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Inappropriate Prescribing
Criteria, Detection and Prevention

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Abstract

Inappropriate prescribing is highly prevalent in older people and is a major healthcare concern because of its association with negative healthcare outcomes including adverse drug events, related morbidity and hospitalization. With changing population demographics resulting in increasing proportions of older people worldwide, improving the quality and safety of prescribing in older people poses a global challenge.

To date a number of different strategies have been used to identify potentially inappropriate prescribing in older people. Over the last two decades,

a number of criteria have been published to assist prescribers in detecting inappropriate prescribing, the majority of which have been explicit sets of criteria, though some are implicit. The majority of these prescribing indicators pertain to overprescribing and misprescribing, with only a minority focussing on the underprescribing of indicated medicines. Additional interventions to optimize prescribing in older people include comprehensive geriatric assessment, clinical pharmacist review, and education of prescribers as well as computerized prescribing with clinical decision support systems.

In this review, we describe the inappropriate prescribing detection tools or criteria most frequently cited in the literature and examine their role in preventing inappropriate prescribing and other related healthcare outcomes. We also discuss other measures commonly used in the detection and prevention of inappropriate prescribing in older people and the evidence supporting their use and their application in everyday clinical practice.

1. Introduction

Inappropriate prescribing is highly prevalent in older people and has become a global healthcare concern because of its association with negative health outcomes including adverse drug events (ADEs), hospitalization and healthcare resource utilization.

In the general adult population, medicines are considered appropriate to prescribe when they have a clear, scientific evidence-based indication, are well tolerated in the majority of patients and are cost effective. However, in the older population, prescribing decisions are often made in the absence of scientific evidence generated by rigorous randomized controlled drug studies because older patients with complex and multiple co-morbidities are frequently excluded from such clinical trials. In addition, age-related physiological changes often result in altered pharmacokinetic and pharmacodynamic responses to medications, thereby reducing the tolerability of many medications in older compared with in younger patients.[1] Compounding this is the increasing prevalence of chronic illnesses that occurs with aging, leading to a greater requirement for the prescription of multiple medications. Such complex factors must be considered when determining the appropriateness of prescribing decisions in older patients.

2. Inappropriate Prescribing: Terminology and Definitions

In the last two decades, much has been written about the definition of medication appropriateness in older patients. A simplistic approach would be to define appropriateness in dichotomous terms, i.e. whether a drug is safe or unsafe in terms of its pharmaceutical properties, or whether or not it is cost effective to prescribe. However, such simple terminology is too restrictive given the complexity of prescribing decisions in older people. A more holistic definition of inappropriate prescribing should encompass the assessment of older persons' prescription medications in the context of their multiple co-morbidities, complex medication regimes, functional and cognitive status, treatment goals and life expectancy. A comprehensive evaluation of prescribing appropriateness should encompass the domains of misprescribing, overprescribing and underprescribing.

(i) *Misprescribing* refers to the prescription of a medication that significantly increases the risk of an ADE. This includes prescribing that involves an incorrect dose, frequency, modality of administration or duration of treatment. In addition, misprescribing includes the use of medications that are likely to cause clinically significant drug-drug or drug-disease

interactions. Safer, equally efficacious alternatives should always be considered.

(ii) *Overprescribing* pertains to the prescription of medications for which no clear clinical indication exists.

(iii) *Underprescribing* pertains to the omission of potentially beneficial medications that are clinically indicated for treatment or prevention of a disease.

3. Inappropriate Prescribing: Criteria for Detection

Medication appropriateness can be measured by evaluating the content or quality of a prescribing decision (i.e. a process measure) and/or the outcome of a prescribing decision (i.e. an outcome measure). An example of a process measure of prescribing appropriateness would be the application of a validated criterion to a patient's prescription and clinical data (e.g. the long-term use of long-acting benzodiazepine is potentially inappropriate in older patients because of the associated increased risk of falls and confusion; therefore, it would be inappropriate to prescribe such a medication for long-term use because of the increased risk of an adverse outcome). An example of an outcome measure would be to evaluate the medications of older patients presenting with falls; a medication that is known to increase the risk of falls, e.g. a long-acting benzodiazepine, would be inappropriate in that instance. Process measures of appropriateness should clearly predict outcome measures. Process and outcome measures of prescribing appropriateness can be evaluated using explicit (criterion-based) or implicit (judgement-based) criteria.

3.1 Explicit Criteria

Explicit criteria are usually developed from literature reviews, expert opinion and consensus techniques. These criteria usually comprise lists of drugs or drug classes and dosages that are known to cause harmful effects in older people. The advantage of explicit criteria is that they can be applied to prescriptions with little or no clinical judgement. However, they usually do not address the burden of co-morbidity frequently found in older people, nor do they take into account patient preference or previously unsuccessful treatment approaches. Commonly used explicit criteria are described in detail below and illustrated in table I.

3.1.1 Beers' Criteria

Beers et al.[2] published the first set of explicit criteria for determining inappropriate prescribing in older patients in 1991. These criteria were based on the consensus opinion of 13 experts in geriatric pharmacotherapy in the US and were originally designed for use in nursing home residents. The original list comprised 30 medications: 19 medications to be avoided irrespective of diagnoses, dose or drug frequency and 11 medications for which certain doses, frequencies and durations of treatment should not be exceeded. The criteria were updated in 1997 so as to be applicable to all patients aged 65 years and over irrespective of place of residence.[3] The second update of the Beers criteria, published in 2003, comprises 48 medications or drug classes to avoid irrespective of diagnosis and 20 medical conditions in which certain drugs should be avoided. Severity ratings pertaining to the outcomes of using such medications are also included in the 2003 iteration of the Beers criteria.[7] The criteria were most recently updated in 2011/2012, addressing three primary areas: (i) criteria for potentially inappropriate medication use in older persons – independent of diagnoses or conditions; (ii) criteria for potentially inappropriate medication use in older persons due to drug-disease/syndrome interactions; and (iii) criteria for potentially inappropriate medication use in older persons for drugs that should be used with caution. This most recent Beers' criteria update is due to be published later in 2012.[15]

The Beers criteria are now widely utilized as a tool for evaluating potentially inappropriate medications in the US. The criteria have been adopted by the American Geriatrics Society. In Europe, several large-scale epidemiological studies have utilized the Beers criteria to quantify the prevalence of inappropriate prescribing in older people in primary, secondary and long-term care

Table I. Comparison of most commonly used explicit and implicit criteria for potentially inappropriate prescribing

Criteria (year)	Country of origin	Validation method	Intended population	Organization of the criteria	Specific advantages	Specific disadvantages
Beers' criteria[2] (1991)	US	Delphi consensus; 13 experts	Nursing home residents aged ≥65 years	30 criteria: 19 drugs to be avoided	Concise; addresses commonly prescribed drugs	Several drugs unavailable outside North America; no drug-drug interaction or duplicate drugs; no underprescribing; poor structure/presentation
Beers' criteria[3] (1997)	US	Delphi consensus; 6 experts	All elderly aged ≥65 years	28 drugs/drug class to avoid independent of diagnoses; 25 drugs/drug classes to avoid with any of 15 medical conditions	Concise explanation of inappropriateness; severity ratings of adverse outcomes	Several drugs unavailable outside North America; no drug-drug interaction or duplicate drugs; no underprescribing; poor structure/presentation
McLeod's criteria[4] (1997)	Canada	Delphi consensus; 32 experts	All elderly aged ≥65 years	38 drugs in 4 categories; 18 drugs contraindicated; 16 drug-disease interactions; 4 drug-drug interactions	Concise explanation of inappropriateness; safer alternatives suggested	Obsolete indicators, e.g. 'β-blockers in heart failure'; no underprescribing; several drugs unavailable outside North America
Improved Prescribing in the Elderly Tool (IPET)[5] (2000)	Canada	Based on McLeod's criteria (not independently validated)	All elderly ≥70 years	14 most frequently encountered McLeod's criteria (in clinical practice)	Concise	Not comprehensive; predominantly cardiovascular and psychotropic drugs; no underprescribing
Zhan's criteria[6] (2001)	US	Delphi consensus; 7 experts	Ambulatory elderly aged ≥70 years	33 drugs (subset of the 1997 Beers criteria); 11 drugs always to avoid; 8 drugs rarely appropriate; 14 drugs indicated in specific circumstances	Less restrictive than previously published criteria in terms of 'always to avoid' drugs	Several drugs unavailable outside of North America; no drug-drug or drug-disease interaction; no underprescribing
Beers' criteria[7] (2003)	US	Delphi consensus; 12 experts	All elderly aged ≥65 years	68 criteria; 48 drugs or drug classes to avoid independent of diagnoses; 20 medical conditions and drugs to be avoided with specific conditions	Concise explanation of inappropriateness; severity rating of adverse outcomes; can be used by computerized clinical information systems	Several drugs unavailable outside North America; controversy over designation of some drugs as inappropriate; no drug-drug interaction or duplicate drugs; no underprescribing

Continued next page

Table I. Contd

Criteria (year)	Country of origin	Validation method	Intended population	Organization of the criteria	Specific advantages	Specific disadvantages
French Consensus Panel List[8] (2007)	France	Delphi consensus; 15 experts	All elderly aged ≥75 years	34 criteria; 29 drugs/drug classes to avoid; 5 criteria on drugs to avoid with specific conditions	Concise explanation of inappropriateness; includes drug duplication; safer alternatives suggested	No clinical studies to date; no underprescribing
Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP) and Screening Tool to Alert doctors to Right Treatment (START)[9] (2008)	Ireland, UK	Delphi consensus; 18 experts	All elderly aged ≥65 years	STOPP: 65 criteria; organized in physiological systems START: 22 criteria addressing underprescribing	Concise explanation of inappropriateness; organized by physiological systems; includes drug-drug and drug-disease interactions; includes drug duplication; includes underprescribing	Does not suggest safer alternatives to inappropriate drugs; does not address certain domains of prescribing appropriateness, e.g. indication, formulation and cost
Australian Prescribing Indicators Tool[10] (2008)	Australia	Not validated	All elderly aged ≥65 years	48 indicators; 18 drug-disease interactions	Includes drug duplication; includes underprescribing	Not validated; derived from Australian data sources, limits international applicability; time consuming to use as footnotes and tables must be read to understand each indicator
Norwegian General Practice (NORGEP) criteria[11] (2009)	Norway	Delphi consensus; 47 experts	Elderly patients aged ≥70 years, in general practice	36 criteria; 21 criteria on drugs and dosages; 15 criteria on drug combinations	Can be applied to medication list with no clinical information	No underprescribing; no drug-disease interactions; no studies to date outside of Norway
Priscus List[12] (2010)	Germany	Delphi consensus; 26 experts	All elderly aged ≥65 years	83 criteria; 15 drug classes	Provides therapeutic alternatives; recommendations on dose adjustments and drug monitoring	No studies to date published outside of Germany
Thailand criteria[13] (2008)	Thailand	Delphi consensus; 16 experts	No age stated	77 criteria	Drug-drug interactions; drug-disease interactions	No studies to date outside of country of origin
Rancourt criteria[14] (2004)	Canada	4 member panel	All elderly aged >65 years in long-term care	111 statements	26 drug-drug interactions; 10 drug duplications	Large number of criteria to get through in clinical practice; data only available on long-term care setting

settings. Gallagher and O'Mahony[16] prospectively applied the 2003 version of the Beers criteria to older patients admitted with acute illness to a university teaching hospital in Ireland and reported an inappropriate prescribing prevalence rate of 32%. In other European studies, potentially inappropriate medications listed in the Beers criteria have been identified in 12–20% of community-dwelling older adults,[17-19] 14–66% of hospitalized older adults[20-22] and almost 40% of nursing home residents.[23,24]

Despite widespread utilization, the Beers criteria have several limitations, particularly with respect to their transferability outside of North America. The Beers criteria include several medications that are not available in European formularies or are rarely prescribed in Europe, some of which are presented in table II. Several of the medications listed in the Beers criteria are rarely used in everyday clinical practice, in particular, in the older patient, e.g. methyldopa and ergot mesyloids. Furthermore, there is much controversy about the inclusion of certain drugs listed in the Beers criteria as being *absolutely* contraindicated in older people, irrespective of diagnosis, e.g. amiodarone, oxybutynin, doxazosin and amitriptyline.

The Beers criteria do not address drug-drug interactions, duplicate drug class prescription and underprescribing of clinically indicated drugs, all of which are important domains of inappropriate prescribing in older patients. From a practical viewpoint, the criteria themselves are not organized in a structured order, which renders them cumbersome and time consuming to use in a busy clinical setting. To date, there are no randomized controlled studies showing that prospective clinical application of the Beers criteria to older patients' prescriptions improves outcomes such as ADEs, morbidity, mortality, hospitalization and cost.

Table II. Drugs listed in Beers' criteria[2,3,7] that are rarely used in European practice

Amphetamines
Carisoprolol
Chlorpropamide
Clidinium
Clonidine
Cyclandelate
Cyclobenzaprine
Cyproheptadine
Discyclomine
Ethacrynic acid
Guanedrel
Guanethidine
Halazepam
Hydroxyzine
Hyoscyamine
Isoxsurpine
Meprobamate
Mesoridazine
Metaxalone
Methocarbamol
Oxaprozin
Pemolin
Phenylpropanolamine
Reserpine
Thioridazine
Trimethobenzamide
Tripelenamine

3.1.2 Improved Prescribing in the Elderly Tool (IPET)

Published in 2000 by Naugler et al.,[5] the Improved Prescribing in the Elderly Tool (IPET) criteria comprise a list of the 14 most commonly encountered instances of inappropriate prescribing identified in clinical practice following the application of a comprehensive set of inappropriate prescribing criteria developed by an expert consensus panel in Canada.[4] The IPET was validated in a prospective study of acutely hospitalized elderly patients that found inappropriate prescribing in 12.5% of patients. The IPET has also been used as an inappropriate prescribing tool in a number of European centres, with considerable variation in the reported rate of inappropriate prescribing between countries (e.g. Ireland 22%,[25] Denmark 3%[18] and Czech Republic 32%[18]). Whilst the IPET criteria are succinct, they have a number of shortcomings, which may explain its limited uptake outside of Canada. Foremost among these shortcomings is the fact that the IPET includes clear-cut errors, notably the recommendation to avoid β-blockers in heart failure. The IPET criteria have a strong emphasis on cardiovascular and psychotropic drugs as well as NSAIDs whilst

other drug categories are under-represented. Examples of IPET criteria include ''NSAIDs in patients with hypertension'' and ''anti-cholinergic drugs to treat side effects of antipsychotic medications''. Three of the 14 categories in the tool relate to the use of tricyclic antidepressants, now infrequently prescribed in older people given the greater tolerability of newer antidepressant drugs with less potential for adverse effects. The IPET criteria also fail to address underprescribing and have not been prospectively studied as an intervention to optimize prescribing appropriateness by way of randomized controlled trials.

3.1.3 Prescribing Appropriateness Index (PAI)

Published in 1998 by Cantrill et al.,[26] the Prescribing Appropriateness Index (PAI) comprises nine indicators of inappropriate prescribing (table III). These indicators rely on excellent documentation of all prescribing decisions in the medical records and are confined to medications listed in the *British National Formulary* thus limiting the use of this tool to countries using this particular formulary. The PAI also has a specific focus on hypertension and little emphasis on other drug classes.

Table III. The Prescribing Appropriateness Index (reproduced from Cantrill et al.,[26] copyright 1998, with permission from BMJ Publishing Group Ltd)

– The indication for the drug is recorded and upheld in the BNF
– The reason for prescribing a drug of limited value is recorded and valid
– If the total daily dose is outside the range stated in the BNF, the prescriber gives a valid reason
– If the dosing frequency is outside the range stated in the BNF, the prescriber gives a valid reason
– A generic product is prescribed if one is available
– If a potentially hazardous drug-drug combination is prescribed, the prescriber shows knowledge of the hazard
– Prescribing for hypertension adheres to evidence-based guidelines in the BNF
– If the duration of therapy is outside the ranges stated in the BNF, the prescriber gives a valid reason
– Compared with alternative treatments in the same therapeutic class, which are just as safe and effective, the drug prescribed is either one of the cheapest or a valid reason is given for using an alternative

BNF = *British National Formulary*.

3.1.4 Zhan's Criteria

The Zhan criteria were devised by a panel of seven experts in geriatrics, pharmacy and pharmacoepidemiology in North America in 2001, using a modified 2-round Delphi consensus method of validation.[6] The criteria divide inappropriate medications into three categories: (i) those that should always be avoided; (ii) those that are rarely appropriate to prescribe; and (iii) those medications that have some indication but are often misused. There are 33 medications listed across these three categories. These 33 potentially inappropriate medications are based on the 1997 version of the Beers criteria. The Zhan criteria are infrequently used as a measure of inappropriate prescribing; one study reported an inappropriate prescribing prevalence rate of 2.5% using these criteria.[6] The Zhan criteria have rarely been used in studies outside of the US, and similarly to the Beers criteria, they include medications that are not available or are infrequently prescribed in Europe. Examples of Zhan criteria are ''antihistamines are appropriate for treatment of allergic reactions and urticaria but not for sedation'' and ''indomethacin may be appropriate as a short course of therapy for acute gouty arthritis though better alternatives exist''.[6]

3.1.5 French Consensus Panel List

Devised by a French panel of 15 experts in geriatric pharmacotherapy, the French Consensus Panel List[8] was published in 2007. Using Delphi consensus methodology, a list of 34 drugs and drug classes to avoid in people aged 75 years and older was validated. The list was based on several sources, including Beers' criteria,[2] McLeod's criteria[4] and Naugler's criteria[5] as well as national practice guidelines in France. However, several drugs listed in the Beers criteria were not included in the French Consensus Panel List either because they were unavailable on the French formulary or no longer in clinical use. Interestingly, drugs listed as always inappropriate in the Beers criteria, e.g. fluoxetine and amiodarone, were judged by the French Consensus Panel List of experts to be appropriate. Twenty-nine drugs or drug classes were identified as being inappropriate in all people 75 years and over and five

criteria involved medications that should be avoided with respect to specific medical conditions. The French Consensus Panel List incorporates duplicate drug class prescribing into its list of inappropriate prescriptions. The list is clearly laid out, with each instance of inappropriate prescribing accompanied by a statement explaining why it is potentially inappropriate as well as listing potential therapeutic alternatives. The criteria do not address underprescribing. To date, no studies have been published that have used these criteria to measure prescribing appropriateness in the clinical setting. Examples of potentially inappropriate prescriptions from the French Consensus Panel List include "the concomitant use of two or more non-steroidal anti-inflammatory drugs (no enhancement of efficacy albeit increase of adverse effect risk)" and "the use of short acting calcium channel blockers (risk of postural hypotension, myocardial infarction, stroke)".

3.1.6 Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP) and Screening Tool to Alert doctors to Right Treatment (START)

Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP) and Screening Tool to Alert doctors to Right Treatment (START) were validated in 2008 using a Delphi consensus methodology by a panel of 18 experts in geriatric pharmacotherapy in Ireland and the UK.[9] The 65 STOPP criteria are arranged according to physiological systems for ease of use, each accompanied by a concise explanation as to why the prescription is potentially inappropriate. They include instances of commonly encountered drug-drug and drug-disease interactions with specific sections devoted to analgesic drugs, drugs that adversely affect older patients at risk of falls and duplicate drug class prescriptions. Examples of STOPP criteria include "digoxin at a long-term dose >125 mcg/day with impaired renal function (increased risk of toxicity)" and "regular opiates for more than 2 weeks in those with chronic constipation without concurrent use of laxatives (risk of severe constipation)".

The 22 START criteria address commonly encountered instances of potentially inappropriate underprescribing, where no contraindication to prescription exists and where life expectancy and functional status justifies the prescription. Examples of START criteria include "regular inhaled corticosteroid for moderate-severe asthma or COPD [chronic obstructive pulmonary disease], where predicted FEV1 [forced expiratory volume] <50%" and "calcium and vitamin D supplement in patients with known osteoporosis (radiological evidence or previous fragility fracture or acquired dorsal kyphosis)".

The STOPP/START criteria have been shown to have good inter-rater reliability between physicians in six European centres.[27] Good inter-rater reliability has also been demonstrated between pharmacists.[28] STOPP criteria have been used as a measure of prescribing appropriateness in European[29] and Asian[30] centres as well as in a variety of clinical settings, i.e. primary care (21%),[31] secondary (hospital) care (35%)[16] and long-term nursing care (60%).[32] Studies using START criteria have detected prescribing omissions in 23% of patients in primary care[31] and in 44–57% of hospitalized older people.[16,32] A recent randomized controlled trial has shown that prospective application of STOPP/START criteria to the prescriptions of acutely ill hospitalized older patients resulted in sustained improvement in all domains of medication appropriateness, as assessed by the Medication Appropriateness Index (MAI) and the Assessment of Underutilization of Medication (AOU) Tool, compared to standard pharmaceutical care alone[33] (see figure 1).

A prospective study of ADEs resulting from medications listed in the STOPP criteria and Beers criteria at the point of admission to hospital showed that 51.7% of criteria-defined and consensus panel-judged ADEs involved medications listed in the STOPP criteria, while 20.4% of confirmed ADEs related to medications listed in the Beers criteria. The risk of a serious avoidable ADE was significantly increased with STOPP-listed drugs (odds ratio [OR] 1.85; 95% CI 1.51, 2.26; $p < 0.001$), while the risk with Beers-listed drugs was not significant (OR 1.28; 95% CI 0.96, 1.72; $p = 0.11$).[34] These data indicate that the presence of STOPP criteria medications represents a significant risk factor for ADEs. However, there

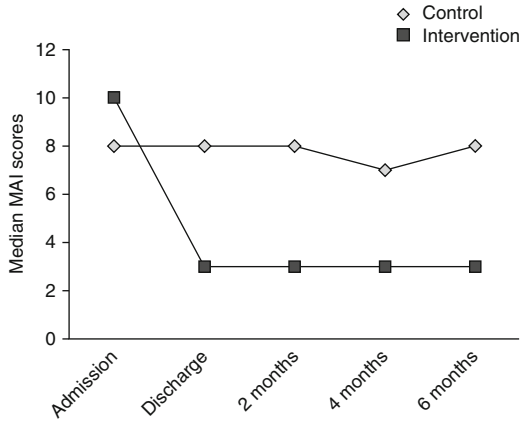

Fig. 1. Medication Appropriateness Index (MAI) scores in the intervention (application of the Screening Tool of Older Persons' potentially inappropriate Prescriptions/Screening Tool to Alert doctors to Right Treatment [STOPP/START] criteria) and control (standard hospital pharmacy care) groups [n = 400].[33]

have been no randomized controlled trials examining the effect of *prospective* application of STOPP criteria on ADE incidence, re-hospitalization or overall healthcare cost, though one such trial is currently underway (trial number NCT01467050).[35] Given the published research data and the reproducibility of the STOPP/START criteria across European centres, these criteria have recently been adopted by the European Union Geriatric Medicine Society (EUGMS). In order to maintain clinical relevance and applicability, the STOPP/START criteria will need regular updating and re-validation.

3.1.7 Australian Prescribing Indicators Tool

Published in 2008,[10] these criteria consist of 48 prescribing indicators with accompanying explanatory footnotes and tables. The target population is any person aged 65 years and older. Unlike the majority of inappropriate prescribing tools described in this paper, the Australian Prescribing Indicators Tool is not formulated from a consensus panel. Instead it is derived from Australian clinical guidelines and indigenous prescribing databases.

The 48 indicators are presented as an unstructured list. Rather than identifying particular drugs or drug classes, the indicators list particular medical conditions and clinical scenarios, e.g. ''patient with a history of falls is not taking psychotropic medications''. The criteria do include indicators that address underprescribing in older people, e.g. ''patient with type 2 diabetes mellitus, hypertension and albuminuria is taking angiotensin-converting enzyme inhibitor or angiotensin receptor blocker''. Tables and footnotes within the criteria provide information on contraindications and precautions to be considered before prescribing new medications to older adults. It also includes indicators that focus on drug-drug and drug-disease interactions. Other important health indicators in this tool that are largely ignored in other sets of inappropriate prescribing criteria include smoking cessation and seasonal vaccinations. The Australian tool has not yet been validated and the evidence base and references supporting the indicators are largely Australian sources, which may limit the use of this tool in other countries.

3.1.8 Norwegian General Practice (NORGEP) Criteria

The Norwegian General Practice (NORGEP) criteria were published in 2009 and were developed by a group of Norwegian geriatricians, clinical pharmacologists and general practitioners, using a Delphi consensus method.[11] The target population for these criteria is ambulatory, independently living, community-based people aged 70 years and older. There are 36 criteria, which are divided into 21 drugs and drug doses that are inappropriate and 15 criteria that address drug-drug interactions. An explanatory statement accompanies most but not all of the criteria. The criteria are presented in two tables, and similar drugs and drug classes are grouped together. The NORGEP criteria do not address underprescribing of drugs, nor do they include drug-disease interactions. There is particular emphasis on drugs affecting the central nervous system. Many of the drugs listed in the NORGEP criteria are rarely used in clinical practice (e.g. trimipramine and chlorprothixene). The applicability of the NORGEP criteria as a tool for measuring prescribing appropriateness has not been evaluated outside of Norway. Examples of NORGEP criteria for potentially inappropriate

medications in those aged ≥70 years include "zopiclone >7.5 mgs/24 hours" and "theophylline: risk of arrhythmias, no documented effect in COPD".

3.1.9 Other Explicit Criteria

Other sets of explicit criteria include the Priscus List published in Germany in 2010[12] the Thailand criteria[13] and the Rancourt criteria[14] from Canada. Details of the validation and layout of these criteria are illustrated in table I.

3.2 Implicit Criteria

Implicit criteria refer to quality indicators of prescribing that a clinician or pharmacist can apply to any prescription, using expert professional judgement. Implicit criteria are not drug or disease specific and consequently rely on a clinician's medical knowledge. Implicit criteria are time consuming to employ (up to 10 minutes per medication for the MAI) and are, as a consequence, deployed mostly as a research tool. However, an advantage of implicit criteria is that they focus on the patient and decisions with regard to prescribing appropriateness at an individual level.

3.2.1 Medication Appropriateness Index (MAI)

The MAI was first published in 1992 by Hanlon et al.[36] and is the most cited of the implicit criteria. This instrument assesses prescribing appropriateness using ten criteria: indication, effectiveness, dose, correct direction, practical directions, drug-drug interactions, drug-disease interactions, duplication, duration and cost (table IV). Each medication receives a rating of being appropriate, marginally appropriate or inappropriate according to each of the ten criteria, with each individual rating receiving a weighted score. The scores are then summated to provide a summary measure of appropriateness for each medication, ranging from zero (indicating a completely *appropriate* prescription) to a maximum score of 18 (indicating a completely *inappropriate* prescription). Comprehensive clinical details, medical knowledge and clinical judgement are required to implement the MAI criteria.

The MAI has been shown to have good intra-rater and inter-rater reliability among hospital pharmacists and hospital physicians,[37] though inter-rater reliability amongst primary care physicians is only moderate, because of difficulty accessing the required clinical details. One study of 397 frail elderly inpatients published in 2004 showed that 92% of patients met at least one MAI criterion, the most common being the use of the most expensive drugs (70%), impractical directions (55%) and incorrect dose (51%).[38] Another study of 384 elderly patients at the point of discharge from hospital showed that 44% were prescribed at least one unnecessary medication.[39] A study by Lund et al.[40] reported that a modified version of the MAI (OR 1.13; 95% CI 1.02, 1.26) predicted more ADEs over a 3-month period than the explicit Beers criteria (OR 1.43; 95% CI 0.67, 3.07).

An advantage of the MAI is that it encompasses elements of drug prescribing that are applicable to any medication and to any clinical condition in any clinical setting. However, the MAI does not address underprescribing and is time consuming to use (approximately 10 minutes per medication) thus limiting its applicability to everyday clinical practice.

Table IV. The Medication Appropriateness Index (reprinted from Hanlon et al.[36] Copyright 1992, with permission from Elsevier)

Criterion	Weighted score
Is there an indication for the drug?	3
Is the medication effective for the condition?	3
Is the dosage correct?	2
Are the directions correct?	2
Are the directions practical?	1
Are there clinically significant drug-drug interactions?	2
Are there clinically significant drug-disease interactions?	2
Is there unnecessary duplication with other drugs?	1
Is the duration of therapy acceptable?	1
Is this drug the least expensive alternative compared to others of equal utility?	1
Total	**18**

3.2.2 Assessment of Underutilization of Medication (AOU) Tool

The AOU tool[41] is based on an instrument reported by Lipton et al.[42] It requires that the

user have a detailed list of medical conditions and current medications for the patient in order to determine prescribing omissions based on existing evidence in the medical literature. Ratings for individual items are dichotomized into ''no prescribing omission'' or ''omission of an indicated drug''. The AOU tool has been shown to have good inter-rater reliability.[41] One study of 196 older patients showed that 64% (125 patients) had evidence of underprescribing according to the AOU instrument.[43]

4. Detection of Inappropriate Prescribing: Additional Approaches

Several other approaches to optimizing prescribing appropriateness have been studied by way of randomized controlled trials. These include comprehensive geriatric assessment (CGA), expert pharmacist review/structured pharmaceutical care, education/audit systems and computerized prescribing/decision support systems. Each of these strategies is outlined below.

4.1 Comprehensive Geriatric Assessment (CGA)

Geriatric medicine services typically comprise a multidisciplinary team of doctors, nurses, therapists and pharmacists, who provide a thorough assessment of older peoples' physical, cognitive and functional abilities as well as detailed analysis of their prescriptions. CGA affords a complete overview of an older persons' health status and functional abilities, enabling the prescriber to make informed prescribing decisions. Several randomized controlled trials[44-46] have shown improvements in all domains of prescribing appropriateness following application of CGA; some of these trials are described in table V. Schmader et al.,[45] in the US, randomized 834 older patients to receive either CGA or usual care. In the subsequent 12-month period, there was a significant reduction in the prevalence of inappropriate prescribing as defined by the MAI criteria, as well as fewer instances of underprescribing in the inpatient intervention group. In Norway, Saltvedt et al.[47] randomized 254 frail older hospital inpatients to CGA or usual care and reported a significantly lower prevalence rate of drug-drug interactions and anticholinergic drug prescriptions in the intervention group at discharge compared with controls. Medications with a high side-effect profile, such as anticholinergics and antipsychotics, were more likely to be discontinued in the intervention group than in the control group. An Australian study[44] reaffirmed that CGA reduces inappropriate prescribing in a study of 154 older people in long-term care where those randomized to the intervention involving the input of a multidisciplinary team had a lower prevalence rate of benzodiazepine prescription than the control group.

Table V. Randomized controlled trials examining the effect of comprehensive geriatric assessment on inappropriate prescribing

Authors, country (year)	Setting; duration	Intervention	Results
Crotty et al.,[44] Australia (2004)	10 nursing homes; 3 month follow-up	2 MDT case conferences 6–12 weeks apart	Greater improvement in prescribing appropriateness in intervention compared with control group (55% decrease vs 10% decrease in MAI scores, $p = 0.004$)
Schmader et al.,[45] USA (2004)	11 Veterans Affairs hospitals and clinics; 834 pts followed up for 12 months	MDT geriatric team review of patients	Improvement in use of unnecessary drugs (–0.6 intervention vs +0.1 control, $p < 0.0001$); improvement in inappropriate prescribing (47% decrease in intervention vs 25% increase in control); decreased risk of ADEs in outpatients
Strandberg et al.,[46] Finland (2006)	Ambulatory care; 400 pts with CVD followed for 3 years	Treatment review by geriatrician with smoking and nutritional advice	Increase in use of evidence-based drugs in intervention groups; improvements in blood pressure and cholesterol levels; no difference in cardiovascular events and mortality

ADE = adverse drug event; **CVD** = cardiovascular disease; **MAI** = Medication Appropriateness Index; **MDT** = multidisciplinary team; **pts** = patients.

The integrated, multi-dimensional process of CGA supports safer prescribing. It is, however, time consuming and resource intensive to deploy, and its availability is limited mostly to those attending hospital services. In clinical practice, it is not feasible for all older patients to have CGA, thereby restricting the application of CGA in the general population.

4.2 Expert Pharmacist Review

An expert pharmacist review involves pharmacists performing a standardized pharmaceutical assessment of older patients' prescriptions coupled with feedback to the patients and their physicians. This approach has been shown to improve prescribing appropriateness in older patients in hospital.[48] It capitalizes on the model of structured interdisciplinary teamwork in a well organized clinical environment in the hospital sector. In another recent randomized controlled trial,[49] a structured pharmacist review coupled with the prevision of detailed drug information to older patients and their carers significantly improved medication appropriateness. However, the cost effectiveness of this approach is uncertain, nor has it been proven to improve clinical outcomes, such as lowering the incidence rates of ADEs. Furthermore, pharmaceutical care is not widely available in secondary care centres across central Europe. Randomized controlled trials using pharmacist intervention are summarized in table VI.

In the UK, the National Health Service advocates implementation of a Medicine Use Review (MUR),[52] a free service offering patients a private consultation with their pharmacist in which medications are reviewed, potential interactions and adverse effects are discussed and an 'action plan' is formed and sent to the patient's general practitioner. There is no evidence that an MUR improves prescribing appropriateness or reduces ADEs. Similarly to CGA, expert pharmacist review is resource intensive and, in the majority of cases, is confined to hospitalized patients, apart from the MUR offered in the UK. Not all pharmacists have specialist training in geriatric pharmacotherapy and the efficacy of this intervention also relies on the availability of the clinical record to the pharmacist. Success of the MUR intervention is dependent on communication between the pharmacist, the patient and their physician. Finally, there are no published randomized controlled trials showing that an MUR reduces ADE incidence or results in any other important positive clinical outcome.

The role of the pharmacist in the optimization of older people's medication is dealt with in detail in the article by Spinewine et al.[53] in the current issue of *Drugs & Aging*.

Table VI. Randomized controlled trials using pharmacist assessment as an intervention

Study (year)	Setting; country; follow-up	Study population	Intervention	Results
Hanlon et al.[50] (1996)	Veterans Affairs clinics; US; 12 months	208 patients	Drug regimen review; written recommendations by pharmacist to physician; patient given advice at each clinic visit by pharmacist	24% decrease (intervention) vs 6% decrease (control) in MAI scores at 3 months ($p = 0.0006$); 28% decrease (intervention) vs 5% decrease (control) at 12 months ($p = 0.0002$)
Crotty et al.[51] (2004)	Patients discharged from hospital to nursing homes; Australia; 8 weeks	110 patients	Pharmaceutical care review by community pharmacist on discharge prescription; subsequent case conference with physicians and pharmacists	Lower MAI scores in intervention group than in control group (2.5 vs 6.5; $p = 0.0006$); no significant difference in ADEs, falls, behaviour or cognition between 2 groups
Spinewine et al.[48] (2006)	27-bed, acute, geriatric unit; Belgium; 3 months	101 patients	Pharmaceutical care by on-site pharmacist from admission to discharge; pharmacist participation on ward round; written instructions given to patient/caregiver	87.8% of interventions fully accepted by physician; 84% of treatment changes persisted 3 months post discharge

ADE = adverse drug event; **MAI** = Medication Appropriateness Index.

4.3 Prescriber Education, Audit and Feedback

Ongoing educational strategies at undergraduate and postgraduate level targeted specifically at those who prescribe for older patients are essential to improving prescribing appropriateness. Studies have shown that most physicians receive inadequate training in geriatric pharmacotherapy.[54,55] In general, interactive approaches with direct feedback appear to be more effective than didactic lectures and dissemination of written material.[56-58] Most of the studies on educational approaches to date pertain to specific drug classes such as antibiotics,[56] analgesics[58] and psychotropic medication.[57]

4.4 Computerized Provider Order Entry with Clinical Decision Support (CPOE/CDS)

Computer-based prescribing systems have been utilized in hospital and community settings with the aim of reducing prescribing errors and improving prescribing appropriateness. These information technology-based interventions provide support at the time of prescription with regard to drug dose, monitoring, interactions and cost. If prescribing programs are linked to a patients clinical and laboratory data, then all categories of inappropriate prescribing could potentially be addressed in a timely manner. Hospital-based, computer-based prescribing systems linked with community pharmacies can assist in reducing transcription errors at points of transition of care. Studies of computer-based interventions in older adults have examined their role in improving prescribing appropriateness.[59,60] Tamblyn et al.[61] randomized 107 family doctors to use either computerized prescribing support or usual practice over 13 months. Results showed no reduction in the discontinuation of inappropriate medications, but there was a significantly lower prevalence of newly prescribed potentially inappropriate medications (as defined by Beers' and Canadian criteria) during the study period. Peterson et al.[62] reported that a hospital-based computerized decision support system specifically for psychotropic medications did result in a reduction in the prescription of inappropriate medications, improvements in the correct dosing of psychotropic medicines and a reduction in the number of inpatient falls. There have been few studies that examine what effect computer-based interventions have on clinical outcomes such as ADEs. One study by Gurwitz et al.[63] evaluated the efficacy of computerized provider order entry (CPOE) and clinical decision support (CDS) compared with usual care in reducing ADEs and found no difference between both groups.

Computer-based prescribing systems have been developed for the general adult population but, to date, none has been developed to specifically address prescribing in older people with complex co-morbidity with altered pharmacokinetics and pharmacodynamics. They are also costly and logistically difficult interventions to implement on a large scale. Computerized prescribing systems are also dependent on the quality of computer programming and many systems allow physicians to override errors highlighted by the system, with consequent medication errors.

5. Inappropriate Prescribing: Prevention

Although expertise and experience in geriatric pharmacotherapy for the prevention of inappropriate prescribing in older people is desirable, it is unrealistic to expect the majority of clinicians who prescribe for older people on a regular basis to possess such knowledge and experience and thereby have it inform their judgement when prescribing. This is particularly relevant when prescribing for older people with complex co-morbidity. Prescribers increasingly utilize electronic sources and software systems to assist in prescribing decisions. In our view, what is needed is a reliable, fast, automated software system for checking older people's prescriptions to ensure that important instances of potential inappropriate prescribing (i.e. those with a high likelihood of incurring serious ADEs) are detected and signalled immediately to the prescriber. A systematic check of (i) drug indication, (ii) drug contraindications, (iii) drug-drug interactions, (iv) drug-disease interactions, (v) the risk of ADEs, through the use of a predictive risk score, and (vi) potentially inappropriate medication criteria with instant feedback to the

prescriber could improve prescribing quality thereby reducing the incidence of ADEs in older people. With regard to ADE prediction on the basis of concurrent ADE risk factors, the GerontoNet ADR Risk Score has recently been proposed.[64] However, this score has not been shown to predict ADEs in other prospective studies.[65]

6. Conclusion

Approaches aimed at detecting inappropriate prescribing have intensified in recent years with the development and validation of a number of strategies, in particular, sets of prescribing indicators or criteria. To remain clinically valid, these criteria will require regular updating and expansion in tandem with the evolving evidence base and the development of new medications. To date, no inappropriate prescribing screening criteria have been tested as an intervention to assess their impact on the incidence of ADEs. This is curious, since the primary purpose of any inappropriate prescribing screening criteria should be the attenuation of ADE incidence rates. Furthermore, criteria that guide prescribing patterns for a subpopulation of frail, older, long-term care residents do not exist. It is unlikely that better detection and prevention of inappropriate prescribing in the future will depend solely on one set of inappropriate prescribing criteria, but rather they will rely on a combination of prescribing quality measures that include drug indication and contraindication data, ADE risk factor analysis, better prescriber education and expert pharmacist review, combined with emerging software technologies.

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