The efficacy of deprescribing interventions on health outcomes in people aged over 65 years: a systematic review protocol

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Review question/objective

The objective of this review is to identify the effectiveness of deprescribing interventions on health-related outcomes.

More specifically, the objectives are to identify:

The effectiveness of deprescribing interventions on health, quality of life and mortality in older people, defined as those aged 65 years and above.

Background

Older people commonly use multiple medicines to manage chronic health conditions. In this population, medicines are frequently associated with adverse drug reactions (ADRs), falls risk and may have a negative impact on both cognition and quality of life.¹ There is often genuine uncertainty whether the benefit or risk of taking the medication is greater.

Medication-related harms are a significant public health risk in the older population. It is estimated that at least 80,000 Australian hospital admissions annually are related to medication use.² Evidence demonstrates that over 40% of ADR-related hospital admissions may be preventable.³ The news does not improve post-discharge, where 17.7% of older people with hospital admissions for ADRs are readmitted...
with a follow-up ADR within three years. The prevalence of medication-related harm highlights the potential for medications to cause significant harm as well as benefit in older people.

There is reasonable doubt if older people benefit from all of their medications. Long-term antihypertensive, diuretic, antipsychotic and hypnotic medications can be ceased in a sizeable minority of older people without symptom return. For example, the second Australian national blood pressure study cohort found that 36% of normotensive older people treated with antihypertensive medications remained normotensive post-withdrawal. This evidence suggests a significant minority of older people take unnecessary medications. The factors and reasons for this are poorly understood, though may include disease progression, physiological ageing, or lifestyle changes.

Deprescribing is hypothesized as an intervention to reduce the risks associated with older people using medicines. Deprescribing balances the expected benefits from medication against the known risks, accounting for potential drug interactions, ADRs, co-morbidities and life expectancy. Deprescribing includes drug withdrawal, drug discontinuation, tapering, or even substitution of the target medicine. Medications are tapered when a rebound syndrome or physiological withdrawal is expected.

First appearing in the literature in 2003, the term deprescribing is a growing area of research. The first review on the topic in 2008 supported evidence that some medications could be safely and successfully withdrawn. A 2009 systematic literature review discussed criteria for inappropriate medications and interventions to reduce their use including, but not limited to, regulatory policies, pharmacist-based, geriatric medicine services and multidisciplinary team-based interventions. A 2012 review investigated the risks of polypharmacy, the challenges of discontinuing medications, interventions to reduce medication prescribing and the effectiveness of interventions to reduce medication exposure and found that although different interventions can reduce medication exposure, the evidence for clinical efficacy and sustainability is both insufficient and conflicting. In 2013, a qualitative systematic review investigated the patient-reported barriers and enablers to deprescribing that discussed patient attitudes and perceptions of medications and found that multiple competing enablers and barriers influence a consumer’s decision to deprescribe a medication.

One of the major drawbacks of these reviews is that they discussed the effect on clinical outcomes of withdrawing only one medication, or only the intervention to withdraw the medication. The proposed systematic review will investigate the effectiveness of deprescribing one or more medications and their effect on clinical outcomes for older people, and more importantly if it is safe.

**Keywords**

deprescribing; drug discontinuation; drug withdrawal; drug tapering; aged; elderly
Inclusion criteria

Types of participants

This review will consider studies that include people aged 65 years and older who are prescribed one or more regular medications at the beginning of the study.

65 years and older will be defined as studies where one of the following applies:

- The mean participant age is 65 years or older.
- Greater than 75% of participants are aged 65 years and older.
- The data from people aged 65 years and older can be extracted.

There will be no limitation on setting; therefore the review will include studies that are community-based, residential care, or hospital-based.

Studies that include only moribund, terminal, or palliative participants will be excluded.

Types of intervention(s)/phenomena of interest

This review will consider studies that evaluate deprescribing by a health professional of one or more regular prescription medications. These interventions include drug withdrawal, drug discontinuation, dose reduction and dose tapering. These will be compared to either no comparator or usual care, namely the continuation of the prescribed medication.

Types of outcomes

This review will consider studies that include the following outcome measures:

1. Mortality
2. Physical Health
   - Physiological Measures (i.e. blood pressure, electrolytes)
   - Psychological Measures (i.e. Cornell Score)
   - Falls
   - Absence of adverse effects attributable to the deprescribed medicine(s)
3. Cognitive function
4. Quality of Life (by standardized measure)
5. Effect on medication regime (measured using a standard); e.g. Number of medications, Drug Burden Index score, Medication Appropriateness Index, Prescribing Quality Index 2.
6. Adverse Drug Withdrawal Events, which can be categorized into:
   - Emergence of a new condition
   - Return of the original condition
   - Physiological withdrawal
   - Idiopathic
Types of studies

This review will consider both experimental and observational study designs including randomized controlled trials, non-randomized controlled trials, quasi-experimental, before and after studies, prospective and retrospective cohort studies, case control studies and analytical cross sectional studies of deprescribing interventions of one or more prescription medications in older people for inclusion.

Search strategy

The search strategy aims to find both published and unpublished studies. A three-step search strategy will be utilized in this review. An initial limited search of MEDLINE and CINAHL will be undertaken, followed by analysis of the text words contained in the title and abstract, and of the index terms used to describe the article. A second search using all identified keywords and index terms will then be undertaken across all included databases. Thirdly, the reference lists of all identified reports and articles will be searched for additional studies. Studies published in English will be considered for inclusion in this review.

Studies published at any time up to the commencement of the search will be considered for inclusion in this review.

The databases to be searched include:

EbscoHost (CINAHL Plus, Health Source: Nursing/Academic Edition, Academic Search Premier), Ovid (Medline, DARE), Scopus and Web of Science.

The search for unpublished studies will include:

Relevant conference proceedings and abstracts, years 2009-current only (database restrictions), will be searched through Elsevier (Embase). Theses and dissertations, in a similar area, will be identified by searching ProQuest (Dissertations and Theses Global)

Initial keywords to be used will be:

• deprescribing
• prescribing OR prescription OR drug OR medication OR polypharmacy
combined with
• inappropriate OR reduc* OR stop* OR withdraw* OR cessation OR ceas* OR discontinu*
combined with
• words to indicate aged 65 years and older: aged OR ageing OR 65 years OR geriatric OR older adult OR older OR elderly OR veteran

Assessment of methodological quality

Papers selected for retrieval will be assessed by two independent reviewers for methodological validity prior to inclusion in the review using standardized critical appraisal instruments from the Joanna Briggs Institute Meta-Analysis of Statistics Assessment and Review Instrument (JBI-MAStARI) (Appendix I). Any disagreements that arise between the reviewers will be resolved through discussion, or with a third reviewer.
Data collection

Data will be extracted from papers included in the review using the standardized data extraction tool from JBI-MASTARI (Appendix II). The data extracted will include specific details about the interventions, populations, study methods and outcomes of significance to the review question and specific objectives. The original authors will be contacted if there is missing information, or to clarify unclear data.

Data synthesis

Quantitative data will, where possible, be pooled in statistical meta-analysis using JBI-MASTARI. All results will be subject to double data entry. Effect sizes expressed as odds ratios (for categorical data) and weighted mean differences (for continuous data) and their 95% confidence intervals will be calculated for analysis of the outcomes for deprescribing each medication or medication class. Heterogeneity will be assessed statistically using the standard Chi-square and also explored using subgroup analyses based on the different study designs included in this review. Where statistical pooling is not possible, the findings will be presented in narrative form including tables and figures to aid in data presentation where appropriate.

Subgroup analysis will be undertaken of deprescribing a single medication rather than deprescribing two or more medications. If possible, a subgroup analysis will be undertaken of participants aged under 80 years and those aged over 80 years, or those with cognitive impairment compared to cognitively intact older people.

Conflicts of interest

None to declare for Professor Rhonda Clifford and Dr Hanan Khalil.

Professor Christopher Etherton-Beer, Dr Kathleen Potter and Mrs Amy Page are working on a deprescribing trial.

Acknowledgements

Mrs Amy Page’s PhD candidacy (of which this research was conducted within) is funded by a University Postgraduate Award (UPA) at the University of Western Australia, School of Medicine and Pharmacology supervised by Professor Christopher Etherton-Beer, Professor Rhonda Clifford, and Dr Kathleen Potter.

Dr Kathleen Potter is funded by an NHMRC Early Career Fellowship.
References


Appendix I: Appraisal instruments

MAStARI appraisal instrument

JBI Critical Appraisal Checklist for Randomised Control / Pseudo-randomised Trial

Reviewer __________________________ Date __________________________

Author __________________________ Year __________ Record Number __________

1. Was the assignment to treatment groups truly random? ☐ Yes ☐ No ☐ Unclear ☐ Not Applicable

2. Were participants blinded to treatment allocation? ☐ Yes ☐ No ☐ Unclear ☐ Not Applicable

3. Was allocation to treatment groups concealed from the allocator? ☐ Yes ☐ No ☐ Unclear ☐ Not Applicable

4. Were the outcomes of people who withdrew described and included in the analysis? ☐ Yes ☐ No ☐ Unclear ☐ Not Applicable

5. Were those assessing outcomes blind to the treatment allocation? ☐ Yes ☐ No ☐ Unclear ☐ Not Applicable

6. Were the control and treatment groups comparable at entry? ☐ Yes ☐ No ☐ Unclear ☐ Not Applicable

7. Were groups treated identically other than for the named interventions? ☐ Yes ☐ No ☐ Unclear ☐ Not Applicable

8. Were outcomes measured in the same way for all groups? ☐ Yes ☐ No ☐ Unclear ☐ Not Applicable

9. Were outcomes measured in a reliable way? ☐ Yes ☐ No ☐ Unclear ☐ Not Applicable

10. Was appropriate statistical analysis used? ☐ Yes ☐ No ☐ Unclear ☐ Not Applicable

Overall appraisal: Include ☐ Exclude ☐ Seek further info. ☐

Comments (Including reason for exclusion)

________________________________________________________________________

________________________________________________________________________
JBI Critical Appraisal Checklist for Descriptive / Case Series

Reviewer __________________________ Date __________________________
Author ____________________________ Year _______ Record Number _______

1. Was study based on a random or pseudo-random sample? □ Yes □ No □ Unclear □ Not Applicable
2. Were the criteria for inclusion in the sample clearly defined? □ Yes □ No □ Unclear □ Not Applicable
3. Were confounding factors identified and strategies to deal with them stated? □ Yes □ No □ Unclear □ Not Applicable
4. Were outcomes assessed using objective criteria? □ Yes □ No □ Unclear □ Not Applicable
5. If comparisons are being made, was there sufficient descriptions of the groups? □ Yes □ No □ Unclear □ Not Applicable
6. Was follow up carried out over a sufficient time period? □ Yes □ No □ Unclear □ Not Applicable
7. Were the outcomes of people who withdrew described and included in the analysis? □ Yes □ No □ Unclear □ Not Applicable
8. Were outcomes measured in a reliable way? □ Yes □ No □ Unclear □ Not Applicable
9. Was appropriate statistical analysis used? □ Yes □ No □ Unclear □ Not Applicable

Overall appraisal: Include □ Exclude □ Seek further info □

Comments (Including reason for exclusion)
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Appendix II: Data extraction instruments

MAStARI data extraction instrument

**JBI Data Extraction Form for Experimental / Observational Studies**

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**Study Method**

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<th>Retrospective</th>
<th>Observational</th>
<th>Other</th>
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**Participants**

Setting

Population

**Sample size**

Group A  
Group B

**Interventions**

Intervention A

Intervention B

Authors Conclusions:

Reviewers Conclusions:
Study results

### Dichotomous data

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### Continuous data

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