

Focus and features of prescribing indications spanning multiple chronic conditions in older adults: A narrative review

Journal of Multimorbidity and Comorbidity

Volume 11: 1–11

© The Author(s) 2021

Article reuse guidelines:

sagepub.com/journals-permissions

DOI: 10.1177/26335565211012876

journals.sagepub.com/home/cob



Carole E Aubert^{1,2,3,4} , Eve A Kerr^{3,4,5}, Mandi L Klamerus³,
Timothy P Hofer^{3,4,5} and Melissa Y Wei^{4,5,6}

Abstract

Background: Inappropriate prescribing is frequent in older adults and associated with adverse outcomes. Prescribing indications aim to optimize prescribing, but little is known about the focus and features of prescribing indications for the most common chronic conditions in older adults. Understanding the conditions, medications, and issues addressed (e.g., patient perspective, drug-disease interaction, adverse drug event) in current prescribing indications may help to identify missing indications and develop standardized measures to improve prescribing quality.

Methods: We searched Ovid/MEDLINE and EMBASE for articles published between 2015 and 2020 reporting prescribing indications for older adults. Prescribing indication included 1) prescribing “criteria,” or statements that guide prescribing action, and 2) prescribing “measures,” or prescribing actions observed in a population. We categorized their focus by conditions, medications and issues addressed, as well as level of evidence provided.

Results: Among 16 sets of prescribing indications, we identified 748 criteria and 47 measures. The most common addressed medications were antihypertensives, analgesics/antirheumatics, and antiplatelets/anticoagulants. The most frequently addressed issues were drug-disease interaction, adverse drug event, administration, better therapeutic alternative, and (co-)prescription omission (20.8–36.1%). Age/functioning, drug-drug interaction, monitoring, and efficacy/safety ratio were found in only 9.9–16.5% of indications. Indications rarely focused on the patient perspective or issues with multiple providers.

Conclusion: Most prescribing indications for chronic conditions in older patients are criteria rather than measures. Indications accounting for patient perspective and multiple providers are limited. The gaps identified in this review may help improve the development of prescribing measures for older adults and ultimately improve quality of care.

Keywords

Criteria, prescribing, measure, older adults, multimorbidity

Received 20 January 2021; accepted: 6 April 2021

¹ Department of General Internal Medicine, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland

² Institute of Primary Health Care (BIHAM), University of Bern, Bern, Switzerland

³ Center for Clinical Management Research, Veterans Affairs Ann Arbor Healthcare System, Ann Arbor, MI, USA

⁴ Institute for Healthcare Policy and Innovation, University of Michigan, Ann Arbor, MI, USA

⁵ Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA

⁶ Department of Medicine, David Geffen School of Medicine at the University of California, Los Angeles, CA, USA

⁷ Center for Healthcare Innovation, Implementation and Policy, Greater Los Angeles VA Healthcare System, Los Angeles, CA, USA

Corresponding author:

Carole E Aubert, Department of General Internal Medicine, Inselspital, Bern University Hospital, Freiburgstrasse, CH-3010 Bern, Switzerland.

Email: caroleelodie.aubert@insel.ch



Creative Commons Non Commercial CC BY-NC: This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 License (<https://creativecommons.org/licenses/by-nc/4.0/>) which permits non-commercial use, reproduction and distribution of the work without further permission provided the original work is attributed as specified on the SAGE and Open Access pages (<https://us.sagepub.com/en-us/nam/open-access-at-sage>).

Introduction

Prescribing is a core element in the chronic care of older patients, particularly among those with multimorbidity. Inappropriate prescribing, including the use of inappropriate medications, prescribing omissions, drug-drug or drug-disease interactions, and prescribing cascades, has been associated with adverse outcomes.^{1,2} Inappropriate prescribing and adverse drug events are particularly frequent in older adults, given the high prevalence of polypharmacy and multimorbidity in this population.^{3,4} Older patients are particularly vulnerable to adverse drug events because of altered pharmacokinetics and pharmacodynamics with aging.⁵ Further, the use of single-disease focused guidelines will inevitably exacerbate polypharmacy when they are simultaneously applied to older patients with multimorbidity.^{6,7}

Prescribing indications for older patients have been developed in attempt to optimize prescribing practices (e.g., prevent inappropriate polypharmacy). These indications include: 1) prescribing “criteria,” which are statements that guide prescribing action, and 2) prescribing “measures” (or indicators), which are prescribing actions observed in a population. Prescribing criteria include statements such as “stop concomitant use of ≥ 2 drugs with anticholinergic properties” and have been promoted in lists or compendiums of medications to avoid, such as the Screening Tool of Older Person’s Prescriptions and Screening Tool to Alert to Right Treatment (STOPP/START) Criteria or the American Geriatrics Society Beers Criteria.^{8,9} Prescribing measures include statements such as “percentage of patients aged >65 years who have been prescribed ≥ 2 drugs with anticholinergic effects concomitantly” and have been promoted by organizations like the National Committee for Quality Assurance (NCQA) and the National Institute for Health and Care Excellence Quality and Outcomes Framework (NICE QOF).^{10,11} While the term “prescribing indications” is most frequently used to describe for which conditions or in which situations a medication should be prescribed, in the current review, we use this term to describe specifically prescribing criteria and measures that have been developed to improve prescribing practices.

Non-adherence with prescribing indications has been associated with adverse outcomes.¹² However, to our knowledge, prescribing indication sets have not yet been broadly implemented in clinical practice, and inappropriate prescribing persists as a considerable problem worldwide. Unlike criteria that are simple recommendations, measures can be used to track and provide feedback on appropriate prescribing.¹³ They are thus more likely to impact prescribing practices than criteria alone, unless criteria are transformed into measures.^{14–18} It is thus important to have prescribing measures for dimensions likely to influence quality and safety for older patients, particularly those with multimorbidity. Such dimensions may extend beyond

condition and medication type to include more clinically cross-cutting issues such as potential for drug-drug or drug-disease interactions, need for monitoring, influence of age or functioning, and need for patient input. However, we currently lack systematically synthesized information about the dimensions and issues covered by existing prescribing criteria and measures, and whether the measures that exist cover the broad range of dimensions. Such information could guide development of future measures and interventions to improve a broad range of prescribing practices for chronic conditions.

Thus, the three aims of this review are to: 1) identify recently developed or updated sets of prescribing indications (i.e., criteria and measures) applicable to chronic medication prescribing for the most common and clinically significant chronic conditions among older adults; 2) assess the domains covered by the prescribing indications, and more specifically by the prescribing measures, particularly given their potential larger impact on prescribing practices compared with criteria; and 3) describe and categorize the focus of the indications based on conditions, medications, issues addressed (e.g., drug-drug interaction, patient perspective, monitoring), and evidence provided.

Methods

Search strategy

We performed a literature search in Ovid/MEDLINE and EMBASE for articles published between January 1, 2015, and May 20, 2020 that reported prescribing indications for chronic medications applicable to the ambulatory care of adults aged 65 years or older, including medications to stop and medications to start (detailed search strategy in Supplementary Text S1). We limited the search to 2015 to focus on the most recent or updated evidence. Prescribing indications included 1) prescribing “criteria,” or statements that guide prescribing action, and 2) prescribing “measures,” or prescribing actions observed in a population.¹⁹ We reviewed articles that published indications based on guidelines but not disease-specific guidelines directly from specialty societies. However, we included single disease-specific sets of indications.

We first selected all publications with at least one prescribing indication that met the inclusion criteria. For each article that only used previously developed indications, we searched the reference list to identify the article that described the actual indication development. We retained that article if it was published in 2015 or later and had not yet been identified through the initial literature search. From the prescribing sets included in the review, we selected only indications related to one or more of the following prevalent and clinically significant chronic conditions in older adults: cognitive impairment/Parkinson’s disease; depression and anxiety; sleep problems; chronic obstructive pulmonary disease and asthma; atrial

fibrillation; heart failure; ischemic cardiac, peripheral, or cerebral vascular disease; hypertension; diabetes mellitus; osteoporosis; thyroid disorders; peptic-related conditions; non-peptic gastrointestinal conditions; urinary disorders (including urinary incontinence, urinary retention, and prostate disorders); and pain and rheumatic disorders. If a prescribing set included indications for those conditions, as well as other conditions, we retained only the indications specific to the above-mentioned conditions. We included indications that did not mention a specific condition if the medication could be used to treat one of the selected conditions (e.g., “stop benzodiazepines”). Finally, we included indications that were not medication-specific (e.g., “stop any duplicate medication”). We categorized the prescribing indications according to conditions mentioned in the indication (when mentioned) and conditions that could be treated by the specific medication. An indication could thus be categorized in several different categories (e.g., “stop benzodiazepines” was classified in “depression/anxiety” and “sleep problems”).

Data extraction

The first author (CEA) conducted the literature search and extracted the data using a standardized database in Microsoft Access (Microsoft Office Professional Plus 2016). The following information was extracted for each article: title, first author, publication year, development location, name of the criteria or measure set when available, prescribing indication type (criteria or measures), development method (literature review, expert suggestion of indications, adaptation from previous list, patient interview, expert panel through RAND Appropriateness Method or other method²⁰), rationale for including a prescribing indication (applicability to a specific population or setting, clinical importance, level of evidence), and whether evidence was provided and/or graded. Data collected on each individual indication included the conditions, medications and issues addressed, level of evidence, and whether the indication was adapted from an indication listed in another set.

We classified medications into the following groups: dementia and Parkinson’s disease medications; antipsychotics; antidepressants; hypnotics (including benzodiazepines, nonbenzodiazepines, sedative antihistamines and other sleep medications); pulmonary medications; antiarrhythmics; antihypertensives; lipid-lowering medications; antiplatelets/anticoagulants; antidiabetics (including insulin); osteoporosis medications (including calcium, vitamin D and antiresorptive agents); thyroid medications; proton pump inhibitors and antacids; other gastrointestinal medications; urinary medications; anticholinergics; analgesics/antirheumatics; and oral corticosteroids. Some indications applied to all medications (e.g., “avoid any duplicate prescription”) and were thus not

classified in a specific medication group (classified as “Not specific” thereafter).

When available in the prescribing sets, the quality of evidence was captured as: 1) GRADE (Grading of Recommendations Assessment, Development, and Evaluation) category,²¹ 2) strength of the recommendation according to the Institute of Medicine (IOM) guidelines,²² and/or 3) reference or type of study provided with the criteria or measure (review or meta-analysis, randomized controlled trial, observational study, guidelines, medication formulary, textbook, previous set of indications).

Categorization of the prescribing indications

First, to identify whether the focus was to avoid, adapt, or start medications, we classified each indication into one or more of the following broad categories: 1) medication or medication combination to always avoid, or to avoid for a specific indication (e.g., “stop beta-blocker in combination with verapamil or diltiazem,” “stop diuretic as first-line treatment for hypertension”); 2) medication to avoid in the presence of a specific disease or condition (e.g., “stop thiazolidinediones in patients with documented heart failure,” “avoid antipsychotics in patients with history of falls”); 3) medication potentially inappropriate unless modifying the dose and/or timing (e.g., “reduce colchicine dose by 50% in older adults or in case of renal failure,” “administer terazosin at bedtime”); 4) medication to start, including co-medications, i.e. joint prescription of two medications required (e.g., “start laxatives in patients receiving opioids regularly,” “start vitamin K antagonists or direct thrombin inhibitors or factor Xa inhibitors in the presence of chronic atrial fibrillation”).

Second, we defined more detailed categories to capture how each indication addressed issues most relevant for appropriate prescribing in older adults, including issues related to the patients, prescribers, medications, and conditions. We assessed whether each indication focused on one or more of the following: 1) patient perspective (preferences, satisfaction, shared-decision making); 2) prescribing by multiple providers; 3) administration (dose, treatment duration, timing, formulation); 4) adverse drug event; 5) age, life expectancy, cognitive or physical functioning; 6) better therapeutic alternative; 7) drug-drug interaction/inappropriate medication combination; 8) drug-disease interaction whereby a disease or condition renders the medication inappropriate, or requires renal dose adjustment (e.g., “thiazolidinediones with documented heart failure,” “metformin if creatinine clearance <30ml/min”); 9) efficacy/safety ratio; 10) monitoring; 11) prescription or co-prescription omission (e.g., “co-prescribe laxative with opioids”).

When similar indications referring to medications of the same group were listed separately (e.g., each tricyclic antidepressant in the EU(7)PIM list),²³ we combined them to eliminate repetition and increase comparability with other

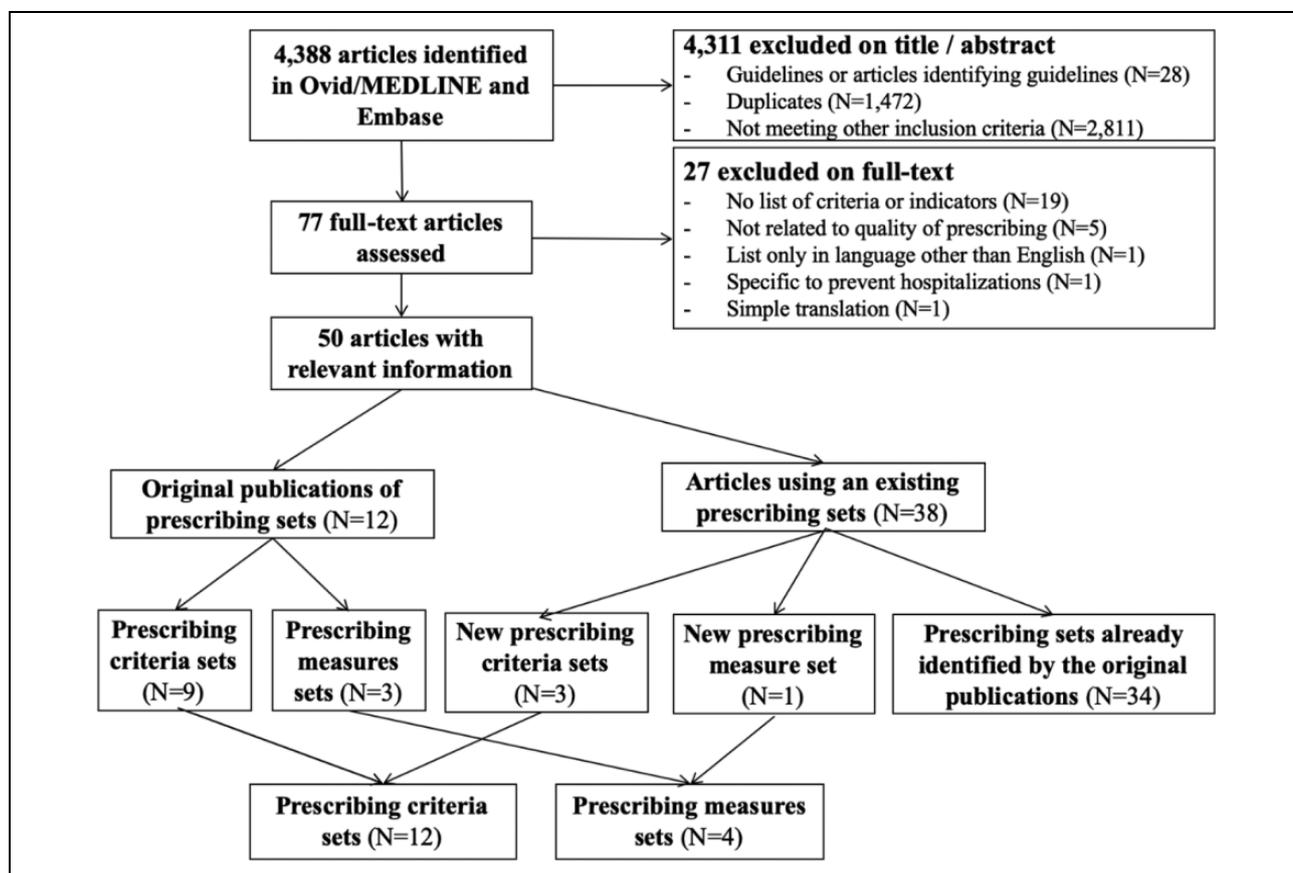


Figure 1. Flow-chart of search result.

prescribing sets that already combined such indications (e.g., the Beers criteria).⁸

Data analysis

For each individual indication, we summarized the number of conditions, medications, and issues addressed. We described frequencies as the percentage of prescribing sets (number of prescribing sets with a characteristic, relative to the total number of prescribing sets), and the percentage of indications (number of indications with a particular characteristic, relative to the total number of indications). We used Stata 16 software (Stata-Corp LP, College Station, TX, USA) for all analyses.

Results

Selection of prescribing sets

We excluded 4,311 out of 4,388 articles identified in Ovid/MEDLINE and EMBASE after review of the title and/or abstract, and 27 additional articles upon full-text review (Figure 1). The 50 remaining articles yielded 16 sets of indications, including 12 sets of prescribing criteria,^{8,9,23–33}

and 4 sets of prescribing measures.^{10,19,34,35} Four of these 16 sets were identified by searching the references of studies employing the indications.^{10,28,29,33}

General characteristics of prescribing sets

Among the 16 sets of indications, 11 (68.8%) were specifically developed for older adults,^{8,9,23–25,27–31,33} and only 1 (6.3%) was developed for multimorbid patients.³² None of the sets was specifically developed for adults in advanced aged groups (e.g., ≥ 75 years old) or older adults with frailty. We extracted 795 indications from these sets (median 50, range 2–123 indications by prescribing set), including 748 (94.1%) prescribing criteria and 47 (5.9%) measures. Many indications addressed similar issues but none were identical (same wording or reference). All indications were developed based on literature review (Table 1). Two sets were based only on guidelines.^{10,35} One study also used patient interviews.²⁹ Seven sets, encompassing 421 (53.0%) prescribing indications, were developed in Europe. Evidence was provided through publication references in 475 (62.5%) indications and the GRADE system and strength of recommendation in 117 (14.7%) indications from 2 (12.5%) prescribing sets^{8,28} (Supplementary Table S1). Among 795 indications, 316 (39.8%) were adapted

Table 1. General description of the indications and prescribing sets.

	N (%) of 795 indications	N (%) of 16 sets
General characteristics		
Prescribing criteria (i.e., not a measure)	748 (94.1)	12 (75.0)
<i>Indications of:</i>		
Medication to start ^a	159 (20.0)	14 (87.5)
Medication to always avoid or to avoid for a specific indication ^b	368 (46.3)	14 (87.5)
Medication to avoid with a specific disease or condition ^c	228 (28.7)	13 (81.3)
Potentially inappropriate medication ^d	106 (13.3)	8 (50.0)
Continent of development		
Europe	421 (53.0)	7 (43.8)
Asia	231 (29.1)	5 (31.3)
North America	85 (10.7)	2 (12.5)
South America	21 (2.6)	1 (6.2)
Australia	37 (4.6)	1 (6.2)
Method of development		
Literature review	NA	16 (100.0)
Uptake/adaptation from previous list(s)	316 (39.8)	8 (50.0)
Uptake/adaptation of guidelines only	30 (3.8)	2 (12.5)
Expert panel	690 (86.8)	12 (75.0)
Patient interviews	102 (10.8)	1 (6.2)
Characteristics for inclusion in the set of prescribing indications		
Applicability to population/setting	NA	9 (56.3)
Clinical importance	NA	9 (56.3)
Evidence	NA	12 (75.0)
Evidence		
Provided	510 (64.2)	10 (62.5)
Graded	117 (14.7)	2 (12.5)

Legend: NA (not available) is mentioned for the indications when the information was not specified for each indication, but only provided as general information in the prescribing set.

^aIncludes potential prescribing omission, and co-prescription required because of another medication.

^bIncludes age-related measures, or measures related to medication combination (e.g., “stop beta-blocker in combination with verapamil or diltiazem”; “avoid statin for primary prevention based on age as single risk factor”).

^cRelated to a medication in the presence of a specific disease or severity of disease (e.g., “stop beta blocker with symptomatic bradycardia (<50/min), type II heart block or complete heart block”).

^dMedication potentially inappropriate if there is no adaptation of administration (dose reduction according to renal function, dose adaptation because of a co-medication, administration timing, e.g. “reduce colchicine dose by 50% in older adults or in case of renal failure”; “administer terazosin at bedtime”).

from a previous list of criteria, most often from the STOPP/START or Beers criteria. Further details on the prescribing sets are provided in Supplementary Table S1.

Chronic conditions and chronic medications addressed in the indications

The number of conditions addressed in each single indication ranged from 1 to 9 (mean 1.7), and the number of medications ranged from 1 to 11 (mean 1.5). Pain and rheumatic disorders were the most frequent focus, appearing in 167 (21.0%) indications (Figure 2, Supplementary Table S2, Supplementary Figure S1). Hypertension, depression/anxiety, cognitive impairment/Parkinson’s disease, heart failure, vascular disorders, atrial fibrillation, and sleep problems were addressed in 10.2–16.0% of all indications. Only 15 (1.9%) indications were not condition specific. Thyroid disorders were least frequently addressed (8 [1.0%] indications). Of note, two prescribing sets focused on a single problem (pain/inflammation and

glucocorticoid-induced osteoporosis).^{30,35} Antihypertensives were the most frequently addressed medications (18.6% of indications), followed by analgesics/antirheumatics (18.1%), antiplatelets/anticoagulants (11.4%) and antidepressants (10.9%) (Figure 2, Supplementary Table S2, Supplementary Figure S1). All other medication groups were addressed in less than 10% of the indications. Only 16 (2.0%) indications were not specific to a medication.

Issues addressed in the indications

Each indication focused on one or more of the following: medications to always avoid (368 [46.3%] indications), medications to avoid with a specific condition (228 [28.7%]), potentially inappropriate medications (106 [13.3%]), and medication to start (159 [20.0%]) (Table 1). We provide the issues addressed in the indications (Table 2), and numbers of indications addressing each issue in each prescribing set (Supplementary Table S3).

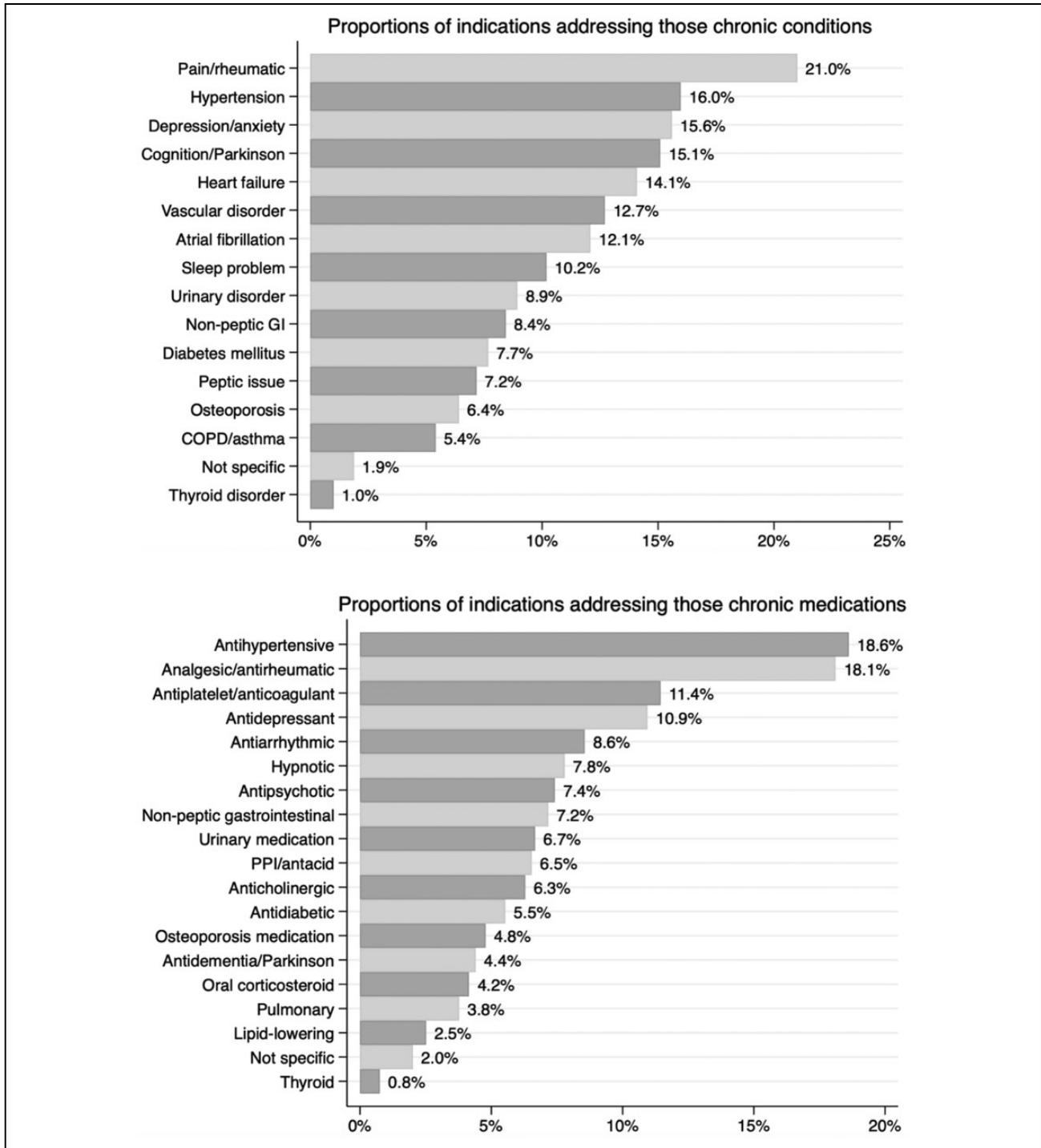


Figure 2. Proportions of indications (N = 795) addressing specific chronic conditions and medications. Abbreviations: COPD; chronic obstructive pulmonary disease; GI, gastrointestinal; PPI, proton pump inhibitor. Legend: Conditions and medications are listed by decreasing prevalence. Percentages are proportions of all indications (N = 795). Antidementia include medications for Parkinson's disease. Osteoporosis medication includes calcium/vitamin D and antiresorptive agents. "Not specific" means that the indication does not address a particular condition or medication (e.g., "Avoid any duplicate medication").

The indications focused primarily on drug-disease interactions (287 [36.1%]), adverse drug events (231 [29.1%]), administration (215 [27.0%]), better therapeutic alternatives (214 [26.9%]), and (co-)prescription omission (165 [20.8%]) (Table 2). Age/life expectancy/functioning,

drug-drug interaction/inappropriate medication combination, monitoring, and efficacy/safety ratio were addressed in 9.9% to 16.5% of all indications. Only 4 (0.5%) indications were related to patient perspective, and none addressed prescribing by multiple providers.

Table 2. Issues addressed in the indication, with examples.

Indication focus and examples (reason)	N (%) of indications
Drug-disease interaction	287 (36.1)
Avoid thiazolidinediones in heart failure with reduced ejection fraction (promote fluid retention and exacerbate heart failure) Stop beta-blockers in diabetes mellitus with frequent hypoglycemic episodes (risk of suppressing hypoglycemic symptoms) Stop metformin if creatinine clearance <30ml/min (risk of lactic acidosis)	
Adverse drug event	231 (29.1)
Stop benzodiazepines (sedative, may cause reduced sensorium, impair balance) Stop neuroleptic drugs (may cause ataxia, Parkinsonism) Avoid peripheral alpha-1 blockers (high risk of orthostatic hypotension; not first-line treatment for hypertension)	
Administration ^a	215 (27.1)
Magnesium hydroxide: maximum dose 5ml/8 h Avoid proton pump inhibitor >8 weeks (long-term high dose associated with <i>Clostridium difficile</i> infection and hip fracture) Avoid use of inhalation corticosteroid as “if necessary” in chronic obstructive pulmonary disease/asthma	
Better therapeutic alternative (explicitly mentioned in the indication)	214 (26.9)
Stop loop diuretic as first-line treatment for hypertension (safer, more effective alternatives available; lack of outcome data) Avoid oral corticosteroids for osteoarthritis (safer alternatives available; unnecessary exposure to systemic side-effects) Stop theophylline as monotherapy for COPD (safer, more effective alternative; narrow therapeutic index)	
New (co-)prescription ^b	165 (20.8)
Start antidepressant treatment in the presence of major depressive disorder Start xanthine-oxidase inhibitors (e.g., allopurinol, febuxostat) with a history of recurrent episodes of gout Recommend vitamin D analogs alone for men/women <50 years with ≥ 7.5 mg/day prednisolone (or equivalent) for ≥ 3 months ^c	
Age/life expectancy/functioning ^d	131 (16.5)
Avoid statins in primary cardiovascular protection in patients with low life expectancy (<2 years) or advanced dementia Avoid pioglitazone (age-related risks include bladder cancer, fractures and heart failure) Avoid opioids with history of falls or fractures (may cause ataxia, impaired psychomotor function, syncope, falls)	
Medication interaction/inappropriate combination	114 (14.3)
Stop beta-blocker in combination with verapamil or diltiazem (risk of heart block) Avoid warfarin with non-steroidal anti-inflammatory drug (increased risk of bleeding) Stop concomitant use of ≥ 2 drugs with anticholinergic properties (risk of increased anticholinergic toxicity)	
Monitoring ^e	93 (11.7)
The percentage of patients with hypothyroidism with thyroid function tests recorded in the preceding 12 months ^c Deprescribe acetylsalicylic acid for primary prevention if age as only risk factor. Monitor for acute coronary syndrome Deprescribe bisphosphonates for primary prevention after 5 years of treatment. Monitor for new fracture over 1 year	
Efficacy/safety ratio ^f	79 (9.9)
Avoid digoxin for heart failure with preserved systolic ventricular function (no clear evidence of benefit) Avoid prasugrel (unfavorable risk/benefit profile, especially for adults aged 75 years and older) Stop any drug prescribed without an evidence-based clinical indication	
Patient perspective ^g	4 (0.5)
The patient was not asked which aspects of pharmaceutical care could be improved for him/her Start statin therapy for secondary prevention in patients with documented atherosclerotic artery. In patients with life expectancy <2 years, terminal dementia, or > 85 years (less likely to benefit, side effects), treatment should be decided by informing the patient/relatives with the shared decision-making principle	

Legend: Issues are classified by decreasing prevalence. The reason associated with the indication is displayed in parentheses, when available. An indication could address several different issues.

^aIncludes issues related to administration timing, dosage, treatment duration, medication formulation.

^bIncludes potential prescribing omissions and co-prescription required because of another medication.

^cPrescribing measure (all others are prescribing criteria).

^dIncludes indications related to cognitive function and physical condition.

^eClinical or paraclinical monitoring. Includes issues related to narrow therapeutic index.

^fNo proven efficacy, or questionable efficacy/safety profile, as defined by FORTA class C: “Drugs with questionable efficacy/safety profiles in the elderly which should be avoided or omitted in the presence of too many drugs, absence of benefits or emerging side effects; explore alternatives.”³¹

^gIncludes patient preferences, satisfaction, and shared-decision making.

Discussion

Among 16 sets of prescribing indications for common and clinically significant chronic conditions in older adults identified through this literature review, most were criteria, while quality measures represented less than 6% of indications. The most frequently addressed medications were antihypertensives, analgesics/antirheumatics, antiplatelets/anticoagulants, and antidepressants. Most indications focused on drug-disease interactions, adverse drug events, administration, availability of a better therapeutic alternative, and (co-)prescription omission. Prescribing indications that considered patient perspectives were rare, and prescribing by multiple healthcare providers was not addressed.

Several key themes emerged from this review. First, we identified numerous prescribing criteria for older adults, but relatively few quality measures. Prescribing criteria, similar to other recommendations to decrease low-value care (e.g., Choosing Wisely),³⁶ are an important first step to improve appropriate prescribing and deprescribing. However, criteria have not yet yielded broad changes in clinical practice.³⁷ This could be due to the absence of a systematic implementation approach, lack of specificity in the indications to support point-of-care decision-making, disagreement with the indications by patients and/or providers, or lack of incentive for noncompliant prescribers.³⁷ Future initiatives should include strategies to facilitate implementation. Performance measures should also be developed, in addition to prescribing criteria, since they have greater specificity and potential to impact prescribing practices.¹³

Second, monitoring was rarely addressed in the indications. Only one prescribing set systematically addressed this issue.³² However, clinical and/or paraclinical monitoring is critical for starting or discontinuing a medication. This includes identifying adverse events due to a new medication, tapering according to withdrawal symptoms, and tracking reemergent symptoms after a medication is discontinued.³⁸ Prescribing indications for chronic conditions are more likely to be successfully implemented and sustained if they specify a clear monitoring and tapering plan to guide providers and patients. Future measures should consider this crucial issue.

Third, most indications focused on potentially inappropriate prescribing, with almost a quarter addressing drug-disease interaction, while only 20% of indications focused on when to start a medication. This suggests greater awareness that doing “more” by prescribing more medications is not always better³⁹ for older adults, especially those with multimorbidity. Prescribing indications that specifically address multimorbidity, age and life expectancy, may improve appropriate prescribing and deprescribing, while applying single disease-based guidelines based on trials that often excluded multimorbid patients,^{40,41} and that focus on treatment intensification

rather than deintensification,⁴² may be inappropriate and detrimental to such patients.^{6,7}

Fourth, prescribing by multiple providers was not addressed, despite that older adults with multimorbidity usually have several specialist providers. Specialists often focus on optimizing single conditions in isolation and may thus overprescribe or inappropriately prescribe particularly in patients with multimorbidity and polypharmacy. Primary care physicians remain critical in these patients because of their predominant role in managing multimorbidity, prescribing chronic medications, and maintaining accurate medication reconciliation. Future prescribing indications should be developed specifically for multimorbid patients and address challenges due to multiple providers.

Patient perspective was also rarely addressed in the indications, whereby only one study used patient interviews to develop indications.²⁹ Patient preferences on topics such as administration time, pharmaceutical formulation, and tapering plan, and active involvement to monitor adverse drug events or withdrawal symptoms of medication discontinuation, are critical for most prescribing issues and should be addressed in future indications.

Prescribing should also be discussed with patients when there is limited evidence such as older or multimorbid patients who are frequently excluded from trials. Identifying patient health priorities and prioritizing their success through shared decision-making could also reduce treatment burden.⁴³ This is particularly important in the presence of multimorbidity given the prevalence and severity of polypharmacy among these patients. Disregarding patient preferences may reduce adherence and successful deprescribing.^{38,44,45}

Finally, while half the prescribing sets, including 40% of all indications, adapted criteria or measures developed previously, there was little evidence of critical revision or removal of indications. While most prescribing sets mentioned assessing the level of evidence, it was not always provided, and it was graded in only two prescribing sets.^{8,28} Although some indications remain relevant, such as avoiding duplicate medications, others may require modification with emerging evidence. Regular updates are conducted for some indications, such as the Beers criteria,⁸ but this is not universal among all current indications. To ensure a robust set of valid measures, future contributions should routinely employ standard evidence for grading practices, assess the most recent evidence, and revise or remove prescribing indications as appropriate.

Strengths and limitations

Our work has several limitations. First, we did not review unpublished or ongoing studies because protocols of non-interventional studies are rarely published in advance and thus difficult to identify. Second, we focused on chronic medications since these comprise the majority of prescribed medications and may require modification in

dynamic disease states. Thus, our findings may not apply to indications for prescribing in acute conditions. Third, we analyzed only prescribing indications related to select chronic conditions to better focus on the most frequent and relevant issues in older adults. Fourth, the review was conducted by a single author, although all classification issues were discussed with the senior authors. Finally, we did not review disease-specific guidelines published by specialty societies to assure the completeness of the indications.

Our study has several strengths. First, we performed a comprehensive review that included Ovid/MEDLINE and EMBASE, and reference lists from the selected articles, reducing the likelihood of missed prescribing sets. Second, we used a broad search strategy that focused on the most common chronic conditions yet did not restrict search terms to those conditions to increase the probability of identifying all relevant prescribing sets. Third, we used a comprehensive and systematic framework to classify issues addressed by the indications. Finally, we included only criteria and measures published in 2015 or later to reflect the most recent evidence.

Conclusion

Our review identified hundreds of criteria, but few measures focused on appropriate prescribing for the most common and clinically significant chronic conditions affecting older adults. Indications, including both criteria and measures, primarily focused on when to deprescribe or adapt prescribing to prevent adverse consequences. While disease-specific guidelines often address intensification,⁴² our review demonstrates that prescribing indications for older persons appropriately emphasize deintensification. However, several important issues related to potentially inappropriate prescribing were rarely addressed in the indications, including patient perspective and prescribing by multiple providers. Indications addressing drug-disease interactions were frequent, highlighting the importance of considering all comorbidities and medications when adjusting a patient's medication regimen. By identifying critical yet rarely addressed issues in current prescribing indications, this review can help guide the development of future quality measures to improve prescribing for older adults with multimorbidity and understand potential barriers to implementation.

Acknowledgments

We would like to thank Judith Ellen Smith from the Taubman Health Sciences Library of the University of Michigan for her help in constructing the literature search.

Author contributions

CEA, EAK, MW and TH designed the study. CEA conducted the literature review, extracted the data, performed the analyses, interpreted the results and wrote the manuscript. MLK developed the database for data abstraction. EAK, MW and TH contributed

to interpretation of the data. EAK, TH, MLK, and MW revised the manuscript critically for important intellectual content. All authors agreed on the final version of the manuscript for submission.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: Dr. Aubert was supported by an Early Postdoc.Mobility grant from the Swiss National Science Foundation (grant P2LAP3_184042). Dr. Wei was supported by the National Institutes of Health, National Institute on Aging (grant K23AG056638). The funders had no role in design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

ORCID iD

Carole E Aubert  <https://orcid.org/0000-0001-8325-8784>

Supplemental material

Supplemental material for this article is available online.

References

- Gallagher P, Barry P and O'Mahony D. Inappropriate prescribing in the elderly. *J Clin Pharm Ther* 2007; 32(2): 113–121.
- Hedna K, Hakkarainen KM, Gyllensten H, et al. Potentially inappropriate prescribing and adverse drug reactions in the elderly: a population-based study. *Eur J Clin Pharmacol* 2015; 71(12): 1525–1533.
- Barnett K, Mercer SW, Norbury M, et al. Epidemiology of multimorbidity and implications for health care, research, and medical education: a cross-sectional study. *Lancet* 2012; 380(9836): 37–43.
- Aubert CE, Streit S, Da Costa BR, et al. Polypharmacy and specific comorbidities in university primary care settings. *Eur J Intern Med* 2016; 35: 35–42.
- Onder G, van der Cammen TJ, Petrovic M, et al. Strategies to reduce the risk of iatrogenic illness in complex older adults. *Age Ageing* 2013; 42(3): 284–291.
- Hughes LD, McMurdo ME and Guthrie B. Guidelines for people not for diseases: the challenges of applying UK clinical guidelines to people with multimorbidity. *Age Ageing* 2013; 42(1): 62–69.
- Boyd CM, Darer J, Boult C, et al. Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases: implications for pay for performance. *JAMA* 2005; 294(6): 716–724.
- By the American Geriatrics Society Beers Criteria RUEP. American Geriatrics Society 2019 updated AGS Beers

- Criteria[®] for potentially inappropriate medication use in older adults. *J Am Geriatr Soc* 2019; 67(4): 674–694.
9. O'Mahony D, O'Sullivan D, Byrne S, et al. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. *Age Ageing* 2015; 44(2): 213–218.
 10. National Institute for Health and Care Excellence (NICE). NICE Quality and Outcomes Framework indicator, <https://www.nice.org.uk/standards-and-indicators/qofindicators> (accessed 5 August 2020).
 11. National Committee for Quality Assurance (NCQA). Healthcare Effectiveness Data and Information Set (HEDIS) and Performance Measurement. <https://www.ncqa.org/hedis> (accessed 18 April 2021).
 12. Hamilton H, Gallagher P, Ryan C, et al. Potentially inappropriate medications defined by STOPP criteria and the risk of adverse drug events in older hospitalized patients. *Arch Intern Med* 2011; 171(11): 1013–1019.
 13. Majeed A, Lester H and Bindman AB. Improving the quality of care with performance indicators. *BMJ* 2007; 335(7626): 916–918.
 14. Asch SM, McGlynn EA, Hogan MM, et al. Comparison of quality of care for patients in the Veterans Health Administration and patients in a national sample. *Ann Intern Med* 2004; 141(12): 938–945.
 15. Kerr EA and Fleming B. Making performance indicators work: experiences of US Veterans Health Administration. *BMJ* 2007; 335(7627): 971–973.
 16. Kerr EA, Lucatoro MA, Holleman R, et al. Monitoring performance for blood pressure management among patients with diabetes mellitus: Too much of a good thing? *Arch Intern Med* 2012; 172(12): 938–945.
 17. Saini SD, Vijan S, Schoenfeld P, et al. Role of quality measurement in inappropriate use of screening for colorectal cancer: retrospective cohort study. *BMJ* 2014; 348: g1247.
 18. Fujita K, Moles RJ and Chen TF. Quality indicators for responsible use of medicines: a systematic review. *BMJ Open* 2018; 8(7): e020437.
 19. Dang CPL, Toh LS, Cooling N, et al. Updating and validating quality prescribing indicators for use in Australian general practice. *Aust J Prim Health* 2019.
 20. RAND/UCLA Appropriateness Method, https://www.rand.org/health-care/surveys_tools/appropriateness.html (accessed 8 August 2020).
 21. Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction—GRADE evidence profiles and summary of findings tables. *J Clin Epidemiol* 2011; 64(4): 383–394.
 22. Institute of Medicine (U.S.). Committee on standards for developing trustworthy clinical practice guidelines. In: Graham R, Mancher M, Wolman DM, et al. (eds) *Clinical practice guidelines we can trust*. Washington, DC: National Academies Press, 2011.
 23. Renom-Guiteras A, Meyer G and Thurmann PA. The EU(7)-PIM list: a list of potentially inappropriate medications for older people consented by experts from seven European countries. *Eur J Clin Pharmacol* 2015; 71(7): 861–875.
 24. Bahat G, Ilhan B, Erdogan T, et al. Turkish inappropriate medication use in the elderly (TIME) criteria to improve prescribing in older adults: TIME-to-STOP/TIME-to-START. *Eur Geriatr Med* 2020; 11(1): 491–498.
 25. Chang CB, Lai HY, Hwang SJ, et al. The updated PIM-Taiwan criteria: a list of potentially inappropriate medications in older people. *Ther Adv Chronic Dis* 2019; 10: 2040622319879602.
 26. Fauziyah S, Andrajati R, Sartika R, et al. Adaptation and validation of the screening tool of older people's prescriptions instrument for the Indonesian population. *J Res Pharm Pract* 2020; 9(1): 24–29.
 27. Kim SO, Jang S, Kim CM, et al. Consensus validated list of potentially inappropriate medication for the elderly and their prevalence in South Korea. *Int J Gerontol* 2015; 9(3): 136–141.
 28. Kojima T, Mizukami K, Tomita N, et al. 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." *Geriatr Gerontol Int* 2016; 16(9): 983–1001.
 29. Mast R, Ahmad A, Hoogenboom SC, et al. Amsterdam tool for clinical medication review: development and testing of a comprehensive tool for pharmacists and general practitioners. *BMC Res Notes* 2015; 8: 642.
 30. Motter FR, Hilmer SN and Paniz VMV. Pain and inflammation management in older adults: a Brazilian consensus of potentially inappropriate medication and their alternative therapies. *Front Pharmacol* 2019; 10: 1408.
 31. Pazan F and Wehling M. The FORTA (Fit for the Aged) List 2018: a crucial update of a clinical tool for the optimization of drug treatment in older adults. *Eur Geriatr Med* 2019; 10: S191.
 32. Rodriguez-Perez A, Alfaro-Lara ER, Albinana-Perez S, et al. Novel tool for deprescribing in chronic patients with multimorbidity: list of evidence-based deprescribing for chronic patients criteria. *Geriatr Gerontol Int* 2017; 17(11): 2200–2207.
 33. Tommelein E, Petrovic M, Somers A, et al. Older patients' prescriptions screening in the community pharmacy: development of the Ghent Older People's Prescriptions community Pharmacy Screening (GheOP³S) tool. *J Public Health (Oxf)* 2016; 38(2): e158–e170.
 34. Spackman E, Clement F, Allan GM, et al. Developing key performance indicators for prescription medication systems. *PLoS One* 2019; 14(1): e0210794.
 35. Suda M, Suyama Y, Ohde S, et al. Effects of quality indicator monitoring for glucocorticoid-induced osteoporosis and trends of drug treatment in a Japanese hospital. *Int J Rheumat Dis* 2018; 21(5): 975–981.
 36. Levinson W, Born K and Wolfson D. Choosing wisely campaigns: a work in progress. *JAMA* 2018; 319(19): 1975–1976.
 37. Grimshaw JM, Patey AM, Kirkham KR, et al. De-implementing wisely: developing the evidence base to reduce low-value care. *BMJ Qual Saf* 2020; 29(5): 409–417.

38. Farrell B and Mangin D. Deprescribing is an essential part of good prescribing. *Am Fam Physician* 2019; 99(1): 7–9.
39. Lipitz-Snyderman A and Bach PB. Overuse of health care services: when less is more . . . more or less. *JAMA Intern Med* 2013; 173(14): 1277–1278.
40. Jadad AR, To MJ, Emara M, et al. Consideration of multiple chronic diseases in randomized controlled trials. *JAMA* 2011; 306(24): 2670–2672.
41. Buffel du Vaure C, Dechartres A, Battin C, et al. Exclusion of patients with concomitant chronic conditions in ongoing randomised controlled trials targeting 10 common chronic conditions and registered at ClinicalTrials.gov: a systematic review of registration details. *BMJ Open* 2016; 6(9): e012265.
42. Markovitz AA, Hofer TP, Froehlich W, et al. An examination of deintensification recommendations in clinical practice guidelines: Stepping up or scaling back? *JAMA Intern Med* 2018; 178(3): 414–416.
43. Tinetti ME, Naik AD, Dindo L, et al. Association of patient priorities-aligned decision-making with patient outcomes and ambulatory health care burden among older adults with multiple chronic conditions: a nonrandomized clinical trial. *JAMA Intern Med* 2019; 179(12): 1688–1697.
44. Clyne B, Cooper JA, Boland F, et al. Beliefs about prescribed medication among older patients with polypharmacy: a mixed methods study in primary care. *Br J Gen Pract* 2017; 67(660): e507–e518.
45. Witticke D, Seidling HM, Klimm HD, et al. Do we prescribe what patients prefer? Pilot study to assess patient preferences for medication regimen characteristics. *Patient Prefer Adherence* 2012; 6: 679–684.