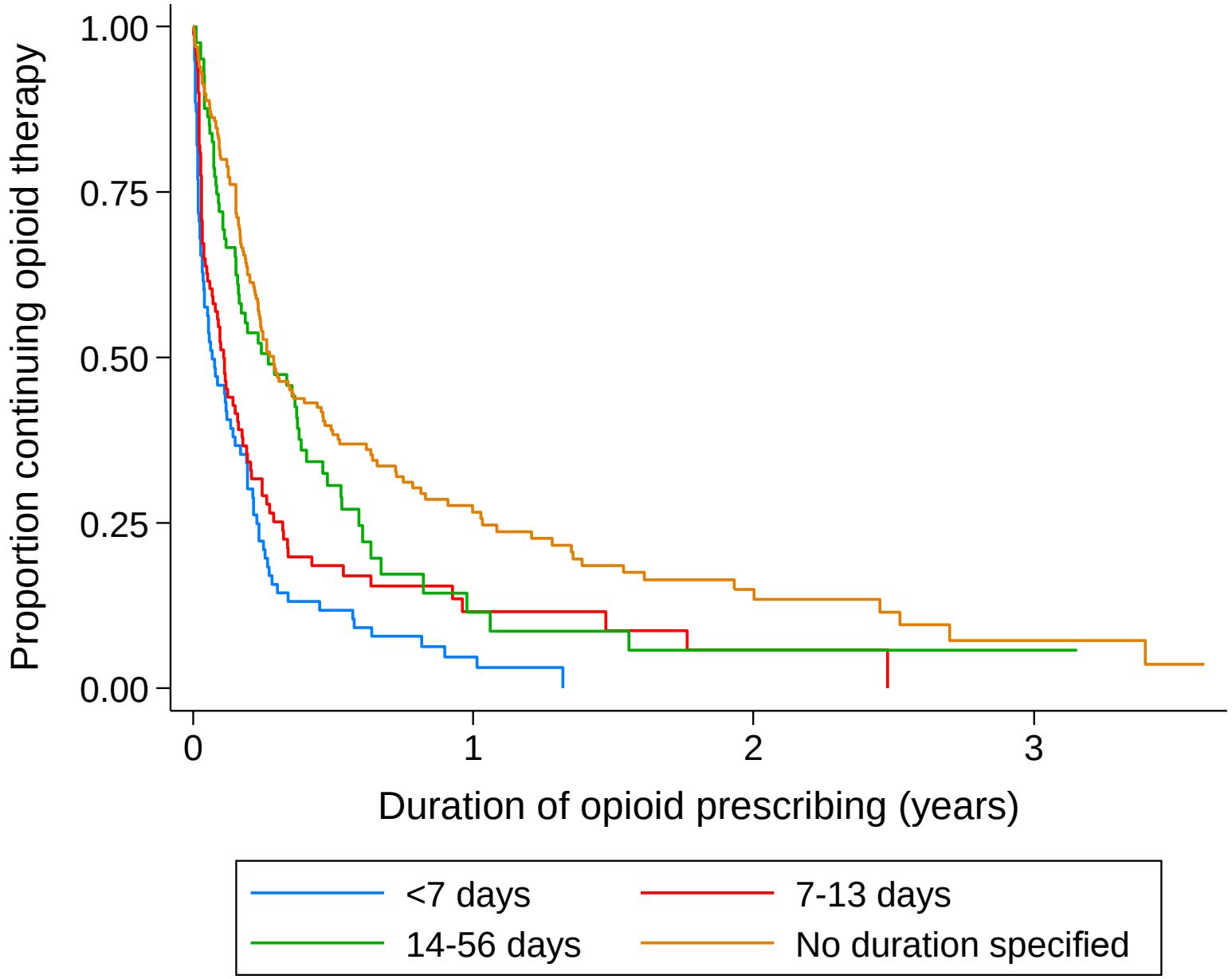
Time to discontinuation

Specified duration of initial hospital discharge prescription was associated with prolonged opioid prescribing in primary care.



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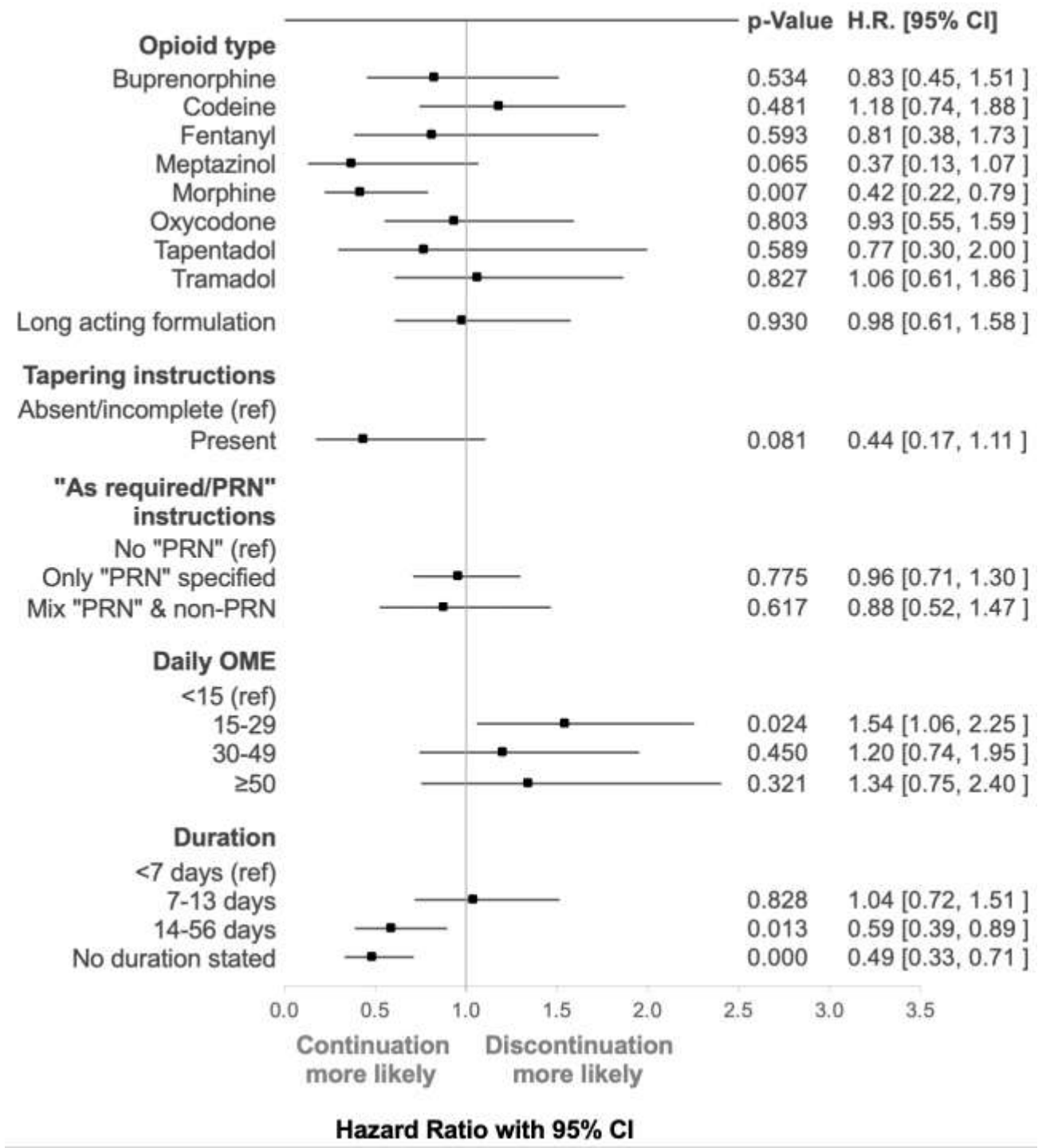
Time to discontinuation

- Initial prescription of morphine was most significantly associated with continuation (i.e. lower chance of discontinuation)
- Longer or no duration being stated was associated with higher likelihood of continuation



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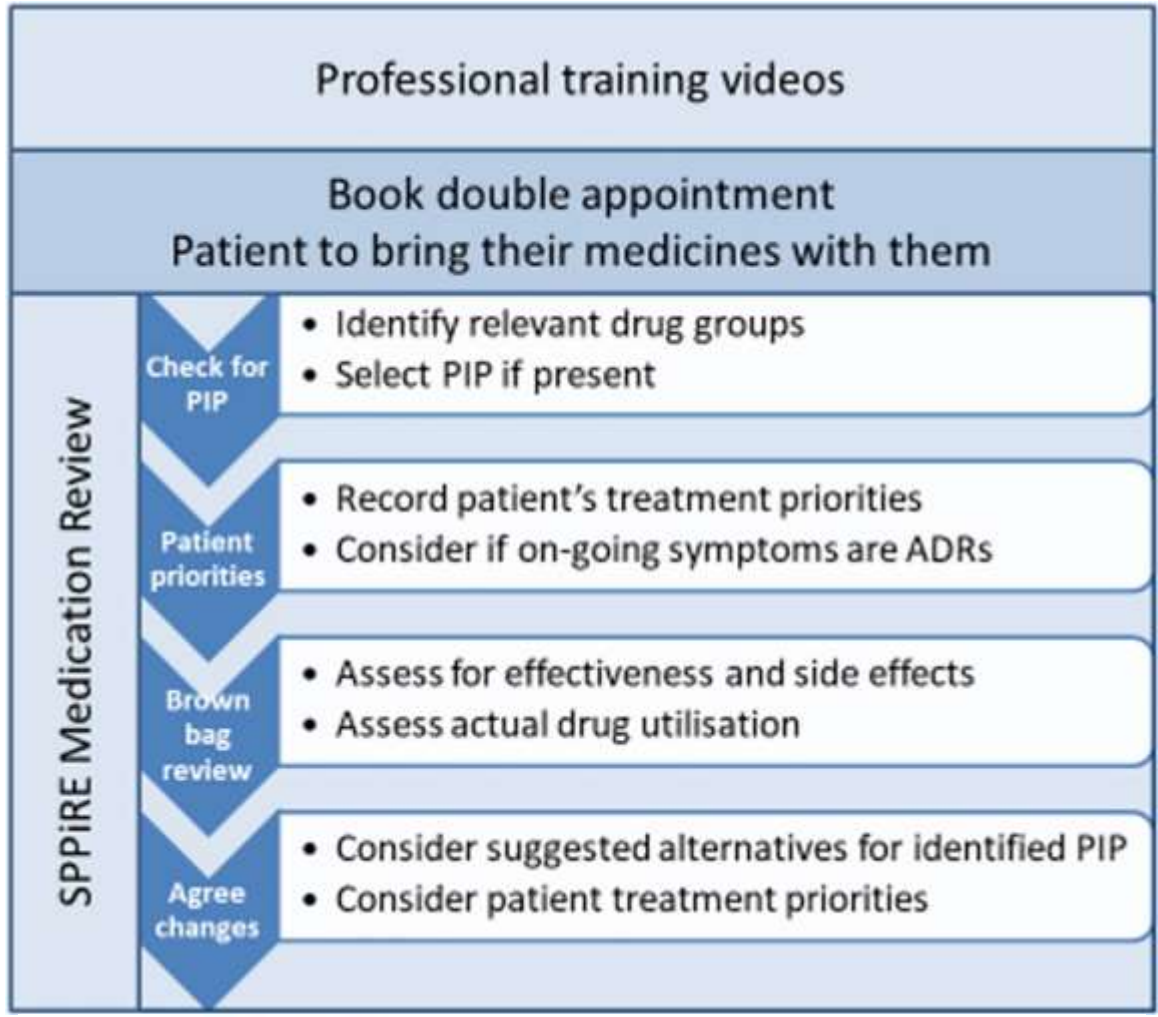
SPPIRE TRIAL

Cluster randomised controlled design

Eligible practices recruited patients:

- Aged ≥ 65 years
- Prescribed ≥ 15 repeat medicines



Project lead: Dr Caroline McCarthy
Principal investigator: Prof. Susan M Smith
SPPiRE Study Team: Frank Moriarty, Emma Wallace, Barbara Clyne, Michelle Flood, Fiona Boland, Tom Fahey, Derek Corrigan, Bridget Kiely, Aisling Croke, James Larkin, Oscar James, Clare Lambert, and Brenda Quigley.
Funding: This research is funded by the HRB Primary Care Clinical Trial's Network, Ireland (https://primarycaretrials.ie/)

PLOS MEDICINE

RESEARCH ARTICLE

GP-delivered medication review of polypharmacy, deprescribing, and patient priorities in older people with multimorbidity in Irish primary care (SPPiRE Study): A cluster randomised controlled trial

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PRIMARY RESULTS

Outcome measure	Intervention (N = 208)	Control (N = 196)	Adjusted difference (95% CI); p-value
Primary outcome measures			
Number of medicines[¥], Mean (SD)	16.02 (3.93)	17.55 (4.10)	0.95[‡] (0.899 to 0.999); p = 0.045
Patients with at least 1 PIP[$], N (%)	181 (87.44)	179 (91.79)	0.39[¶] (0.140 to 1.064); p = 0.066
Secondary outcome measures			
Prescribing-related measures	**N = 208**	**N = 196**	
Number of medicines stopped, Mean (SD)	3.97 (3.15)	2.92 (3.17)	1.48[‡] (1.171 to 1.871); p = 0.001
Number of medicines started, Mean (SD)	3.02 (3.03)	2.67 (2.91)	1.12[‡] (0.826 to 1.513); p = 0.470
Proportion prescribed ≥15 medicines, N (%)	132 (63.46)	161 (82.14)	0.37[¶] (0.193 to 0.719); p = 0.003
Number of PIP, Mean (SD)	2.16 (1.44)	2.35 (1.43)	0.92[‡] (0.813 to 1.057); p = 0.256
Proportion with any reduction in PIP, N (%)	73 (35.10)	58 (29.51)	1.42[¶] (0.892 to 2.255); p = 0.140
Proportion with at least 1 high-risk PIP, N (%)	117 (57.07)	119 (62.30)	0.93[¶] (0.528 to 1.642); p = 0.806

- Out of >800 medicines stopped in the intervention group, 15 ADWEs were reported (1.8%), one of which was classified as serious.
- No difference in healthcare utilisation
- No differences identified in PROMs (EQ-5D, MTBQ, rPATD)

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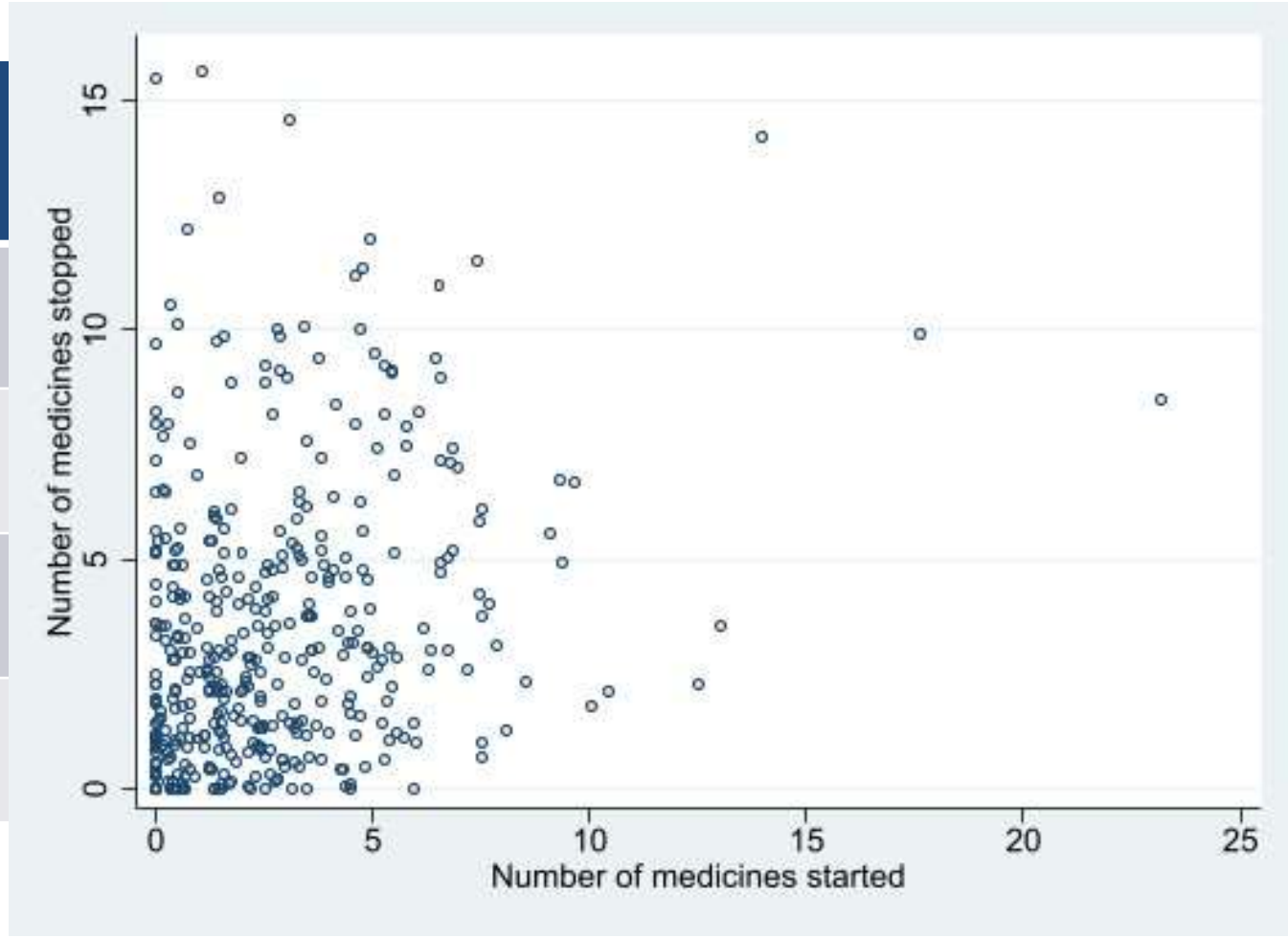
Medication changes	Intervention	Control
Discontinuations, n Mean (SD)	809 3.9 (2.9)	573 2.9 (3.1)
Initiations, n Mean (SD)	591 2.8 (2.7)	498 2.5 (2.6)
Switches, n Mean (SD)	72 0.3 (0.6)	54 0.3 (06)
All changes, n Mean (SD)	1472 7.1 (4.7)	1125 5.7 (4.6)



McCarthy C, Flood M, Clyne B, Smith SM, Wallace E, Boland F, Moriarty F. Medication changes and potentially inappropriate prescribing in older patients with significant polypharmacy. Int J Clin Pharm. 2023 ;45(1):191-200.

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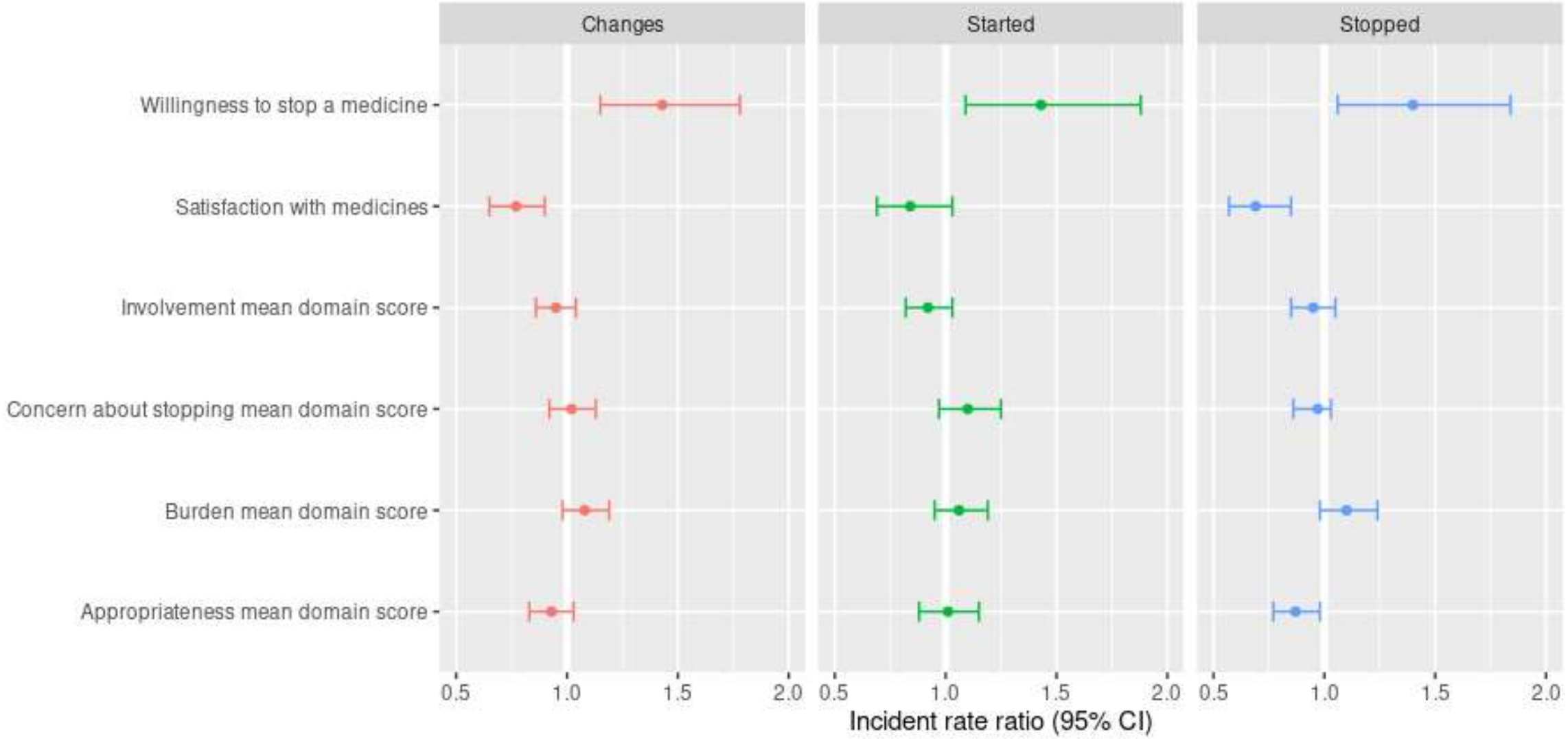

McCarthy C, Flood M, Clyne B, Smith SM, Boland F, Wallace E, Moriarty F. Association between patient attitudes towards deprescribing and subsequent prescription changes. Basic Clin Pharmacol Toxicol. 2023. doi: 10.1111/bcpt.13859.

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TOOLS TO SUPPORT

- STOPP/START criteria (version 3 published this year)
- Scottish Government Polypharmacy Guidance (3rd edition)
- Deprescribing-specific guidance

Domain	Steps	
Aims	1.	What matters to the patient?
Need	2.	Identify essential drug therapy
	3.	Does the patient take unnecessary drug therapy?
Effectiveness	4.	Are therapeutic objectives being achieved?
Safety	5.	Does the patient have ADR/Side Effects or is at risk of ADRs/Side Effects? Does the patient know what to do if they're ill?
Cost-effectiveness	6.	Is drug therapy cost-effective?
Patient centeredness	7.	Is the patient willing and able to take drug therapy as intended?

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DEPRESCRIBING

Deprescribing is the planned and supervised process of dose reduction or stopping of medication that might be causing harm, or no longer be of benefit.

Deprescribing is part of good prescribing – backing off when doses are too high, or stopping medications that are no longer needed.

www.deprescribing.org

Systematic Review | Full Access

A systematic review of the emerging definition of 'deprescribing' with network analysis: implications for future research and clinical practice.

Emily Reeve, Danijela Gnjidic, Janet Long, Sarah Hilmer

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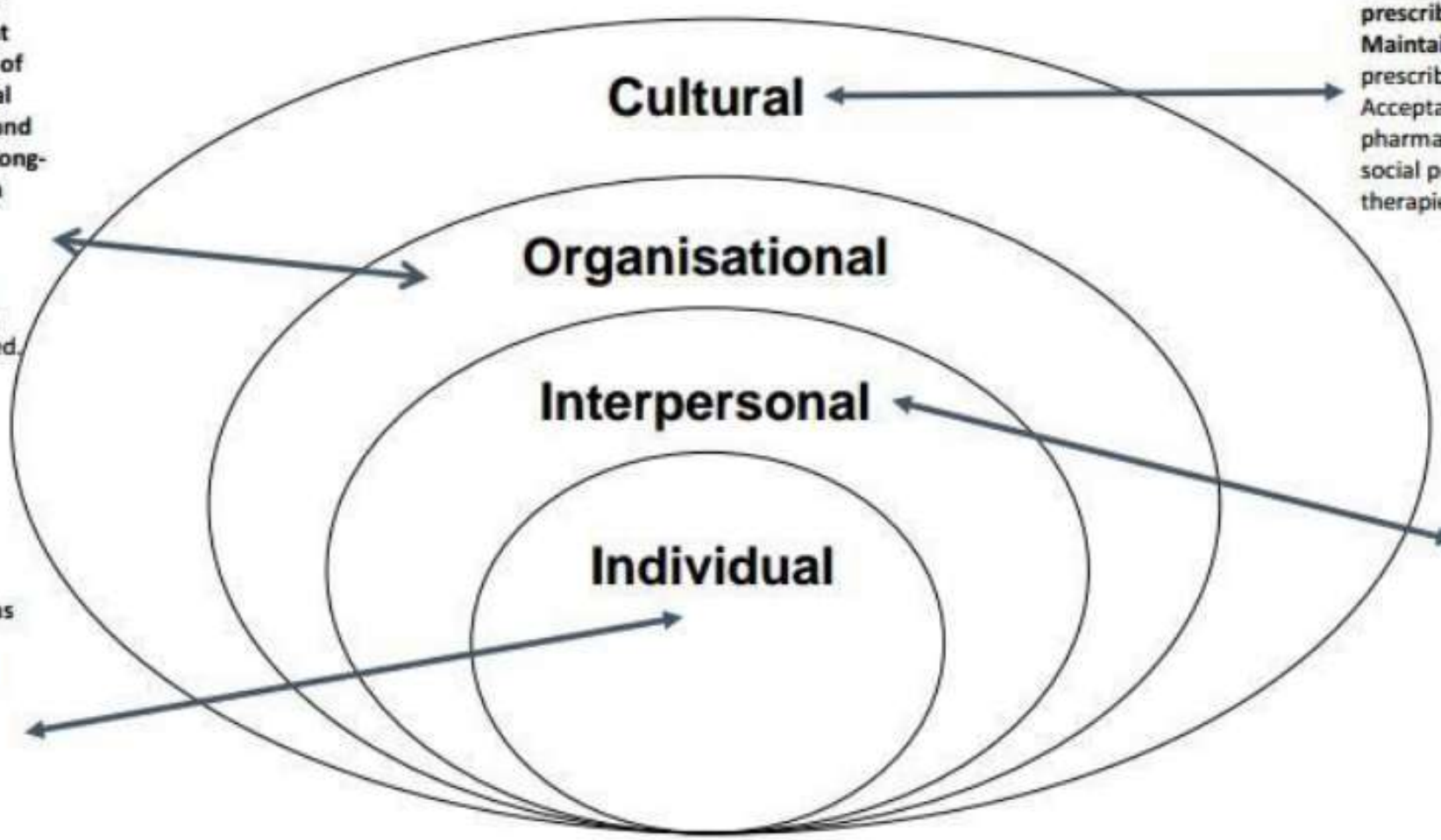

Single disease focused evidence-base and guidance. Evidence-base lacking for older patients. Insufficient tools and resources. Lack of shared IT between general practice, secondary care and community pharmacist. Long-term residential care with restrictive regimes and resource constraints. Improved multimorbidity evidence-based guidance, tools and resources needed.

Prescribing culture: diagnosis of, and prescribing for, new conditions. Maintaining the status quo. Prudent prescribing culture needed. Acceptability and availability of non-pharmacological alternatives such as social prescribing, and talking therapies advocated.

Patient uncertainties. *"Doctor knows best".* Impaired cognition / reliance on others for support. Prevailing attitudes and assumptions towards older patients. Improvements needed in patient and prescriber awareness, knowledge, understanding. Patient-centred care. Patient perspective. Tailored approaches for different patients.

Fragmented care. Prescriber uncertainties. Professional etiquette. Fears. Improvements needed in: communication, continuity of care, collaboration. Shared decision making. Multidisciplinary team working. GP/pharmacist/advanced nurse practitioner.

Doherty AJ, etal . Barriers and facilitators to deprescribing in primary care: a systematic review. BJGP Open. 2020 Aug 25;4(3):bjgpopen20X101096. doi: 10.3399/bjgpopen20X101096.

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SAFETY CONCERNS

- Adverse drug withdrawal events: “clinically significant set of symptoms or signs caused by the removal of a drug”
  - e.g. rebound acid secretion after stopping a PPI
  - Tapering to mitigate risk
- Return of the medical condition which the drug was being used to treat (indicating that the medication was having a benefit)
  - Monitoring important (if a symptomatic treatment, or marker available)

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HOW TO DEPRESCRIBE?

1. Ascertain all drugs the patient is currently taking and the reasons for each one
2. Consider overall risk of drug-induced harm in individual patients in determining the required intensity of deprescribing intervention
3. Assess each drug for its eligibility to be discontinued: • No valid indication • Part of a prescribing cascade • Actual/potential harm of a drug clearly outweighs any potential benefit • Disease and/or symptom control drug is ineffective or symptoms have completely resolved • Preventive drug is unlikely to confer any patient-important benefit over the patient's remaining lifespan • Drugs are imposing unacceptable treatment burden
4. Prioritise drugs for discontinuation
5. Implement and monitor drug discontinuation regiment

Scott IA, Hilmer SN, Reeve E, et al. Reducing Inappropriate Polypharmacy: The Process of Deprescribing. *JAMA Intern Med.* 2015;175(5):827–834. doi:10.1001/jamainternmed.2015.0324

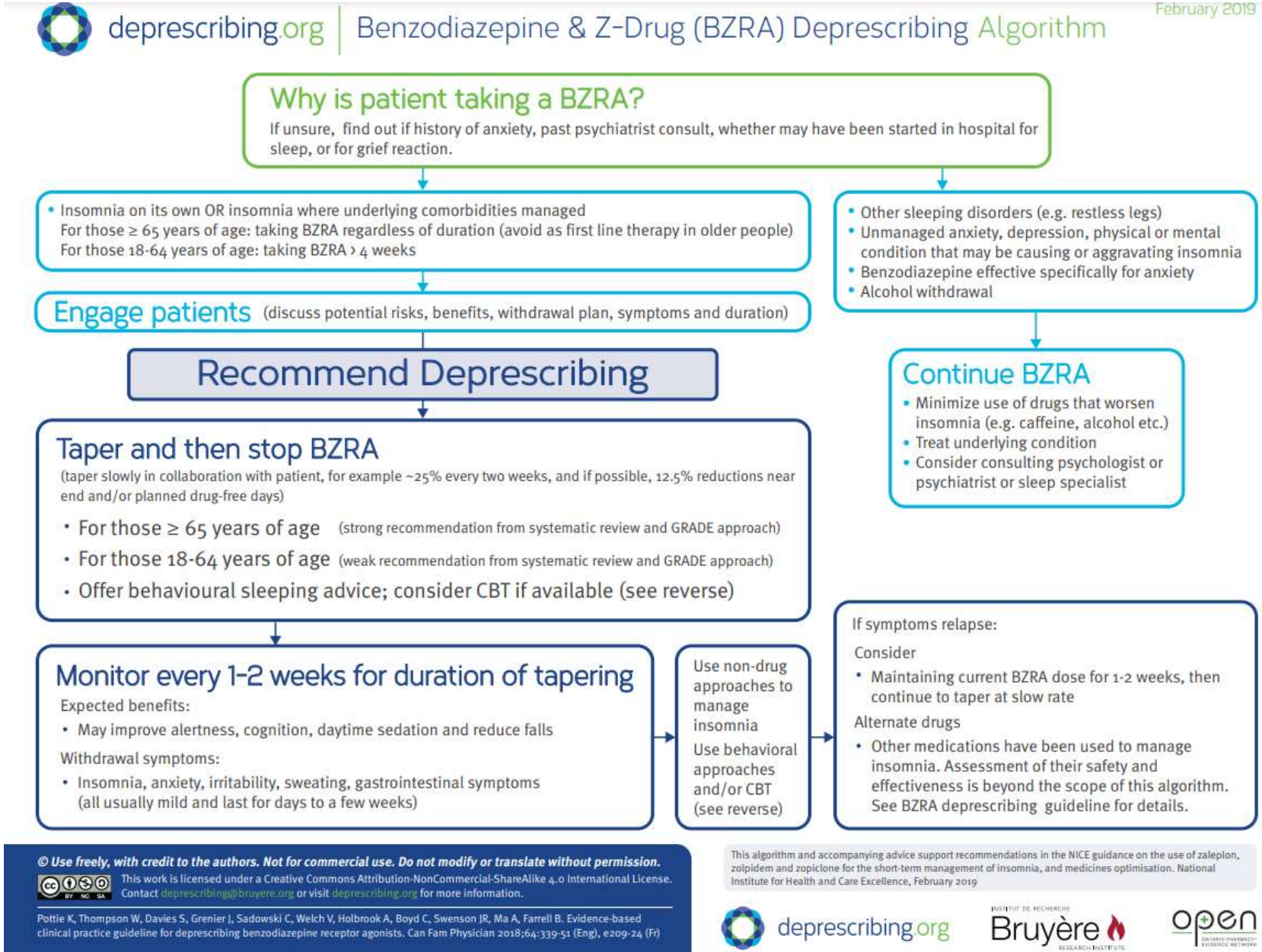
1. those with the greatest harm and least benefit;
2. those easiest to discontinue, ie, lowest likelihood of withdrawal reactions or disease rebound;
3. those that the patient is most willing to discontinue first (to gain buy-in to deprescribing other drugs)

Suggested approach is to rank drugs from high harm/low benefit to low harm/high benefit and discontinue the former in sequential order

DEPRESCRIBING GUIDELINES

- Guidelines (with algorithms) developed for specific drugs
- Cover need for medication, process of deprescribing, and monitoring
- Available for BZRAs, PPIs, antidiabetics, antipyschotics and cholinesterase inhibitors

www.deprescribing.org



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FUTURE WORK

Developing Innovative Analytical Methods for research ON Deprescribing (DIAMOND)

To develop and advance novel methods to research deprescribing by harnessing big data

To apply these methods to generate new evidence that improves our understanding of the benefits and harms of deprescribing

Postdoctoral researcher position

June 2024

Pharmacist PhD student (funded - stipend)

December 2023

CONCLUSIONS

Better data needed

Shift our understanding of medication use patterns and issues to target

Supportive resources are improving

Tools and evidence to inform decisions on stopping medications to address barriers

Need upstream/downstream interventions

Prevent and address the need for medicines optimisation

Reduce medication-related harm

Through additive effects of multiple interventions at various levels

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25 October 2023

Thank you

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Prof. Susan Smith (PI – SPPiRE study)
Prof. Rose Anne Kenny (PI – TILDA)

Funders: Health Research Board

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