Reducing Potentially Inappropriate Medications in Older Adults: A Way Forward

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RÉSUMÉ

La réduction des médicaments potentiellement inappropriés (MPI) chez les personnes âgées est un enjeu important selon de nombreux cliniciens et chercheurs à travers le monde, car ces médicaments accroissent significativement la morbidité et la mortalité dans la population plus âgée. La prévalence des MPI est un problème répandu malgré l'existence de plusieurs critères explicites et implicites de réduction des MPI chez les personnes âgées, les plus courants étant les critères de Beers, les critères STOPP/START et plusieurs critères nationaux spécifiques. Cette revue non systématique visait à examiner les critères de référence pour la réduction des MPI et à clarifier le rôle de certaines mesures, dont la déprescription, pour optimiser la prescription des médicaments chez les personnes âgées. Des recherches par mots-clés et termes MeSH ont été menées dans des bases de données électroniques. Les nombreux critères disponibles ont chacun leurs avantages et inconvénients. La déprescription, qui vise à réduire l'utilisation des MPI, a considérablement gagné en importance dans les initiatives associées à l'amélioration des pratiques de prescription. La déprescription est une approche méthodique qui implique l'arrêt graduel, éclairé et individualisé des médicaments inappropriés, avec un suivi rigoureux des patients pour assurer la détection d'événements indésirables ou de symptômes de rebond. Une approche combinée centrée sur le patient et le soignant favorise la collaboration entre les prescripteurs et les pharmaciens afin de réduire le nombre de MPI chez les personnes âgées.

ABSTRACT

Reducing potentially inappropriate medications (PIMs) in older adults is an area of sustained interest for many clinicians and researchers across the globe, as PIMs contribute to a significant burden of morbidity and mortality in the aging population. The prevalence of PIMs is a pervasive problem despite the presence of several explicit and implicit criteria for reducing PIMs in older adults, the most common being the Beers criteria, the Screening Tool of Older Persons' potentially inappropriate Prescriptions/Screening Tool to Alert doctors to the Right Treatment (STOPP/START) criteria, and several country-specific criteria. This narrative review aims to discuss the frequently used published criteria for reducing PIMs, and elucidates the role of certain measures, especially de-prescribing, to optimise medication prescription in older adults. Electronic databases were searched using keywords and MeSH terms. The numerous available criteria have their specific advantages and drawbacks. De-prescribing, an initiative to reduce the use of PIMs, has gained significant importance in improving appropriate prescribing practices. De-prescribing is a methodical approach to gradually stopping inappropriate medications judiciously for each patient and simultaneously monitoring the patient carefully for the onset of adverse events or rebound symptoms. A combined caregiver–patient-centred approach encourages the collaboration between prescribers and pharmacists to reduce PIMs in older adults.

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Introduction

Several medications need to be prescribed cautiously in older adults, because of age-related variations in pharmacokinetics and pharmacodynamics (Anathhanam, Powis, Cracknell, & Robson, 2012). There is consistent evidence implicating inappropriate prescribing as a potential predictor of negative health outcomes, including adverse events, drug interactions, hospital admissions, increasing health care costs, and an increase in both morbidity and mortality in older adults (Page, Linnebur, Bryant, & Ruscin, 2010; Spinewine et al., 2007). The term "potentially inappropriate medications" (PIMs) refers to those medications that should not be prescribed for most older adults because the risk of adverse events outweighs the clinical benefits, particularly when there is evidence in favour of safer and more effective alternative treatments, including non-pharmacological measures (Sehgal et al., 2013) such as lifestyle modification, weight reduction, regular physical exercises, smoking cessation, and reduction in alcohol consumption (Shinde, Shinde, Khatri, & Hande, 2013).

Epidemiology of PIMs

Prescription of PIMs to older adults has received significant consideration worldwide for several decades, and is a pervasive public health concern, with reported figures of 5.2 per cent to more than 85 per cent of older adults being exposed to PIMs (Bala, Narayan, & Nishtala, 2018). Studies have demonstrated significant associations between inappropriate medication use and higher health care costs (Fick, 2001; Fick, Mion, Beers, & Waller, 2008; Fu et al., 2007). A systematic review found that prescription of PIMs had a statistically significant effect on health care utilization, including hospitalization, inpatient and outpatient visits, and emergency department visits among older adults (Hyttinen et al., 2017). The prescription of PIMs in older adults has been on the rise globally, which can be attributed to the widespread increase in the prescription of medications for the management of multiple chronic medical illnesses (Ailabouni, Mangin, & Nishtala, 2017). A study conducted in community dwelling older adults found that more than half of the study population were prescribed PIMs (Al Odhayani, Tourkmani, Alshehri, Alqahtani, & Mishriky, 2017).

Prescribing medications to older adults is complicated in the presence of cognitive decline, multiple morbidities, and frailty (Poudel, 2015). Clinicians perceive deficits in self-efficacy (relating to knowledge, skills, and decision support), and feasibility (resource availability and work practices) as hindrances to addressing the risk–benefit ratio of prescribing medications to older adults (Anderson, Stowasser, Freeman, & Scott, 2014). When formulating therapeutic aims for older adults, clinicians have to consider the indications for prescribing, the time-to-benefit, co-morbid conditions, concomitant medications, side effects, compliance, patient preferences, and the patent's remaining life expectancy (Beers et al., 1991; Spinewine et al., 2007). It is plausible that as more medications become available, and longevity continues to increase, there will be a further increase in the consumption of prescription medications among older adults, and the incidence of potentially inappropriate prescribing will continue to grow proportionately (Gallagher, Barry, & O'Mahony, 2007). In view of the high rate of prescription of PIMs in the older population, it is important to discuss the practical applications of the existing PIMs criteria, and identify methods to reduce the occurrence of PIMs. We have attempted to describe the popular explicit and implicit criteria globally for assessing appropriate prescribing in older adults, and have suggested methods to reduce inappropriate prescribing, which include meticulously reviewing the prescriptions during assessments. We have emphasized de-prescribing as an efficient way forward (Al Odhayani et al., 2017).

Sources and Selection Criteria

The current study is a narrative review of the existing criteria for appropriate prescribing in older adults. The Ovid MEDLINE®, Embase, PubMed, Scopus, and International Pharmaceutical Abstracts databases were searched using the keywords prescribing criteria, prescribing indicators, deprescribing, appropriate prescribing, and older adults (including synonyms), by the MeSH or major descriptor headings. The search was

limited to studies undertaken in humans, which were published in English during the past 30 years (1987–2017), and in individuals over 65 years of age. In addition, a citation analysis with the aid of Web of Science was conducted to track prospective citing of references of the selected articles. Reference lists of retrieved articles were studied for the purpose of finding additional articles not identified in the original database searches. Studies that were pertinent to the description of appropriate prescribing in older adults were selected. The most recent studies conducted globally were prioritized. For this review, the discussion is limited to the most common criteria employed internationally to assess appropriate prescribing in clinical practice and research.

Summary of the Criteria Measuring PIMs

Several criteria have been implemented internationally to reduce the prevalence of the prescription of PIMs in older adults (Tables 1–4).

Explicit Criteria

These criteria are established by expert consensus, and used to generate lists of medications to be avoided in older adults, or in the presence of specific co-morbidities. It is often easier to implement explicit criteria in routine clinical practice, because no extensive clinical judgement is required for their implementation, and the number of medications and clinical conditions specified is limited. Explicit criteria are often utilized in studies of health outcomes and prevalence associated with PIMs (Chang & Chan, 2010).

Several of these criteria are completely explicit or have both implicit and explicit measures embedded in them, and are usually drug or disease oriented, rather than being patient oriented (Morin, Fastbom, Laroche, & Johnell, 2015). Most explicit criteria are based on the sequential Beers criteria, which could be attributed to the fact that each updated version of the Beers criteria encompasses most of the contemporary medications and ailments (Dimitrow, Airaksinen, Kivelä, Lyles, & Leikola, 2011). The explicit criteria include listings of medications to be avoided in older adults, which are perceived to have increased possibilities of negative health outcomes. Expert opinions, literature reviews, and consensus statements are typically considered in the development of the explicit criteria, because there is insufficient evidence from randomised controlled trials to guide prescribing to older adults. However, it is important to note that explicit criteria may not encompass all aspects that define the quality of prescribing for older adults (Spinewine et al., 2007), and they must be updated and validated regularly (Dimitrow et al., 2011).

These criteria are re-classifications of previous international PIMs criteria, and were developed by a panel of experts through the Delphi method. Very few studies have been conducted internationally to validate the reliability of the aforementioned criteria, and the majority do not circumvent under-prescribing of medications (Chang & Chan, 2010; Lucchetti & Lucchetti, 2017; O'Connor, Gallagher, & O'Mahony, 2012).

Implicit Criteria

When utilising implicit criteria for reducing inappropriate prescribing, the focus is generally on the patient, rather than on medications or diseases per se. Implicit criteria may be the most sensitive approach, as they account for the patients' preferences; nonetheless, they are time consuming, and the outcomes are dependent on the prescriber's knowledge and attitudes and can have low reliability (Spinewine et al., 2007). Implicit criteria may be employed as a supplement, but not as a substitute for clinical judgment, when optimising medication use in older adults (Pattanaworasate, Emmerton, Pulver, & Winckel, 2010).

The ideal criteria should consider the management of co-morbid disorders, under-prescribing of guideline-recommended medications, drug interactions, polypharmacy, patient preferences, life expectancy, and clinical information about the older adults (Basger, Chen, & Moles, 2008).

The Way Forward

The health and functional status of the geriatric population vary widely; so a "one size fits all" approach to prescribing is sub-optimal for meeting individual patient needs (Bpac[nz], 2010; Hanlon & Schmader, 2013). Individual assessments that review the need for continuing each medication help in simplifying treatment regimens, and may decrease the prescribing of PIMs. A Cochrane review in 2013 demonstrated that medication reviews of inpatients, led by physicians, pharmacists, and other health care professionals, resulted in a 36 per cent reduction in emergency department visits (Christensen & Lundh, 2016). As the illness progresses, and if it is evident that the therapy is not appropriate, a tailored approach for discontinuing medications may be favoured (Holmes, Hayley, Alexander, & Sachs, 2006). The physician has a limited role in effective prescribing in clinical practice as the prevailing professional and organisational culture towards quality influences the outcome to a larger extent. Interactive and continuous education, which includes discussion of evidence, local consensus, feedback on performance (by peers), and personal and group learning techniques facilitate appropriate prescribing (Grol & Grimshaw, 2003).

Table 1: Globally most commonly used explicit criteria

Criteria	Basis of Criteria	Type of Care	Content	Usefulness	Drawbacks	Results of Studies Conducted	Validity and Generalisability
Beers Criteria 2015, USA	1. Seminal criteria for assessing PIMs (Beers et al., 1991) 2. Based on medications available in the United States (Steinman et al., 2015) 3. To alert prescribers about medications that are frequently problematic, and therefore should be avoided in majority of older adults (Steinman et al., 2015) 4. Criteria based on pharmacological groups of drugs (American Geriatrics Society Beers Criteria Update Expert Panel, 2015)	Ambulatory, acute, and institutionalized settings of care, except hospice and palliative care (American Geriatrics Society Beers Criteria Update Expert Panel, 2015)	Lists medications, that are potentially inappropriate and hence could be avoided in general in older adults, and prescribed at reduced dosage or with caution to older adults with certain diseases or syndromes (American Geriatrics Society Beers Criteria Update Expert Panel, 2015)	1. For monitoring the quality of prescribing across varied settings (Gnjidic et al., 2012) 2. Increased awareness among health professionals about inappropriate medication prescription in older adults (Gnjidic et al., 2012)	1. Do not identify all cases of potentially inappropriate prescribing 2. Do not predict functional decline in community-dwelling older people 3. Cannot address under-prescribing, over-treatment (e.g., unnecessary prolongation of therapy) or alternatives to medications not to be prescribed. 4. Not applicable to patients in palliative and hospice care (Gnjidic et al., 2012)	A study conducted in hospital-discharged older patients found a prevalence of potentially inappropriate prescribing of 63%, which was mostly associated with psychiatric–behavioural disorders. (Bo, et al.) A study conducted in long-term-care facilities in Canada found a prevalence of PIMs of 81–86%. (Andrew et al., 2018)	1. Systematic literature review and evaluation of the evidence base by the Delphi consensus (American Geriatrics Society Beers Criteria Update Expert Panel, 2015) 2. The predictive validity of Beers criteria in different settings suggests generalisability of the evidence about adverse events and costs (Jano & Aparasu, 2007)

Continued

Table 1: Continued

Criteria	Basis of Criteria	Type of Care	Content	Usefulness	Drawbacks	Results of Studies Conducted	Validity and Generalisability
Screening Tool of Older Person's Prescriptions and Screening Tool to Alert doctors to Right Treatment (STOPP/START), Criteria 2015 Version, Ireland	1. Developed as a screening tool to identify problems at the individual patient level (Nauta et al., 2017) 2. Adopted globally for assessment of inappropriate prescribing. (O'Mahony et al., 2015) 3. Structured according to the physiological systems, and addressed to pharmacological groups of drugs. (O'Mahony et al., 2015)	Primary care setting, acute hospital care, and in nursing home care (O'Mahony et al., 2015)	1. 114 criteria for measuring the appropriateness of the prescribed medications 2. Lists appropriate as well as inappropriate medications prescribed 3. It has implicit and explicit criteria (O'Mahony et al., 2015)	1. To identify PIMs and potential prescribing omissions (Nauta et al., 2017) 2. Increasingly used to assess the prescribing quality at the levels of both the practitioner and the practice (Nauta et al., 2017) 3. Can be utilised to support medication reviews, as it is a comprehensive screening tool that enables the prescribers to appraise the health of the older population, in the context of their co-morbidities (Saddiq & Kauser, 2017) 4. Computerised application of the criteria can support the routine assessment of prescribing for older adults, by reducing the time to analyse inappropriate prescriptions with the 114 criteria (Nauta et al., 2017) 5. The potential to incorporate the criteria into electronic medical record databases, which are now widely used for evaluation and feedback purposes in primary care, needs further exploration.	1. Adequately large prospective trials are needed to determine if rigorous application of the STOPP and START tools have tangible benefits in terms of a decrease in adverse drug reactions, cost, hospitalization, and mortality. (Ryan et al., 2009) 2. The practical applicability with respect to clinical and financial benefits in daily general practice and community pharmacy is not yet established. (Ryan et al., 2009) 3. There are very few doses of medications mentioned that are inappropriate. 4. The majority of drug-related problems of community-dwelling older adults are seldom associated with STOPP/START criteria. (Ryan et al., 2009; Verdoorn et al., 2015) 5. The criteria should preferably be combined with implicit criteria. (Verdoorn et al., 2015)	1. 41.5% of the in-patients in a hospital in Spain were prescribed PIMs, the most common being benzodiazepine, antithrombotics, and opioids. (Pardo-Cabello et al., 2018) 2. STOP-Frail is an explicit list of 27 PIMs, which can be applied to frail older adults with limited life expectancy in any health care setting. (Lavan et al., 2017) 3. A systematic review of the STOPP/START criteria conducted in Nova Scotia, Canada observed reduced PIM rates in all studies, and a reduction in falls, delirium episodes, length of stay in hospitals, care visits, and medication costs, but no improvement in quality of life and mortality. (Hill-Taylor et al., 2016)	1. Delphi consensus conducted (O'Mahony & Gallagher, 2008) 2. Good Inter-rater reliability when tested between multiple physicians practicing independently in different European centres. (Gallagher et al., 2009) 3. Generalizable across different European countries and languages. (Gallagher et al., 2009)

Note. PIM = potentially inappropriate medications.

Table 2: Popular country-specific criteria for assessing potentially inappropriate medications (PIMs)

Criteria	Description	Usefulness	Validity	Drawbacks Including Generalisability
Australian prescribing appropriateness criteria (APAC) 2008 (Basger et al., 2008) (Basger et al., 2012) (Bell et al., 2012; O'Connor et al., 2012)	1. Applicable to older adults in the community, a hospital, a residential home, a care home, or a nursing home. 2. Structured according to the physiological systems, and addressing pharmacological groups of drugs. 3. Lists appropriate as well as inappropriate medications prescribed. 4. Has implicit and explicit criteria.	1. Addresses optimal and sub-optimal prescribing of medications. 2. Provides evidence-based treatment in the oldest old. 3. Encourages shared decision making. 4. Encompasses medication duplication and under-prescribing. 5. The guidelines used to derive the criteria may be applied to develop various country-specific criteria.	1. The APAC criteria cross-referenced the 50 highest-volume medications prescribed to elderly Australians in 2006 with the most common reasons for patients consulting general practitioners. 2. The tool is derived from an analysis of the most common medications dispensed in Australia, and the most common conditions for which older adults residing in Australia receive medical care. 3. Delphi consensus conducted.	Because of the differences in the prescribing patterns in various countries, these criteria may have limited generalisability worldwide.
Improved Prescribing in the Elderly Tool, Canada 2000 (Barry et al., 2006; Naugler et al., 2000) (O'Mahony & Gallagher, 2008)	1. Updated version of the Mc Leod criteria. 2. Comprises 10 drug–disease interactions, two inappropriate medication classes, and two recommendations for the duration of therapy. 3. Criteria based on pharmacological groups of drugs.	1. A tool for quick analysis of PIMs 2. Lists inappropriate medications prescribed.	No information on validity.	Mainly comprises psychotropic and cardiovascular medications, and overlooks many other well- recognised inappropriate prescriptions; hence, may not be generalised to prescribing in older adults.
The French Consensus panel list, 2007 (Laroche et al., 2007) (Chang & Chan, 2010)	1. Developed from the Beers lists, the Canadian criteria, the criteria adapted to French practice, and the guidelines of the French Medicine Agency on medication prescribing in older adults. 2. Thirty-four inappropriate practices in prescribing with recommendations of alternative therapies (29 medications or medication classes that should be avoided, five drug–disease interactions). 3. Criteria based on pharmacological groups of drugs and structured according to five syndromes. 4. Lists inappropriate medications prescribed.	1. Provides a concise explanation of inappropriateness. 2. Includes medication duplication. 3. Safer alternatives are suggested.	Delphi consensus conducted.	The guidelines are adapted referring to the French drug formulary, and there are very few studies conducted to assess the criteria. Hence, it is not feasible to generalise the criteria.

Continued

Table 2: Continued

Criteria	Description	Usefulness	Validity	Drawbacks Including Generalisability
Fit for the aged (FORTA), 2015 (Wehling et al., 2016) (Pazan et al., 2018) (Pazan & Wehling, 2017)	1. A total of 273 items consisting of the most frequently used substances for the long-term medication therapy of older adults. 2. Twenty-nine diagnoses/indication areas were assigned positive and negative labels ranging from A–B–C–D according to the state of evidence according to risk/benefits and age appropriateness. 3. Criteria structured according to the physiological systems. 4. Lists appropriate as well as inappropriate medications prescribed.	1. Supports the screening for inappropriate medications and the omission of important medications, including sub-optimal treatment in older adults. 2. Has been shown to improve the quality of pharmacotherapy, and may ameliorate clinical end-points including adverse reactions.	1. Delphi consensus validations of country/region-specific FORTA lists were conducted in the United Kingdom/Ireland, France, Poland, Italy, Spain, the Nordic countries, and The Netherlands. 2. Validated in a randomized, controlled, prospective trial.	The application of FORTA is very challenging, and the beneficial results cannot be generalised, because no international studies have been conducted applying FORTA.
The PRISCUS list, Germany, 2008 (Holt et al., 2010; O'Connor et al., 2012) (Morin et al., 2015)	1. A total of 131 criteria derived from the pre-existing criteria. 2. Criteria based on pharmacological groups of drugs. 3. Eighty-three drugs were termed PIMs according to the drug class. 4. Lists inappropriate medications prescribed.	Provides therapeutic alternatives and recommendations on dose adjustment, and facilitates medication monitoring.	Delphi consensus conducted.	1. Most adverse drug events in older adults were not associated with the PRISCUS list medications, hence generalisability is challenging. 2. There are no criteria for assessing the combination of medications. 3. Do not include over-the-counter medications.
The Norwegian General Practice (NORGEP) Criteria, Norway, 2009 (Morin et al., 2015; Rognstad et al., 2009) (Fastbom & Johnell, 2015; O'Connor et al., 2012)	1. Thirty-seven explicit criteria based on pre-existing criteria and clinical experience. 2. Intended for use in general practice and for home-dwelling older adults. 3. Criteria based on pharmacological groups of drugs. 4. Lists inappropriate medications prescribed.	1. Inclusive of the de-prescribing component as well. 2. Addresses medication combinations.	Delphi consensus conducted.	1. Criticised for including several medications that are seldom utilized in clinical practice; therefore, not generalisable. 2. Do not include drug–disease interactions.

Table 3: Miscellaneous country specific criteria

Austrian consensus panel list (Mann et al., 2012)

The quality indicators for Assessing Care of Vulnerable Elders (ACOVE) (San-José et al., 2014)
The EU(7) PIM list (Renom-Guiteras et al., 2015)
The Health Plan Employer Data and Information Set (HEDIS) criteria (Pugh et al., 2006)
The List of Potentially Inappropriate Drugs for the elderly in Korea (Kim et al., 2015)
The comprehensive protocol by Matanovic et al. (Matanovic & Vlahovic-Palcevski, 2012)
The PIM-Taiwan criteria (Chang et al., 2012)
The criteria for high-risk medication use in Thai older patients (Winit-Watjana et al., 2008)
The Zhan classification (Barnett, Perry, Langstaff, & Kaboli, 2006)

De-prescribing

De-prescribing is an initiative to decrease the use of redundant medications, especially PIMs, and it encourages the use of non-pharmacological alternatives, supervised by a health care professional, with the objective of managing polypharmacy and improving health outcomes (Reeve, Gnjidic, Long, & Hilmer, 2015). Rational withdrawal of medications in older adults may be one of the best clinical decisions for significant clinical benefits, including improved adherence. It can also reduce the inevitable negative consequences of polypharmacy, including medication burden and costs of complex medication regimens (Bpac^nz , 2010; Ní Chróinín, Ní Chróinín, & Beveridge, 2015). Appropriate cessation of medications in older adults encompasses factors such as the patient's residual life expectancy, avoiding preventive treatments for those with a reduced survival prognosis, excluding medications with questionable evidence of effectiveness, and promoting the prescription of medications with favourable risk–benefit ratios. (O'Mahony & Gallagher, 2008; Scott, Gray, Martin, Pillans, & Mitchell, 2013). In 2003, Woodward proposed the following five principles of de-prescribing: review all current medications, identify medications to be targeted for cessation, prepare a de-prescribing regimen, discuss with patients and carers, and frequent review and support (Woodward, 2003)

Scientific Evidence of Benefits of De-prescribing
In a trial composed of 119 older adults, 332 medications (2.8 medications per patient on an average) were discontinued utilising an algorithm, leading to a decline in mortality by 24 per cent, a significant reduction in the referral rates to acute care facilities, and reduction in health care costs (Garfinkel, Zur-Gil, & Ben-Israel, 2007; Scott et al., 2013). In a similar study conducted in Israel, 58 per cent of medications were withdrawn with an 81 per cent success rate, without major untoward effects, and with almost 90 per cent of the patients reporting a holistic improvement in health (Garfinkel & Mangin, 2010; Scott et al., 2013). A systematic review conducted in Australia in 2008 observed that withdrawal of benzodiazepines and psychotropics diminished the

number of falls, and improved cognition and psycho-motor functioning in older adults (Iyer, Naganathan, McLachlan, & Le Couteur, 2008). Likewise, a randomised controlled study in the United Kingdom in 2009 demonstrated a decline in mortality when antipsychotics were withdrawn in nursing home patients presenting with dementia (Ballard et al., 2009). In a recent clinical trial, it was observed that patients with a lower remaining life expectancy could safely discontinue statins, and the discontinuation was associated with a better quality of life and a decrease in medication costs (Kutner et al., 2015). The List of Evidence-baSed depreScribing for CHRONic patients (LESS-CHRON) criteria constitute the first explicit criteria to assist clinicians in deprescribing PIMs. Each of the 27 criteria consists of indications for which the medications are prescribed, clinical situations that offer an opportunity to de-prescribe, clinical variables to be monitored, and the minimum time to follow the patient after de-prescribing (Rodríguez-Pérez et al., 2017). The Current medication, Elevated risk, Assess, Sort, Eliminate (CEASE) de-prescribing framework, a de-prescribing five step protocol has been developed by the Australian Deprescribing Network, which includes taking a comprehensive medication history, identifying PIMs, determining whether the PIMs can be terminated, planning the withdrawal regimen (tapering where necessary), and the provision of monitoring, support, and documentation. It focuses on engaging patients throughout the sequence, with the aim of improving long-term health outcomes (Reeve, Shakib, Hendrix, Roberts, & Wiese, 2014a)

Barriers to De-prescribing
For most prescribers, prescribing medications is much easier than de-prescribing, possibly because of insufficient awareness of de-prescribing (Lai & Fok, 2017). A study surveying family physicians in Vancouver observed that they were reluctant to de-prescribe the medications prescribed by another practitioner or specialist, and many physicians felt that they lacked the knowledge and skills to de-prescribe in a safe and effective manner out of fear of initiating an adverse

Table 4: Implicit criteria adopted globally for assessment of PIMs

Criteria	Description	Usefulness	Disadvantages
Medication Appropriateness Index, USA, 1994 (Fitzgerald et al., 1997) (Anrys et al., 2016; Hanlon & Schmader, 2013) (Koria et al., 2018)	1. First implicit criteria used in research and clinical practice. 2. Ten criteria worded as questions that allow three rating choices according to the appropriateness. 3. Requires clinical information and acumen for its application. 4. A study conducted recently in Australia demonstrated the reduction in the Medication Appropriateness Index scores post intervention.	1. Applicable to all older adults. 2. Lists appropriate as well as inappropriate medications prescribed. 3. Criteria based on pharmacological groups of drugs.	1. Does not prioritise which medications should be modified. 2. Seldom addresses aspects of suboptimal prescribing (i.e., polypharmacy or under-use of essential medications). 3. May be subjected to reliability issues when there is more than a single evaluator.
The Systematic Tool to Reduce Inappropriate Prescribing (STRIP), 2012 (Drenth-van Maanen et al., 2017) (Meulendijk et al., 2015)	1. Includes a combination of implicit criteria and the STOPP/START explicit criteria. 2. Actively involves the patient, and includes patients' medication histories and preferences. 3. Promotes cooperation among different health care providers (physicians, pharmacists, and home care nurses). 4. Focuses on the evaluation and monitoring of changes in the medication regimen. 5. The comprehensive pharmacotherapeutic analysis in STRIP includes under-prescribing, over-treatment, potential adverse effects, recommended dosage adjustments, medication effectiveness, clinical interactions, and medication adherence, including practical challenges with medication use.	1. Applicable to all older adults. 2. Lists appropriate as well as inappropriate medications prescribed. 3. Has been included as part of a Dutch multidisciplinary guideline on polypharmacy in older adults. 4. The STRIP assistant is a Web application. 5. Criteria structured according to the physiological systems. 6. It has both implicit and explicit criteria.	1. Can be tedious, and respondents perceived using the STRIP Assistant as only marginally acceptable. 2. Has not been validated in clinical practice, and hence lacks sufficient relevance.
The revised Swedish indicators (2010) (Fastbom & Johnell, 2015) (Morin et al., 2015)	1. Classified as (a) Drug-specific (encompassing choice, indication, and dosage of medications; aspects of polypharmacy; and drug interactions) (b) Diagnosis-specific (incorporating rational, irrational, and hazardous drug use in 11 common disorders in older adults)	1. They include criteria on medication omissions 2. Applicable to all older adults. 3. Lists inappropriate medications prescribed. 4. Structured according to the physiological systems, and addressing pharmacological groups of drugs. 5. It has both implicit and explicit criteria.	Dearth of information regarding patient adherence to the pharmacological therapy, and further research is required to assess the proposed improved health status of older adults.

Note. STOPP/START = Screening Tool of Older Persons' potentially inappropriate Prescriptions/Screening Tool to Alert doctors to the Right Treatment; STRIP = Systematic Tool to Reduce Inappropriate Prescribing

effect (Harriman, Howard, & McCracken, 2014). In another study, it was noticed that the physicians were not in favour of discontinuing medications because they usually followed the prescribing guidelines, and de-prescribing often requires discussing the patient's limited life expectancy, which is challenging (Schuling, Gebben, Veehof, & Haaijer-Ruskamp, 2012). A systematic review in 2013 explored the views of patients and observed that the fear of non-specific consequences makes patients reluctant to agree to cessation (Reeve et al., 2013). Sudden withdrawal of a medication could result in a physiological response, termed as "withdrawal reaction", which could be prevented (or minimised) by tapering the dose before withdrawing a medication. Ceasing a particular medication may result in alteration of the pharmacokinetics and pharmacodynamics of other medications. The potential for negatively and irreversibly affecting the medical condition is of a greater concern (Reeve et al, 2014b). Other barriers to de-prescribing include lack of time and support, the anxiety of withdrawal reactions, and unfortunate experiences with cessation of medications in the past. To overcome these barriers to de-prescribing, it is imperative to educate the prescribers and patients about the problems of inappropriate prescribing and to develop guidelines for de-prescribing (Lai & Fok, 2017).

During medication reviews, it is essential to minimise or discontinue the utilization of inappropriate medications, commence or optimise the utilization of appropriate medications, account for a cautious dosage of medications, consider the impact of renal function on drug clearance, and review any drug interactions (Masnoon, Shakib, Kalisch-Ellett, & Caughey, 2018).

Ongoing Research
The Canadian Frailty Network, through the Networks of Centres of Excellence Program, is dedicated to improving the health care of older Canadians living with frailty, and as a part of its mandate, convened a stakeholders' meeting to seek their perspectives on appropriate medication prescription. The priorities identified were: (1) augmented efforts towards developing innovations focused on facilitating prescribing of appropriate medications, and/or de-prescribing in older adults living with frailty; (2) facilitating research for developing or improving models that facilitate pharmacists to be actively involved in the process of monitoring and assessing use of PIMs; and (3) encouraging further research into the values and preferences held by older adults living with frailty with respect to medication use (Muscedere et al., 2017).

De-prescribing is an area of continuing research, as clinicians recognise the significance of a parallel strategy to re-evaluate the prescription of medications.

There is ongoing research to supplement the beneficial evidence for deprescribing by focusing on relevant patient outcomes such as a reduction in falls, hospital admissions, and mortality; and improvement in sleep quality, cognitive function, independence in activities of daily living, and quality of life (Lai & Fok, 2017). De-prescribing may be more beneficial than continuing intensive treatment regimens in older adults presenting with severe co-morbidities (e.g., patients presenting with end-stages of dementia or with a poor functional status); this has motivated researchers to address de-intensification of medical therapy, which implies discontinuation of medications in situations in which the potential problems outweigh the benefits (Green & Leff, 2016). The Canadian Deprescribing Network continues to develop and advance de-prescribing across Canada, in a collaboration with a wide range of stakeholders to bring about real transformation in Canadian health care (Tannenbaum et al., 2017). De-prescribing has the potential to improve health outcomes; however, the clinical benefits and associated risks can be determined only after the development and validation of a systematic de-prescribing process. An account of the reduction in mortality and morbidity will necessitate large randomized controlled trials, requiring hundreds or even thousands of participants in each arm, so the conduct of these trials may, unfortunately, not be feasible (Reeve et al., 2014b). To achieve appropriate polypharmacy, de-prescribing cannot be considered in isolation for optimising the medications of older adults, as potentially inappropriate omissions have also been found to be prevalent in this vulnerable population (Cadogan, Ryan, & Hughes, 2016). Consideration should be given to integrating the de-prescribing process with other interventions to reduce PIM prevalence.

Strength of the Review

This review provides a glimpse of the benefits of and gaps in the existing criteria for inappropriate prescribing, with respect to the latest scientific evidence. The review also describes the potential methods useful in prescribing appropriate medications, and emphasizes de-prescribing.

Limitation of the Review

The literature search was restricted to manuscripts published in English. In addition, the search terms may not be adequate, although the most-relevant criteria were included, and a manual search of the reference lists from the articles searched was also performed. Most of the explicit criteria are based on the Beers criteria, which may have produced a bias and possibly false conclusions.

Conclusion

Inappropriate prescribing of medications in older adults remains a major international health concern. Excluding the Beers criteria and the Screening Tool of Older Persons' potentially inappropriate Prescriptions/Screening Tool to Alert doctors to the Right Treatment (STOPP/START) criteria, most of the existing criteria for measuring PIMs are not comprehensive, and are generally not being used globally as a criterion for prescribing in all older adults. A way forward to reduce PIMs is to encourage de-prescribing, which is a positive, patient-centred intervention, and requires shared decision making, informed patient consent, close monitoring of effects, and consideration of the cumulative risk from multiple medications caused by pharmacokinetic and pharmacodynamic interactions—the same prescribing principles that apply when the therapy is initiated. The development of evidence-based de-prescribing guidelines and the inclusion of de-prescribing modules in all chronic disease guidelines are a priority for the adequate care of older adults.

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