


BMJ Open Optimising prescribing practices in older adults with multimorbidity: a scoping review of guidelines

Penny Lun ¹, Felicia Law,² Esther Ho,³ Keng Teng Tan,⁴ Wendy Ang,⁵ Yasmin Munro,⁶ Yew Yoong Ding^{1,3}

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¹Geriatric Education and Research Institute, Singapore

²Geriatric Medicine, National Healthcare Group Woodlands Health Campus, Singapore

³Geriatric Medicine, Tan Tock Seng Hospital, Singapore

⁴Pharmacy, Tan Tock Seng Hospital, Singapore

⁵Pharmacy, Changi General Hospital, Singapore

⁶Medical Library, Lee Kong Chian School of Medicine, Singapore

Correspondence to

Penny Lun;
lun.penny.sy@geri.com.sg

ABSTRACT

Objective Inappropriate polypharmacy occurs when multiple medications are prescribed without clear indications or where harms outweigh their benefits. The aims of this scoping review are to (1) identify prescribing guidelines that are available for older adults with multimorbidity and (2) to identify cross-cutting themes used in these guidelines.

Design Scoping review.

Data sources PubMed, Embase, Web of Science, the Cochrane Library databases, Cumulative Index to Nursing and Allied Health Literature, grey literature sources, six key geriatrics journals, and reference lists of identified review papers. The search was conducted in November 2018 and updated in September 2019.

Study selection General prescribing guidelines tailored to or for adults including older adults with multimorbidity.

Data extraction Data for publication description, guideline characteristics, information for users and criteria were extracted. The synthesis contains summarised qualitative descriptions of the studies and guideline characteristics as well as identified cross-cutting themes.

Results Our search strategy yielded 10 427 unique citations, of which 70 fulfilled the inclusion criteria for synthesis. Among these, there were 61 unique guidelines and tools which used implicit, explicit, mixed or other approaches in the prescriber decision-making process. There are 11 cross-cutting themes identified in the guidelines. Prescriber-related themes are: conduct a comprehensive assessment before prescribing, identify patients' needs, goals and priorities, adopt shared decision-making, consider evidence-based recommendations, use clinical prescribing tools, incorporate multidisciplinary inputs and embrace technology-enabled prescribing. Wider organisation-related and system-related themes related to education, training and the work environment are also identified.

Conclusions From guidelines and tools identified, eleven cross-cutting themes provide a usable knowledge base when seeking to optimise prescribing among older adults with multimorbidity. Incorporating these themes in an approach that uses mixed criteria and implementation information could facilitate greater uptake of published prescribing recommendations.

INTRODUCTION

According to the WHO, global life expectancy increased by 5.5 years on average between

Strengths and limitations of this study

- This scoping review adopts the five-stage methodological framework developed by Arksey and O'Malley.
- Comprehensive search including grey literature broaden the findings and results.
- Broad results presented an overview of prescribing guidelines for older adults with multimorbidity despite challenges of the synthesis.
- Consultation with experts and stakeholders was not performed.
- Quality of the guidelines was not appraised.

2000 and 2016.¹ With rising life expectancies, the prevalence of multimorbidity among older adults will increase.² Multimorbidity is defined as having two or more chronic conditions.³ It often leads to polypharmacy, which is described as having five or more concurrent regular medications, although there is no agreement on its criteria to date.^{4 5} Inappropriate polypharmacy occurs when multiple medications are prescribed without clear indications or where harms outweigh their benefits.² A recent systematic review and meta-analysis of 33 studies found statistically significant association between adverse drug events, hospitalisations and potentially inappropriate medications (PIM).⁶

One of the factors that contributes to polypharmacy and PIM in patients with multimorbidity is the lack of evidence and guidance on multi-disease management, since most clinical guidelines and evidence from research trials target single diseases.² Moreover, older adults are frequently excluded from clinical trials, making prescribing for this population even more challenging.

To mitigate this challenge, general guidelines on multimorbidity management have been published by professional groups in recent years,^{7 8} with some of these designed specifically for older adults.⁹ In addition,

there have also been new guidelines on prescribing,¹⁰ as well as development of PIM lists specific to older adults.^{11 12} Clinicians in university research settings and university hospitals have also developed treatment principles and clinical tools to guide the process of prescribing for this group with complex needs. Some emerging trends in the recommendations are the focus placed on engaging patients in shared-decision making that take their preferences and priorities into consideration. Studies have shown that doctors' and caregivers' perspectives may be incongruent from that of patients',^{13 14} which make shared decision-making even more salient. As such, guidelines on multimorbidity and polypharmacy tend to place an importance on identifying patients' needs, priorities and preferences through communicating with patients and their caregivers.¹⁵

Objective

We aim to identify and compile the available guidelines for medication prescribing in older adults with multimorbidity via a scoping review. In addition, using this as a knowledge base, we intend to elicit common themes in the approaches used, in order to develop a list of practical suggestions which could help optimise prescribing within hospital outpatient clinics for this group of patients. We chose to perform a scoping review rather than a systematic review to capture the breadth of evidence on the subject.

METHODS

The five-stage methodological framework developed by Arksey and O'Malley¹⁶ was adopted to guide our scoping review. The optional consultation with experts was not performed, as this step will be integrated into a separate stakeholder engagement when designing a care intervention to improve prescribing. In addition, advancements proposed by Levac, Colquhoun and O'Brien¹⁷ and the Joanna Briggs Institute¹⁸ were incorporated where applicable. As scoping reviews focus largely on capturing the breadth of relevant publications, quality assessments were not performed.

Stage 1: identifying the research question

Our initial scoping review question was formulated in the context of a broader project to design a care intervention to reduce potentially inappropriate prescribing in outpatient care: What medication prescribing guidelines are available on older adults with multimorbidity? However, on review of the relevant literature, a further question was added to capture the essence of these guidelines: What are the cross-cutting themes in these prescribing guidelines? This expansion will help to identify key themes that can be incorporated for medication management in a care intervention to improve prescribing for older adults with multimorbidity.

Stage 2: identifying relevant studies

With guidance from a medical librarian (YM) experienced in evidence searching, a core search strategy was

devised in PubMed and adapted across Embase, Web of Science, the Cochrane Library, and Cumulative Index to Nursing and Allied Health Literature using the appropriate syntax. Online supplemental file 1 presents our PubMed search strategy. JBI's mnemonic population, concept, and context¹⁸ was used to inform our search strategy (see online supplemental file 2). In exploring guidelines, we also expanded the scope to include related approaches such as tools, lists, checklists and criteria that were developed or proposed to optimise prescribing.

The search was conducted in November 2018 and subsequently updated in September 2019. We limited our searches to the English language only, with publication dates from January 1998 onwards. The reasons for imposing these limits were limitations in resources and currency of guidelines. In addition, various grey literature sources and six key geriatrics journals were searched in December 2018 and updated in September 2019. Simplified keywords were used to augment the coverage in *Journal of the American Geriatrics Society*, *Age and Ageing*, *The Journals of Gerontology Series A*, *Archives of Gerontology and Geriatrics*, *BMC Geriatrics* and *European Geriatric Medicine*. Supplementary searches based on reference lists of systematic reviews were performed. Online supplemental file 3 provides information on the grey literature and key journal searches.

Stage 3: study selection

Article selection was conducted independently in the Covidence software¹⁹ by three reviewers (PL, FL, EH). One of the reviewers (PL) screened titles and abstracts of all the articles, while the role of the second reviewer was divided between the other two reviewers (FL, EH). This arrangement was repeated for the next stage of full text screening. Conflicts were resolved through discussion between the two reviewers concerned, with adjudication by a fourth reviewer (YYD) where necessary. We included guidelines and strategies for adults of all ages if they did not exclude older adults in their applications. We also focused on guidelines and strategies that were not disease specific, not restricted to specific medication classes, or settings. Studies that set out to measure epidemiological outcomes or cost were also excluded. Broader guidelines that focused on the overall management of older adults with multimorbidity were also included, as their principles on treatment have direct impact on the prescribing process. In line with Arksey and O'Malley's framework¹⁶ and recommendations from Levac *et al*,¹⁷ the eligibility criteria were iterated during the review process following discussions among the reviewers. **Table 1** presents the study eligibility criteria. In keeping with the goals of scoping reviews to include all relevant articles, quality assessments were not performed.¹⁶

Stage 4: charting the data

Due to the large volume of included articles, the task of charting the data was divided between two reviewers (PL and FL). An extraction spreadsheet was created to

Table 1 Eligibility criteria for study

	Inclusion criteria	Exclusion criteria
Population	<ol style="list-style-type: none"> Older adults only Adults including older adults 	Paediatrics, children, young adults, middle-aged adults.
Concept	<ol style="list-style-type: none"> General prescribing guidelines, criteria, checklists, lists, tools, approaches, recommendations. Study aims to improve physician prescribing process for older adults with multimorbidity. 	<ol style="list-style-type: none"> If guidelines are restricted to specific diseases or therapeutic classes (eg, antibiotics, benzodiazepines). Interventions and not guidelines. Study aims: Exclusively to measure or predict epidemiological outcomes or cost using the guidelines, tools, approach, and so on.
Context	Tailored for older patients with multimorbidity in outpatient setting (including primary care).	Tailored for patients with specific diseases, with comorbidity, or inpatient or residential settings.
Filter	Publications from Jan 1998 to present; English publications.	Publications before Jan 1998; non-English publications.
Study types	Published guidelines, research studies, reports, grey literature.	Protocols, epidemiological studies using guidelines, abstracts, reviews.

capture publication description, guideline characteristics, information for users and criteria. The extraction sheet was tested by the reviewers prior to independent data extraction. Subsequently, one reviewer (PL) reviewed all the extracted data to ensure their completeness and consistency. In addition, 10% of the final extractions were crossed checked by three reviewers (PL, FL, EH).

Stage 5: collating, summarising and reporting the results

The extracted data were collated and summarised by one of the reviewers (PL). Publication description and information about the guidelines are presented in the form of frequencies and percentages. To capture the range of themes presented in the guidelines, criteria identified were categorised. The reviewers then conducted several rounds of iterative discussions to agree to the categorisation, where possible, into broader finalised themes (PL, FL, EH, YYD). This scoping review is reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Review (PRISMA-ScR).²⁰

RESULTS

Our search strategy yielded 10 427 unique citations for the first stage title and abstract screening, including additional sources identified from grey literature, key journals and reference lists of systematic reviews identified. Among these, 152 studies were selected for the second stage of full-text screening, which in turn led to the final list of 70 studies that fulfilled our inclusion criteria. Online supplemental file 4 provides references of the included studies. A PRISMA flow diagram in figure 1 shows the screening process for the review.²¹

Characteristics of included articles

Most shortlisted articles were publications in scientific journals (n=64, 91%), whereas the remaining articles were from grey literature sources (n=6, 9%), such as

governmental reports. Among regions, Europe had the largest representation of included articles. Notably, publications on this topic have increased almost fourfold in the last 10 years, compared with the previous decade. Table 2 presents the publication information.

Characteristics of the guidelines and tools

In total, 61 unique guidelines and tools were identified from the final list of 70 articles that fulfilled our inclusion criteria. Since we adopted a broader definition of guidelines that included tools, our results captured criteria, approaches and lists on appropriate prescribing. To make sense of the broad range of information, we grouped them into implicit, explicit, mixed criteria, and others, in line with the categories generally used in tools that evaluate appropriateness in prescribing.^{22–24} Table 3 shows the characteristics of these guidelines.

Most of the guidelines are categorised as either implicit criteria (n=18, 30%) or explicit criteria (n=20, 33%). Implicit criteria require the prescriber to apply clinical knowledge and judgement to make decisions. These tend to be patient focused, rather than drug or disease focused.^{22–24} In other words, the prescriber would need to tailor his prescribing decisions to the specific conditions of the patient within the constraints of the implicit criteria, which often requiring reliance on knowledge of existing literature and clinical experience. As such, the clinical decision could vary and tend to be more time consuming.²⁵ Based on the above principles that define implicit criteria, we have categorised guidelines or approaches that involve lists of evaluation questions as part of the process of reviewing patients' treatment and prescriptions under implicit criteria.^{9 26 27}

As described in the literature, explicit criteria in theory could be assessed with less need for clinical judgement.²² Some examples include Beers criteria and Screening Tools of the Older Persons' Prescriptions/Screening Tool to Alert to Right Treatment (STOPP)/(START). Explicit

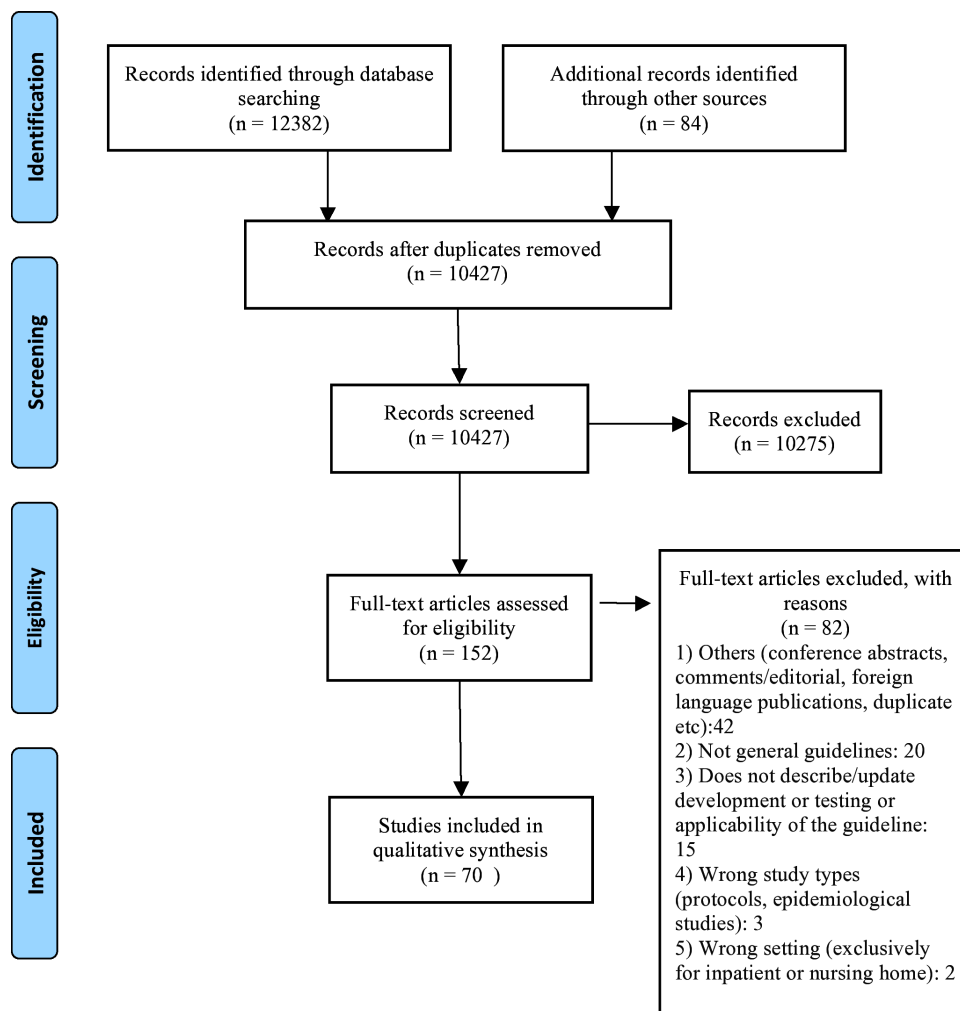


Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram of study selection process.

criteria could come in the form of potential prescribing omissions, medication cluster lists, drug–disease or drug–drug interactions that should be avoided, or specific medications that are rarely appropriate. In addition, some PIM are defined by dosage, length of use or drug regimen. To further assist physicians in prescribing, some tools also include suggested alternatives or replacement medications, or medication to consider starting for selected conditions.

In the mixed criteria category, both explicit and implicit approaches are employed in the decision-making process.²³ One example is the Australian Prescribing Appropriateness Criteria which encompass a list of medications to avoid, as well as recommendations to exercise clinical judgement in reviewing the need for additional therapy, tests, ineffective treatment and monitoring for certain medications.²⁸ In addition, two of these guidelines also included additional broader system-level principles, such as providing education or training on inappropriate prescribing, research priorities, and adaptation of work environment.^{10 29}

The remaining category of ‘others’ represents a mix of tools and guidelines that are implemented in computer decision support systems^{30 31} and guidelines that focused

on broader system needs, such as care models and research,^{32 33} general medical care, and a tool on prioritising outcomes.³⁴ Online supplemental file 5 provides the list of included studies according to our categorisation.

Overall, the aims of the guidelines were largely focused on improving the prescribing process through optimisation or deprescribing, except for 18% (n=11) that were focused on improving the overall clinical management. Most of the guidelines were developed through engaging experts in Delphi or consensus studies (n=33, 54%), whereas 13% (n=8) described other methods, such as conducting surveys, discussions or interviews.

Information for guideline users

Two-thirds of the guidelines identified described incorporation of the evidence base (n=42, 69%) by including evidence summaries, scoping and other literature reviews, or existing guidelines and tools. One-fifth of them reported updates, plans to update, or mentioned need for guidelines to be updated (n=12, 20%). These studies tended to be on tools, such as country- or region-specific PIM lists, which need to be updated due to new medications and advancement, updates on treatment outcomes, or changing policies which would affect availability of

Table 2 Publication information

Publications by:	Frequency (n=70)	Percentage
Region		
Europe*	38	54
USA	13	19
AUS/NZ	6	8.5
Asia	6	9.5
International†	7	10
First author affiliation		
Medicine	18	26
Pharmacology	18	26
Professional organisations/ governmental bodies	17	24
Other university departments	9	13
University hospitals	6	8
Others	2	3
Year published		
2001–2005	3	4
2006–2010	12	17
2011–2015	32	46
2016–2019 (part year)	23	33
Publication type		
Scientific journals	64	91
Grey literature	6	9

*Some studies involved multiple countries.

†Any combinations of authors from ≥ 2 continents.

medications in a specific market. More than half of the articles reported that the guidelines offered an implementation plan or had information that prescribers could use to facilitate the prescribing and decision process (n=35, 56%). For example, American Geriatric Society's Guiding Principles on the Care of Older Adults with Multimorbidity identified barriers to, and mitigating factors for, its implementation, in addition to providing tips and scripts to support the action steps proposed.⁹

Cross-cutting themes

Although identified guidelines have differences in their approach and criteria, their cross-cutting themes represent key concepts for improving prescribing practice in older adults with multimorbidity. The elicited themes and associated practical actions that prescribers can consider adopting are presented in table 4. Table 5 presents themes related to the wider health organisation and health system, with identified areas for change to be considered. These suggested actions are tailored to outpatient specialist clinics within the hospital setting, where there are access to multidisciplinary teams such as the pharmacy services,

Table 3 Characteristics of guidelines

Guideline categories	Frequency (n=61)	Percentage
Types		
Implicit criteria	18	30
Explicit criteria	20	33
Mixed criteria	16	26
Others	7	11
Target population		
Older adults only	51	83
Adults (including older adults)	9	15
No age restrictions	1	2
Aims		
Improving medication/optimize prescribing	24	39
Identify PIM	18	30
Clinical management	11	18
Deprescribing	6	10
Others*	2	3
Development method		
Delphi/Consensus study	33	54
Other methods†	8	13
not described	20	33
Evidence based	42	69
Implementation tool or usage information	35	56
Update needed	12	20
Training needed	9	15
Patient preference or shared decision-making	33	54
Provides information for discussion or patient information brochure	18	30

*Patients' priorities, prevent medication errors.

†Surveys, discussions, interviews.

physio/occupational/speech therapy services, nutrition and medical social work departments, and so on.

DISCUSSION

Current clinical practice guidelines were largely formulated from a single disease perspective and have limited applications to patients with multimorbidity. This is especially so for older adults who experience age-related pharmacokinetic and pharmacodynamic changes that alter the way they respond to medications.³⁵ We seek to identify the scope and extend on what guidelines are available. To our knowledge, this is the first scoping review to identify the principles and themes in these guidelines, which

**Table 4** Prescriber-related themes

Final theme	Expansion of theme	Suggested practical actions
Conduct comprehensive assessment before prescribing ^{7 8 10 26 29-31 35 45-70}	<ul style="list-style-type: none"> ▶ Conduct comprehensive assessment to understand patient's medical (including assessment for frailty and dementia), psychosocial and functional aspects of health as well as possible prognosis. ▶ The knowledge gathered from comprehensive assessment will guide prescribing decisions. ▶ Consider overall treatment, including using objective measures for clinical improvement as part of regular follow-up, consultations, and monitoring. 	Integrate Comprehensive Geriatric Assessment at intake and/or relevant treatment trajectory points, so that information on patient's medical, psychosocial, and physical function are updated.
Use clinical prescribing tools ^{8 10-12 27-29 31 46 52 55 56 58 60 61 63 68 70-98}	These tools could either assess the quality of medication prescription, aid in identifying PIM or PMO, or advise on optimising medications through a series of evaluation questions.	Integrate use of a prescribing tool for medication review (physicians, pharmacists)
Identify patient's needs, goals and priorities ^{7-10 26 32-35 45 47-56 58 60-63 65-68}	<ul style="list-style-type: none"> ▶ Identify needs, goals, and care priorities from patients' perspectives. ▶ Consider patients' values, health beliefs, characteristics and attitudes towards treatment, treatment goals (including adequacy of symptom control), medication management and adherence, social and economic factors (including costs and affordability of treatment), and care arrangement 	Actively ask patients for their needs, goals and care priorities during clinic consults. This can be facilitated by use of a tool or checklist.
Consider evidence-based recommendations ^{7-10 33 35 45 46 48-51 53-58 60-69}	<ul style="list-style-type: none"> ▶ Apply current evidence to assess or estimate risks and benefits of treatment and the impact on health, quality of life, burden of care and lifestyles. ▶ Recommend non-pharmacological alternatives or reduce unnecessary medical procedures when appropriate. 	<ul style="list-style-type: none"> ▶ Setting up an internal repository that help expand knowledge and to share experiences of clinicians encountering complex prescribing cases. ▶ Incorporate up-to-date evidence on risks and benefits of treatment (where available) when prescribing ▶ Offer and discuss suitable alternatives for treatment where appropriate
Adopt shared decision-making ^{7-9 33 35 45 49 54-56 58-61 65-68 84}	<ul style="list-style-type: none"> ▶ Develop a therapeutic alliance and good patient rapport. ▶ Maintain an open communication with other healthcare professionals involved in patients' care. ▶ Involve patients, caregivers and families in shared decision making with the goal towards an individualised care plan that is aligned to patient's health goals. ▶ Provide patient education and counselling. 	<ul style="list-style-type: none"> ▶ Provide patient and caregivers with adequate information on their clinical condition and associated treatment via education and counselling ▶ Integrate shared-decision making with patients and their caregivers during intake or at relevant treatment trajectory points. ▶ Communicate with other prescribers and healthcare professionals via discussions, progress notes, memos, and so on.
Incorporate multidisciplinary inputs ^{7 8 29 32 49 55 67 68 73}	<ul style="list-style-type: none"> ▶ Obtain multidisciplinary team's input on their evaluations of patient's conditions and care situation. ▶ Consider use of care coordination, integrated care approach. ▶ Consult with experts outside of the core team. 	<ul style="list-style-type: none"> ▶ Refer patient to multidisciplinary team when necessary (eg, Pharmacist review for medication reconciliation at initial presentation to clinic and after each discharge from inpatient admission). ▶ Set up a platform for multidisciplinary input (eg, clinic rounds/discussions)
Embrace technology-enabled prescribing ^{7 8 29-31 33 52}	Use technology in the prescribing and clinical management process, such as alerts to detect potentially inappropriate medications in the electronic health record system, or patient feedback of conditions to physicians.	<ul style="list-style-type: none"> ▶ Set up alerts in electronic health record system on potentially inappropriate medication for older adults. ▶ Encourage use of clinical decision platforms that provide quick review of clinical information via an App

can then be incorporated into the outpatient setting or considered in the design of an intervention to reduce PIP in this vulnerable population.

Gaps in current guidelines

A difficulty with implementing guidelines is the uptake among its potential users. On one hand, it is important to consider quality of a guideline, such as the scope and purpose, stakeholder involvement, rigour of development, clarity of presentation and applicability identified in the Appraisal of Guidelines for REsearch and Evaluation instrument,³⁶ but not knowing what to do could present implementation barriers for healthcare professionals.³⁷

Adding usage or implementation support information could help to increase uptake or use of guidelines.³⁷

One of the key findings from our review is that most guidelines did not incorporate implementation tools for users, even though there is a need for such user guidance.³⁸ While we found that about half of articles described guidelines with some usage information, very few of them included comprehensive implementation information similar to what the National Institute for Health and Care Excellence (NICE) provides for clinical management of multimorbidity to encourage uptake and use of the guidance in clinical practice.⁸ However, this

Table 5 Wider health organisation-related or system-related themes

Final theme	Expansion of theme	Suggested interventions
Education and training on polypharmacy ^{7 10 29 68}	Physicians, pharmacists or other healthcare professionals should receive education or training on geriatric pharmacology/ pharmacotherapy	Provide regular learning or training sessions, based on updated evidence in the literature.
Adapt work environment ²⁹	Adapt the work environment to reduce prescription errors, such as by enhancing the clinical management process (eg, reduce distractions, create a culture of caution).	Adopt a culture of caution, allowing time to routinely review medication prescription lists.
Broader health system related issues ^{7 10 32 33 62 66}	<ul style="list-style-type: none"> ▶ To include and increase research on older adults (eg, randomised controlled trials, improving care models) ▶ To adopt uniform coding of patients' health problems ▶ To consider healthcare cost effectiveness 	Setting up local institutions with cross collaborations to facilitate research at practice settings.
Establishing a clear definition of multimorbidity ^{8 52}	To have a clear definition and understanding of what multimorbidity means, so as to identify the right patient for treatment.	Establish a clear definition of multimorbidity (eg, patient being cared for by at least 3 specialists with >10 daily medications) and identify a way to flag these patients (physicians-identified or via electronic health record system set-up)

could in part be due to our search not capturing some separate publications that provided implementation tools later. For example, applications of STOPP/START³⁹ and the Screening Tool for Older Person's Appropriate Prescriptions for Japanese (STOPP-J)⁴⁰ were further specified and operationalised for clinicians, while Fit for The Aged (FORTA) could be accessed through an App that was developed.⁴¹ On the other hand, about a third of guidelines had information that support discussion with patients, such as information brochures developed specifically for them, as a lack of knowledge of this information may amplify implementation challenges for healthcare professionals.³⁷

Consideration to use a mixed approach

A point to note on the category with an explicit approach is that they are tools that came in the form of lists of PIM or medication clusters that tended to be country specific. Transferability of such tools may be limited by the availability of medications in specific countries.²² However, prescribing appropriateness should not be solely dependent on using drug data as a measure, as the focus should be on using various dimensions of appropriateness.²² The complexity of choosing one medication over another could reduce risk in one aspect but increase harm in another.⁴² Using such tools alone could potentially result in suboptimal decision-making when caring for older adults with multimorbidity.

Nevertheless, thoughtful incorporation of these tools in clinical practice may improve prescribing for older adults with multimorbidity. A study by Blozik *et al* highlighted that although explicit and implicit tools exist, these have not been systematically included in current clinical practice guidelines.⁴³ In response, they recommended cross

referencing such instruments in the care of multimorbid patients.⁴³ As such, adopting a mixed approach might be a way to mitigate short comings in either an implicit or explicit criteria approach. Notably, most of the guidelines formulated by governments or governmental bodies fall into this mixed-approach category. Hence, it would be important to consider incorporating mixed-criteria approach to assist decision-making when prescribing, while providing guidance or steps to facilitate their implementations.

Identifying cross-cutting themes

Examining the themes that are commonly addressed across guidelines helped identify important practical actions and potential interventions to optimise prescribing. Of these themes, five emerged as prevailing recommendations for prescribing and care for older adults with multimorbidity: conduct a comprehensive assessment before prescribing; use clinical prescribing tools; identify patients' needs, goals and priorities; consider evidence-based recommendations; and adopt shared decision-making. These five themes can serve as the minimum recommended prescribing actions that could be adopted by clinical programmes and services delivering outpatient care to older adults with multimorbidity. The remaining themes 'incorporate multi-disciplinary inputs' and 'embrace technology-enabled prescribing' and wider health organization-related and system-related themes were less commonly identified as recommendations, perhaps as prerequisite infrastructure needs to be in place in the practice setting for their adoption. These remaining themes could serve as optional actions, depending on appropriateness to the settings. Thus, reorganising the cross-cutting themes signalled



what could be considered at the microlevel, vis-à-vis themes that are at the mesolevel or macrolevel.

Implications on clinical practice and research

The practical actions and suggested interventions based on the cross-cutting themes reflected how it could look like in an ideal outpatient setting with adequate manpower and resources. A Comprehensive Geriatric Assessment would be routinely done in geriatric clinics, while medication reconciliation and medication review might happen at more ad hoc basis, depending on needs of the patients. However, due to the constant pressure of continuous patient load flow and time/cost constraints, some of the practical actions might not translate to feasible actions.

For example, using an implicit tool such as the Medication Appropriateness Index²⁷ in clinical practice is not appropriate, due to time needed for the review. On the other hand, adopting an explicit tool would have the challenge of applicability, as they are tailored to the medications and formularies of the country where the tool was originally developed. This might require adaptations and tailoring to specific health systems, which require resources. As such, both kinds of prescribing tools might present acceptability and feasibility issues that make their implementations in routine clinical practice challenging. A possible solution could be first using a PIM list of choice that is most applicable to the context of the country of use, if tailored or adapted PIM list is not available. On identification of PIM, further implicit criteria could be applied to those medications, which would provide systematic guidance to the physicians in their prescribing decision-making process.

In addition, the suggested practical actions under 'Consider evidence-based recommendations' require time and resources to be taken away from clinical work. Prior to implementation of the repository, information and resources that clinicians find helpful would first need to be identified, before searching and compilation in the repository. Hence, in order to facilitate use of the practical actions on a day-to-day basis, themes that are most feasible and in need of prioritising should be identified in one's setting. They can then be carried out as an implementation study to understand the process, identifying barriers and facilitators involving stakeholders in context. Although the end outcome of the intervention or practical action might deviate from the original intended version, it might still be worth putting a theme or themes into practice.

Overall, making sense of the heterogeneous information assembled in this review was challenging. The concepts summarised via themes have closely linked practical actions to each other, making it hard to be disentangled. The advantage of separating the themes is the ability to focus on one and not the other, if resources and time are limited. However, because some of the concepts have overlaps and are very much interlinked, implementation of even one of the themes could impact other areas

of needs, potentially facilitating the prescribing process. For example, while highly important, having a separate assessment on patients' needs, goals and priorities in the routine clinical settings might not be practical or feasible. However, some of answers might surface during the Comprehensive Geriatric Assessments, even if direct questions were not asked, which would be helpful information towards a physician's prescribing decisions.

Limitations

Despite using a broad suite of literature search terms, it is still likely that relevant studies were missed, especially by use of filters (language and year). As such, we are likely to have missed earlier guidelines and criteria published, as well as updates or implementation tools that were published separately that were not captured in our search strategy. On the other hand, limiting articles to those published in the previous 20 years ensures their saliency to contemporary prescribing. Thematic synthesis was conducted by one author (PL), which could limit the robustness of interpretation. However, given that data extraction criteria were predetermined, the need for ground interpretations in the coding process was minimised. The subsequent multiple iterative discussions among the reviewers calibrated joint understanding, and the final selection of themes reflects collective judgement. Although the quality of a guideline is an important factor in determining whether it should be implemented in public health,⁴⁴ we did not perform quality appraisal on the guidelines to achieve the goal of including all relevant articles.

CONCLUSIONS

Our scoping review was undertaken to provide a usable knowledge base when developing care interventions to optimise prescribing among older adults with multimorbidity. As implementation of guidelines often presents challenges in clinical settings,³⁷ finding ways to incorporate their elements into clinical improvement initiatives could facilitate greater uptake of published prescribing recommendations. We found 61 unique guidelines that included tools, criteria and approaches with 11 cross-cutting themes to be considered, with practical actions and suggested interventions. The need to employ a mixed approach, incorporating thoughtful use of explicit tools and providing useful implementation information should be strongly considered in efforts to optimise prescribing practices in older adults with multimorbidity.

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ORCID iD

Penny Lun <http://orcid.org/0000-0001-8125-7411>

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Supplementary File 1 – Pubmed Search Strategy

#1	"Aged"[Mesh]
#2	((((aged[Title/Abstract] OR elderly[Title/Abstract] OR senior[Title/Abstract] OR seniors[Title/Abstract] OR older person[Title/Abstract] OR older persons[Title/Abstract] OR older people[Title/Abstract] OR older adult[Title/Abstract] OR older adults[Title/Abstract] OR older patient[Title/Abstract] OR older patients[Title/Abstract])) OR (aged[Text Word] OR elderly[Text Word] OR senior[Text Word] OR seniors[Text Word] OR older person[Text Word] OR older persons[Text Word] OR older people[Text Word] OR older adult[Text Word] OR older adults[Text Word] OR older patient[Text Word] OR older patients[Text Word])))
#3	"Comorbidity"[Mesh]
#4	((((comorbidity[Title/Abstract] OR multimorbidity[Title/Abstract])) OR (comorbidity[Text Word] OR multimorbidity[Text Word])))
#5	#1 OR #2
#6	#3 OR #4
#7	#5 AND #6
#8	((("Inappropriate Prescribing"[Mesh]) OR "Drug Prescriptions"[Mesh]) OR "Potentially Inappropriate Medication List"[Mesh])
#9	((((prescribing[Title/Abstract] OR prescription[Title/Abstract] OR prescriptions[Title/Abstract] OR medication[Title/Abstract] OR medications[Title/Abstract] OR medicine[Title/Abstract] OR medicines[Title/Abstract] OR drug prescription[Title/Abstract] OR drug prescriptions[Title/Abstract] OR inappropriate prescribing[Title/Abstract])) OR (prescribing[Text Word] OR prescription[Text Word] OR prescriptions[Text Word] OR medication[Text Word] OR medications[Text Word] OR medicine[Text Word] OR medicines[Text Word] OR drug prescription[Text Word] OR drug prescriptions[Text Word] OR inappropriate prescribing[Text Word])))
#10	#8 OR #9
#11	Guideline[Publication Type]
#12	((((guideline[Title/Abstract] OR tool[Title/Abstract] OR tools[Title/Abstract] OR guidelines[Title/Abstract] OR checklist[Title/Abstract] OR checklists[Title/Abstract] OR criteria[Title/Abstract] OR list[Title/Abstract] OR lists[Title/Abstract])) OR (guideline[Text Word] OR guidelines[Text Word] OR tool[Text Word] OR tools[Text Word] OR checklist[Text Word] OR checklists[Text Word] OR criteria[Text Word] OR list[Text Word] OR lists[Text Word])))
#13	#11 OR #12
#14	#10 AND #13
#15	#7 AND #14
#16	(#7 AND #14) Filters: Publication date from 1998/01/01 to 2018/12/31; English

Supplementary File 2: Search terms based on PCC

	Terms
Population	<ul style="list-style-type: none">aged, elderly, seniors, older adult(s), older patient(s), older people, older person(s)
Concept	<ul style="list-style-type: none">prescribing, prescription(s), drug prescriptions, medicine(s), inappropriate prescribing, potentially inappropriate medication listguideline(s), list(s), checklist(s), tool(s), criteria
Context	<ul style="list-style-type: none">multimorbidity, comorbidity

Supplementary File 3: Searches in grey literature and key journals

A search for grey literature was carried out in December 2018 with the following resources: World Health Organisation (<http://www.who.int>), Google Scholar (<https://scholar.google.com/>), Google (<https://www.google.com.sg/>), Ministry of Health, Singapore (<https://www.moh.gov.sg/>), SG Press Centre (<https://www.gov.sg/resources/sgpc>), DR-NTU (Open Access) (<https://dr.ntu.edu.sg/>), ScholarBank@NUS (<https://scholarbank.nus.edu.sg/>), using keywords such as 'prescribing guidelines' and 'multimorbidity'.

Electronic-searching of selected key e-journals were also carried out for the following titles: Journal of the American Geriatrics Society, Age and Ageing, The Journals of Gerontology Series A, Archives of Gerontology and Geriatrics, BMC Geriatrics, and European Geriatric Medicine using keywords 'guidelines', 'prescribing guidelines' and 'multimorbidity'.

A search update was then performed in September 2019 for the same set of resources, with the following included in addition to the above-mentioned resources: US Preventive Services Task Force (USPSTF) (<https://www.uspreventiveservicestaskforce.org/>) and GuidelineCentral (<https://www.guidelinecentral.com/>), Clinical Practice Guidelines Archive (<https://www.ahrq.gov/prevention/guidelines/archive.html>), Emergency Care Research Institute (<https://www.ecri.org/about/>) and Institute for Healthcare Improvement (<http://www.ihl.org/>). Keywords such as 'prescribing guidelines' and 'multimorbidity' were used in the search update as well. Electronic-searching of selected key e-journals were also carried out for the above-mentioned titles using keywords 'guidelines', 'prescribing guidelines' and 'multimorbidity'.

Supplementary file 4: Included studies for the review

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Supplementary file 5: List of studies by guideline types

Author, Year	Title
1) Implicit Criteria	
Barnett et al, 2015	Patient-centred management of polypharmacy: a process for practice
Boyd et al, 2019	Decision Making for Older Adults With Multiple Chronic Conditions: Executive Summary for the American Geriatrics Society Guiding Principles on the Care of Older Adults With Multimorbidity
Burt et al, 2018	Developing a measure of polypharmacy appropriateness in primary care: systematic review and expert consensus study
Drenth-van Maanen et al, 2009	Prescribing Optimization Method for Improving Prescribing in Elderly Patients Receiving Polypharmacy: Results of Application to Case Histories by General Practitioners
Durso, 2007	Prioritizing care for older adults with multiple comorbidities: Working in the 'zone of complexity'
Garfinkel et al, 2015	Routine deprescribing of chronic medications to combat polypharmacy
Hilmer et al, 2012	Thinking through the medication list - appropriate prescribing and deprescribing in robust and frail older patients
American Geriatrics Society, 2012 ¹	Patient-Centered Care for Older Adults with Multiple Chronic Conditions: A Stepwise Approach from the American Geriatrics Society
American Geriatrics Society, 2012 ¹	Guiding Principles for the Care of Older Adults with Multimorbidity: An Approach for Clinicians
Muth et al, 2014	The Ariadne principles: how to handle multimorbidity in primary care consultation
Palmer et al, 2018	Multimorbidity care model: Recommendations from the consensus meeting of the Joint Action on Chronic Diseases and Promoting Healthy Ageing across the Life Cycle (JA-CHRODIS)
Scott et al, 2015	Reducing Inappropriate Polypharmacy: The Process of Deprescribing
Sinott et al, 2015	What to give the patient who has everything? A qualitative study of prescribing for multimorbidity in primary care
Todd et al, 2018	The deprescribing rainbow: a conceptual framework highlighting the importance of patient context when stopping medication in older people
Wilson et al, 2015	Prescribing to fit the needs of older people - the NHS Scotland Polypharmacy Guidance, 2nd edition
Best Practice Advocacy Centre	Polypharmacy in primary care: Managing a clinical conundrum

NZ, 2014	
Tully et al, 2005	Development and Face Validity of Explicit indicators of Appropriateness of Long Term Prescribing
Lewis, 2004	Using the NO TEARS tool for medication review
Hanlon and Schmader, 2013	The Medication Appropriateness Index at 20: Where It Started, Where It Has Been, and Where It May Be Going
2) Explicit Criteria	
Winit-Watjana et al, 2008	Criteria for high-risk medication use in Thai older patients
Van der Linden et al, 2014	Development and validation of the RASP list (Rationalization of Home Medication by an Adjusted STOPP list in Older Patients): A novel tool in the management of geriatric polypharmacy
Tommeiein et al, 2015	Older patients' prescriptions screening in the community pharmacy: development of the Ghent Older People's Prescriptions community Pharmacy Screening (GheOP3S) tool
Rognstad et al, 2009	The Norwegian General Practice (NORGE) criteria for assessing potentially inappropriate prescriptions to elderly patients
Rodriguez-Pérez et al, 2017	Novel tool for deprescribing in chronic patients with multimorbidity: List of Evidence-Based Deprescribing for Chronic Patients criteria
Renom-Guiteras et al, 2015	The EU(7)-PIM list: A list of potentially inappropriate medications for older people consented by experts from seven European countries
Mann et al, 2012	Potentially inappropriate medication in geriatric patients: the Austrian consensus panel list
Maio et al, 2010	Using explicit criteria to evaluate the quality of prescribing in elderly Italian outpatients: a cohort study: Prescribing in elderly outpatients
Laroche et al, 2007	Potentially inappropriate medications in the elderly: a French consensus panel list
Kojima et al, 2016	Screening Tool for Older Persons' Appropriate Prescriptions for Japanese: Report of the Japan Geriatrics Society Working Group on "Guidelines for medical treatment and its safety in the elderly"
Kim et al, 2015	Consensus Validated List of Potentially Inappropriate Medication for the Elderly and Their Prevalence in South Korea
Kim et al, 2010	Development of a List of Potentially Inappropriate Drugs for the Korean Elderly Using the Delphi Method
Holt et al, 2010	Potentially Inappropriate Medications in the Elderly
Chang et al, 2012	Using published criteria to develop a list of potentially inappropriate medications for elderly patients in Taiwan
Bachyrycz et al, 2012	Development and Dissemination of a Statewide System to Minimize Use of Potentially Inappropriate

	Medications (PIMs)
The American Geriatrics Society Beers Criteria Update Expert Panel, 2019 ²	American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults
The American Geriatrics Society Beers Criteria Update Expert Panel, 2015 ²	American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults
The American Geriatrics Society Beers Criteria Update Expert Panel, 2012 ²	American Geriatrics Society Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults
Fick et al, 2003 ²	Updating the Beers Criteria for Potentially Inappropriate Medication Use in Older Adults: Results of a US Consensus Panel of Experts
Wehling, 2015 ³	How to Use the FORTA ("Fit fOR The Aged") List to Improve Pharmacotherapy in the Elderly
Wehling et al, 2016 ³	VALFORTA: a randomised trial to validate the FORTA (Fit fOR The Aged) classification
Kuhn-Thiel et al, 2014 ³	Consensus validation of the FORTA (Fit for the Aged) List: A clinical tool for increasing the appropriateness of pharmacotherapy in the elderly
Pazan et al, 2018	The EURO-FORTA (Fit fOR The Aged) List: International Consensus Validation of a Clinical Tool for Improved Drug Treatment in Older People
O'Mahony et al, 2010 ⁴	STOPP & START criteria: A new approach to detecting potentially inappropriate prescribing in old age
O'Mahony et al, 2015 ⁴	STOPP/START criteria for potentially inappropriate prescribing in older people: version 2
Hill Taylor et al, 2013 ⁴	Application of the STOPP/START criteria: a systematic review of the prevalence of potentially inappropriate prescribing in older adults, and evidence of clinical, humanistic and economic impact
Herefordshire Clinical Commissioning Group, 2016	STOPP START Toolkit Supporting Medication Review
3) Mixed criteria	
Bergman-Evans & Adams, 2006	Evidence-based Guideline Improving medication management for older adults clients
Lavan et al, 2016	Methods to reduce prescribing errors in elderly patients with multimorbidity
Mangin et al, 2018	International Group for Reducing Inappropriate Medication Use & Polypharmacy (IGRIMUP): Position

	Statement and 10 Recommendations for Action
Marengoni, 2015	Best Practices for Drug Prescribing in Older Adults: A Call for Action
NICE, 2016	Multimorbidity: clinical assessment and management
All Wales Medicines Strategy Group, 2014	Polypharmacy: Guidance for Prescribing
Sarkar, 2017	Geriatric Poly-Pharmacy: A Growing Epidemic. How to Prevent It?
Scottish Government Polypharmacy Model of Care Group, 2018	Polypharmacy Guidance: Realistic prescribing 3rd edition, 2018.
Sergi et al, 2011	Polypharmacy in the elderly: Can comprehensive geriatric assessment reduce inappropriate medication use?
Sivagnanam, 2016	Deprescription: The prescription metabolism
The Guidelines group of Hesse, 2014	Recommendations for treating adult and geriatric patients on multimедication
Vrdoljak & Borovac, 2015	Medication in the elderly - considerations and therapy prescription guidelines
Department of Health UK, 2001	Medicines and older people-implementing medications-related aspects of the NSF for older people
Lenaerts et al, 2013	Appropriate prescribing for Older people: A new tool for General Practitioner
Drenth-van Maanen, 2017	The Systematic Tool to Reduce Inappropriate Prescribing (STRIP): Combining implicit and explicit prescribing tools to improve appropriate prescribing
Basger et al, 2012 ⁵	Validation of prescribing appropriateness criteria for older Australians using the RAND/UCLA appropriateness method
Basger et al, 2008 ⁵	Inappropriate Medication Use and Prescribing Indicators in Elderly Australians: Development of a Prescribing Indicators Tool
4) Others	
Muche-Borowski et al, 2017	Development of a meta-algorithm for guiding primary care encounters for patients with multimorbidity using evidence-based and case-based guideline development methodology
Schippinger et al, 2018	Optimizing medical care for geriatric patients in Austria: defining a top five list of “Choosing Wisely” recommendations using the Delphi technique
Roughead et al, 2011	Multimorbidity, care complexity and prescribing for the elderly

Rieckert et al, 2018	Reduction of inappropriate medication in older populations by electronic decision support (the PRIMA-eDS study): a qualitative study of practical implementation in primary care
Niehoff et al, 2016	Development of the Tool to Reduce Inappropriate Medications (TRIM): A Clinical Decision Support System to Improve Medication Prescribing for Older Adults
Van Summeren et al, 2017	Outcome prioritisation tool for medication review in older patients with multimorbidity: a pilot study in general practice
Vetrano et al, 2017	An International Perspective on Chronic Multimorbidity: Approaching the Elephant in the Room

¹⁻⁵ only counting once for each unique tool for summary under information on guidelines