Prescribing in Elderly People 1

Appropriate prescribing in elderly people: how well can it be measured and optimised?

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Prescription of medicines is a fundamental component of the care of elderly people, and optimisation of drug prescribing for this group of patients has become an important public-health issue worldwide. Several characteristics of ageing and geriatric medicine affect medication prescribing for elderly people and render the selection of appropriate pharmacotherapy a challenging and complex process. In the first paper in this series we aim to define and categorise appropriate prescribing in elderly people, critically review the instruments that are available to measure it and discuss their predictive validity, critically review recent randomised controlled intervention studies that assessed the effect of optimisation strategies on the appropriateness of prescribing in elderly patients, and suggest directions for future research and practice.

Introduction

Prescription of medicines is a fundamental component of the care of elderly people. Several characteristics of ageing and geriatric medicine affect medication prescribing for these people and render the selection of appropriate pharmacotherapy a challenging and complex process. Interindividual variability in health, disease, and disability increases substantially with ageing, which is a gerontological principle known as aged heterogeneity.2 This heterogeneity means that the health status of elderly people ranges widely from those who are fit to those who are frail, which makes generalisation of prescribing decisions difficult for clinicians.

Although there are increasing numbers of fit, healthy elderly people, there are also increasing numbers of those who are vulnerable and frail and have limited physiological reserve, reduced homoeostasis, dysregulations in immune and inflammation mechanisms, several comorbidities, and take many drugs.3,4 These individuals claim a disproportionate share of medical care and medication use and make prescribing decisions complex. Some syndromes related to age, especially cognitive impairment, affect the ability of elderly people to engage with health services. For example, elderly people with dementia have increased difficulty with taking drugs, and dementia impedes their ability to make autonomous decisions about their medicines. Finally, frail elderly people have age-related impairments in the hepatic metabolism and renal clearance of medications, and enhanced pharmacodynamic sensitivity to specific drugs.5

Evidence suggests that the use of drugs in elderly people is often inappropriate partly because of the complexities of prescribing as well as other patient, provider, and health-system factors. Inappropriate prescribing can cause substantial morbidity, and represents a clinical and economic burden to patients and society.6,7 Inappropriate prescribing in elderly people has therefore become an important public-health issue worldwide.

In this review we aim to define and categorise appropriate prescribing in elderly people, critically review the instruments that are available to measure it and discuss their predictive validity, critically review recent randomised controlled intervention studies that assessed the effect of optimisation strategies on the appropriateness of prescribing in elderly patients, and suggest directions for future research and practice.

Search strategy and selection criteria

We searched Medline (1970–2006), International Pharmaceutical Abstracts (1970–2006), and the Cochrane Database. We used the following keywords to identify papers on measuring appropriate prescribing in elderly people: “aged”, “frail elderly”, “drug therapy”, “drug utilisation”, “drug utilisation review”, “elderly”, “measure”, “medication errors”, “prescription drugs”, “polypharmacy”, “quality indicator”, and “quality of health care”. Additional publications were identified by a manual search of references of relevant papers. After identification of papers on measuring appropriate prescribing in older people, we reviewed those that examined the predictive validity of the measures on the basis of the Donabedian Model that defines quality in terms of structure, processes, and outcomes of health care.1 All studies included were published in the past decade, measured one or more appropriate prescribing process measures, measured one or more patient health outcomes (eg, adverse drug reactions, death, etc), and involved older people (65 years and older). To identify articles on interventions to improve prescribing, we used a combination of the following search terms: “suboptimal”, “appropriateness”, “underuse”, “misuse”, “medication”, “drug therapy”, “aged”, “frail elderly”, “trial”, “randomised controlled trial”, and “intervention”. We also did a manual search of the reference lists from identified articles and the author’s article files, book chapters, and recent reviews to identify additional articles. All articles used a randomised controlled study design, were published in the past decade, measured change in one or more inappropriate prescribing practices with either explicit criteria or implicit measures of inappropriate prescribing in both intervention and control groups, and involved only older adults (65 years and older).
**Definition and categories of appropriate prescribing**

What is appropriate prescribing and how is it different for elderly people? Appropriate prescribing is a general phrase encompassing and compressing a range of values and behaviours to express in a simple term the quality of prescribing. Many other words are used to describe prescribing quality, such as good, poor, appropriate or inappropriate, optimal or suboptimal, and error. Additionally, some terms are specific to some types of inappropriate prescribing—e.g., underprescribing refers to failure to prescribe drugs that are needed, overprescribing refers to prescribing more drugs than are clinically needed, and misprescribing refers to incorrectly prescribing a drug that is needed. We have chosen “appropriate” as a term that implies the quality is what it should be achieved in practice, rather than very high (extremely good), or low (poor or erroneous).

Three of the most important sets of values in judging appropriateness are what the patient wants; scientific, technical rationalism (including the clinical pharmacology of the drug); and the general good. The last value is a mixture of issues, including societal and family-related consequences of prescribing. A judgment of appropriateness will therefore depend on consideration of the facts and circumstances in all three domains. Any measure of appropriateness will inevitably reduce this complexity; however, much of the published work has condensed the notion of appropriateness to simply pharmacological appropriateness—i.e., whether a drug was seen as safe and effective, or sometimes cost-effective. Most performance indicators provide a measurable lower limit of pharmacological appropriateness, rather than a continuous scale of prescribing quality.

Appropriate prescribing in elderly people has its own additional problems, but does not fundamentally change the domains of decisionmaking. Several factors that are specific to frail elderly people increase the complexity of prescribing. Furthermore, clinical evidence for the effects of drugs in elderly people is scarce, goals of treatment might change, and social and economic factors might be different or more important for these patients than for a younger population.

**Measures of appropriateness of prescribing**

Appropriateness of prescribing can be assessed by process or outcome measures that are explicit (criterion-based) or implicit (judgment-based). Process measures assess whether the prescription accords with accepted standards—they are direct measures of performance. However, they might be costly to apply, and might not have face validity for patients. Also, to be valid, process measures should have causal links to important outcomes. Outcome measures are indicators of adverse outcomes (e.g., adverse drug events and hospital admissions) that are secondary to inappropriate prescribing.

Explicit indicators are usually developed from published reviews, expert opinions, and consensus techniques. Expert opinion is usually needed in geriatric medicine because evidence-based aspects of treatments are frequently absent. These measures are usually drug-orientated or disease-oriented, and can be applied with little or no clinical judgment. However, explicit criteria might not take into account all factors that define high quality health care for the individual. They generally do not address the burden of comorbid disease and patients' preferences. Additionally, consensus approaches have little evidence of validity and reliability. Explicit measures with little clinical detail can be applied on large prescribing databases, but with measures that have increasing amounts of clinical details, valid data from computerised databases are difficult to obtain. In implicit approaches, a clinician uses information from the patient and published work to make judgments about appropriateness. The focus is usually on the patient rather than on drugs or diseases. These approaches are potentially the most sensitive and can account for patients' preferences, but they are time-consuming, depend on the user's knowledge and attitudes, and can have low reliability. There is no ideal measure, but the strengths and weaknesses of both approaches should be considered. Panel 1 provides examples of measures of inappropriate prescribing.

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**Panel 1: Examples of explicit and implicit process and outcome measures of appropriateness, applied to benzodiazepine prescribing**

**Process**

**Explicit**

Prescription of long-acting benzodiazepines is inappropriate (because of extended sedation and increased risk of falls). (Process measure based on prescription data).

Prescription of a benzodiazepine is inappropriate if prescribed for insomnia (no valid indication), in patients with history of fall (contraindication) and no attempt to withdraw the drug. (Process measure based on prescription and clinical data).

**Implicit**

If patient is prescribed a long-acting benzodiazepine for insomnia for 5 years, the clinician identifies additional risk factors for falls. The patient is open to attempt progressive discontinuation, and then the clinician assesses that the choice of the drug and the duration of treatment are inappropriate.

**Outcome**

**Explicit**

Patient admitted to hospital for fall and taking a long-acting benzodiazepine indicates that the benzodiazepine prescription is inappropriate. (Measure that includes an adverse outcome component—i.e., fall).

**Implicit**

If patient admitted to hospital for falls and confusion (ie, outcome), medication history shows chronic use of benzodiazepine, and use of sedating agents in the previous 3 days for a cold, then the clinician evaluates that admission was drug-related and preventable (avoidance of concomitant sedating agents in a patient at risk of falls).

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*Some patients on chronic benzodiazepines, who are not willing to undergo substitution treatment and controlled withdrawal, have benzodiazepine dependency and are at risk of withdrawal symptoms, and discontinuation of benzodiazepines is not advised. This effect can be taken into consideration in the implicit approach, but is not accounted for in the explicit criteria.*
Explicit or criterion-based process measures

Explicit criteria used with prescription data alone or with clinical data are commonly used to detect inappropriate prescribing. Most criteria constitute a floor of quality below which no patient should go. Panel 2 explores their transferability between countries. Criteria to detect overprescribing consist of a list of invalid indications to prescribe a specific drug or class of drugs. The most common application has been to detect high amounts of overprescribing of neuroleptic drugs for patients in nursing homes.24,35

Criteria to detect underprescribing usually state that a drug should be prescribed to treat or prevent a specific condition, unless there is a contraindication. These criteria have been applied to different areas, such as heart failure6,37 and atrial fibrillation,7 pain,6 and depression.6 The prevalence of underuse is usually high (above 40% of patients). The main restrictions of present studies are that few have examined underuse of medicines for several medical conditions simultaneously,14–16 and criteria do not allow for factors such as life expectancy and time needed to derive clinical benefit as legitimate reasons for underprescribing.6

Misprescribing criteria usually focus on choice of drug, dose, drug interactions, duration of therapy, duplication, and follow-up. The drug-to-avoid criteria have been the most frequently used. They consist of a list of drugs that should be avoided in elderly people because of the risks of use outweigh benefits. These lists were developed and updated by Beers and co-workers20–22 in the USA and McLeod and colleagues25 in Canada. No similar initiative based on expert consensus has been reported in Europe. The lists include drugs that should be avoided in any circumstances, doses that should never be exceeded, and drugs to avoid in patients with specific disorders. These criteria have been frequently used in aggregate on large databases. A study in Europe30 found that 20% of elderly patients cared for at home used at least one inappropriate drug as defined by the Beers or McLeod criteria, but there were substantial differences between countries.

There are disadvantages with the use of lists of so-called bad drugs as a sole measurement for inappropriate prescribing in elderly people. First, the inclusion of some drugs is subject to controversy,6 and there is insufficient evidence to support inclusion of several drugs.8 Furthermore, this approach sometimes identifies appropriate prescribing as inappropriate (poor specificity). Second, the prescription of drugs that should be avoided is a relatively minor problem compared with other categories of inappropriate prescribing such as underuse of medicines, medication monitoring, or drug disease interactions.6 Third, the reliability of the process to generate such lists is not established.

Other misprescribing criteria go beyond this drug-to-avoid perspective. For example, explicit drug-use-review criteria were developed to detect dosage, duplication, interactions, and duration problems for eight classes of drugs.9 New criteria are being developed to assess the quality of laboratory monitoring of drug therapy.50 Drug interaction criteria will be examined in more detail in the second paper in this series.

Initiatives have attempted to develop and to validate sets of explicit criteria.20,31–33 These sets consist of criteria of overprescribing, misprescribing, and underprescribing for several drugs or diseases, which provides an overview of appropriateness of prescribing for patients. The most comprehensive project—the Assessing Care Of The Vulnerable Elder (ACOVE) project—used systematic reviews of publications, expert opinion, and the guidance of expert groups and stakeholders in the USA to develop a set of quality-of-care indicators that are relevant to vulnerable elders.52,53 68 (29%) indicators refer to medication. Higashi and colleagues43 reported a prevalence of inappropriateness of 3% in the drug-to-avoid domain, 36% in the medication-monitoring domain, and 50% in the underprescribing domain. The ACOVE indicators have several merits. First, geriatric conditions (eg, dementia, falls) are included. Second, indicators pertain to treatment, prevention, monitoring, education, and documentation, and they encompass overprescribing, misprescribing, and underprescribing. Third, most indicators are applicable to people with advanced dementia and poor prognosis.6 Only few data on inter-rater reliability have been published with the ACOVE criteria.40

Implicit or judgment-based process measures

When an individual clinician judges the appropriateness of a patient’s regimen in the context of research, the findings might be non-valid, not reproducible, or not generalisable, which could have been the case in studies for which no data on the validity or reliability of measurements were provided.20,34 These limitations are, nevertheless, remediable—reliability can be improved with detailed specifications, instruments to obtain data, and by training data collectors,34 as done with the Medication Appropriateness Index (MAI).47

The MAI is a measure of prescribing appropriateness that assesses ten elements of prescribing: indication, effectiveness, dose, correct directions, practical directions,
Table 1: Association between misprescribing detected by process measures, and adverse patient outcomes

<table>
<thead>
<tr>
<th>Sample</th>
<th>Criteriaa</th>
<th>Results†</th>
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<tbody>
<tr>
<td>Gupta et al72</td>
<td>19332 Medicaid beneficiaries, USA</td>
<td>Beers 1997 (do not use)</td>
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<tr>
<td>Fick et al73</td>
<td>2336 managed care patients, USA</td>
<td>Beers 1997 (do not use)</td>
</tr>
<tr>
<td>Fu et al74</td>
<td>2305 community-dwellers (MEPS), USA</td>
<td>Beers 1997 (do not use)</td>
</tr>
<tr>
<td>Lanohe et al75</td>
<td>2018 patients admitted to the acute geriatric unit of a teaching hospital, France</td>
<td>Beers 1997 (do not use)</td>
</tr>
<tr>
<td>Franic et al76</td>
<td>444 community-dwellers (MEPS), USA</td>
<td>Beers 2003 (do not use)</td>
</tr>
<tr>
<td>Zuckerman et al77</td>
<td>487 383 community-dwellers, USA</td>
<td>Beers 2003 (do not use)</td>
</tr>
<tr>
<td>Risk et al78</td>
<td>406 Medicare-managed care patients, USA</td>
<td>McLeod and Beers 1997 (do not use)</td>
</tr>
<tr>
<td>Perri et al79</td>
<td>1117 residents in 15 Georgia nursing homes, USA</td>
<td>Beers 1997 (do not use, dose)</td>
</tr>
<tr>
<td>Raivio et al80</td>
<td>425 patients admitted to seven nursing homes and two hospitals, Finland</td>
<td>Beers 1997 (do not use, dose)</td>
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<tr>
<td>Onder et al81</td>
<td>5152 patients in 81 hospitals, Italy</td>
<td>Beers 2003 (do not use, dose)</td>
</tr>
<tr>
<td>Page et al82</td>
<td>389 admitted to two adult internal medicine services</td>
<td>Beers 2003 (do not use, dose)</td>
</tr>
<tr>
<td>Aparasu et al83</td>
<td>471 community-dwellers (MEPS) taking a psychotropic drug, USA</td>
<td>Beers psychotropic (do not use, drug-disease interaction)</td>
</tr>
<tr>
<td>Chang et al84</td>
<td>882 patients in outpatient clinics, Taiwan</td>
<td>Beers 1997 (do not use, drug-disease, interaction)</td>
</tr>
<tr>
<td>Lau et al85</td>
<td>3372 nursing home residents (MEPS), USA</td>
<td>Beers 1997 (do not use, dose, drug-disease interaction)</td>
</tr>
<tr>
<td>Hanlon et al86</td>
<td>3234 community dwellers (Duke EPESE), USA</td>
<td>(1) DUR criteria and (2) Beers 1997 (do not use)</td>
</tr>
<tr>
<td>Fillenbaum et al87</td>
<td>3165 community-dwellers (Duke EPESE), USA</td>
<td>(1) DUR criteria and (2) Beers 1997 (do not use)</td>
</tr>
<tr>
<td>Klarin et al88</td>
<td>785 ambulatory and nursing home patients in a rural area, Sweden</td>
<td>Beers 1997 (high severity do not use), McLeod (drug-disease interactions), duplication, drug-drug interactions</td>
</tr>
<tr>
<td>Schmader et al89</td>
<td>208 community-dwellers, USA</td>
<td>MAI (summed score)</td>
</tr>
</tbody>
</table>

β—regression coefficient. DUR—drug use review. EPESE—Established Populations for Epidemiologic Studies of the Elderly. HR—hazard ratio. HRQOL—health-related quality of life. MAI—medication appropriateness index. MEPS—Medical Expenditure Panel Survey. OR—odds ratio. RR—relative risk. *For the drug-to-avoid criteria, data in brackets refer to the subtype of criteria used in the study: do not use refers to drugs that should be avoided in any circumstances, dose refers to doses of drugs that should not be exceeded, and drug-disease interaction refers to drugs to avoid in patients with specific conditions. †Risk of adverse outcomes in patients prescribed inappropriate drugs, as compared with patients not prescribed inappropriate drugs.

drug-drug interactions, drug-disease interactions, duplication, duration, and cost. Although clinical judgment is needed to assess some criteria (which is why the MAI is classified in implicit measures), the index has operational definitions and explicit instructions, which standardise the rating process. The ratings generate a weighted score that serves as a summary measure of prescribing appropriateness.³³ Three questions of the MAI (indication, effectiveness, and duplication) can be used to detect unnecessary polypharmacy,⁶⁹ and high rates of inappropriateness have been detected. For example, 92% of frail elderly inpatients included in a health-services intervention study had at least one drug with one or more inappropriate ratings, and 44% had at least one unnecessary drug.⁶⁹ The MAI has good intrarater and inter-rater reliability, and face and content validity.⁷³,⁷⁴ However, it is time-consuming and does not assess underprescribing.

Underprescribing can be detected with the Assessment of Underutilization of Medication. The assessment needs a health professional to match a list of chronic medical disorders to the prescribed medications to establish whether there is an omission of a needed drug.⁴² A small study showed good inter-rater reliability,⁴ and in two studies,⁷⁴ 25–60% of patients had evidence of under-prescribing.

Is there a link between process measures and adverse health outcomes? To be valid, process measures should have causal links with important outcomes (eg, mortality, morbidity, adverse
drug events, quality of life). To the best of our knowledge there are no studies linking overprescribing (unnecessary polypharmacy) with adverse health outcomes. Several studies reported a link between underuse of cardiovascular drugs and adverse health outcomes such as mortality. The restriction of drug use because of cost considerations is linked to adverse clinical outcomes and a decrease in self-reported health status. At least 18 studies have looked at the predictive validity of process measures with respect to misprescribing (mainly the drug-to-avoid criteria; table 1).

Some studies showed a positive relation between inappropriate prescribing and mortality, use of health-care services, adverse drug events, and quality of life, whereas others reported mixed or negative results. Most studies, however, had important limitations in the methods—no adjustment for important confounders (eg, comorbidity, polymedication), temporal relation between the process and the outcome not addressed, duration and dose response relation not addressed, short follow-up, small and select sample, and clinically meaningless differences observed.

In summary, the evidence is mixed and contradictory that inappropriate prescribing, defined by process measures, is associated with adverse patient outcomes. No clear conclusions can be made about the predictive validity of specific measures, except for criteria for underuse of drugs for cardiovascular disease. The important questions, therefore, are: do existing process measures measure the wrong things, or just a small subset of the right things, or is it simply the design of studies that needs to be strengthened? Should other aspects of appropriateness, such as measures of continuity of care, patients’ involvement, or of patients’ adherence, be included in the new models? Future studies that test the predictive validity of measures of inappropriate prescribing for elderly people are needed to better inform health policy.

Outcome measures

New measures have been developed that detect inappropriate prescriptions which cause harm to the patient. Juurlink and colleagues investigated the association of hospital admission for drug toxic effects and use of interacting drugs in the preceding week. Other researchers attempted to develop indicators of preventable drug-related morbidity. These indicators can be used in epidemiological databases, with linkages via appropriately coded disorders, medications, and other patient characteristics. However, their specificity and sensitivity might not be satisfactory; they could be difficult to operationalise, and only a few indicators refer to geriatric conditions.

Perspectives on measuring appropriateness

In summary, diverse process measures are available to quantify overprescribing, misprescribing, and under-prescribing in elderly patients. There is no ideal measure, and the choice should depend on study objectives and available data. However, assessment of prescribing appropriateness should go beyond the use of measures that rely exclusively on drug data, and the use of instruments addressing several dimensions of appropriateness for patients should be encouraged. Importantly, the predictive validity of process measures remains to be proven.

We believe that the needs of individual patients, and society as a whole, have been overlooked. Most measures of appropriateness do not extend beyond pharmacological appropriateness, with the occasional marker of cost containment, and we believe this approach is inadequate. The notion of pharmacological appropriateness does not always coincide with what could be called overall appropriateness (accounting for the perspectives of patients, prescribers, and pharmacology). However, there are substantial challenges in going beyond measures based on scientific rationality and available, measurable data. Objectives for future research will be to operationalise and validate instruments that go beyond pharmacological appropriateness, and to assess the predictive validity of present and future instruments. Meanwhile, many of the measures mentioned above have suggested that prescribing for elderly people is often inappropriate, and have been used in optimisation studies.

Approaches for optimisation of prescribing

Approaches for optimisation of prescribing in younger patients might not be applicable to frail, elderly patients. Older patients usually have several comorbidities, associated polypharmacy, and objectives of treatment that may differ from that of younger adults. The application of guidelines for specific chronic disorders is not always suited to this older population, and enrolment in several separate programmes for the management of multiple disease (eg, diabetes, heart failure) might not be the best option for caring for elderly patients with several chronic disorders, since this approach may lead to fragmentation of care. Specific adaptations should therefore be considered.

14 studies met our inclusion criteria. Overall, two studies used an educational type of intervention, one used a computerised decision support system, three used pharmacist interventions, and five used a geriatric medicine service approach. Geriatric medicine service approaches generally consist of a multidisciplinary team including a geriatrician and other health-care providers with specialised geriatrics training (eg, nurses, pharmacists, psychiatrists). The study by Stranberg and colleagues was the only trial to include only one of these aspects—namely, the input of a geriatrician. Finally, two studies used a multidisciplinary approach without geriatric medicine services, and one used a multifaceted intervention. Only three studies were done in Europe, and the others in North America or Australia. All studies were undertaken in ambulatory-care settings except for those by Schmader.
### Educational approaches

<table>
<thead>
<tr>
<th>Setting</th>
<th>Unit of randomisation and number randomised</th>
<th>Intervention</th>
<th>Duration</th>
<th>Results (process measures of appropriate prescribing [P] and patient health outcomes [O])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pimlott et al.105</td>
<td>Ambulatory care, Canada 372 family doctors</td>
<td>Mailed prescribing feedback and education materials on the prescription of benzodiazepines</td>
<td>Three mailings over 6 months</td>
<td>P: Absolute decrease of 0.7% in prescribing of long-acting benzodiazepines in intervention group, and increase of 1.1% in control group (p=0.036); no difference in long-term benzodiazepine therapy, and in combination treatment with other psychoactive drugs</td>
</tr>
<tr>
<td>Rahme et al.106</td>
<td>Ambulatory care, Quebec, Canada Eight towns [cluster], 249 family doctors</td>
<td>Small-group workshop and decision tree to manage osteoarthritis</td>
<td>10 months</td>
<td>P: Better adherence to guidelines with workshop and decision tree (OR 1.8, 95% CI 1.3–2.4); weak evidence that workshop plus decision tree is more effective than decision tree alone</td>
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### Computerised decision support systems

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<thead>
<tr>
<th>Setting</th>
<th>Unit of randomisation and number randomised</th>
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<th>Duration</th>
<th>Results (process measures of appropriate prescribing [P] and patient health outcomes [O])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tamblyn et al.102</td>
<td>Ambulatory care, Canada 107 family doctors</td>
<td>Computerised decision support system</td>
<td>13 months</td>
<td>P: Lower prescription of new inappropriate drugs (Canadian criteria, drug-to-avoid, drug-drug and drug-disease interactions, duration and duplication) in the intervention group vs control group (RR 0.82, 95% CI 0.69–0.98); no difference in the discontinuation of inappropriate drugs (1.06, 0.89–1.26)</td>
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### Clinical pharmacy

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<tr>
<th>Setting</th>
<th>Unit of randomisation and number randomised</th>
<th>Intervention</th>
<th>Duration</th>
<th>Results (process measures of appropriate prescribing [P] and patient health outcomes [O])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hanlon et al.103</td>
<td>Veteran Affairs General Medicine clinic, USA 208 patients</td>
<td>DRR and written drug therapy recommendations for physician; patient counselling at each clinic visit</td>
<td>12 months</td>
<td>P: Higher decline in inappropriate prescribing scores (MAI) in intervention vs control group, at 3 months (24% vs 6% decrease; p=0.0006), and 12 months (28% vs 5% decrease; p=0.0002) O: No significant differences in adverse drug events, health related quality of life, or health services use</td>
</tr>
<tr>
<td>Kanka et al.104</td>
<td>Ambulatory care, Scotland 332 patients</td>
<td>Pharmaceutical care plan completed and given to family doctor</td>
<td>3 months</td>
<td>P: More drug-related problems resolved in intervention than in control group (82.7% vs 41.2%, p&lt;0.05) O: No difference in health related quality of life or health services use</td>
</tr>
<tr>
<td>Crotty et al.105</td>
<td>Hospital to nursing home, Australia 110 patients</td>
<td>Transfer medication list to community pharmacist, DRR by community pharmacist, and case conference with doctors and pharmacists</td>
<td>8 weeks</td>
<td>P: Scores of inappropriate prescribing (MAI) at follow-up lower in the intervention than in control group (25% vs 65%, p=0.006); at follow-up, 22% decrease vs 91% increase, respectively O: Better pain control and less hospital use; no difference in adverse drug events, falls/mobility, behaviour/cognition</td>
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</table>

### Geriatric medicine services

<table>
<thead>
<tr>
<th>Setting</th>
<th>Unit of randomisation and number randomised</th>
<th>Intervention</th>
<th>Duration</th>
<th>Results (process measures of appropriate prescribing [P] and patient health outcomes [O])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coleman et al.106</td>
<td>Nine primary care physician practices, USA Nine intervention practices [cluster], nine family doctors, 159 patients</td>
<td>Chronic care clinic including visit with geriatrician, nurse, and pharmacist</td>
<td>24 months</td>
<td>P: No significant improvements in the prescription of high-risk medications at 12 months (2.94 high-risk medications per patient in the intervention group vs 3.26 in the control group; p=0.20); no difference in selection of geriatric syndromes</td>
</tr>
<tr>
<td>Schmader et al.107</td>
<td>11 Veteran Affairs hospitals and clinics, USA 834 patients</td>
<td>Multidisciplinary geriatric team care (including a geriatrician) for inpatients and outpatients (2+2 factorial design)</td>
<td>12 months</td>
<td>P: Higher improvements in the number of unnecessary drugs in intervention than in control patients (–0.6 vs +0.1, p=0.0001), and number of conditions with underuse (–0.4 vs +0.1, p=0.001) in inpatients. Higher improvements in the number of conditions with underuse in intervention than in control outpatients (–0.2 vs +0.1, p=0.004) O: Decreased risk of serious adverse drug reactions in outpatients</td>
</tr>
<tr>
<td>Saltvedt et al.108</td>
<td>Single Hospital, Norway 254 patients</td>
<td>Multidisciplinary geriatric team care (including a geriatrician)</td>
<td>Until hospital discharge</td>
<td>P: Lower prevalence of potential drug-drug interactions in intervention than in control group at discharge (p=0.009), 36% decrease from admission to discharge vs 17%, respectively, and of anticholinergic medications (p=0.03, 78% vs 10% decrease, respectively), no difference in prescription of Beers’ drugs (p=0.05, 60% vs 33%) respectively</td>
</tr>
<tr>
<td>Crotty et al.109</td>
<td>Ten residential care homes, Australia Ten facilities [cluster], 154 residents</td>
<td>Two multidisciplinary case conference (including a geriatrician), 6–12 weeks apart</td>
<td>3 months</td>
<td>P: Higher improvements in prescribing appropriateness in intervention than in control group (55% vs 10% decrease in MAI scores; p=0.004) O: No differences in resident behaviour</td>
</tr>
<tr>
<td>Strandberg et al.110</td>
<td>Ambulatory care, Finland 400 patients with CVD</td>
<td>Geriatrician-driven treatment review plus nutritional and smoking recommendations</td>
<td>3 years</td>
<td>P: Significant increase in the use of evidence-based drugs in the intervention compared with control group (β blockers p=0.02, ACE-1 p=0.0001, ARAs p=0.007, statins p=0.0001) O: Significant improvements in blood pressure and cholesterol levels, but no difference in major cardiovascular events and total mortality</td>
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UN. There were mixed findings on the effect of educational approaches. Simon and colleagues reported that intervention with physicians via academic detailing might not enhance computerised decision support interventions. However, the investigators used a non-traditional academic detailing approach, in which the main focus differed from appropriate prescribing. Table 3 shows the advantages and disadvantages of approaches that we have critically reviewed. In several cases, no or only little effect on appropriateness of prescribing was reported, which could have been because of no direct interaction with the main prescriber, or a low participation rate of health-care professionals, mainly for educational interventions and case conferences. Environmental barriers certainly have an important role and should be addressed adequately. The data also show that, whenever possible, the intervention should be provided at the time of prescribing rather than retrospectively—ie, after an initial prescription has been issued.

Several weaknesses can be reported in terms of the process measures used—five studies looked only at prescription data to assess appropriateness, without taking into account clinical data; two studies used explicit measures that were not fully validated; and Keska and co-workers used implicit measures without reporting data on their validity and reliability. In contrast, robust measures, such as the Medication Appropriateness Index or a combination of implicit and explicit measures of overprescribing, misprescribing, and underprescribing, were used in other trials.

Nine studies assessed the effect on patient health outcomes, such as adverse drug events, mortality, morbidity, or quality of life. Most did not find an effect (either positive or negative), which is probably because most studies were underpowered to detect differences in patient health outcomes or the outcome measures were not responsive enough to the intervention. This issue is an important limitation of present studies.

There are some potential restrictions of our review. Some studies (usually with negative findings) might not have been published and therefore could not be included. Other studies of interest could not be included because they did not use a randomised controlled design or because they did not specifically use valid measures of appropriate prescribing in the control and intervention group. Two studies had to be excluded because of a lower age limit. Similarly, we did not look at other intervention types (eg, regulatory approaches) because they have not been rigorously studied with a randomised controlled trial. We were unable to do quantitative synthesis (ie, meta-analysis) because of the heterogeneity of the interventions, their settings, and outcome measures.

How do approaches tackle the causes of inappropriate prescribing?

Inappropriate prescribing has been attributed to several causes that should be addressed when approaches for optimisation are considered. Conceptually, prescribing can be regarded as a function of the patient, prescriber, and environment. First, the clinical needs of the patient should be the primary determinant of prescribing decisions. Appropriate prescribing should aim to promote the use of evidence-based therapies and keep the use of drugs for which there is no clinical need or where there is dubious efficacy to a minimum. The patients themselves can influence prescribing decisions on the basis of their expectations. Second, prescribing is done mainly by physicians who will use their own clinical experience and attitudes to make the final decision. A contributory factor to inappropriate prescribing is the inadequate training in

Table 2: Summary of randomised controlled studies to improve inappropriate prescribing in elderly people

<table>
<thead>
<tr>
<th>Study</th>
<th>Setting</th>
<th>Participants</th>
<th>Intervention</th>
<th>Duration</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simon et al</td>
<td>15 health maintenance organisation practices, USA</td>
<td>13 clinics (cluster) 126 doctors, 26 805 patients</td>
<td>Multifaceted, computerised decision support with or without academic detailing</td>
<td>3 months</td>
<td>P: 57% decrease in prescribing of inappropriate drugs (Beers) with computerised alerts (p=0.75); academic detailing had no effect (p=0.52)</td>
</tr>
<tr>
<td>Allard et al</td>
<td>Ambulatory care, Quebec, Canada</td>
<td>266 patients</td>
<td>DRR by single interdisciplinary team (two physicians, one pharmacist, and one nurse) and written recommendations given to family doctor</td>
<td>12 months</td>
<td>P: The mean number of potentially inappropriate prescription (Quebec consensus panel: drug interactions, therapeutic overlapping, drugs of limited use) declined by 0.24 in the intervention group and by 0.15 in the control group (p=0.001); 37% of intervention patients had no team DRR, and those with team DRR were twice as likely to have fewer potentially inappropriate prescriptions</td>
</tr>
<tr>
<td>Meredith et al</td>
<td>Healthcare homes, NY and LA, USA</td>
<td>259 patients</td>
<td>DRR by pharmacist and nurse to identify problems that were then presented to the physician</td>
<td>From 6 weeks to 90 days</td>
<td>P: Overall medication use improved for 50% of intervention patients and 38% of control patients (p=0.051); more duplicative drugs stopped in intervention group (p=0.003) and more appropriate cardiac drugs (p=0.027); no effect on appropriate prescribing of psychotropic drugs and NSAIDs (p=0.05; DUR criteria)</td>
</tr>
</tbody>
</table>

ACE-I=angiotensin-converting enzyme inhibitor. ARA=angiotensin II receptor antagonist. ADEs=adverse drug events. ADRs=adverse drug reactions. CVD=cardiovascular disease. DRR=drug regimen review. DUR=drug use review. MAI=Medication Appropriateness Index. NSAID=non-steroidal anti-inflammatory drug. * These studies were specifically designed to assess the effect of the clinical pharmacist who made recommendations to prescribers. Clinical pharmacists can also work within geriatric medicine teams, and this was the case in most geriatric medicine service studies included in this review. The difference is that such trials were designed to assess the effect of the whole geriatric team, and not of clinical pharmacists themselves.

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Table 3: Advantages and disadvantages of approaches to improve prescribing in elderly patients

<table>
<thead>
<tr>
<th>Description</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Educational approaches</td>
<td>Can be passive (eg, didactic courses, dissemination of printed material), or more interactive (eg, academic detailing), Audit and feedback can be added to enhance the effect</td>
<td>Directly addresses the absence of training in geriatric pharmacotherapy, Can promote changes in prescribing behaviours, Personalised, interactive, and multidisciplinary approaches most likely to be effective</td>
</tr>
<tr>
<td>CPOE and CDSS</td>
<td>Support with regard to drug interactions, dosage, choice of drug, and monitoring, Effect of CPOE based on the use of prescription data only, whereas CDSS uses prescription and clinical data to provide support</td>
<td>Potentially powerful tools to prevent adverse drug events, Support at the time of prescribing, All categories of inappropriate prescribing can be addressed, if prescription data are linked to clinical data</td>
</tr>
<tr>
<td>Clinical pharmacists</td>
<td>Provide pharmaceutical care and drug regimen review</td>
<td>Specialist clinical pharmacists have expertise in geriatric pharmacology and pharmacotherapy, Drug regimen review can potentially improve all categories of inappropriate prescribing</td>
</tr>
<tr>
<td>Geriatric medicine services</td>
<td>Usually an interdisciplinary team composed of geriatricians, nurses, and other specialised health-care professionals (sometimes pharmacists) delivers medical care that includes optimisation of the drug regimen, Comprehensive geriatric assessment is the usual process of care</td>
<td>Can potentially address most causes of inappropriate prescribing, Every team member brings specific competences with regard to drug use, Service is tailored to meet the needs of elderly people, and criteria to enter the programme are related to frailty and functional decline</td>
</tr>
<tr>
<td>Multidisciplinary approaches</td>
<td>Usually a group of health-care professionals undertake drug regimen review of individual patients</td>
<td>Can address distinct causes of inappropriate prescribing, Every team member brings specific competences with regard to medicines use</td>
</tr>
<tr>
<td>Multifaceted approaches</td>
<td>Interventions that incorporate two or more distinct strategies (eg, academic detailing and CDSS)</td>
<td>Can address distinct causes of inappropriate prescribing, More likely to work than single interventions</td>
</tr>
</tbody>
</table>

CDSS=computerised decision support system. CPOE=computerised physician order entry.

How should prescribing be optimised in the future?
From a clinical research perspective, further robust information is urgently needed about the risks and benefits of drugs in elderly patients. The type of evidence that clinical trials provides is restricted with respect to generalisability, because trials usually exclude older, frail patients, and even when a trial is targeted to elderly people, the population enrolled is usually highly selected. Future trials complemented by evidence from well-designed non-experimental studies that estimate causal effects could address this inequity.

From an interventional and health-care research perspective, even though data provide useful insights into the effectiveness of different approaches, several questions remain unanswered. The effect on important health outcomes and health-care costs still needs to be proven (some interventions can potentially decrease direct
costs, but there is yet no guarantee that effective strategies will generate economic savings in the long-term). This process is a challenging task that will need the implementation of multicentre studies with large samples and outcome measures that are clinically relevant and responsive to the intervention (i.e., adverse drug events, and outcome measures that are clinically relevant and responsive to the intervention). The effect of multifaceted approaches should also be assessed.

Another important perspective relates to the widespread diffusion of effective approaches. Despite the substantial resources devoted to developing and testing the effectiveness of interventions to improve prescribing, widespread diffusion of successful methods has not yet been achieved. This failure could be because of several reasons. First, researchers often do little to put together and disseminate interventions beyond traditional methods such as publication in academic journals. At the end of a particular study, researchers generally do not have the resources to assist others in implementation of successful approaches. Further, the translation of research into practice depends on the resources needed to implement the intervention, as well as the characteristics and resources of the organisation adopting the approach. The issue of who should meet the cost for such interventions might prevent diffusion of innovation.

Direct transfer of interventions between different settings or between the same setting in different countries might not be possible. The US approach to prescribing in nursing homes will not necessarily work within other countries and indeed, other countries have not used this method. A complex pharmaceutical care intervention tested in US nursing homes needed adaptation before it could be implemented in nursing homes in Northern Ireland. Differences in the practice environment and culture should be considered if interventions are to be successfully transferred into different settings and countries.

The involvement of patients or their carers in decisionmaking relevant to prescribing is a real challenge, especially in a frail elderly population. However, this approach seems promising. Evidence suggests that a patient’s decision to take or not to take drugs might be part of a negotiation process rather than a final stance, and that changing patients’ behaviour is more likely if patients are helped to make decisions for themselves rather than being told what to do. Encouraging adherence in this population for whom multiple drug therapy is common will need careful prescribing, assessment of benefit, and avoidance of adverse effects. Changes in the attitudes of prescribers towards sharing prescribing decisions are needed, in addition to the improvements in communication that could arise from information technology.

Information technology should improve the use of drugs. Prescribing in the future will use three interacting information reference and guideline database, and clinical information that is patient-specific. Integrated prescribing systems offer promise, but tailoring such systems to the unique concerns of the geriatric patient population is warranted. Improvements in the specificity of alerting systems might improve their clinical usefulness.

Finally, prescribing is no longer viewed as a solitary activity undertaken by physicians. Prescribing authority in the UK has been extended to other health professions, notably nursing and pharmacy. Continual assessment of pharmacist prescribing suggests that it has been positively received by the medical profession. There has been very little objective robust data for the effect of prescribing by pharmacists on patient outcome, so further assessment will be needed.

Conflict of interest statement
We declare that we have no conflict of interest.

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