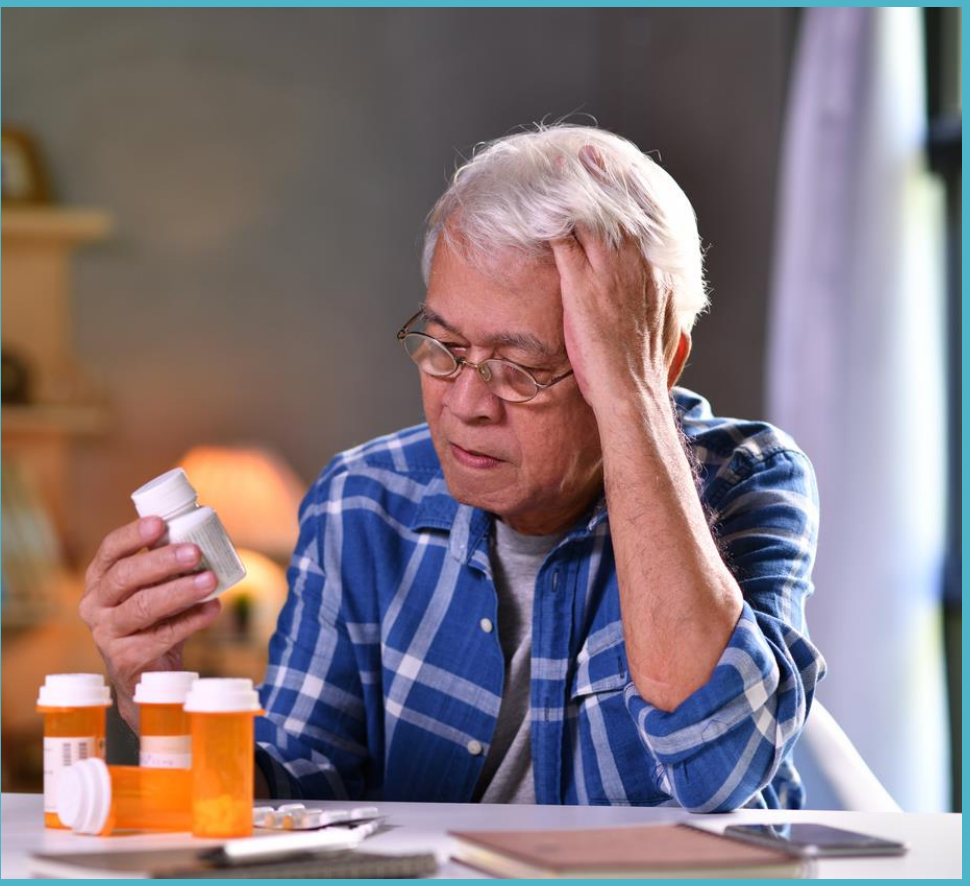

Deprescribing Interventions: Learnings from an Overview of Systematic Reviews

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Agenda

Upon completion of this presentation, you should be able to:

✓ Understand the approach and rationale to conducting an overview of systematic reviews.

✓ Discuss study methods and results as it relates to vulnerable subgroups and downstream outcomes.

✓ Describe opportunities to enhance future deprescribing research

Background

- Deprescribing has been described as a priority for older patients and to address significant polypharmacy and quality of prescribing.
- Deprescribing is the process of discontinuing, or reducing the dose of, medications that are no longer needed, or where risks outweigh benefits or are inconsistent with goals of care
- Despite several studies in this area, rigorous evidence to guide deprescribing is limited, and future priorities for deprescribing research and practice remain unclear.

Background

- Challenges contributing to the heterogeneity of evidence include:
  - lack of a consistent definition of deprescribing
  - challenges with outcome measurement
  - poor reporting of studies
  - variation in study design
- Effectiveness of deprescribing interventions might differ according to patient characteristics, thus information according to subgroups is needed.

Objectives

- ✓ Examine whether deprescribing interventions lead to a difference in outcomes amongst older adults.
- ✓ Synthesize results according to the focus of the intervention (i.e., deprescribing specific medication targets, or general deprescribing such as comprehensive medication reviews).
- ✓ Examine the effectiveness of deprescribing interventions according to patient- subgroup characteristics (i.e., advanced age (aged 80+), dementia, frailty, and multimorbidity), and by intervention type and setting.

Importance: With limited health care resources, which deprescribing efforts will provide the most benefit?

Features of an Overview

- Overview of systematic reviews (i.e., overviews) have gained widespread acceptance to compile evidence from multiple systematic reviews of interventions into one accessible and usable document.
- Also referred to as umbrella reviews, meta-reviews, reviews of reviews, synthesis of systematic reviews.
- Overviews have evolved to address a growing need to filter the information overload, improve access to targeted information and inform healthcare decision-making
- Important for summarizing existing research or highlighting the absence of evidence

Hunt et al. Systematic Reviews 2018; 7:39

Challenges of Conducting an Overview

- Overlap between reviews
- Definition for systematic review
- Assessment of methodological quality of reviews
- Quality of reporting withing reviews
- Summarizing key findings in brief accessible format

Pollock et al. Syst Rev. 2017;6(1):145; ; Luny et al. BMC Medical Research Methodology 2021;21:140

Methods

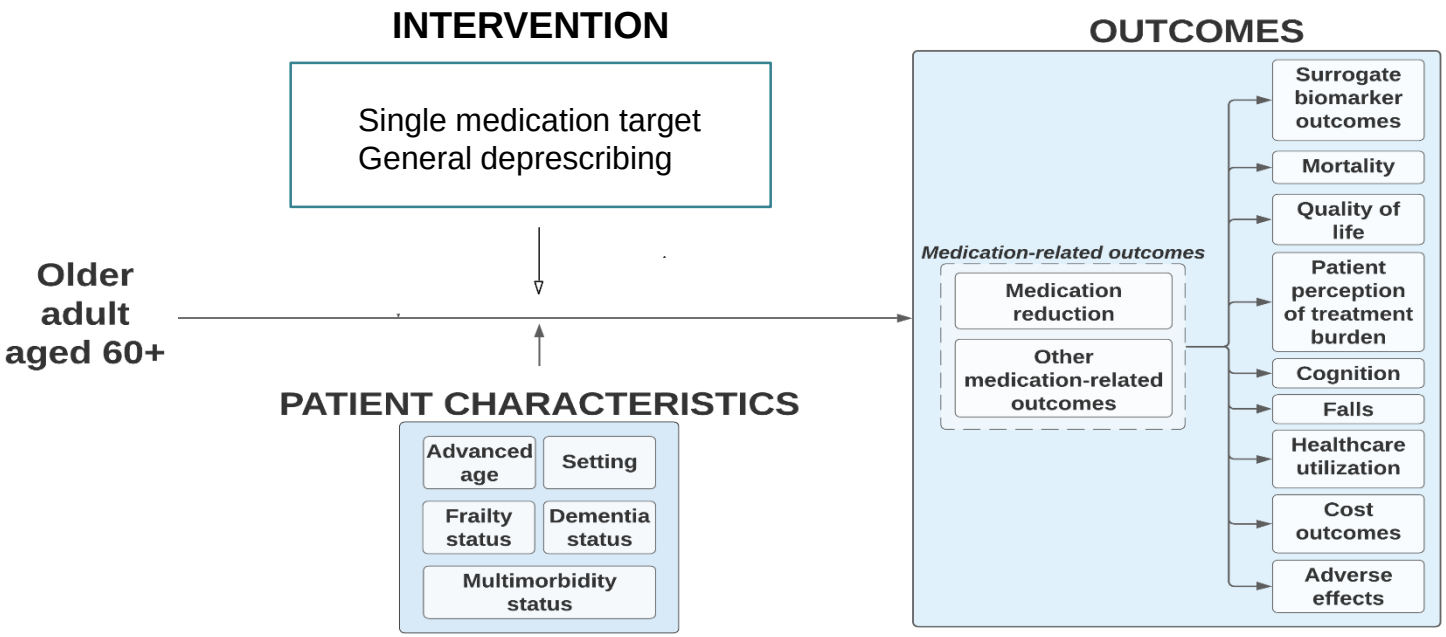
- Developed and registered protocol with PROSPERO
- Population, Intervention, Comparators, Outcomes, Study Design (PICOS)

P	Mean age of 60 years and older
I	Interventions with a deprescribing focus: ○ Specific medication targets (e.g., single medication, medication class or therapeutic category). ○ General deprescribing (e.g., comprehensive medication reviews, reduce polypharmacy or PIMs). Interventions of investigator-initiated medication withdrawal.
C	Reviews including comparisons with ‘usual care’ and/or medication continuation.
S	Randomized trials, non-randomized trials, controlled before-after studies, interrupted time series studies and repeated measures studies.

Outcomes

Outcome Themes	Specific Outcomes
Medication reduction	• Number of medications prescribed, pre- and post-intervention • Dose reduction • Discontinuation
Other medication-related outcomes	• Potentially inappropriate medications (e.g., STOPP criteria) • Medication appropriateness • Adherence
Other outcomes	Surrogate biomarkers Mortality Quality of life Healthcare use Patient treatment burden Falls Cognition ADEs Cost

Conceptual Model



Methods

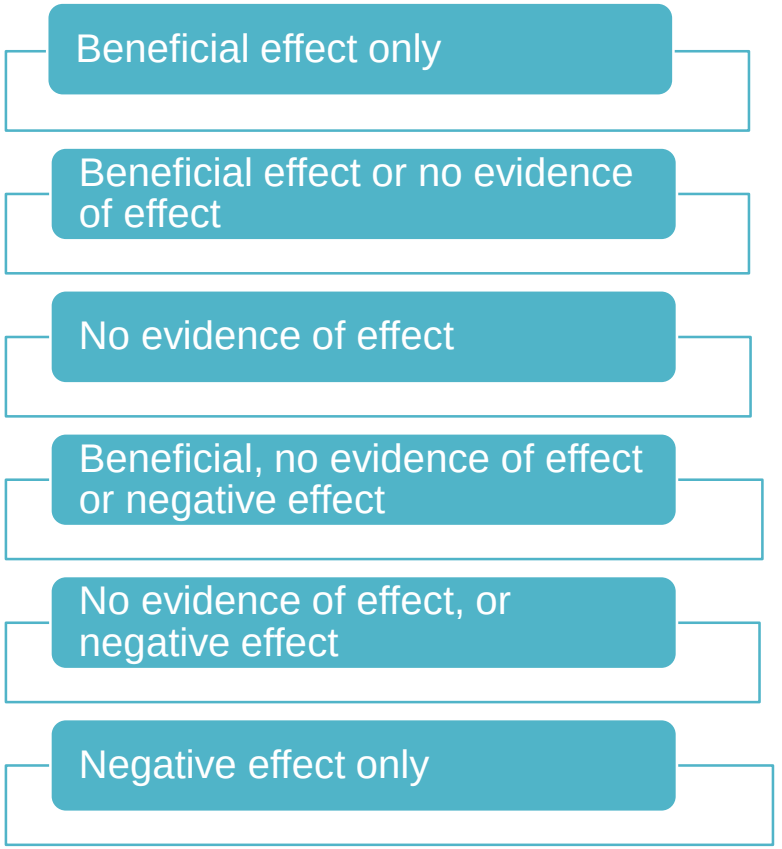
- Developed search strategy with research librarian
- Searched 11 databases from January 2005 to October 2020
- Titles/abstracts and full-text articles screened by 3 reviewers
- Data extracted in duplicate
- Assessed quality of reviews using Multiple Systematic Reviews (AMSTAR 2)
- Addressed overlap by presenting matrix of primary studies and reviews and calculating the corrected coverage area (CCA) index

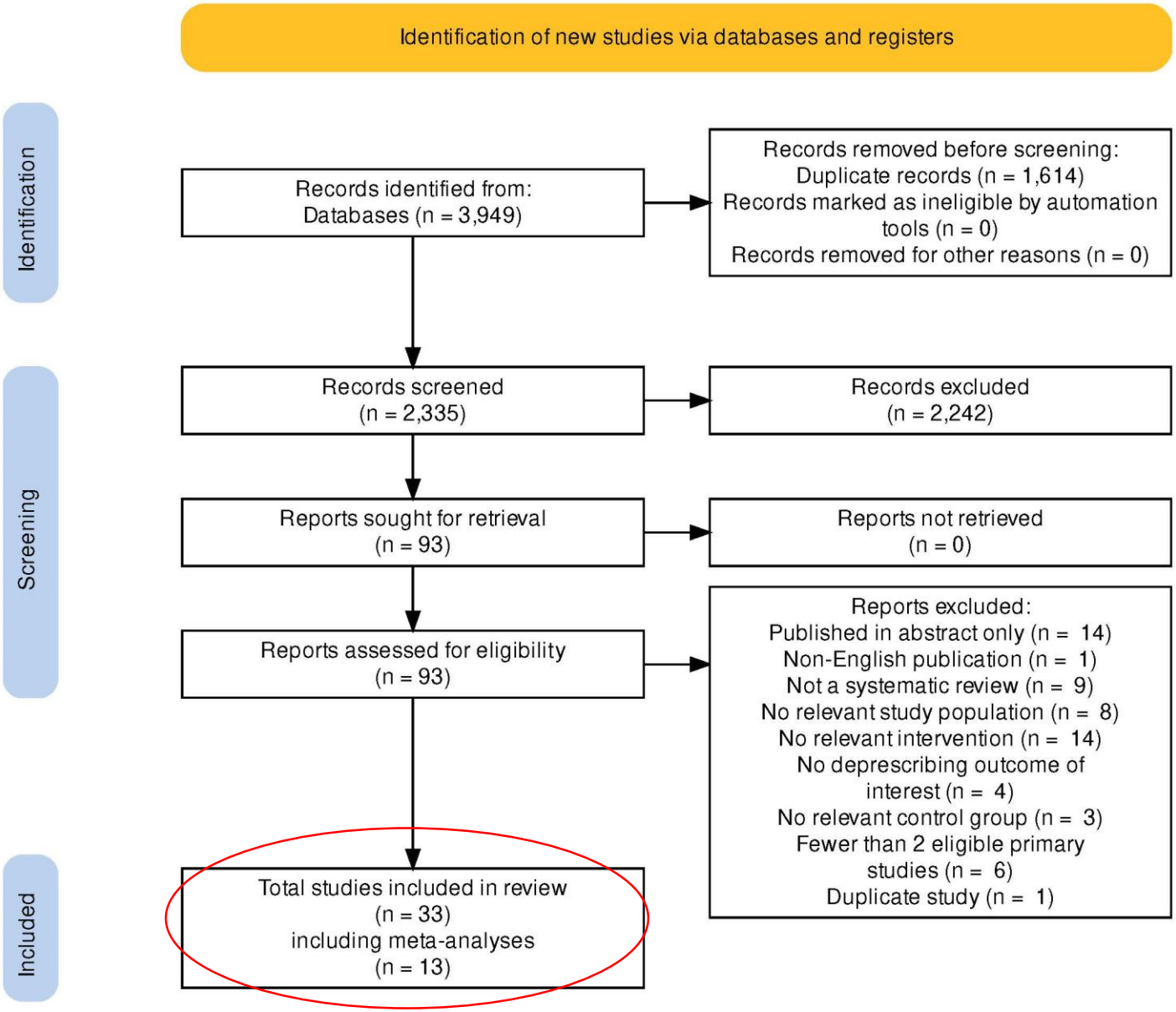
Methods

STEP 1: REVIEW SUMMARY

- Characteristics of reviews
- Author conclusions
- Summary of meta-analyses

STEP 2: NARRATIVE SYNTHESIS




Identification of new studies via databases and registers
Identification
Screening
Included
Records identified from:
Databases (n = 3,949)
Records removed before screening:
Duplicate records (n = 1,614)
Records marked as ineligible by automation tools (n = 0)
Records removed for other reasons (n = 0)
Records screened
(n = 2,335)
Records excluded
(n = 2,242)
Reports sought for retrieval
(n = 93)
Reports not retrieved
(n = 0)
Reports assessed for eligibility
(n = 93)
Reports excluded:
Published in abstract only (n = 14)
Non-English publication (n = 1)
Not a systematic review (n = 9)
No relevant study population (n = 8)
No relevant intervention (n = 14)
No deprescribing outcome of interest (n = 4)
No relevant control group (n = 3)
Fewer than 2 eligible primary studies (n = 6)
Duplicate study (n = 1)
Total studies included in review
(n = 33)
including meta-analyses
(n = 13)

Results: Step 1

Summary of Reviews

Intervention Focus

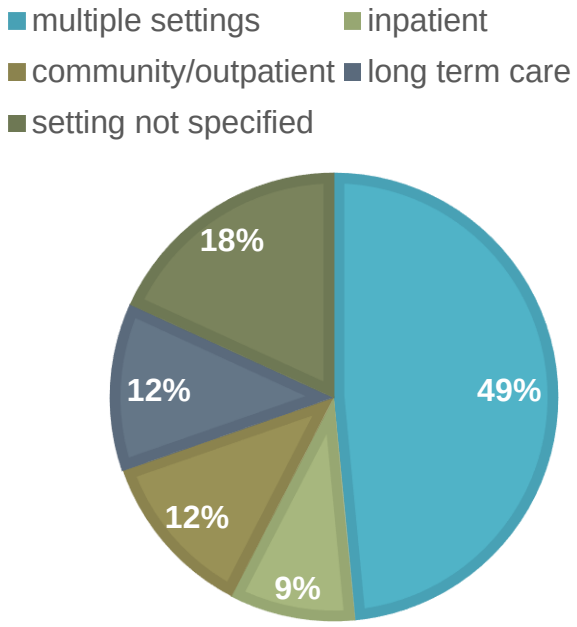
13 reviews	Focused on specific medication targets • antihyperglycemics, anticholinergics, antihypertensives, psychotropics, proton-pump inhibitors
19 reviews	Focused on general deprescribing • reducing PIMs or polypharmacy
1 review	Included primary studies that focused on specific medication targets and general deprescribing

Assessment of review quality

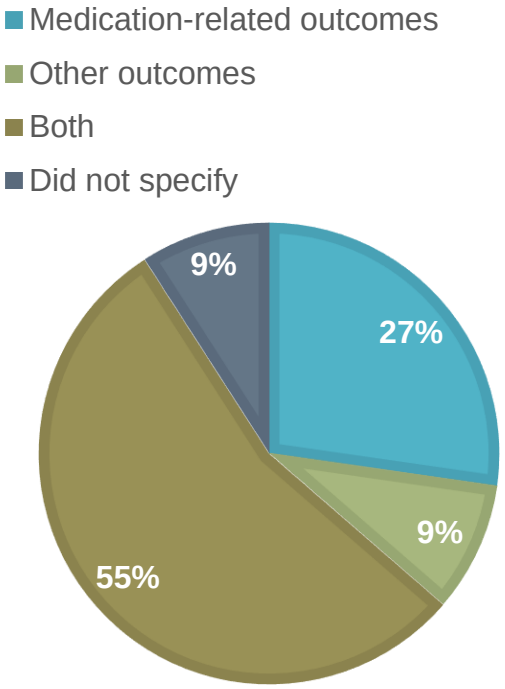
- 29 rated as “critically low”; 4 as “low”

Summary of Review Characteristics

SETTING



OUTCOMES

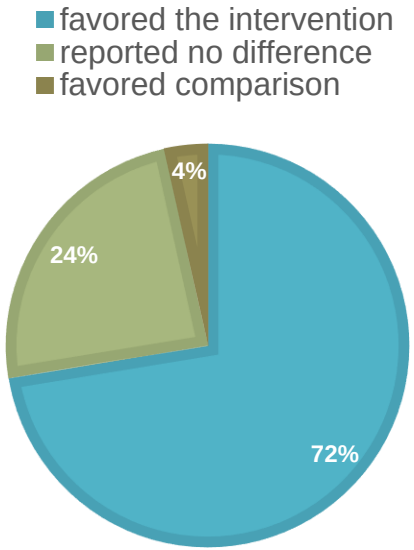


Summary of Review Characteristics

- 9 reviews specified an objective of evaluating harms of deprescribing.
  - 5 reviews defined which outcomes were considered harms
- 8 reviews specified adverse drug- withdrawal events as an outcome of interest.

Summary of meta-analyses Medication-related outcomes

- Ten of the 33 reviews included a meta-analysis of *medication-related* outcomes.
- Included 29 comparisons examining discontinuation, change in medication or appropriateness.



Summary of meta-analyses Medication-related outcomes

Review	Medication-related outcome	# of comparisons or outcomes	Favored intervention	No evidence of an effect
Nishtala 2008	Hypnotics, antipsychotics	2	1	1
Parr 2009	BZD	7	4	2
Page 2016	Number, PIMs, BZD	3	2	1
Walsh 2016	MAI	2	2	
Dalton 2018	PIM	1	1	
Sheehan 2018	Psychotropic	1	1	
Hansen 2018	Number, MAI	5	4	1
Rankin 2018	MAI, PIMs	3	2	1
Dou 2019	BZD	3	2	1
Almutairi 2020	MAI	2	2	

MAI, Medication appropriateness index; PIM, potentially inappropriate medication

Summary of meta-analyses *Other* outcomes

	# of reviews	Favored intervention	No evidence of an effect	Mixed
Mortality	5	**1**[2]	**3**[1,4,5]	**1**[3]
Hospitalization	3		**3**[1,2,5]	
Quality of life	2		**2**[1,5]	
Falls	2		**1**[1]	**1**[3]
BPSD/NPI	2		**2**[1,3]	
Cognition	1		**1**[1]	
Adverse drug events	1		**1**[1]	
ADWEs	1		**1**[3]	

[1]Almutairi 2020, [2]Bloomfield 2020, [3]Page 2016, [4]Johansson 2018, [5]Reeve 2020

Results: Step 2

Narrative Synthesis by Outcome

Medication-related outcomes

Summary of findings of eligible studies across reviews

	Beneficial effect only	Beneficial or no effect	No effect	Mixed	No effect or negative effect	Negative effect only
Medication reduction/ discontinuation (n=28)	19	6	1	1		1
Other medication related outcomes (n=13)	6	5	1	1		

Other Outcomes

Summary of findings of eligible studies across reviews

	Beneficial effect only	Beneficial or no effect	No effect	Mixed	No effect or negative effect	Negative effect only
Mortality (n=15)		4	11			
Quality of life (n=15)		5	6	1	3	
Adverse drug events (n=16)	6	1	6	1	1	1
Hospitalization (n=11)		4	7			
Cognition (n=9)	1	1	6		1	
Falls (n=8)	1	5	2			
Surrogate biomarkers (n=6)			2	1	1	2
Patient perception of treatment burden (n=3)	2	1				
Costs (n=1)		1				

Results: Subgroups

Data from meta-analyses or narrative synthesis

Subgroups

Subgroup	#	Meta-analysis results	Narrative synthesis
Age	1	Mortality: no evidence of effect • < 80 yrs (OR 0.64; CI 0.4-1.04)[1] • ≥ 80 yrs (OR 0.88; CI 0.74-1.31)	
Dementia	3	Mortality: no evidence of effect • dementia (OR 0.89; 0.63, 1.27)[1] • Intact cognition (OR 0.64; 0.36, 1.13) Psychotropic use (in people with impaired cognition): reduced • OR 0.24; 0.14, 0.39[2]	inappropriate antipsychotic use (in people with dementia): reduced[3]
Frailty	1		Unnecessary med: reduced[4]
Setting	12	Medication use: reduced • outpatient setting (MD -0.80; -1.40, -0.21)[5] • hospital setting (MD-0.50; -1.36, 0.37)	**Evidence of benefit**: LTC: 1 of 4 reviews[6] Hospital: 3 of 3 reviews [7-9] Outpatient: 2 of 4 reviews[10,11]

[1]Page 2016, [2]Sheehan 2018, [3]Thompson Coon, [4]Tjia 2013, [5]Hansen 2018, [6]Hoyle 2018, [7]Dalton, [8]Thillainadesan 2018, [9]Walsh 2016, [10]Parr 2009, [11]Kallio 2018

Subgroups

Subgroup	#	Meta-analysis results
Intervention type	6	Number of medications: reduced • patient centered (MD -1.01; -2.00, -0.03)[1] • health-care professional centered (MD -0.51; -0.80, -0.22) Medication appropriateness: improved • medication review (RR 0.62; 0.41, 0.93)[2] • computerized decision support (RR 0.78; 0.64, 0.95) • multidisciplinary meetings (RR 0.97, 0.92, 1.03) • staff education (RR 0.66; 0.43, 1.01) BZD use: reduced • brief interventions,[3] psychological interventions with and without gradual dose reduction,[3] cognitive behavioral therapy,[4] educational programs[4] • therapeutic substitution.[3,4] Mortality: reduced • patient specific interventions (OR 0.62; 0.43, 0.88)[5] • educational programs (OR 1.21; 0.86, 1.69)[5] • CMRs (OR 0.74; 0.58, 0.95)[6] Hospitalization: no evidence of effect • CMRs (RR 1.07; 0.92, 1.26)[6]

[1]Hansen 2018, [2]Almutairi 2020, [3]Parr 2009, [4]Dou 2019, [5]Page 2016, [6]Bloomfield 2020

Summary

- First overview of systematic reviews of deprescribing
- Narrative synthesis according to outcome
  - Deprescribing interventions generally resulted in medication reduction but resulted in mixed effects or no evidence of an effect for other outcomes.
  - Outcome of ADEs were reported in nearly half of reviews; only 1 found an increase.
- Summary of results from meta-analyses
  - Few meta-analyses reported on other outcomes
  - Mixed (e.g., mortality, falls) or no evidence of an effect (e.g., hospital admissions, adverse effects, quality of life, cognitive function).
- Few reviews focused on how intervention effects varied according to patient characteristics such as older age, dementia, frailty or multimorbidity.

Summary

- Many primary studies not designed or powered to examine downstream outcomes.
  - Important to interpret “no evidence effect” within this context.
- Low quality of included reviews
- Examining harm of deprescribing was often not specified as an objective
- Interventions categorized differently across reviews
- Difficult to prioritize which medications or patient groups would benefit most from deprescribing efforts.

Research Implications

- Define and examine potential harms of deprescribing
- Develop and use a standardized set of outcome measures, which include patient-centered, clinical, health utilization and cost outcomes
- Conduct intervention studies of sufficient sample size and duration to be able to capture such outcomes
- Examine the effect of deprescribing on specific vulnerable subgroups, such as people with frailty, dementia, multimorbidity, and the very old.
- Develop a taxonomy of intervention types

Strengths and Limitations

STRENGTHS

- Comprehensive overview of systematic reviews using established methods.
- Addressed a unique gap by summarizing the proliferation of evidence from recent reviews.
- Adapted a core outcome set for polypharmacy research to conceptualize the results

LIMITATIONS

- Included only English- language publications
- Large recently published deprescribing trials not captured.
- Extracted data was dependent on reporting by authors of the reviews, which varied in quality and style.
- Unable to estimate the association between success on medication-related outcomes and impact on downstream outcomes.

Conclusions

- Interventions generally resulted in medication reduction.
- Information about other outcomes was not routinely examined, and where included, studies were likely underpowered.
- The evidence, though of low-quality, suggests deprescribing was not associated with increased adverse events, and had little evidence of effect on mortality, quality of life and health-care use.
- Few reviews examined effects on vulnerable subgroups.
- Given harms of polypharmacy and use of high-risk medications, clinicians should continue to look for opportunities to deprescribe inappropriate medications and practice shared decision-making, keeping in mind patient-specific goals in deprescribing medications.


THANK YOU!
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