BMJ Open

Outcomes associated with prescribed medications in older adults with multimorbidity: protocol for a scoping review

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To cite: Watt J, Tricco AC, Vyas M, *et al*. Outcomes associated with prescribed medications in older adults with multimorbidity: protocol for a scoping review. *BMJ Open* 2017;**7**:e014529. doi:10.1136/bmjopen-2016-014529

► Prepublication history and additional material is available. To view please visit the journal (http://dx.doi.org/10.1136/bmjopen-2016-014529).

Received 4 October 2016
Revised 26 January 2017
Accepted 30 January 2017

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ABSTRACT

Introduction: Multimorbidity becomes increasingly prevalent with ageing. Polypharmacy is often associated with multimorbidity because patients accrue medications to treat each individual disease; however, there is uncertainty around the generalisability of disease-specific guidelines. Namely, the extrapolation of results from studies conducted in younger patients to older adults with multimorbidity. The main objective of this scoping review is to explore our current knowledge of the outcomes that older adults with multimorbidity experience from taking prescribed medications.

Methods and analysis: A scoping review will be conducted to explore what is known about the outcomes experienced by older adults with multimorbidity who are taking guideline-recommended medications and to identify areas for future research. In addition to searching the grey literature, the following databases will be searched from 1990 onward: MEDLINE, EMBASE, PsycINFO and the Cochrane Library. Experimental, quasi-experimental and non-experimental studies consisting of patients ≥65 years old who have two or more comorbid conditions (explicitly grouped together for the purpose of analysis) and who are being prescribed a guideline-recommended prescription medication for a chronic condition will be considered for inclusion in our scoping review. We will describe patient (eg, mortality, morbidity, quality of life) and health system (eg, number of emergency department visits or hospitalisations, cost to third-party payer) outcomes associated with the prescription of medications for older adults who have two or more chronic comorbid conditions. Two reviewers will complete all screening and data abstraction independently. Data will be synthesised with descriptive statistics.

Ethics and dissemination: Ethics approval is not required because this is a scoping review of published literature. Results will be disseminated through conference presentations and publication in a peer-reviewed journal.

Strengths and limitations of this study

- The field of research concerning appropriate prescribing in older adults with multiple chronic conditions (multimorbidity) is evolving. A scoping review is a feasible strategy to identify gaps in the current literature to guide future research.
- This will be the first scoping review to systematically identify studies that were conducted to ascertain outcomes of prescribed medications in older adults with an identified cluster of two or more chronic medical conditions (explicitly grouped together for the purpose of analysis).
- Our literature search strategy is expansive, including both the published and grey literature.
- Despite our expansive search strategy, it is possible that articles appropriate for inclusion will be missed given that the effects of patient comorbidities are often explored in subgroup analyses that are not described in a study's title or abstract.

INTRODUCTION

Multimorbidity is a term used to describe a patient who has two or more chronic health conditions such as coronary artery disease, diabetes mellitus and depression. Multimorbidity and polypharmacy are highly prevalent among adults aged 65 years and older. Over half of older adults are afflicted by multimorbidity and nearly a quarter of older adults are prescribed at least five medications.[1 2] Patients with multimorbidity are at increased risk for polypharmacy. This relates to the pill burden associated with medications prescribed as per disease-specific guidelines and the subsequent prescribing cascade that can result from treating medication-related adverse effects.[3] There are several other concerns that clinicians must consider when prescribing medications for older adults with multimorbidity: the applicability of each guideline to their individual patients, patients' preferences for certain treatments and not others, and the potential unintended consequences

that can arise from taking medications, such as adverse drug events and decreased medication compliance.[4–6] These considerations create uncertainty in decision-making around the appropriate prescribing of medications for clinicians and patients with multimorbidity.

Clinicians are becoming increasingly aware of the need for a greater evidence base to guide clinical decision-making for this complex population of older adults with multimorbidity and polypharmacy.[7 8] Recently, research has focused on characterising the prevalence of multimorbidity in older adults and the clusters of diseases that are found in patients with multimorbidity.[9 10] Other research is beginning to focus on how medications affect patients with specific clusters of comorbidities.[11] For example, Tinetti *et al*[11] found that β blockers had a beneficial effect on mortality for patients being prescribed this medication for a guideline-recommended indication, except among those patients with the disease cluster of hypertension, hyperlipidaemia, depression and coronary artery disease. It is necessary to identify important outcomes (eg, quality and length of life, adverse drug effects) that can facilitate discussions around informed consent for patients and clinicians who are considering use of multiple medications. It is also important to ascertain the gaps in the literature concerning what is known around the prescribing of guideline-recommended medications for older patients with multimorbidity.

The objectives of this study are to describe: (1) patient (eg, mortality, morbidity, quality of life) and health system (eg, number of emergency department visits or hospitalisations, cost to third-party payer) outcomes associated with the prescription of medications for older adults who have two or more chronic comorbid conditions (explicitly grouped together for the purpose of analysis); (2) medications, outcomes and clusters of comorbid conditions that are being studied; and (3) the methodology (eg, study designs, statistical modelling techniques) that researchers are using to study these patient and health system outcomes in patients with multimorbidity. For example, we are interested in knowing whether an older adult with both diabetes mellitus and hypertension who is taking a specific antihypertensive medication is more likely to fall than an older adult with these two comorbidities who is not taking this medication. Given the exploratory nature of these research questions, a scoping review will be undertaken to assess the breadth and depth of knowledge around this topic. Synthesis of research on this topic can help researchers and policymakers to understand the current state of the evidence and identify areas for future research.

METHODS AND ANALYSIS

Study design

A scoping review will be conducted to synthesise our current knowledge of patient and health system outcomes relating to the prescription of medications for adults ≥65 years old who have two or more chronic medical conditions (explicitly grouped together for the purpose of analysis). Scoping reviews are meant to provide users and researchers with an overview of a topic so as to identify key concepts, knowledge gaps and types of evidence within an evolving field of research.[12] Unlike a systematic review, the research questions outlined by study authors of a scoping review are often quite broad.[12] A scoping review is appropriate because the purpose of this study is to describe a wide range of patient groups, comorbidity clusters, medications, outcomes and research methodologies, as they relate to patients with multimorbidity so that researchers can understand areas within the field that require further study.[12] This study will be conducted as per the methodology outlined in the Joanna Briggs Institute Reviewers' Manual and reported as per the PRISMA statement.[13 14] It has been registered with Open Science Framework.[15]

Eligibility criteria

Our three research questions are:

1. What is known about the effect of prescribed medications on patient or health system outcomes in adults ≥65 years old who have two or more chronic medical conditions that are explicitly grouped together for the purpose of analysis? For example, are older adults with the comorbid diagnoses of coronary artery disease and depression more likely to achieve clinical remission from their depression if they are prescribed an antidepressant than those patients with coronary artery disease and depression who are not treated with an antidepressant?
2. What outcomes, medications and disease clusters have been studied to ascertain the effect of prescribed medications on adults ≥65 years old who have two or more chronic medical conditions that are explicitly grouped together for the purpose of analysis?
3. What research methods (ie, study designs, statistical modelling techniques) are being used in the studies that focus on this topic?

Our PICOS eligibility criteria were developed from our research questions, as follows:[16]

Population

Adults who are ≥65 years old with an identified cluster of chronic medical conditions (defined as the explicit grouping of two or more chronic medical conditions for the purpose of quantitative analysis by the original study's authors) will be included in this scoping review. Chronic diseases will include, but not be limited to, coronary artery disease, diabetes mellitus, chronic obstructive lung disease and depression. Rates of multimorbidity and polypharmacy are highest among older adults.[1 2] Capturing studies that include patients ≥65 years old will ensure that we can describe the effects of medications on patients with multimorbidity in each of the three generally described cohorts of older adults: young-old

(age 65–74 years), middle-old (age 75–84 years) and oldest-old (age ≥85 years).[17]

Intervention and comparator

The intervention can be any guideline-recommended medication prescribed for the treatment of one or more comorbidities among older adults. The comparator group will be older adults with the same identified cluster of chronic medical conditions who are not receiving the guideline-recommended medication. We will search the literature to identify whether or not a medication is recommended by any clinical guideline published in English for the treatment of one or more of the comorbidities identified in the disease cluster.

Outcomes

Given the exploratory nature of this study, any patient or health system outcome will be considered for study inclusion. This could include, but will not be limited to, the following patient outcomes: mortality, adverse drug events, quality of life measures, medication adherence and disease-specific outcomes (ie, glycaemic or blood pressure control). Health system outcomes such as healthcare usage will also be included.

Study design

Experimental, quasi-experimental and non-experimental studies published in English will be considered for inclusion in this scoping review. It is important to include all study designs so as to not limit our ability to identify disease clusters, medications prescribed and outcomes among older adults with multimorbidity. Systematic reviews on related subject matter will be retained so that their reference lists can be scanned for other potential studies to be included in our scoping review.

Search strategy

An information specialist developed a search strategy for our clinical question (see online supplementary appendix 1 for the MEDLINE search strategy). It was peer reviewed by a second information specialist using the Peer Review of Electronic Search Strategies (PRESS) checklist.[18] The following databases will be searched for citations published in English: MEDLINE, EMBASE, the Cochrane Library and PsycINFO. The search will be restricted to papers published from 1990 onwards because previous research has shown that few studies were published on multimorbidity prior to 1990.[19 20] A validated age-specific search filter will be used to better identify those studies that include patients ≥65 years old.[21] Searches of the grey literature will be conducted using the Canadian Agency for Drugs and Technologies in Health (CADTH) tool,[22] Google Scholar and relevant topic-related conference proceedings and websites such as those of the American Geriatrics Society (AGS) and the Society for General Internal Medicine (SGIM). Reference lists of included studies and related systematic reviews will be reviewed to identify additional relevant studies.

Study selection

Using the PICOS eligibility criteria, two levels of screening will be completed independently using *Synthesi*. SR (proprietary online software developed at St Michael's Hospital, Toronto, Canada). Level 1 screening will consist of two reviewers independently reviewing the title and abstract of each article retrieved from the literature search to determine if the article meets the criteria for inclusion. Level 2 screening will consist of two reviewers independently reviewing the full text of each article retained from level 1 screening. If a conference abstract is retrieved for level 2 screening, study authors will be contacted for further information to ensure the study meets our outlined eligibility criteria, as required. Whenever it is unclear whether or not a study meets our outlined eligibility criteria, study authors will be contacted for further information. When multiple studies report outcomes from the same data set, the largest study will be included in the results of our scoping review. The other studies will be retained as companion reports.

A calibration exercise will occur whereby each reviewer will independently screen 10% of a random sample of citations at the beginning of each level of screening to ensure appropriate inter-rater agreement (at least 80% agreement). For disagreements among reviewers, the article in question will be discussed between the two reviewers until consensus is reached as to whether or not the article should be included. If there is ongoing disagreement, a third reviewer will be consulted to come to a final decision about an article's inclusion.

Data abstraction

Data will be abstracted independently in duplicate from those studies retained from level 2 screening using a data abstraction form compiled a priori. The form will be piloted on a random sample of five included studies to ensure the form is being used correctly by each of the reviewers. The form will be modified as necessary to ensure clarity for reviewers. Data abstraction will begin when at least 80% agreement is reached by each of the reviewers in the sample of piloted studies. Disagreements will be resolved in the same manner as described above for screening.

Data pertaining to study characteristics, study outcomes and patient characteristics will be abstracted. Abstracted data pertaining to study characteristics will include authorship, year and journal of publication, study design, inclusion and exclusion criteria, duration of patient follow-up, geographic region in which study was conducted, patient care setting (ie, inpatient or outpatient), number of patients enrolled in the study, comorbidity cluster(s) identified, medication(s) prescribed, outcome(s) examined, how results are reported (ie, adjusted vs unadjusted outcomes), and statistical modelling techniques used by study authors. Each reported outcome relating to our study question will be abstracted from included studies. Outcomes could

include patient-level or health system-level outcomes such as the risk of morbidity of mortality, quality of life, perceptions around quality of care or cost to the healthcare system. Abstracted data pertaining to patient characteristics may include average age and body mass index (mean or median plus SD or IQR); percentage of participants who are female, are frail (defined as per the study investigators), smoke cigarettes or drink alcohol; percentage of participants who have functional impairment (ie, activities of daily living and instrumental activities of daily living), cognitive impairment (ie, major and minor neurocognitive disorder), hypertension, dyslipidaemia, coronary artery disease, cancer, asthma, chronic obstructive pulmonary disease, arthritis, diabetes mellitus, depression, anxiety, a history of stroke or other comorbidities; the number of patients within each cluster of comorbidities; and the number of patients prescribed medication(s) within each cluster of comorbidities. Where authors have documented reasons for choosing to study certain clusters of diseases, medications or outcomes, this information will be abstracted.

Methodological quality assessment

No assessment of methodological quality will be completed, as this is a scoping review,[13] which is consistent with other published scoping reviews on clinical topics.[23]

Data synthesis

Quantitative syntheses will be undertaken to explore the content of the studies included in this scoping review. The effect measures reported by each study will be summarised in a table that outlines each study's first author, year of publication, design, multimorbidity cluster(s), exclusion criteria, outcome(s), guideline-recommended medication(s), comparator(s), average age of patients and percentage of female patients. Descriptive statistics will be used to summarise the number of included studies; geographic regions of the world where the studies were conducted; total number of patients included in the scoping review; number of studies that were conducted in each healthcare setting; number of study designs; and number of studies that reported each comorbidity cluster, medication prescription and outcome. For example, we will report the number of articles that identify each cluster of comorbidities and how many of these articles report specific outcomes associated with the use of a particular medication (eg, three studies assessed the odds of mortality in older adults with the comorbid diagnoses of coronary artery disease and diabetes mellitus who were prescribed metformin for glycaemic control compared with those who were not prescribed metformin). These categorical data will be summarised with frequencies and percentages. Data will be further categorised as to: (1) outcomes being studied (eg, patient-level or health system-level outcomes), (2) disease clusters included in study analyses relating to each outcome, (3) medications prescribed by healthcare providers for patients with the identified cluster of chronic medical conditions leading to the described study outcome(s) and (4) study designs.

ETHICS AND DISSEMINATION

There is a growing body of literature around older adults with multimorbidity, but more research is needed to characterise the benefits and harms around prescribing medications to multimorbid older adults with specific clusters of disease. As such, the purpose of this scoping review will be to provide a synthesis of the current breadth and depth of knowledge in this evolving area of research and no ethics approval will be needed. The results of this study will be disseminated through presentations at clinical conferences and publication in a peer-reviewed journal.

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Acknowledgements The authors wish to thank Jessie McGowan for designing the literature search strategy and Elise Cogo for peer reviewing the literature search strategy using the PRESS statement.

Contributors JW and SES conceived and designed the study and drafted the protocol. ACT helped to design the study and edit the protocol. MV, KK, SS, MA and SW helped to edit the protocol. All authors read and approved the final protocol prior to its submission.

Funding JW is funded by the Ontario Ministry of Health and Long-Term Care Clinician Investigator Program, the Eliot Phillipson Clinician Scientist Training Program, and the Canadian Institutes for Health Research (CIHR) Canada Graduate Scholarships-Master's Program.

Competing interests None declared.

Provenance and peer review Not commissioned; externally peer reviewed.

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