UCL Université catholique de Louvain

Faculté de Médecine

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APPROPRIATE USE OF MEDICINES IN CARE OF THE ELDERLY

-

FACTORS UNDERLYING INAPPROPRIATENESS, AND IMPACT OF THE CLINICAL PHARMACIST

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Do the one thing you think you cannot do.
Fail at it. Try again. Do better the second time.
The only people who never tumble are those who never mount the high wire.
This is your moment. Own it.

Oprah Winfrey, 1954.

Avoir encore devant soi cette chance
De vivre sans vieillir
Avant le temps du silence
Le regarder venir comme un présent
Le vivre en se disant que demain est en avance.

Calogero, vieillir.

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Voilà presque 4 ans que je me suis lancée dans l'aventure… Aventure dont l'issue était au départ incertaine (comme c'est le cas pour tout doctorant qui débute), mais aussi aventure un peu curieuse au sein de l'Ecole de Pharmacie, puisqu'il ne s'agissait pas de recherche fondamentale mais bien de pharmacie clinique.

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Contents

Abbreviations list

ACEI	Angiotensin-converting enzyme inhibitor
ACOVE	Assessing care of the vulnerable elder
ADE	Adverse drug event
ADL	Activities of daily living
ADR	Adverse drug reaction
ATC	Anatomical Therapeutic Chemical
CDSS	Computerised decision support system
CMH	Cochran-Mantel-Haenszel
CPOE	Computerised prescription order entry
DRP	Drug-related problem
GEM	Geriatric evaluation and management
GP	General practitioner
HCP	Health care professional
MAI	Medication Appropriateness Index
NHS	National Health Service (United Kingdom)
NSF	National Service Framework
OBRA	Omnibus Budget Reconciliation Act
OR	Odds ratio
PDRM	Preventable drug-related morbidity
RCT	Randomised controlled trial
SD	Standard deviation
SEM	Standard error of the mean
SPSS	Statistical Package for Social Sciences
UK	United Kingdom
US	United States

Foreword

The present work was initiated in 2002, in the context of a desire to develop clinical pharmacy at our University. Clinical pharmacy has been flourishing in other countries such as the United States, Canada, and the United Kingdom for more than 30 years, and there is good evidence to support its value in improving quality of care. In Belgium in 2002, the scope of patient-centred clinical pharmacy services was very limited, but several opportunities for developing clinical pharmacy had been identified.[1] These included (a) the willingness, at local and national levels, to improve the quality of use of medicines in acute care, and to reduce costs, (b) a forthcoming shift in drug financing policy, and (c) a reduction in the number of practising doctors in the near future. In parallel, several measures were being taken to overcome the perceived barriers, such as the implementation of new educational programs. The time to attempt to launch patient-centred clinical pharmacy had come.

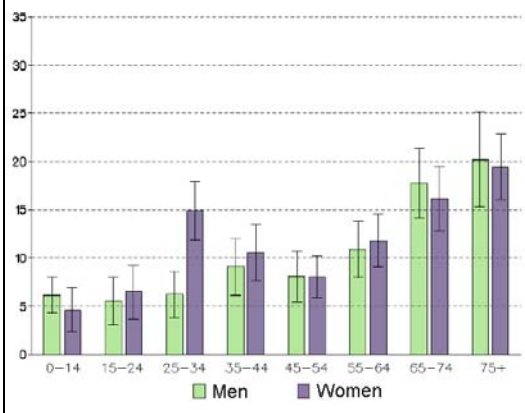
To gain acceptance, it was essential (i) to start with a well-defined pilot project targeting a specific population that would be likely to benefit from clinical pharmacy services, and (ii) to combine this clinical project with a research project that would rigorously evaluate the impact of the service. Elderly patients admitted to acute care were targeted. This group of patients was selected for several reasons:

- The population is ageing, and people aged 65 and over often have comorbidities, are hospitalised more often than their younger counterparts, and they are the highest consumers of drugs.

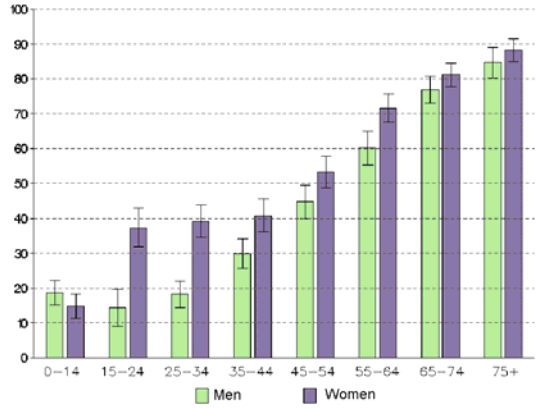
Some figures on ageing and medicines in Belgium:

- Life expectancy in Belgium has continued to rise over the last 10 years. In 2003 it was 75.9 years for men and 81.7 for women.
- In a recent survey, one quarter of persons aged 65-74 years and 40% of persons aged 75 and older had taken at least 5 drugs in the preceding 24 hours.

Percentage of the population admitted to hospital over the last 12 months [2]



Percentage of the population having taken at least one prescribed medicine over the last 24 hours [2]



- Elderly patients are at high risk of drug-related problems, for several reasons: age-related changes in the pharmacokinetics and pharmacodynamics of medicines; higher incidence of polymedication; lack of knowledge of the prescriber specific to the use of medicines in the elderly; frequent cognitive and physical impairment; multiple prescribers.
- There is strong evidence from the literature that use of medicines in that population is often far from ideal. More than 50% of adverse drug events are potentially preventable. Opportunities for improvement can occur at several steps of medication use process (prescription, administration, follow-up, education, and compliance).

This manuscript is the outcome of this pilot project that combined clinical and research activities focusing on elderly inpatients. The **Introduction** covers three topics. First, appropriateness of use of medicines in elderly patients is discussed under two main questions: how can it be measured, and how can it be optimised? [a] Second, elements of organisation of care in Belgium and that are relevant to this Thesis are provided. Third, an international perspective on the scope and impact of clinical pharmacy services in 2002 is provided, and lessons for development in Belgium are discussed. The **Results** of the main original studies are then presented. The first section describes the baseline level of appropriateness of use of medicines for elderly inpatients, and focuses more specifically on the factors underlying inappropriateness. The second and third sections report the implementation and impact of a collaborative approach including the clinical pharmacist on the appropriateness of prescribing, using a randomised controlled design. Finally, questions and perspectives arising from this work are discussed in the **Discussion and perspectives** part.

References

1. Spinewine A, Dhillon S. Clinical pharmacy practice: implications for pharmacy education in Belgium. Pharmacy Education 2002;2:75-81.
2. Health Survey, Belgium, 2004. Available as an electronic file at: http://statbel.fgov.be/port/hea_fr.asp. Last accessed: March 2006.

[a] Content and structure have been guided by a desire to publish this work as a Review paper. The editors of The Lancet have commissioned myself as the coordinator of a group of international investigators to write a series of review-type articles on prescribing in elderly people. This section of the Introduction is the first draft for two of the three review-type papers of the series.

1.

Introduction

1. Appropriate prescribing in elderly people: How can it be measured?

1.1. Introduction

Prescribing medicines is a fundamental component of the care of older people. Recent data indicate that the majority of older persons take at least one prescribed drug, with more than one-third of patients taking four or more prescribed drugs.[1-3] However, overwhelming evidence indicates that the use of medicines in elderly people is often inappropriate.

One of the first report of inappropriate prescribing in the elderly – more than 20 years ago – said that about one quarter of elderly patients admitted to the general medical and geriatric beds of a teaching hospital were prescribed a contraindicated or adversely interacting drug, and that at least 65.5% could have been avoided.[4] A substantial amount of original studies and related reviews on inappropriate prescribing in older people living in different settings have been published since then. They consistently show that inappropriate prescribing increases with age, is prevalent in the elderly, and that it represents both a clinical and economical burden to patients and society.[5-7] Inappropriate prescribing in older people has therefore become a significant public health issue worldwide. But what measures of appropriateness were used in these studies?

Measuring appropriateness of prescribing in older people is challenging, and much more complicated than in younger persons.[8;9] Complexity is convened by several factors such as the lack of clinical evidence specific to that population, the presence of comorbidities, variable goals of treatment, preferences for care, life expectancy, and social resources. In the present paper, we will discuss how "appropriate prescribing[b] in older people" can be defined and categorised. Then we will critically review the instruments that are available to measure it, and suggest directions for future research.

1.2. Search strategy and selection criteria

We searched MEDLINE (1970-2006) and the Cochrane Database of effective practice and organisation of care group. The following keywords were used: aged, drug therapy, prescription drugs, drug utilisation, drug utilisation review, medication errors, quality of health care, polypharmacy, geriatric assessment, quality indicator. We largely selected publications in the past 5 years, but did not exclude commonly referenced and highly regarded older publications. Additional publications were

[b] Prescribing is only one aspect of the use of medicines in older patients. Other aspects refer to dispensing, administration, counselling, and transfer of information between care settings. Although the whole process is important to consider, prescribing deserves special caution, because it is the step where the majority of preventable errors leading to adverse drug events (ADEs) occur.[10-12] The prescribing process will be the main focus of the present review.

identified by a manual search of references of relevant papers. Several review articles were included because they provide comprehensive overviews that are beyond the scope of this review.

1.3. Definition of appropriateness of prescribing in older people

The literature is replete with various terms that pertain to the quality of prescribing (eg optimal/suboptimal, good/poor, appropriate/inappropriate, error), yet there is no consensus on the definition of each term. It is beyond the scope of this introduction to debate on the terminology. The term "appropriateness" will be used to refer to quality of prescribing (and more precisely, to the quality of the prescribing decision).

Appropriateness of prescribing is a balance of scientific rationalism (pharmacological rationality), the needs of individual patients (whole view of the patient), and population constraints (economic issues).[13-15] Several definitions focused exclusively on pharmacological appropriateness, which usually refers to efficacy and safety. For example, according to Beers and colleagues, the use of a medication is labelled as appropriate if its use has potential benefits that outweigh potential risks.[16] This type of definition is too restrictive, because appropriate prescribing goes beyond simply pharmacological rationality. The cost issue is important to consider both from a societal perspective (older people consume the majority of resources for drugs) and from an individual perspective (cost issues frequently impair compliance). Furthermore, the perspective of the patient must be included when considering appropriateness.[14;17] Several studies have suggested that no or limited patient involvement and communication in reaching a prescribing decision can lead to poor outcomes.[18;19] Increasing patient involvement has therefore become a major consideration in improving health care.

There are 3 major categories of inappropriate prescribing: over-prescribing, under-prescribing and mis-prescribing.[6;20] Evaluations of the appropriateness of prescribing in older people should evaluate each of these domains to provide the most thorough measure. Overprescribing can be defined as the prescription of more medications than are clinically indicated. This definition has replaced the older and less valid concept of overprescribing as the use of multiple drugs (i.e. polypharmacy). Misprescribing is defined as the prescription of medications that does not agree with accepted medical standards.[13;21] In other words, a medication is indicated but prescribed incorrectly. Misprescribing refers to several aspects of prescribing such as: choice of medicine, dose, modalities of administration, duration of therapy, drug interactions, monitoring, cost. Underprescribing – an aspect of inappropriate prescribing that has long been underestimated - is the omission of drug therapy that is indicated for the treatment or prevention of a disease or condition.[6]

1.4. Measures of appropriateness of prescribing in older people

Appropriateness of prescribing can be evaluated using process or outcome, and implicit (judgment-based) or explicit (criterion-based) measures.[22] There is no ideal measure or gold standard, but the strengths and weaknesses of each type of measure must be considered. The main types of measures and their characteristics are summarised in Figure 1, and examples are given in Table 1.

Process measures evaluate if the prescribing decision is appropriate, in other words if the prescription is in line with accepted standards. They are a direct measure of performance, and are useful and timely measures of the effect of quality interventions.[23;24] However, they may be costly to apply, and may lack face validity for patients.[24] Also, to be valid, process measures should have causal links to important outcomes.[25]

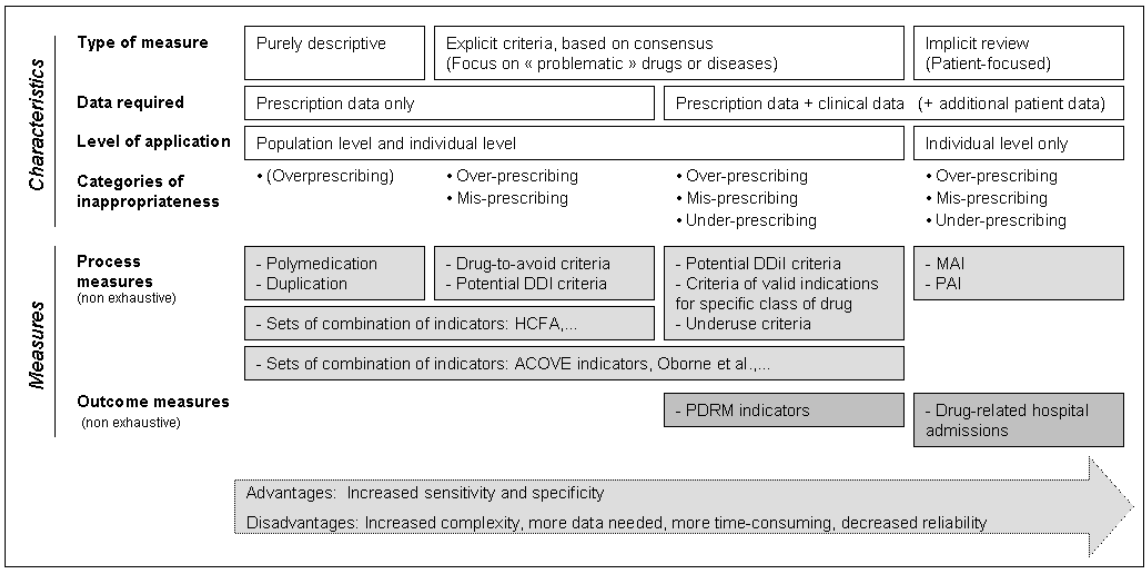
Outcome measures include as inappropriate prescriptions only those that result in harm to the patient such as ADEs or hospitalisation. The causal link is, however, not always straightforward, because the outcome of a prescribing act is often subject to significant uncertainty that the prescriber cannot influence.[14]

The above classification of process versus outcome measures is widely used in the literature. In contrast, the explicit versus implicit approach has been less described, but is – in our opinion – an important perspective.

Explicit indicators of appropriate prescribing for older people are usually developed based on extensive literature reviews, expert opinions and consensus techniques. Gathering expert opinion is often required in geriatrics because evidence-based aspects of treatments are frequently lacking for older people.[26] Recent European recommendations on the development and use of these indicators were made.[27] These measures are usually drug- or disease-oriented. Their main advantages are that they require no or little clinical judgment to apply, and can be used in large administrative databases. However, there are legitimate concerns that explicit criteria may be too rigid and cannot take into account all factors that define individualised high quality of health-care.[28] They often do not address the burden of comorbid disease,[9;29] and they rarely incorporate patient preferences. In addition, consensus approaches have limited evidence on validity and reliability.[26]

In implicit approaches, a clinician utilises information from the patient and from the scientific medical literature to make judgements regarding appropriateness. The focus is usually on the patient rather than on a specific drug or disease. These approaches are potentially the most sensitive, can account for patient preferences, but they are time consuming, depend on the users' knowledge and attitudes, and may have low inter-rater reliability.

Figure 1: Categories of measures of appropriateness of prescribing in elderly patients, and main characteristics



Abbreviations: ACEI: angiotensin-converting enzyme inhibitor; ACOVE: assessing care of the vulnerable elderly; CHF: chronic heart failure; DDI: drug-drug interaction; DDiI: drug-disease interaction; MAI: Medication Appropriateness Index; PAI: Prescription Appropriateness Index; PDRM: preventable drug-related morbidity.

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

	Process	Outcome
Explicit	- Prescription of long-acting benzodiazepines is inappropriate (due to prolonged sedation, and increased risk of falls).[16;30-32] - Prescription of a benzodiazepine is inappropriate if prescribed for insomnia (no valid indication), in patients with history of fall (contra-indication) and no attempt to withdraw the drug.[33-35]	- Patient admitted to hospital for fall (fall=outcome), and taking a long-acting benzodiazepine → the benzodiazepine prescription is inappropriate. [36-38]
Implicit	- Patient 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 → the clinician evaluates that the choice of the drug and the duration of treatment are inappropriate.	- Patient admitted to hospital for falls and confusion (=outcome); medication history reveals chronic use of benzodiazepine, and additional use of several sedating agents in the previous 3 days, for a cold → the clinician evaluates that admission was drug-related and preventable (avoidance of concomitant sedating agents in a patient at risk of falls).

Using this dual classification (process/outcome, explicit/implicit), we will review each type of existing measures separately. Their characteristics and psychometric properties are summarised in Table 2.

1.4.1. Process measures

1.4.1.1. Explicit process measures based on prescription data alone

These measures are the easiest to apply because they require only limited information to apply (namely prescription data). They mainly include polymedication, drugs-to-avoid criteria, and drug-drug interactions criteria.

First, the concomitant use of multiple drugs (polymedication) was often used as a criteria of inappropriate prescribing. For example, in 1999 the Health Care Financing Administration in the United States (US) adopted the use of nine or more medications as a quality indicator to identify potential quality problems in nursing home residents.[39] Similarly, several intervention studies used the number of drugs per patient as the sole measure of appropriate prescribing.[40-43] The use of this criterion should be discouraged. In fact, even though the number of prescribed drugs increases the likelihood of ADEs,[44] it is not a valid measure of appropriateness because many older people with comorbidities benefit from multiple medications. Instead, the accent should be on the use of medications that are clinically indicated.

Second, groups of experts have developed lists of drugs that should be avoided in the elderly, because the risk of using them outweighs the benefit.[16;32;45] The Beers' list – the most widely known - was developed by a group of thirteen national experts in the US in 1991, and included 19 medications that should be avoided, and 11 doses, frequencies, or durations of medication prescription that should not be exceeded.[16] This list was updated in 1997 and again in 2003,[30;31] and drug-disease interactions and severity ratings have been added. There are several limitations to using such lists. First, they have poor sensitivity. Medications frequently implicated in preventable ADEs often do not appear on the lists.[46] Likewise, recent data show that the magnitude of the problem of "drug-to-avoid" is small compared to problems of underuse of medicines or medication monitoring.[47] Second, they sometimes identify appropriate prescribing as inappropriate (poor specificity). The inclusion of some drugs is subject to controversies,[48] and solid evidence to support inclusion of several drugs on the list is lacking.[49] Third, the reliability of the process of generating such lists is not established. A similar consensus approach was followed by a Canadian panel, and only a minority of the criteria figured on both the US and Canadian lists.[32] These second and third limitations illustrate that we must go beyond trusting expert opinion and seek validation of the criteria in research settings. Finally, generalisability to other countries (external validity) is not straightforward. Many (almost half) of the drugs on the

Beers' list are not available in European countries,[50-52] and conversely some inappropriate drugs (with similar potentially harmful properties) that are not available in the US may be marketed outside the US. Despite these limitations, the "drug-to-avoid" criteria are still used in the vast majority of observation studies worldwide, probably because they are simple to apply. However, as claimed by several authors, we must move away from only using lists of "bad drugs" as sole measurement for inappropriate medication use in older people.[53-55]

Third, drug-drug interactions in older patients with polymedication are often a major concern for prescribers. Most studies looking at their incidence in geriatrics relied on computerised detection programs flagging potential moderate and severe drug interactions. These studies found that potential interactions are common.[56-60] However, these databases are not geriatric-specific, and, more importantly, they overestimate the true clinical significance (low specificity). In fact, clinically significant drug-drug interactions are much less frequent.[61] It is therefore necessary to increase the validity of drug-drug interaction criteria by (i) focusing on drug interactions with sufficient clinical significance,[62] (ii) targeting drug-drug interactions relevant to the geriatric population – such as the concomitant use of anticholinergics and acetylcholinesterase inhibitors,[63;64] (iii) linking prescribing data with adverse outcomes – such as done by Juurlink et al.[65]

1.4.1.2. Explicit process measures based on prescription and clinical data

These indicators constitute a higher standard than indicators based on prescription data alone, because clinical information of the patient is accounted for and permits a finer analysis. Indicators can cover over-, mis-, and under-prescribing.

Indicators of overprescribing and misprescribing (with regard to choice of drug, dose, duration, follow-up, drug-disease interactions) have been developed by groups of experts and consensus methods. The majority of these indicators target high-risk drugs, i.e. psychotropic drugs (including neuroleptics[66-69] and benzodiazepines[33;35]) and cardiovascular medicines.[33;35;70] Lists of drug-disease interactions were developed together with the lists of drug-to-avoid in elderly patients.[30-32] Similarly to drug-drug interactions, the clinical relevance is sometimes debatable. Interactions between drugs and geriatric conditions (such as incontinence, syncope, falls, cognitive impairment) should be further examined, but their application require that these conditions are better recorded in medical records.

Over the last decade, underprescribing criteria were also used (mainly in the US, very little in Europe) to detect underprescribing in the following areas: ACE inhibitors and β-blockers in heart failure[71-74] and post-myocardial infarction,[75;76] bisphosphonates, calcium and vitamin D in osteoporosis and after a fracture,[77;78] anticoagulant in atrial fibrillation,[79;80] pain,[81;82] depression.[83] In contrast to over- or mis-prescribing criteria, most of these indicators do not rely on consensus methods. They are

grounded in solid evidence that shows that underuse is related to increased morbidity and mortality, both in younger and older adults. Most of these indicators are therefore not geriatric-specific. A limitation is that they do not account for potential valid decisions not to prescribe drugs (eg short life-expectancy, decisions to limit prescriptions to the drugs that are the most needed, in patients with multiple comorbidities).

1.4.1.3. Sets of explicit process measures

Recent local and national initiatives have attempted to develop and to validate sets of indicators relevant to the quality of drug use in older people in the community, in long-term care, or in hospitals.[33-35;84-86] These sets usually comprise purely descriptive as well as explicit criteria of over-, mis-, and under-prescribing, for several drugs or diseases. A more global picture of appropriateness of prescribing at the patient level can therefore be obtained, and the use of these sets should be encouraged in the future. Unfortunately, data can be difficult to collect when clinical documentation in the medical record or in administrative databases is poor.[87;88]

The most recent and comprehensive project – the Assessing Care Of the Vulnerable Elder (ACOVE) project - used systematic literature reviews, expert opinion, and the guidance of expert groups and stakeholders in the US to develop a comprehensive set of quality-of-care indicators that are relevant to vulnerable elders.[84;89] Sixty-eight (29%) indicators refer to medication.[89;90] Although several indicators were taken from previous work, they have the following merits: (i) geriatric conditions of importance to older people were included; these are conditions for which greater deficiencies in quality of care exist[91]; (ii) indicators pertain to treatment, prevention, monitoring, education and documentation, and they encompass over-, mis-, and under-prescribing; (iii) most indicators are applicable to older people with advanced dementia and poor prognosis.[92] Only limited data on inter-rater reliability has been published.[24]

1.4.1.4. Implicit process measures

As mentioned earlier, when an individual clinician judges the appropriateness of a patient's regimen, the findings may be non-valid, not reproducible or not generalisable, especially if there is a high degree of individualisation and no systematic approach. This could have been the case in studies for which no data on the validity or reliability of the measurements were provided.[4;93;94] These limitations are, nevertheless, remediable: reliability can be improved with detailed specifications, data collection instruments, and by systematically training data collectors,[25] as done with the Medication Appropriateness Index (MAI).[95] For individual patients, the MAI evaluates each medication using 10

criteria that take into account efficacy, safety and cost aspects of appropriateness.[95] All criteria are defined operationally and worded as questions that require an implicit rating of appropriateness on a 3-point Likert scale. Support to answer each question is provided through explicit definitions and specific instructions for use.[95] The 10 ratings can then be combined to produce a weighted score per medication.[96] This instrument is currently the most comprehensive – and therefore time-consuming - instrument to measure appropriateness of prescribing in older outpatients and inpatients, provided that it is combined with implicit measurement of underuse.[97] The MAI has good reliability and face and content validity,[95;96;98-100] that could nevertheless be further enhanced by some modifications.[101]

1.4.2. Is there a link between process measures and adverse outcomes (predictive validity)?

Despite the vast amount of data on inappropriate prescribing in the elderly, it is surprising that there is currently no convincing evidence on their predictive validity. Using mainly explicit criteria, some studies found a positive relationship with mortality, use of healthcare services, ADEs, cost, quality-of-life,[102-108] while others found mixed or negative results.[52;66;109-114] Most studies, however, had important methodological limitations: lack of adjustment for important confounders (e.g. comorbidity, polymedication), temporal relationship between the process and the outcome not addressed, duration- and dose-response relationship not addressed, short follow-up period, small and select sample, clinically meaningless differences observed. The burning question, therefore, is: existing process measures do they measure the wrong things, or is it simply the design of studies that need to be strengthened? Will it be necessary to include other aspects of appropriateness, such as measures of continuity of care or of compliance, in the new models? Both questions need to be addressed, and this issue of predictive validity will be one of the most exciting research area on appropriateness of prescribing in older people in the near future.

1.4.3. Outcome measures

Similarly to process measures, implicit or explicit approaches can be used. On the one hand, structured implicit reviews can be performed to identify ADEs and admissions to hospital that are secondary to inappropriate prescribing.[10-12;115-117] This yields valuable information on the relative contribution of inappropriate prescribing as a source of ADEs. There is, however, no data on the reliability of such evaluations in older patients. On the other hand, explicit outcomes and related processes of inappropriate prescribing can be defined. For example, Juurlink et al. looked at the association of hospital admission for drug toxicity (eg hypoglycemia) and use of an interaction medication in the preceding week (eg sulfonylurea and sulfonamide antibiotic).[65] Other researchers

have attempted to develop indicators of preventable drug-related morbidity (PDRM), through literature review and consensus methods.[36-38;118;119] Each indicator has an outcome that is foreseeable and recognizable (eg chronic constipation), and a causality (process of care) that is identifiable and controllable (eg regular use of a strong opioid analgesic without concurrent administration of a stimulant laxative). They can be used in epidemiological databases, with linkages via appropriately coded disorders, medications, and other patient or clinical characteristics.[38] However, there are important limitations that make their wider use too premature: their specificity and sensibility may not be satisfactory,[120] they may be difficult to operationalise, and only a minority of indicators directly refer to geriatric conditions.

1.5. Can explicit indicators be transferred between countries?

Because the development of quality indicators is resource intensive, it is desirable that explicit indicators can be shared internationally. The Beers criteria are not transferable to a non negligible extent, due to differences in drugs marketed between countries.[50-52] The situation is somewhat different for indicators that do not exclusively rely on specific drugs. For example, a recent study found that the ACOVE indicators in the treatment and follow-up domains were transferable from the US to the United Kingdom (UK).[121] Similar findings were reported with other sets of indicators.[33;122] However, these studies also highlight that indicators cannot be transferred from one country to another (or even from one setting to another) without going through a process of modification, due to important contextual differences between countries.[33;122]

Table 2: Characteristics and psychometric properties of most common instruments of appropriateness of prescribing in elderly patients (based on the literature and on author's view)

1.6. Perspectives

Going back to our definition of appropriateness of prescribing, it is clear that most current measures of appropriateness do not go beyond pharmacological rationality. The needs of individual patients, and population constraints, have been overlooked. There is increased recognition that these perspectives are important to consider, and their inclusion might potentially improve the predictive validity of current measures of appropriateness of prescribing. Objectives for future research will be (1) to operationalise and to validate instruments that go beyond pharmacological rationality, and that take into account patients' and doctors' views, and (2) to further evaluate the predictive validity of current and developing instruments, using appropriate designs.

Work is ongoing to develop broader measures of appropriateness of prescribing. Barber et al. assessed pharmacological measures of prescribing appropriateness (i.e. MAI) against complex, contextual, multidimensional accounts of reality that accounted for the perspectives of the patients, prescriber and pharmacology.[14] Although in many cases pharmacological appropriateness coincided with overall appropriateness (ie including the patient's views and contextual factors), measures restricted to pharmacological appropriateness may be insufficient if most prescribing is appropriate. However, measures that take into account other perspectives than pharmacology and cost can be difficult to operationalise,[123] and further work is needed.

1.7. Conclusion

Because appropriateness is an abstract concept whose assessment necessarily entails value judgments, it is extremely difficult to produce a valid, reliable and generalisable definition of appropriateness that can be used as the basis for measuring appropriateness of care in various clinical settings.[124] The focus of measures of appropriate prescribing has evolved from the drug to the disease, and to some extent to the patient. Currently, process and outcome measures are available to quantify over-, mis-, and under-prescribing in elderly patients. There is no ideal measure, but the use of indicators that rely exclusively on prescription data should be abandoned. An important limitation of current process measures is that their predictive validity on adverse outcomes remains unproved. The inclusion of addititional aspects related to appropriate prescribing, including an account of the patient's perspectives, should be considered in the future.

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2. Approaches for optimisation of drug prescribing in elderly people

2.1. Introduction

Evidence indicates that inappropriate prescribing of medicines in elderly people is prevalent, and is associated with increased morbidity and mortality, increased costs, and decreased quality-of-life. Inappropriate prescribing has therefore become a significant public health issue worldwide, and an urgent need to implement effective optimisation strategies has emerged.

Several countries have implemented national strategies to improve prescribing of medicines in older patients. For example, the National Service Framework (NSF) for Older People in the UK has defined five main types of interventions to improve prescribing and use of medicines in older people: prescribing advice/support, active monitoring of treatment, review of repeat prescribing systems, medication review with patients and their carers, education and training.[1]

In the present article, we will first discuss how current strategies for improvement address the factors underlying inappropriate prescribing. In a second time, we will review the most recent evidence of the impact of different approaches that aim to optimise medications prescribing in older patients.

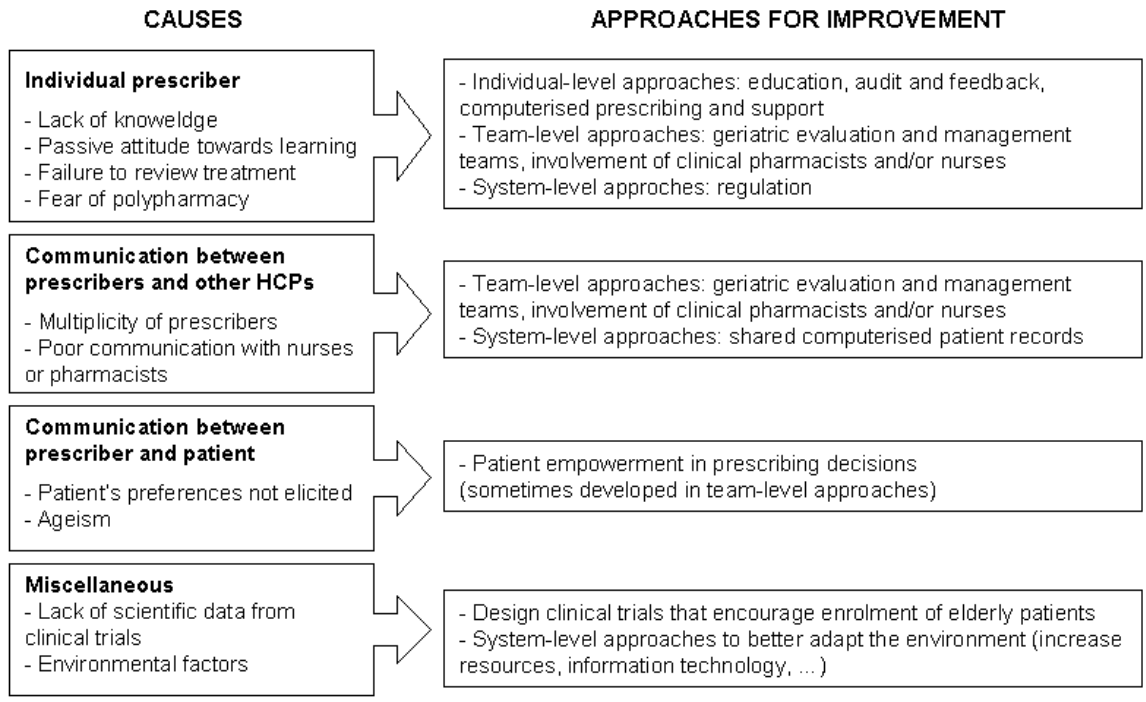
2.2. Search strategy and selection criteria

We used the same Search Strategy as described in the first section of this Introduction. Additional keywords included: randomised controlled trial, prospective studies, pharmaceutical services, computerised medical record systems, feedback, education, clinical decision support systems, nurse clinicians, nurse practitioners.

2.3. Link between causes of inappropriate prescribing and optimisation strategies

To be effective, optimisation strategies must take into account the causes of inappropriate prescribing.[2-4] Causes can originate from the individual prescriber, from its relationship with other HCPs or with patient, or from the environment. Figure 3 summarises causal factors and related approaches for improvement. Some of these approaches have already been broadly implemented (individual-level and team-level approaches), while others require important efforts to be implemented (such as patient empowerment, clinical trials).

Figure 2: Causes of inappropriate prescribing in older people, and related approaches for improvement



At this stage, two additional factors are crucial to consider.

First, effective approaches to optimise prescribing in younger patients are not directly transferable to older patients. Older patients often have several comorbidities, polymedication, objectives of treatment that may differ from that of younger adults, and they are more frequently transferred between settings of care than younger patients. For these reasons, optimising drug therapy in older patients is more complex than for younger patients. For example, it is more complicated than just applying clinical guidelines for specific chronic conditions,[5;6] and simultaneous enrolment in multiple disease management programs (eg diabetes, hypertension) may not be the best option for caring for elderly patients with multiple chronic conditions.[7] The focus of optimisation strategies should, therefore, be on the frail geriatric patient rather than on single diseases.

Second, there also needs to be consideration of transferability of strategies between different settings. The issue of environment must be considered: what will work in acute care will not necessarily work in ambulatory care, what will work in the US will not necessarily work in the UK, for example. Environmental factors specific to the Belgian setting will be discussed in other chapters of this thesis.

2.4. Current approaches to optimise prescribing in elderly patients

2.4.1. Regulation

Regulatory approaches impose restrictions on the use of certain drugs, and were mainly implemented in the US. The Omnibus Budget Reconciliation Act 1987 (OBRA 87) regulation aimed to improve the use of psychotropic drugs in nursing homes. Data - mainly from observational retrospective studies - indicate that this regulation led to marked decreases in psychotropic drug use.[8] However, regulatory approaches are restrictive and limited to specific medications or drug-related problems (DRPs), and they are not sufficient to bring about changes in prescribing.[8;9] More personalized approaches should be used instead.[9]

2.4.2. Education, audit and feedback

Educational and feedback approaches have been widely used to promote changes in prescribing behaviours, and they are often used in combination. First, in the care of elderly patients, educational approaches are potentially of high relevance because most physicians (and other HCPs) receive inadequate training in geriatric pharmacotherapy.[10-13] Educational strategies targeting practising physicians can be passive (eg didactic courses, dissemination of printed material alone), or more interactive (eg academic detailing). Academic detailing refers to repeated face-to-face delivery of educational messages to individual prescribers, by doctors or pharmacists.[14] Second, auditing prescribing practice and then providing feedback to physicians on the quality of their prescribing is another potential optimisation strategy.

Previous literature reviews found that passive educational approaches are likely to be ineffective, while more interactive educational and feedback strategies can improve the quality of prescribing.[2;15-20] Furthermore, previous studies showed that interventions in long-term care settings should also target nurses, because they play a prominent role in the use of medicines, and more precisely in the use of drugs prescribed as-needed, antipsychotics, and laxatives.[2;21;22] However, most studies almost exclusively focused on psychotropic medicines, and the impact may not be sustained without continued intervention.[8;20]

More recent studies performed in primary care and long-term care used education and feedback to improve the use of psychotropic drugs, [23-25] the use of analgesics,[26;27] the avoidance of potentially inappropriate drugs,[28;29] and the management of patients at risk of stroke[25;30] or osteoporosis.[31] A detailed analysis of the interventions confirms that the more personalised, interactive and multidisciplinary, the more effectives the strategies are: (1) educational and feedback interventions targeting physicians together with other healthcare professionals (nurses, pharmacists)[23;27;29;30] tended

to report better results than interventions directed at physicians alone;[24;26;28] (2) interventions that relied on mailed educational and feedback material, without interactive and direct contacts with a "trainer", were not or weakly effective;[24;28] (3) interactive educational sessions without feedback were not more effective than passive education.[26] One study found that academic detailing provided separately to physicians and nurses in a residential care setting did not improve clinical practice in the area of falls reduction and stroke prevention.[25] In the hospital setting, one recent study found that comprehensive multidisciplinary educational program decreased the use of antibiotics in a geriatric hospital.[32] These results are encouraging, but further work is needed to evaluate (i) the sustainability of these interventions, and (ii) their impact on broader measurements of appropriateness.

2.4.3. Computerised prescribing and decision support

Computerised prescription order entry (CPOE) and computerised decision support systems (CDSS) are potentially powerful tools to prevent errors that lead to serious drug-related injuries.[33-37] The increased risk of such injuries in older people further enhances the attractivity of these systems for the geriatric population. CDSS can provide support with regard to drug interactions, choice of drug, dosages, monitoring. CPOE can also improve communication among providers during transitions of older people among sites and providers.[38]

However, there are important limitations to the use of CPOE and CDSS in today's care of elderly people. First, these systems are challenging to implement, not only in the hospital setting, but mainly in the long-term care and ambulatory settings.[7] Second, existing CDSSs were developed for adults in general, and do not account for considerations that are specific to the elderly, such as low dosages and routes of administration. Adaptations are needed before the systems can be used with elderly patients.[39] Third, it has been reported that therapeutic flags generated by computerised systems are often overridden by physicians, therefore decreasing their potential impact.[40] An older adult with comorbidities and polymedication might generate a substantial number of recommendations, too many of them being unimportant, while other important warnings may be ignored.[38] Fourth, recent evidence indicates that medication errors and ADEs have been linked to computerised systems.[41-44] The literature may have overestimated the effectiveness of these systems,[45] and analysing the failures in interactions between humans and computerised systems is needed to improve their safety.[43;46] Finally, it should not be assumed that the effectiveness of a computerised prescribing system in one country is any guide to its effectiveness in another.[45]

To date, a limited number of studies have evaluated the use of CPOE or CDSS with elderly people in acute care,[47;48] outpatient care,[49;50] and long-term care.[39;51;52] Most of them used systems that were adapted to the geriatric population, which is encouraging.[39;47;49-52] Several of these studies were descriptive, and did not measure the impact on process or outcome measures of appropriate

prescribing.[39;48;50-52] Two controlled studies have been published so far. Peterson et al. observed that CDSS improved the appropriateness of prescribing of psychotropic drugs in elderly patients in acute care,[47] and Tamblyn et al. observed a reduced initiation of drug-to-avoid by general practitioners.[49] However, similarly to previous studies in younger adults, a substantial number of alerts were overriden by prescribers in both studies, therefore decreasing the potential impact of these systems.

In conclusion, although this approach is of great interest, there is still along way to go before CPOE/CDSS can be claimed to be effective and feasible to improve prescribing of medicines in older patients.

2.4.4. Multidisciplinary approaches

Multidisciplinary approaches for the care of older patients are among the most effective approaches, they are applicable in all settings of care (but local adaptations are needed), and they can address the three categories of causes of inappropriate prescribing. Teams elevate the importance of non-physician input, and teams make fewer mistakes than do individuals, especially when each team member knows his or her own responsibilities as well as those of other team members.[53]

In geriatric evaluation and management (GEM) approaches, an integrated team composed of geriatric physicians, nurses and other HCPs (sometimes pharmacists) deliver medical and psychosocial care. Medical care includes a review of the medications prescribed, with the goal of identifying and preventing DRPs. Non-physician input in medication review mainly comes from clinical pharmacists and nurses. A recent qualitative study found that the multidisciplinary approach can promote a better use of medicines.[4] Several controlled studies evaluated the impact of GEM teamwork versus that of general adult care, in acute or clinic-based settings. The earliest studies were limited by the use of unvalid measures of prescribing appropriateness, namely the number of medicines prescribed.[54-56] A recent controlled study found that GEM teams can decrease overuse, underuse, and misuse of medicines, and decrease adverse drug reactions, in comparison to general adult care.[57] There is almost no similar European data, therefore limiting the generalisability of findings. A Norwegian study reported that drug treatment in a GEM (without pharmacist involvement) was more appropriate than on general medical units in terms of fewer inappropriate drugs and fewer drug-drug interactions.[58] A recent French study showed that the number of potentially inappropriate drugs decreased from admission to discharge on a medical geriatric unit.[59] However, clinical data of the patient were not accounted for in the evaluations. Similar teamwork approaches exist in nursing home and ambulatory (non clinic-based) care settings, but a geriatrician is usually not involved, and the interaction usually occurs between GPs, nurses, and pharmacists.

The aforementioned studies evaluated the impact of the team as a whole. One can wonder what is the added value of non-physicians (non-geriatricians). There is little data on the impact of nurses on

appropriate prescribing for elderly patients. A recent study found that the quality of drug use is positively associated with the quality of nurse-physician communication and with regular multidisciplinary team discussions addressing drug therapy.[60] In contrast, the impact of clinical pharmacists has been widely studied, and is discussed in the next paragraph.

2.4.5. Clinical pharmacy and pharmaceutical care

Clinical pharmacists are uniquely qualified to provide pharmaceutical care to elderly patients, and there is nowadays international acceptance of their role.[c] The NSF for Older People in the UK insisted on the role of pharmacists in optimising use of medicines in elderly patients,[1] and similar positions were taken in the US.[61] Clinical pharmacy is not widely implemented in Europe (except in the UK), but several recent reports have shown that pharmaceutical care for older people is developing.[62;63] When clinical pharmacists provide pharmaceutical care to individual patients, they perform medication reviews. A medication review is a structured, critical examination of a patient's medicines with the objective of reaching an agreement with the patient about treatment, optimising the impact of medicines, minimising the number of DRPs, and reducing waste.[64]

There is considerable evidence that clinical pharmacists providing medication reviews can decrease the occurrence of DRPs in the elderly. Most evidence comes from randomised controlled studies[55;57;62;65-78] and prospective pre-post studies[79-84] that were conducted in acute care settings,[55;79] ambulatory settings (including outpatient clinics),[62;65-73;81;82;85;86] long-term care settings,[74;75;83;84;87] or upon transfer between settings.[76;78] Several of them used validated measures of appropriateness of prescribing, such as the Medication Appropriateness Index,[57;65;78;87] drug-to-avoid criteria,[66;83;84] or other sets of explicit criteria.[71] Table 1 in annexe (p37-38) summarises randomised controlled trials of medication reviews performed by clinical pharmacists, with reported impact on appropriateness of prescribing. Successful interventions require that clinical pharmacists work in close liaison with the prescriber, and have access to the full clinical record of the patient.[64;88] Several studies that did not meet these conditions reported only weak impact or even detrimental effects.[67;89] The main limitation of these studies (together with studies on other optimisation approaches) is that the impact on mortality and morbidity outcomes is not well demonstrated, neither for the economic and humanistic outcomes.

[c] In addition to pharmaceutical care provided at the patient level, clinical pharmacists can also get involved in education and feedback for HCPs, in the development and implementation of computerised prescribing systems (see relevant paragraphs). Clinical pharmacy is discussed in more details in the third section of the Introduction.

2.5. Perspectives on other approaches

Additional approaches to optimise prescribing in elderly patients exist, but have not been widely tested yet. These include:

- Further involve patients or their carers in treatment decisions, and provide appropriate education. In other words, improve provider-patient communication and provide increased time for this communication.[3;90] This is a key theme of the NHS plan.[1] Some studies that intended to improve prescribing have targeted the patient in addition to the prescriber.[31;91] More data is needed on the impact of patient empowerment on appropriateness of prescribing, and new measures of appropriate prescribing should be developed for this purpose.[92]
- Give prescribing responsibilities to other professions; this is happening now in the UK, for pharmacists and nurses.
- Because clinical pharmacists are a scarce resource in several countries, drug regimen reviews by general practitioners themselves or by nurses could be an alternative. Preliminary evidence indicates that reviews by GPs can decrease drug consumption in nursing home patients,[93] and that training GPs in the methods used by pharmacists may result in an enhanced ability to detect pharmaceutical care issues,[94] but more rigorous data are needed.
- Improving communication between prescribers through technological improvements to share medication histories will save time and improve the safety of elderly patients who often have multiple prescribers. This new technology seems inevitable, but it is still a challenge in most countries.

2.6. Conclusions

One of the greatest opportunities to improve patient outcomes comes from more effective delivery of existing therapies rather than from discovering new treatments.[95] Strategies for optimisation should tackle the causes of inappropriate prescribing, including factors that are specific to the geriatric patient and to the practice environment. While earlier strategies focused on regulation and passive educational approaches, focus has moved towards more integrated approaches composed of multidisciplinary teamwork with clinical pharmacists or other multifaceted approaches. These approaches improve prescribing for elderly people, but additional data is needed on their relative efficacy and cost-effectiveness. Other promising approaches, including increasing patient empowerment, need to be tested.

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Annexe: Summary of randomised controlled trials measuring the impact of clinical pharmacists providing medication review on the appropriateness prescribing and related outcomes

Reference	Sample	Intervention	Design	Measure of appropriateness of prescribing, and impact	Other measures of impact and results		Comments
					Process measures	Outcomes measures	
Hospital setting							
Crotty 2005	110 older adults awaiting transfer from 3 hospitals to 85 LTC facilities (Australia)	Pharmacist transition coordinator	Randomised controlled, single blind	Change in MAI from baseline to 8-week follow-up: 3.2 to 2.5 for intervention, 3.7 to 6.5 for control (p=0.007)	DRPs identified at admission to LTC ↑ nb of drugs, 2 versus 1 per patient	(C): hospital usage among survivors (RRR 0.38), ADE (no diff), falls (no diff), worsening mobility (no diff), worsening pain (RRR0.55), worsening behaviors (no diff), increased confusion (no diff)	- Low baseline MAI because inpatients cared for by multidisciplinary GEM team
Lipton 1992, 1994	236 patients ≥65, discharged on ≥ 3 regular medications (US)	Pharmacist consultation at discharge and post-discharge	Randomised controlled, blinded	Implicit review using standardised instrument with 7 explicit review criteria: 82 v 93% had ≥1 problem in 1 of 6 drug categories (p.05), mean score 0.59 v 0.76 (p.01)	Number of drugs	(C) Better drug knowledge and compliance; health service use: no effect (E) service charges: no effect	- Substantial proportion of intervention patients nonetheless had prescribing problems; - limited scope of the intervention
Ambulatory care setting							
Coleman 1999	169 frail patients ≥65 in 9 chronic care clinics (US)	Clinic involved a pharmacist visit to reduce polypharmacy and high-risk drugs	Cluster randomised controlled, 2 years follow-up	High-risk medications 1 year before, 12 and 24 months follow-up: 3.92, 3.26 and 2.54 for C; 1.99, 2.94 and 1.86 for I → no significant difference		(C): care for geriatric syndromes: no improvement (E): no effect on cost of medical care and utilisation (H): higher levels of satisfaction	- Multi-component strategy (Pharmacist = 1 component) - Limited study power - Low participation level
Hanlon 1996 Schmader 1997 Cowper 1998	208 outpatients taking ≥ 5 regularly scheduled medicines (US)	Clinical pharmacist	Randomised, controlled, blinded 1 year follow-up	MAI: ↓ in inappropriate prescribing scores: 24% v 6% improvement at 3 months, sustained at 12 months (p=;0006)	Number of medicines: no difference Acceptance of recommendations: 55% enacted v 20%	(C) ADEs: fewer patients with ADEs (30% v 40%, p=0.19) Medication knowledge and compliance: no difference (E) similar drug costs; $7.5-30/1-unit improvement in MAI (H) HRQL (SF-36): no difference; patient health care satisfaction: no difference	- Potential for contamination at the physician level

Reference	Sample	Intervention	Design	Measure of appropriateness of prescribing, and impact	Other measures of impact and results		Comments
					Process measures	Outcomes measures	
Krska 2001	332 ambulatory patients, ≥65yrs, with ≥ 2 chronic diseases and taking ≥ 4 regular medicines (UK)	Clinical pharmacist performing medications review (in-home patient interviews, PC plans given to GPs)	Randomised, controlled, open-label	Pharmaceutical care issues (PCIs) identified through implicit review: more PCIs of all types resolved at 3 months	Acceptance and resolution of care issues identified: 96% acceptance and 70% resolution rates	(C) contact with health and social services: no difference (E) medicines costs: no change (H) HRQOL (SF-36): no change	- sample size too small to detect a difference in health services use - the same pharmacists performed all measures - potential confounding effect for GPs
Meredith 2002	259 Medicare patients, ≥65, admitted to home healthcare agencies, with ≥1 study medication problem (US)	Pharmacist and nurse reviewed medication problems and presented a plan to the physician	Randomised controlled 6-week follow-up	4 medication problems and predetermined objective criteria: duplication, CV problems, psychotropic drugs and confusion/fall/orthostasis, NSAIDs and risk of ulcer complication → difference for duplication and CV medicines	NR	(C): deterioration of health, new fall: no differences	- Generalisability (22% patients included)?
Nursing home setting							
Crotty 2004	154 residents (with difficult behavior and ≥5 prescribed drugs) from 10 high-level aged care facilities (Australia)	Case conference by residential care staff, including pharmacist	Cluster randomised controlled	Change in MAI from baseline to 3 months follow-up: difference in change between groups ($p<0.001$): 7.4 to 3.5 for intervention, 4.1 to 3.7 (and 6 to 6.2 for 2nd control)	NR	(C): residents behavior (NHBPScale): no differences at follow-up and in change across groups (E): monthly drug costs: no difference between change in PBS total costs	- Used 2 controls: control facilities, and controls within facility to assess educational bias (carry-over effect) – no significant difference observed - MAI by an independent pharmacist - GP present at the point of decision-making

Abbreviations: ADE: adverse drug event; AOU: assessment of underutilisation index; BAS: before-after-study; BP: blood pressure; (C): clinical outcome; CI: contra-indication; DDI: drug-drug interaction; (E): economic outcome; GP: general practitioner; (H): humanistic outcome; LTC: long-term care; NR: not reported; HRQL: health-related quality-of-life; LTC: long-term care; MAI: medication appropriateness index; NR: not reported; RCT: randomised controlled trial; UK: United Kingdom; US: United States

3. Organisation of health care in Belgium

This section aims to provide baseline information on health care in Belgium, for readers who are not familiar with the Belgian healthcare system. After an explanation of the basic principles of healthcare in Belgium, several aspects that are relevant to the present thesis (i.e. acute care and care of the elderly) are briefly presented.

The Belgian healthcare system

Belgium has a compulsory health care system based on the social health insurance model. Health care is publicly funded and mainly privately provided. The federal government regulates and supervises all sectors of the social security system, including health insurance. However, responsibility for almost all preventive care and health promotion has been transferred to the communities and regions. This explains why the system is frequently quoted as being heterogeneous and fragmented. Other key features of the Belgian health care system are: (i) liberal ideas of medicine: the majority of providers are self-employed, are paid per item of service (fee-for-service) and enjoy complete freedom of diagnosis and prescription; and (ii) patients are free to choose both their health care provider and their hospital. For the individual patient, one of the main advantages of the Belgian healthcare system is its high quality, freedom of choice of general practitioner, responsiveness and almost total coverage of the insurance system. However, the system is vulnerable to abuse, inefficiency, over-supply and over-consumption of services. A series of reforms in primary and secondary care have intended to contain costs while maintaining the essential structure of the system. This also applies to pharmaceutical expenditure. Attempts to stabilise expenditure have involved price-cuts and lower reimbursements. A long term national policy was also developed for promoting rational prescribing and use of drugs.

Acute care

The hospital sector forms an important part of the Belgian health care. The hospitals consume approximately 55% of the total contribution to the health insurance system (inpatient and outpatient departments). In 2003 there were 218 not-for-profit hospitals: 149 general hospitals and 69 psychiatric hospitals. The majority of hospitals (147) are private. The hospital legislation and financing mechanism are the same in both the public and private sector. Since the beginning of the eighties, the Belgian hospital sector has been restructured in order to better adapt its services to evolving needs: reduction of the number of hospital beds and redeployment to residential care homes, psychiatric care centres or sheltered housing for psychiatric patients, more geriatric previsions, shorter stays, expansion

of day-hospitalisation, scaled-up capacity [between 1980 and 2003, the number of hospitals dropped from 521 to 218 and the average capacity of a hospital rose from 177 to 325 beds].

Hospital financing, previously based on structural features such as the number of accredited beds, now takes the "justified activity of the hospital" into account. The justified activity is based on the case-mix of the hospital and the average national length of stay per diagnosis-related group. This change in the financing system from per diem rates to a prospective diagnosis-related group payment scheme has been quite successful in controlling costs.

With regard to quality, a policy has been adopted on evaluating medical practices and establishing standards or directives aimed at improving the quality of medical practice. This evaluation is based on clinical and financial information at the patient or hospital level. Over the last few years, there has also been an increased attention to clinical risk management in hospitals, and several research projects were funded by public health authorities. These projects aimed to describe the adoption of clinical risk management in Belgian hospitals, the attitude of health care professionals towards risk management, and the tools that could be used in daily practice to evaluate patient safety. Although it appears that there is limited clinical risk management procedures in Belgium (including limited reporting, analysis and follow-up of critical incidents, and limited training), it is very clear that it is gaining increasing interest, and that hospitals will be required to adopt structured and comprehensive measures toward clinical risk management in the near future, in order to improve patient safety.

Care of the elderly

The elderly care infrastructure comprises home care and community services, short- and long-term residential care, and hospital care. Home care and community services have been developed to accommodate the preference of senior citizens to remain in their own homes, and new initiatives are developed to expand home and community care in Belgium. Residential care includes rest homes and nursing homes (125.000 beds in Belgium for a population of 10 millions inhabitants with 16% older than 65). In 2002, 6% of the population aged 65 and over, 13% of the population aged 75 and older, and 34% of that aged 85 and older lived in residential care. The number of nursing home beds has increased by 65% from 1984 to 2001, and it is estimated that 170.000 additional beds will be needed by 2050, taking into account the compression of the morbidity perspectives. Each nursing home must have a medical coordinator. These persons are GPs who are responsible to coordinate quality initiatives, the medications policy, and training of the personnel. They progressively start to work in network with home care on the one hand, and with hospital geriatric units on the other hand

With regard to acute care, elderly people in Belgium – as in other developed countries – are hospitalised more often and for longer periods of time than younger adults. The majority of elderly patients admitted to hospital are admitted through the emergency department. Since 1984, geriatric

wards are distinguished as separate entities, and in 1986 geriatric medicine was recognised as a new competence for internists. These steps recognised the need for comprehensive geriatric assessment, evaluation, and management of frail older patients. Since 2005, geriatric medicine is recognized as a full medical specialty (six years training).

The theoretical provision of geriatric beds in acute hospitals is 5/1000 inhabitants aged 65 and over. There are currently 750 geriatric beds over the country, organised in about 220 geriatric departments composed of 300 units of 24 beds. Diagnosis, treatment, rehabilitation and discharge planning are provided by a multidisciplinary team. The average length of stay is 19 ± 5 days (median 16). There are 160 to 200 geriatricians censed (calculations varies according to the rate of activity). The acute geriatric beds are permanently in over occupation. In consequence, a new national program has been created to provide, in addition to acute geriatric units, internal geriatric liaison consulting, and geriatric day hospital.

Continuity of care

When an older patient is admitted to hospital, written information is provided by the general practitioner on the past medical history of the patient, reason(s) for referring to hospital, treatment (list of medications prescribed), and social context. No standard form is used for this, and the quantity of information can substantially vary from one admission to another. The information relative to medicines is often very limited (lack of information on OTC medicines, on duration of treatment, doses, …). When the patient comes from a nursing home, a copy of the medication sheet used by the nurses is usually provided.

Upon transfer from the hospital to the community or to the nursing home, the house officer in charge of the patient writes a summary of the admission, for the general practitioner. No standard form is used (except if it has been designed locally, for a single hospital or unit), and information on medicines is generally limited to a list of drugs, and limited information on treatment changes. No information is provided to the community pharmacist.

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4. Clinical pharmacy, a new patient-centred pharmaceutical approach: international perspective, and opportunities for development in Belgium

Spinewine A.

Louvain Medical 2003;122:127-139.

Abstract:
Clinical pharmacy is a patient-centred pharmaceutical practice. The main objective is to ensure the most appropriate and safe use of medicines. A second related objective is to optimise medicines use at the lowest possible costs. Clinical pharmacy services have existed for many years in North America and the UK, and they can be provided from the hospital pharmacy department (centralised services) or on the wards (decentralised services). There is robust evidence of their positive clinical and economical impact. This new pharmaceutical practice could be developed in Belgium, based on the expected impact, and on real current opportunities in the Belgian healthcare situation.

For the readers who do not understand French, the following paper first reviews the development of clinical pharmacy and pharmaceutical care abroad. A historical perspective is taken, and the different types of clinical pharmacy services are explained. Then the impact of different clinical pharmacy services is reviewed, and the methodology used for evaluation of impact is discussed. In the second section, the current scope of practice for Belgian hospital pharmacists is reviewed. Opportunities and barriers for a future development of clinical pharmacy practice in Belgium are discussed, and elements of strategic planning are provided.

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LA PHARMACIE CLINIQUE, UNE NOUVELLE ORIENTATION PHARMACEUTIQUE AU SERVICE DES PATIENTS: RÉALISATIONS À L'ÉTRANGER ET POSSIBILITÉS EN BELGIQUE

A. SPINEWINE[1]

Mots clefs: évaluation; hôpital; patient; pharmacie clinique; pharmacoéconomie; pharmacothérapie

RÉSUMÉ

La pharmacie clinique est une pratique pharmaceutique centrée sur le patient. Son premier objectif est d'assurer un usage aussi efficace et aussi sûr que possible des médicaments. Un deuxième objectif, lié au premier, est d'assurer une optimisation de l'usage des médicaments susceptible d'en diminuer le coût global. Elle se pratique depuis de nombreuses années en Amérique du Nord et en Angleterre, de façon centralisée (depuis la pharmacie de l'hôpital) et décentralisée (dans les unités de soins). L'effet attendu, tant au niveau clinique qu'économique, a été démontré dans de nombreuses études. Cette discipline pourrait être développée en Belgique en raison des nombreux avantages espérés et de réelles opportunités dans le cadre de l'évolution actuelle des soins de santé dans notre pays.

INTRODUCTION

Le concept de pharmacie clinique, souvent associé à celui plus global de soins pharmaceutiques, fait référence à une nouvelle pratique pharmaceutique centrée sur le patient (1). Formé de longue date à la connaissance du médicament en termes de propriétés chimiques et pharmacologiques, le pharmacien ne s'est intéressé que plus récemment à l'aspect pharmacothérapeutique. Or, en tant que spécialiste du médicament, le pharmacien peut apporter une plus-value dans la qualité des soins au patient. Cette fonction est complémentaire de celle des médecins. Hepler et Strand ont défini les soins pharmaceutiques comme l'engagement du pharmacien à assumer envers les patients la responsabilité de l'atteinte clinique des objectifs préventifs, curatifs ou palliatifs de la pharmacothérapie (2) mise en place et décidée par le médecin. Cet engagement peut s'exercer vis-à-vis d'un patient ou d'un groupe de patients précis, aussi bien en milieu ambulatoire qu'hospitalier. Il peut aussi s'envisager dans un cadre sociétal (3). Cet article a pour but de montrer quelles ont été les réalisations et l'impact de la pharmacie clinique à l'étranger. Nous nous concentrerons essentiellement sur la pratique en milieu hospitalier. Nous examinerons ensuite dans quelle mesure un tel développement est utile et souhaitable en Belgique.

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1. PRATIQUE ET IMPACT DE LA PHARMACIE CLINIQUE À L'ÉTRANGER

1.1. HISTORIQUE ET RAISONS DU DÉVELOPPEMENT

Le concept de pharmacie clinique et son développement sont principalement d'origine nord-américaine (Etats-Unis, Canada) et anglaise. Les pharmaciens ont en fait répondu à un besoin au départ spécifique, mais ensuite plus global, d'assurer un usage rationnel des médicaments (4).

Deux grandes orientations ont été suivies. En Amérique du Nord d'abord, il s'est agi initialement de mettre au service des patients l'expertise des pharmaciens dans le domaine de la pharmacocinétique et du monitoring thérapeutique. Ceci a conduit les pharmaciens à contribuer de façon importante à l'optimisation générale des traitements (4). En parallèle, les pharmaciens se sont progressivement intégrés dans les équipes d'investigateurs cliniques. Un grand nombre d'études cliniques se déroulent aujourd'hui aux Etats-Unis et au Canada avec une participation active des pharmaciens dans la conception même de l'étude, et ce, dans différents domaines cliniques (5-9). En Angleterre ensuite, des études bien documentées ont mis en évidence un besoin urgent d'amélioration de la qualité de prescription et d'administration des médicaments, en terme de prévention d'effets secondaires, d'interactions médicamenteuses, ou d'erreurs d'administration. Ceci a conduit au développement d'un nouveau système de prescription et de dispensation, ainsi qu'à la présence de pharmaciens dans les services cliniques (10-12). Enfin, dans l'ensemble de ces pays, divers changements économiques et sociaux dans l'organisation des soins de santé ont également contribué au développement de services de pharmacie clinique (4).

Restreinte au départ à des services très ciblés envers un nombre limité de bénéficiaires, la pharmacie clinique a connu depuis lors une expansion très importante (13). Plusieurs éléments déterminants ont permis cette évolution. Tout d'abord, l'intérêt de la pharmacie clinique a été reconnu par les autorités sanitaires à l'échelle locale et nationale dans les pays considérés (certains de ces services font actuellement l'objet d'un système de remboursement spécifique). Par ailleurs, des sociétés scientifiques et professionnelles très actives ont été créées. En termes de formation, le curriculum d'étude du pharmacien a été adapté. En particulier, la pharmacothérapie et l'approche inhérente aux soins pharmaceutiques, de même que les stages en milieu hospitalier, y tiennent une place de choix (14). La publication par des pharmaciens de livres de référence de pharmacothérapie ou de publications scientifiques témoigne de la compétence qu'ils ont ainsi pu acquérir dans ce domaine (15-17).

L'intérêt qu'ont trouvé tous les acteurs du monde médical dans la pharmacie clinique est démontré par le fait qu'aujourd'hui un hôpital universitaire au Canada, aux Etats-Unis ou en Angleterre compte en moyenne un pharmacien pour dix à trente lits, par comparaison à un pharmacien pour cent à cent cinquante lits en Belgique.

En Europe, on assiste depuis une dizaine d'années au développement de services pharmaceutiques centralisés visant à une amélioration de la qualité et de la rentabilité des thérapeutiques. De façon plus ponctuelle et plus restreinte, certains projets de services décentralisés où les pharmaciens sont intégrés dans les équipes médicales ont été créés (18-22). Les changements nécessaires au niveau du curriculum se mettent progressivement en place dans les universités (23).

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1.2. SERVICES ET FONCTIONS

Dans ses implantations nord-américaine et anglaise en milieu hospitalier, la pharmacie clinique s'exerce tant dans le cadre de services centralisés (au départ de la pharmacie de l'hôpital ou de la direction hospitalière) que de services décentralisés (on parlera alors plus directement, notamment dans le cas de la pharmacie d'étage, de services centrés sur le patient) (24,25). Ces services sont présentés au tableau I. Tous répondent à la même volonté d'optimisation de la qualité d'utilisation des médicaments.

1.3. IMPACT DE LA PHARMACIE CLINIQUE

Tout au long de son implémentation, la pharmacie clinique a fait l'objet d'études d'évaluation objectives, dont un grand nombre ont été publiées dans des revues scientifiques. Une analyse critique de la méthodologie utilisée dans ces études n'est pas l'objet de notre discussion. Toutefois nous avons tenu à illustrer les différentes mesures d'impact utilisées (voir tableau II). De façon générale, les études ont démontré que les services de pharmacie clinique sont bien acceptés au sein de l'hôpital, qu'ils permettent d'améliorer l'efficacité des traitements médicamenteux et de réduire les risques et les coûts liés à ces traitements (26-31). Ces résultats obtenus ont été récemment reconnus par l'American College of Physicians et l'American Society of Internal Medicine, qui ont souligné le bénéfice d'une collaboration médecins-pharmaciens dans l'amélioration de la qualité des soins pour le bien des patients (32).

A. Impact global à l'échelle nationale aux Etats-Unis

Le tableau III montre les résultats d'une série d'études d'observation menées à l'échelle nationale aux Etats-Unis (33-35). Le message essentiel est que l'implémentation de services centralisés et décentralisés de pharmacie clinique dans les hôpitaux étudiés permet, après une période de mise en place,

TABLEAU I

Services de pharmacie clinique développés en Amérique du Nord et en Angleterre

1. Services centralisés (au niveau de l'hôpital)
- Comité médico-pharmaceutique
- Information sur les médicaments au personnel (para)médical
- Etudes d'évaluation de l'utilisation des médicaments
- Aide aux essais cliniques
- Pharmacovigilance

2. Services décentralisés (en relation directe avec le patient – au sein d'une unité de soins)
- Anamnèse médicamenteuse à l'admission
- Suivi des traitements des patients
- Participation aux tours de salle
- Consultations pharmacocinétiques
- Conseil au patient (éducation)
- A la sortie du patient: résumé du traitement instauré et communication au généraliste et au pharmacien d'officine, éducation du patient
- Services cliniques spécifiques (intégration à l'équipe multidisciplinaire, service de consultation): pharmacocinétique, pédiatrie, gériatrie, oncologie, contrôle de la douleur, anticoagulation, antibiothérapie, nutrition parentérale, ...

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TABLEAU II

Moyens d'évaluation de l'impact de services de pharmacie clinique

L'impact de services de pharmacie clinique peut être évalué par des mesures directes relatives au service fourni ("process measures") ou par des mesures de conséquence ("outcome measures"). Cette classification peut s'appliquer de manière générale à l'évaluation de tout service de soins de santé (78). Chaque étude d'impact devrait idéalement combiner ces deux types de mesure.

1. Mesures relatives au service fourni

Caractéristiques: Propriétés du service implémenté, essentiellement propriétés des interventions faites par les pharmaciens

Exemples: Type d'interventions faites par les pharmaciens, importance clinique, acceptation par le corps médical, charge de travail,...

2. Mesures de conséquences

Caractéristiques: Conséquences cliniques, économiques et humaines de l'implémentation du service de pharmacie clinique. Ces mesures peuvent être réalisées soit avant et après l'implémentation du service de pharmacie clinique (on parle alors de contrôle historique), soit de façon concomitante chez des patients/médecins/hôpitaux bénéficiant ou non du service évalué (contrôle simultané).

Exemples:
- Mesures cliniques: Efficacité des traitements, effets secondaires des médicaments, morbidité et mortalité, durée de séjour, compliance du patient,...
- Mesures économiques: Coûts pharmaceutiques, coûts hospitaliers, coûts indirects divers
- Mesures humaines: Qualité de vie, satisfaction des patients et du corps médical

TABLEAU III

Impact de la pharmacie clinique aux Etats-Unis suivant les études de Bond (33-35)

Objectifs: Mesurer la relation entre la présence de services de pharmacie clinique (centralisés et décentralisés) et certains paramètres cliniques et économiques prédéfinis

Méthode: Études d'observation, données prospectives (1992)
Analyse par régression uni- et multi-variée

Echantillon: Plus de 1000 hôpitaux (1016 à 1081 suivant l'étude), c'est-à-dire environ 30% de l'ensemble des hôpitaux américains

Résultats:
(1) Impact clinique
- Présence de divers services centralisés et décentralisés associée à une mortalité hospitalière et un taux d'erreurs de médication plus faibles ($p<0.05$)
- 40478 vies sauvées chaque année de par la présence de ces services

(2) Impact économique
- Présence de divers services centralisés et décentralisés associée à des coûts hospitaliers plus bas ($p<0.05$)
- 5.1 milliards de dollars d'économies par an de par la présence de ces services

(3) Influence du nombre de pharmaciens cliniciens
- Augmentation du nombre de pharmaciens cliniciens par nombre de lits associée à une diminution de la durée de séjour, du taux d'erreurs de médication et des coûts hospitaliers ($p<0.05$)

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de sauver des vies tout en ne coûtant pas davantage à la société, et même en faisant souvent réaliser des économies substantielles. Bien que ce type d'étude ne permette pas de prouver une relation de cause à effet, la taille de l'échantillon, la multiplication des mesures d'efficacité utilisées ainsi que les méthodes d'analyse donnent un fort niveau de crédibilité aux conclusions qu'en tirent les auteurs. Ces résultats nationaux positifs se retrouvent aussi bien pour les services centralisés (36, 37) que décentralisés dans des études expérimentales à plus petite échelle.

B. Impact des pharmaciens cliniciens présents dans les services cliniques

L'utilité de ces services doit être envisagée ici sur base du rôle direct que peut jouer le pharmacien soit de façon rétroactive (en analysant les prescriptions de façon rétrospective) soit proactive (en intervenant au moment même de la prescription). Le premier type d'action a été étudié par Barber et al. (38) qui ont analysé l'ensemble des interventions (n=3501) faites pendant une semaine par 248 pharmaciens anglais révisant les prescriptions de 27 hôpitaux. Les pharmaciens passaient en moyenne 1h30 dans chaque service (avec une moyenne de 22 patients/service). Les trois interventions les plus fréquentes concernaient le choix d'un régime thérapeutique (dose, fréquence) (29%); l'ajout ou la suppression d'un médicament (21%); ou le choix d'un médicament plus approprié (14%). Dans 83% des cas, les interventions furent considérées comme positives et acceptées par le corps médical avec pour conséquence un changement dans le traitement ou dans son suivi. Des résultats similaires ont été obtenus par Hawkey et al. (39). Les études comprenant des mesures d'«outcome» (conséquences cliniques et économiques) sont également favorables puisqu'elles montrent une diminution significative de la durée de séjour et des coûts pharmaceutiques et hospitaliers (40), et ceci sur des séries importantes (41-43). Par exemple, une étude contrôlée avec 3081 patients admis dans des services de médecine générale et de chirurgie a mis en évidence un rapport bénéfice-coût de 6:1 (41). Les résultats sont plus épars et plus variables en ce qui concerne l'impact d'interventions pharmaceutiques sur la qualité de vie des patients (44), et une amélioration dans la méthodologie de ces études s'avère sans doute nécessaire.

C. Le pharmacien clinicien et le patient individuel

A côté du rôle qu'il peut jouer dans un service médical ou chirurgical de manière générale, le pharmacien peut également apporter son expertise dans des situations individuelles spécifiques où le risque d'événements iatrogéniques médicamenteux est particulièrement élevé. Ceci a été démontré pour des patients admis aux soins intensifs (45), aux urgences (46), en gériatrie (47), en psychiatrie (48,49) ou en pédiatrie (50); ou encore pour des patients sous anticoagulants oraux (51), souffrant d'insuffisance cardiaque (52, 53), ou recevant des médicaments nécessitant un monitoring thérapeutique (54). Des exemples d'études d'impact relatives à plusieurs de ces services sont reprises dans le tableau IV. Dans chacun de ces domaines, le pharmacien joue la plupart du temps un rôle proactif, c'est-à-dire qu'il intervient au moment où une décision de traitement est prise. Cette intervention précoce est d'ailleurs une des conditions du succès, comme le démontre l'étude de Leape (45).

Bien que cet article ne traite pas des réalisations non hospitalières des soins pharmaceutiques, il semble intéressant de mentionner que ce type de service clinique s'est

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TABLEAU IV

Exemples d'études d'impact de services décentralisés de pharmacie clinique dans des unités de soins spécifiques (ou chez des patients spécifiques)

Intervention	*Type d'étude*	*Résultats*	*Réf*
Participation du pharmacien clinicien au tour de salle des soins intensifs (rôle proactif)	Prospective Randomisée Contrôlée 275 patients	99% des interventions acceptées ↓ événéments iatrogéniques médicamenteux (p<0.001) ↓ coûts de séjour ($270.000/an)	45
Consultations pharmaceutiques lors de l'initation d'un anticoagulant oral	Pré-post 120 patients	↓ durée de séjour (p=0.009) ↓ n patients et patients-jour avec INR > 3.5 et > 6.0 (p<0.001) ↓ n saignements ↓ n interactions médicamenteuses sévères (p=0.02)	51
Equipe multidisciplinaire gériatrie - pharmacien responsable de l'aspect pharmacothérapie	Prospective Randomisée 436 patients (75 ans et +)	↓ n médicaments prescrits (p<0.05) ↓ incohérences indication - médicament (p<0.025) ↓ choix inappropriés de médication (effets secondaires, meilleure alternative - p<0.005)	47
Intervention du pharmacien clinicien dans le traitement de l'insuffisance cardiaque	Prospective Randomisée Contrôlée 181 patients	↓ mortalité totale + complications d'insuffisance cardiaque à 6 mois (p=0.05) ↑ doses d'IEC prescrites (p<0.001) ↑ utilisation de vasodilatateurs chez les intolérants aux IEC (p=0.02)	53
Pharmaciens cliniciens dans un service de pediatrie (2 hôpitaux)	Prospective Non-contrôlée 101022 prescriptions	Détection et prévention d'erreurs de prescription (qualifiées d'erreurs par le pharmacien *et* le prescripteur): 1.56 erreurs prévenues / 100 patient-jour, 4.7/1000 prescriptions	50
Service de pharmacie clinique en psychiatrie	Pré-post 93 patients	↑ scores cliniques à la sortie (diverses échelles de mesure utilisées) ↓ effets secondaires (symptômes extra-pyramidaux) durée de séjour et coûts pharmaceutiques similaires	49
Services de pharmacocinétique	Méta-analyse 27 études	↑ % patients avec Cp dans l'intervalle thérapeutique ↑ % échantillons collectés de façon appropriée ↑ % résultats utilisés de façon appropriée	54

Abréviations: Cp: concentrations plasmatiques; IEC: inhibiteur de l'enzyme de conversion; INR: International Normalized Ratio; n: nombre; p: valeur statistique p; %: pourcentage
Etudes «pré-post»: études avec contrôle historique, c'est-à-dire avec mesures avant et après implémentation du service de pharmacie clinique

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fortement étendu à des patients non hospitalisés. Le pharmacien intervient alors soit au sein d'une équipe médicale faisant des consultations (55-57), soit seul dans la pharmacie de ville (58,59). De nombreuses interventions ont ciblé des patients âgés (60-64).

Un domaine où le rôle du pharmacien vis-à-vis du patient individuel peut aussi être très important est l'anamnèse médicamenteuse où une information de qualité est essentielle (65-68). Enfin, le pharmacien peut intervenir de façon efficace dans le suivi et la bonne mise en œuvre des prescriptions faites à la sortie de l'hôpital (y compris le conseil au patient et la communication avec le pharmacien de ville) (69-72).

2. PERSPECTIVES EN BELGIQUE

2.1. SITUATION ACTUELLE

Même si les tâches cliniques du pharmacien sont reconnues dans les textes légaux belges depuis une dizaine d'années (AR du 04 mars 1991*), la pharmacie clinique, telle qu'elle est développée en Amérique du Nord ou en Angleterre, reste encore une vision du futur en ce qui concerne la Belgique. Ceci ressort d'une étude menée en 2001, qui a tenté d'analyser spécifiquement la situation belge au départ de cadres de réflexion de l'école anglaise de pharmacie clinique (73). Néanmoins, certains services centralisés de pharmacie clinique existent et jouent déjà un rôle important au sein de l'hôpital. Un bon exemple est celui des comités médico-pharmaceutiques, dont les missions ont été récemment fortement élargies (AR 20 août 2000). En plus de l'établissement et de la mise à jour du formulaire thérapeutique, ce comité est chargé de «la proposition de mesures en vue d'améliorer la consommation de médicaments et d'éviter les erreurs de prescription», de la «rédaction d'un rapport annuel reprenant la consommation de médicaments à l'hôpital (...), [ainsi que] les mesures prises en vue d'une prescription plus rationnelle». Il persiste toutefois un manque de moyens spécifiques pour permettre de développer ces comités. Certains hôpitaux universitaires ont réalisé des études d'évaluation de l'utilisation de certains médicaments coûteux et/ou utilisés fréquemment de façon irrationnelle (74). Ces études restent toutefois limitées parce que longues à réaliser et demandant un personnel formé à ce type de travail. Les pharmaciens sont également actifs dans les domaines des études cliniques, de l'information aux médecins et infirmières, et du Drug Monitoring, ce dernier étant exercé cependant le plus souvent au départ du laboratoire. D'autres mesures centralisées ont été prises par de nombreux hôpitaux afin d'améliorer la qualité de distribution et d'administration des médicaments, comme par exemple la dispensation individuelle, la prescription informatisée ou encore la préparation centralisée des cytostatiques. Par contre, les services décentralisés sont quasi inexistants, à l'exception de quelques projets relativement récents dans des hôpitaux universitaires. Aux Cliniques Universitaires Saint-Luc ainsi qu'aux Cliniques Universitaires de Mont-Godinne, par exemple, des pharmaciens hospitaliers sont directement impliqués depuis plusieurs années dans l'optimisation des chimiothérapies anticancéreuses. Ailleurs, on rapporte l'intégration d'un pharmacien hospitalier dans une unité de soins intensifs (75, 76), ou encore une implication des pharmaciens dans une unité de gériatrie, afin d'y évaluer l'importance d'effets secondaires médicamenteux.

*Pour information, les tâches des pharmaciens hospitaliers en Belgique sont variées et plus larges que celles des pharmaciens nord-américains. Par exemple la gestion du matériel médical et des implants, ainsi que le contrôle de la stérilisation n'est pas à charge du pharmacien hospitalier américain.

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2.2. INTÉRÊT ET POSSIBILITÉS D'UN DÉVELOPPEMENT FUTUR

Au vu des résultats d'études publiées à l'étranger, l'intérêt clinique et économique des activités de pharmacie clinique décrites précédemment apparaît réel tant pour les patients que pour la société de ces pays. Nous pensons donc qu'il peut en être de même en Belgique. Cependant, il existe également des facteurs propres à notre pays et à sa situation actuelle que nous désirons souligner ici. Ces facteurs ont été identifiés par le biais d'une étude récente (73) et ressortent de discussions et échanges avec de nombreuses personnes potentiellement impliquées dans le développement de la pharmacie clinique. Ces facteurs sont présentés au tableau V.

La volonté politique d'instaurer un meilleur usage des médicaments est liée à celle visant tant à diminuer le coût des médicaments actuels qu'à dégager les moyens financiers nécessaires à l'introduction de thérapeutiques dites innovantes*. Dans les deux cas de figure, le pharmacien peut contribuer de manière efficace à la mise en œuvre de cette politique.

L'informatisation des prescriptions constitue également un élément important pour les pharmaciens à plusieurs points de vue. Tout d'abord, les prescriptions informatisées sont plus claires et complètes que les ordonnances manuscrites. Ceci permet une meilleure qualité de distribution des médicaments. Ensuite la prescription informatisée génère une base de données d'intérêt certain: elle permet à l'ensemble de l'équipe soignante d'avoir une vue d'ensemble des traitements mis en place pour chaque patient, et de plus elle fournit une aide à la détection d'interactions ou d'incompatibilités. La prescription informatisée constitue une opportunité de dialogue constructif entre le pharmacien et le prescripteur.

L'évolution vers une forfaitarisation des soins médicaux et pharmaceutiques conduira à développer de plus en plus des approches objectives en terme de choix thérapeutiques. Les expériences étrangères dans ce domaine se sont révélées très convaincantes pour une justification pharmacoéconomique de la pharmacie clinique. De tels résultats devraient être applicables en Belgique.

Enfin, il est clair que la volonté politique de diminuer le nombre de médecins mènera

*Un effort important au niveau fédéral a été réalisé en vue d'accélérer le processus d'enregistrement et de remboursement des médicaments, dans le but de ne pas laisser la Belgique privée de médicaments innovants pour des raisons administratives. Ces dernières étaient cependant souvent liées à des questions de disponibilités budgétaires. La présence de pharmaciens-cliniciens peut certainement représenter un élément utile à l'utilisation optimale et raisonnable de ces nouveaux médicaments coûteux.

TABLEAU V

Potentiel de développement futur de la pharmacie clinique en Belgique d'après des pharmaciens hospitaliers belges (73)

Facteurs favorisants	*Difficultés*
– Volonté politique d'améliorer la qualité d'utilisation des médicaments – Informatisation des prescriptions – Changement de politique de financement des médicaments (forfaitarisation) et volonté de diminuer le coût des soins de santé – Diminution du nombre de médecins dans un futur proche (numerus clausus)	– Manque de temps et de moyens (pharmaciens hospitaliers) – Problèmes d'acceptation de la part du corps médical – Formation universitaire insuffisante / inappropriée

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à une certaine redéfinition des tâches, le médecin devant, par la force des choses, se concentrer sur les domaines où lui seul peut agir (c'est-à-dire le diagnostic et les décisions thérapeutiques globales). Il sera donc amené à confier à d'autres la mise en œuvre pratique des décisions qu'il prend. Le partenariat avec les pharmaciens, spécialistes des médicaments, est donc intéressant*. Ceci doit se comprendre dans le cadre de la constitution d'équipes médicales prenant en charge le patient (au delà du dialogue singulier médecin-patient qui doit être à la base de toute démarche diagnostique et thérapeutique et qui garde donc toute son importance). Ces équipes doivent être des lieux de dialogue où des disciplines complémentaires s'associent.

Le contexte actuel apparaît donc favorable au développement de projets pilotes de services décentralisés de pharmacie clinique, et ceux-ci pourraient être ciblés spécifiquement en fonction des besoins et des priorités locales et nationales** (77). Ce développement pourrait se faire, au départ de la pharmacie de l'hôpital, par l'intégration progressive de pharmaciens formés au bon usage des médicaments dans des services ciblés. Dans ce cadre, une orientation vers les patients à risque élevé d'effets secondaires et d'interactions médicamenteuses apparaît certainement comme prioritaire.

2.3. DIFFICULTÉS ATTENDUES

Le tableau V résume également les principales difficultés qui seront vraisemblablement rencontrées. Tout d'abord, il est certain qu'une augmentation relative du nombre de pharmaciens hospitaliers s'avère nécessaire pour pouvoir pratiquer la pharmacie clinique de façon efficace et il faut donc trouver ici le cadre institutionnel et financier qui permette cette augmentation. Une manière de répondre à cette difficulté sera de montrer que le rapport bénéfice-coût de l'activité du pharmacien clinicien est favorable. Une autre difficulté est l'acceptation de l'intervention des pharmaciens par le corps médical. Ceci nécessite tout d'abord que le pharmacien soit compétent et assure la responsabilité de ses interventions. Il faut ensuite que les objectifs de la collaboration soient clairs dès le départ. Lorsque cela est assuré, les études réalisées à l'étranger ont démontré que, malgré les craintes exprimées au départ, les interventions des pharmaciens sont généralement très bien acceptées.

2.4. ETAPES À PARCOURIR

Le tableau VI résume les étapes à suivre dans le développement de tels projets. Il est important de bien saisir que les pharmaciens «d'étage» n'ont en aucun cas pour fonction ou pour but de remplacer le médecin ou de s'approprier une partie de ses fonctions. Ils sont là pour apporter une *plus-value* en terme de qualité d'utilisation des médicaments. Par ailleurs, aucun service clinique n'est et ne sera jamais obligé de s'associer des pharmaciens s'il juge leur présence inutile ou contre-indiquée. Néanmoins, nous pensons

* Des réflexions sont en cours pour la formation et la mise en place de personnel apportant au médecin une aide dans des domaines spécifiques («physician assistants» [ou «assistants-médecins»], «therapeutic nurses» [ou "infirmières en charge de traitements"]). La place des pharmaciens-cliniciens n'est pas encore à l'ordre du jour de ces discussions, mais ceci pourrait être un développement intéressant.

** Il est intéressant de noter qu'une collaboration se met en place à l'échelle nationale, ce qui semble utile pour promouvoir davantage l'intérêt potentiel de la pharmacie clinique. Dans ce cadre, l'association belge des pharmaciens hospitaliers sensibilise progressivement les pharmaciens hospitaliers au potentiel de la pharmacie clinique. Parallèlement, la Belgique était responsable de l'organisation du congrès annuel de la Société Européenne de Pharmacie Clinique en novembre 2001. Enfin, un groupe de travail composé de pharmaciens et de médecins s'est constitué afin d'échanger les informations relatives aux études belges sur la qualité d'utilisation des médicaments en milieu hospitalier. Ce groupe fera bientôt partie de la Société belge de Pharmacoépidémiologie.

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TABLEAU VI

Etapes à suivre dans l'établissement de services décentralisés de pharmacie clinique en Belgique

1. Préparation de la pharmacie de l'hôpital
   - Assurer une volonté de changement de la part des pharmaciens hospitaliers; définir les objectifs à atteindre et les moyens à mettre en œuvre
   - Optimiser le système de distribution des médicaments, la gestion et l'organisation afin de libérer du temps pour les tâches cliniques
   - Disposer des ressources nécessaires relatives à l'information sur les médicaments (pharmaciens compétents en recherche et analyse de littérature; ressources matérielles)
   - Identifier les besoins de mise à jour des connaissances et compétences; assurer une formation appropriée

2. Préparation des personnes clés au niveau de l'hôpital
   - Sensibiliser la direction hospitalière à la volonté de changement et aux objectifs fixés
   - Se mettre d'accord sur les objectifs d'une collaboration pharmaciens-médecins et sur les étapes à suivre

3. Développement d'un projet pilote
   - Tenir compte des besoins et de la demande locale dans le choix du service clinique, ainsi que des résultats d'expériences étrangères
   - Limiter le projet à un nombre restreint de patients ou à un seul service, dans lequel un seul (ou un nombre restreint) pharmacien(s) intervient
   - Préparer les outils nécessaires au travail des pharmaciens hospitaliers dans l'unité
   - Etablir un premier contact avec l'unité: connaissance de son mode de fonctionnement, des rôles et responsabilités des différents intervenants; définition claire du rôle du pharmacien et des détails pratiques de son travail dans l'unité
   - Une fois le projet démarré: se donner le temps nécessaire à l'intégration et à la mise en place d'un service efficace
   - Evaluer de façon régulière et avec les différents intervenants le travail du pharmacien et la collaboration au sein de l'équipe

4. Evaluation et réajustement
   - Analyser les résultats obtenus (sur base des interventions faites par le pharmacien) par rapport aux objectifs fixés
   - Présenter le bilan aux personnes-clés
   - Définir les objectifs et modalités d'un développement futur

que dans la mesure où l'évaluation objective des projets mis en place s'avère positive, elle devrait mener à une expansion progressive des activités des pharmaciens cliniciens.

2.5. IMPLICATIONS POUR LA FORMATION DES PHARMACIENS

Il est évident que la formation actuelle des pharmaciens doit être adaptée afin que les étudiants acquièrent les connaissances et compétences relatives à leurs fonctions cliniques (73). Cela nécessite que la formation universitaire soit plus centrée sur le patient, et inclue davantage de notions de pharmacothérapie à tous les niveaux de l'enseignement. De plus les pharmaciens devraient avoir l'opportunité de communiquer avec les patients et avec les médecins tout au long de leur formation et certainement pendant leurs dernières années d'étude*. Le but est de condui-

*Actuellement un nombre limité d'étudiants de dernière année de l'UCL ont la possibilité de réaliser un mois de stage dans un service clinique. Il serait souhaitable d'étendre ce stage à une proportion plus importante d'étudiants et également d'augmenter la durée et la fréquence de ces stages.

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re pharmaciens et médecins à une meilleure compréhension de leurs activités respectives et de construire la base d'un espace de collaboration où chacun garde sa spécificité et sa compétence propre.

CONCLUSION

Développer la pharmacie clinique est à la fois un défi et une évolution normale et même souhaitable de l'activité pharmaceutique en Belgique. Défi, dans la mesure où il imposera au pharmacien d'acquérir les compétences nécessaires, de prendre sa part de responsabilités dans les soins à donner au patient, et d'établir avec le monde médical un dialogue fructueux. Evolution normale et souhaitable dans la mesure où l'expérience nord-américaine et anglaise montre tout l'intérêt de la pharmacie clinique dans le cadre d'une réelle optimisation de l'usage des médicaments. Le développement de cette discipline s'est fait en vingt à trente ans dans ces pays et il n'y a pas de raison de penser que cela puisse se faire plus rapidement en Belgique, tenant compte de la nécessité de mettre en place les moyens de formation et les cadres institutionnels requis. Il s'agit donc ici d'un projet à long terme et pas d'une innovation «rapide et ponctuelle». En outre, il faudra sans doute trouver la voie propre à notre pays. La valeur des résultats attendus justifie certainement à nos yeux les efforts à consentir.

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2.

Objectives

The main research hypothesis was that pharmaceutical care[d] provided to elderly patients improves the quality of use of medicines. To that end, the first step was to understand the baseline level of appropriateness of use of medicines, and the second step was to evaluate the impact of pharmaceutical care on relevant process and outcome measures. The objectives of these two sections were as follows:

- To identify the processes leading to inappropriate use of medicines in older patients admitted on acute geriatric wards in Belgium, with regard to prescribing, counselling, and transfer of information to the general practitioner;
- To measure the appropriateness of prescribing in this population, using validated instruments;

- To evaluate the feasibility of providing pharmaceutical care at an acute geriatric ward;
- To describe the characteristics of interventions made by the clinical pharmacist, to measure their acceptance by prescribers and their clinical significance, and to measure their persistence after discharge;
- To quantify the impact of pharmaceutical care on validated measures of appropriateness of prescribing.

[d] Although some authors make distinctions between « clinical pharmacy » and « pharmaceutical care », we will use these terms interchangeably. The term « clinical pharmacy » has the advantage to be better understood by Belgian health care professionals who are not familiar with this practice, while « pharmaceutical care » better reflects what the clinical pharmacist actually does for individual patients.

3.

Results

FOREWORD

This Chapter has 3 sections.

In the first section, the results of the qualitative study that aimed to identify the factors underlying inappropriate use of medicines are provided.

The second section reports the phase of implementation of the clinical pharmacy service, as well as a description of the interventions made by the clinical pharmacist.

In the third section, the impact of pharmaceutical care on the quality of use of medicines in elderly inpatients is described. This study was a randomised controlled trial, and used three measures of appropriateness of prescribing in elderly patients (Medication Appropriateness Index, Beers criteria, and ACOVE criteria of underprescribing) as primary outcome measure. These were developed by international experts and validated in their respective countries. We had to adapt these measures to our local situation, and to make sure that inter-rater reliability was adequate. This was quite straightforward for the Beers and ACOVE criteria, whereas an in-depth validation was required for the Medication Appropriateness Index. The results of this validation are reported just before the results of the randomised controlled trial. Finally, additional data related to this intervention study are given. This includes a comparison of the relative value of pharmaceutical care and of a computerised prescribing system.

3.1.

Appropriateness of use of medicines in elderly inpatients: qualitative study

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Papers

Appropriateness of use of medicines in elderly inpatients: qualitative study

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Abstract

Objectives To explore the processes leading to inappropriate use of medicines for elderly patients admitted for acute care.
Design Qualitative study with semistructured interviews with doctors, nurses, and pharmacists; focus groups with inpatients; and observation on the ward by clinical pharmacists for one month.
Setting Five acute wards for care of the elderly in Belgium.
Participants 5 doctors, 4 nurses, and 3 pharmacists from five acute wards for the interviews; all professionals and patients on two acute wards for the observation and 17 patients (from the same two wards) for the focus groups.
Results Several factors contributed to inappropriate prescribing, counselling, and transfer of information on medicines to primary care. Firstly, review of treatment was driven by acute considerations, the transfer of information on medicines from primary to secondary care was limited, and prescribing was often not tailored to elderly patients. Secondly, some doctors had a passive attitude towards learning: they thought it would take too long to find the information they needed about medicines and lacked self directed learning. Finally, a paternalistic doctor-patient relationship and difficulties in sharing decisions about treatment between prescribers led to inappropriate use of medicines. Several factors, such as the input of geriatricians and good communication between members of the multidisciplinary geriatric team, led to better use of medicines.
Conclusions In this setting, improvements targeted at the abilities of individuals, better doctor-patient and doctor-doctor relationships, and systems for transferring information between care settings will increase the appropriate use of medicines in elderly people.

Introduction

Elderly patients are frequent users of health services and medicines. Research, however, has identified problems in the effective use of medicines in this population.[1 2] Adverse drug reactions are implicated in 5-17% of hospital admissions.[1] Elderly people are also less likely to receive treatments indicated by guidelines,[3] such as those for patients admitted to hospital with myocardial infarction.[4] In addition, discrepancies with medicines prescribed in the hospital occur after discharge.[5] Although many quantitative studies have identified deficiencies, only limited work has been carried out on the reasons for these problems.

To optimise the provision of care in hospital and around discharge for elderly people, the national service framework for older people in the United Kingdom and similar strategies in other countries have encouraged the development of programmes of "care of the elderly." In this approach, multidisciplinary teams deliver medical, psychosocial, and rehabilitative care. The "single assessment process" was later developed to ensure that professional resources are used effectively.[6] There is, however, limited qualitative or quantitative data on the appropriateness of use of medicines in elderly people admitted to acute care for the elderly wards.[7 8]

We explored the appropriateness of use of medicines for patients admitted to wards for care of the elderly from the perspectives of healthcare professionals and patients. We considered prescribing, counselling, and information given to the general practitioner at discharge.

Methods

Study design

We used individual semistructured interviews to explore the perspectives of relevant healthcare professionals. Observations on the ward were conducted to complement findings from interviews and to uncover behaviours that healthcare professionals may be unaware of. Finally, because pilot work showed some difficulties in stimulating discussion in individual interviews, we used focus groups to examine the views of elderly inpatients on issues relevant to them (changes in treatment and counselling).

Sampling strategy

The study was conducted on five acute wards for care of the elderly in five Belgian hospitals, purposively selected to include teaching and non-teaching, rural and urban settings. A multidisciplinary team of doctors, nurses, physiotherapists, social workers, and occupational therapists cared for patients. The purposive sample of five doctors and four nurses working on these five wards reflected variety in terms of position and experience (table). Three doctors were geriatricians, the others were house officers. We purposively selected three hospital pharmacists with relevant experience to complement the views of doctors and nurses.

Patients were recruited from two wards, one in an urban setting and the other rural. We purposively selected individuals able to share personal experience relating to changes in treatment and counselling. Such patients had to be stable and not

P+ *Details of the research process, interview schedules, and observation grid are on bmj.com*

Summary of participants' characteristics

Characteristics	Doctors (n=5)	Nurses (n=4)	Pharmacists (n=3)	Patients (n=17*)
No of women	3	2	3	10
Age range (years)	25-41	31-44	25-28	73-92
Teaching:non-teaching setting	3:2	2:2	3:0	17:0
Experience in care of elderly (years)	1-10	1-30	NA	—
Mean No of medicines on admission (range)	—	—	—	7 (3-12)
Mean No of changes in treatment (range)	—	—	—	7 (3-12)

NA: not applicable because pharmacists in Belgium are not directly involved in care of patients on wards. These pharmacists were not involved in other parts of study.
*Four focus groups comprised three patients each. Five patients were interviewed individually.

confused; have no cognitive impairment; have had at least one modification in chronic medication; and had to manage their own medication at home. Two focus groups were conducted on each ward. Pilot work suggested that three to four patients per group worked best. The doctors identified eligible patients (table).

Observations occurred on the wards where focus groups took place over a one month period. Healthcare professionals, patients, and heads of departments gave informed consent after they had received oral and written information (see bmj.com).

Instruments and data collection

Interviews—AS conducted interviews using a guide piloted with two healthcare professionals external to the main study. Each interview lasted about an hour. Questions were open ended and covered perceived appropriateness of prescribing, counselling, and sharing of information relating to medicines, together with factors contributing to inappropriateness (see bmj.com).

Focus groups—An experienced independent researcher who was not involved in the rest of the study moderated each group. Key questions pertained to knowledge of treatment, satisfaction with changes in treatment, and information received (see bmj.com). Each discussion lasted about 45 minutes.

Observation—Two clinical pharmacists (AS and another pharmacist not involved in the rest of the study) observed all the main activities on two wards. Healthcare professionals were informed of their role, but did not know the extent of their observations. Observers described events relating to the use of medicines. When they identified inappropriate use (according to their clinical judgment) they informally discussed this with prescribers. Both observers took notes to remind them of key events and used an observation grid to write these notes up in more detail later (see bmj.com).

Data processing and analysis

All interviews (focus groups and the informal discussions with prescribers) were taped, transcribed, and entered into QSR NVivo (version 1.2) for support in coding and analysis. We used the principles of grounded theory[9] to analyse the data with an inductive approach combining biomedical and sociological perspectives (see bmj.com).

Results

Most interviewees (especially those from teaching settings) admitted that prescribing was sometimes inappropriate and that counselling of patients was insufficient. Observations and data from focus groups corroborated these findings. In addition, one geriatrician and all pharmacists thought that the information shared with the general practitioner on discharge was insufficient. Observers confirmed that it was often limited to a list of medications.

Three main categories underlying inappropriate use of medicines emerged (box). All three contributed to inappropriate prescribing. The third category (paternalistic decision making) contributed to most instances of inappropriate counselling and ineffective transfer of information.

Reliance on general acute care and short term treatment

Most participants thought that they devoted considerable time to acute problems and that prescribing for chronic diseases was overlooked. Observations confirmed this. Reasons included insufficient incentives to review chronic problems in an acute care setting.

I think that doctors pay a lot of attention to the acute problem, but they don't give enough consideration to other medicines that patients are on. For example, a patient had been admitted for syncope secondary to atrial fibrillation. They started to give digoxin to control the fibrillation. But at the same time, pain care, for example, was inadequate: the patient was on paracetamol and amitriptyline at home, and these were not re-prescribed in the hospital (observer 2).

Undermedication, it's important, but we don't consider that issue enough. It's clear that we don't treat hypertension enough, for example. And that's maybe more difficult in the hospital because we are in acute care, and so we first see the problem that brings the patient into hospital (doctor 5, geriatrician).

In addition, medicines (mainly for chronic conditions) were sometimes not appropriately reviewed because there was no written information on indication and follow-up or because this information was not readily available. This was identified through observations and subsequently validated by most prescribers.

Patient on fentanyl patch in nursing home, continued during admission. No indication in the medical notes; no report of pain; patient not communicative. When asked by the geriatrician, the house officer said she didn't know the indication. No change was made to the treatment afterwards, and there was no comment in the discharge letter. On being asked, the house officer later told me that treatment hadn't been reviewed because the indication wasn't known (observer 1).

Finally, several interviewees said that prescribing was often not tailored to elderly patients. For example, the dose was not adjusted to renal status, medicines for which risks outweighed benefits were used, or the formulation was inappropriate. This mainly happened with junior doctors and external consultants.

Categories underlying inappropriate use of medicines

Reliance on general acute care and short term treatment
- Review of treatment driven by acute considerations; other considerations overlooked
- Limited transfer of information on medicines from primary to secondary care
- "One size fits all": prescribing behaviour not tailored to the older patient

Passive attitude towards learning
- Anticipated inefficiency in searching for medicines information
- Reliance on being taught (teacher centred) rather than self directed learning

Paternalistic decision making
- Patients thought to be conservative
- Patients declared as unable to comprehend
- Ageism
- Difficulty in sharing decisions about treatment with other prescribers

When house officers come on our ward, they haven't necessarily been trained in geriatrics. So they arrive here, and then they start with 10 mg of morphine every four hours. That's too much (doctor 2, geriatrician).

The formulations prescribed aren't always suited to the ability of an elderly person to swallow the medicine or to receive an injection, for example. . . The doctor doesn't necessarily think about it [the formulation prescribed]. I would even say that, except for Dr X [geriatrician], who is used to doing so, the house officers don't have this instinct (nurse 2).

Passive attitude towards achieving learning outcomes

In some cases doctors acknowledged that questions on medication (especially relating to interactions and side effects), when not answered by a colleague, remained unanswered because of anticipated inefficiency in accessing information on medicines. Observers also reported this.

[House officer talking about drug interactions with warfarin, leading to increased international normalised ratio—that is, overanticoagulation] I still don't really know them well. And to always go and look in the compendium [a reference book with scientific information on licensed medicines] is a bit difficult in terms of time. I think that's the main reason why we don't check (doctor 3, house officer).

In addition, several doctors thought that the learning process of house officers was passive and teacher centred rather than active and self directed. Doctors gave two explanations for this: low perceived interest and motivation on medication matters during undergraduate studies, and lack of time for active learning during training. As a consequence, junior doctors relied heavily on superiors' comments. There was a risk of passive application of "recipes" (also with medicines requiring special considerations on prescribing, see below). Observations corroborated this finding.

When we were studying, it was not really compulsory for us to take a serious interest in the literature. And I used to always say to myself "when I'm a house officer, I will read it up." Well in everyday practice we rely very much on our superiors' comments. I hardly ever go and look up what to do myself, what is the right thing to do . . . Also because that takes longer to do (doctor 1, house officer).

Observation in relation to the care of an 80 year old man complaining of insomnia] The geriatrician suggested that the house officer prescribe a preparation of chloral hydrate. The house officer prescribed it, using the formula available in the office. She later told me that she didn't know this drug at all, but that apparently the geriatrician was used to prescribing it. Contraindications and drug interactions had not been considered (observer 1).

Paternalistic decision making

Most participants agreed with the identified factors relative to paternalism, but several doctors said that the first three did not always occur (see box). Most doctors and nurses thought that changes in treatment were often difficult to implement because patients were attached to their usual medicines.

For example, for an antidepressant that had been given for a minor depression and that the patient is on for life, that nobody tried to stop a year or so later, well they [patients] are attached to it, it's difficult to go against that (doctor 2, geriatrician).

Conservatism also applied to counselling. One nurse described the unwillingness to inform patients of side effects.

I've noticed before, too, that they [patients] weren't told about known side effects because it was thought that they would be afraid of taking the medicine or that they would start feeling those side effects (nurse 4).

Several interviewees thought that the problem underlying conservatism was insufficient decision sharing.

I think that if somebody explains to the patient why he or she is given this medicine, the patient could understand. Here patients mightn't understand, quite simply because they [doctors or nurses] don't know how to explain things to them (pharmacist 3).

I think that too often, they don't ask what the patient thinks. For example, when a patient comes into hospital, they replace his laxative, X, by another laxative, Y. It mightn't seem that important, but for the elderly person it is. Even just from a psychological point of view, I would say (nurse 3).

Shortage of time and an assumption of inability to comprehend were other reasons for insufficient counselling.

Some of the patients wouldn't take it in [information on the indication of each medicine], because, well, two thirds of our patients have cognitive impairment, after all (doctor 4, geriatrician).

The attitude of most patients regarding treatment decisions reinforced a paternalistic model.

The doctors tell me, "We'll stop this one and give you something else that will work better." Well, for me that's fine. I have boundless confidence in them.

With regard to counselling, however, about half of patients expressed dissatisfaction with not being informed about changes.

I'm completely lost . . . My medicines were replaced by different ones, but I don't know who decided that . . . and I don't know what they are. . . . I would like to know what I'm taking and what I am being treated for. I like to know the "why" (patient).

The group discussions helped patients clarify their thoughts but they did not change their views.

One doctor cited ageism to explain underuse of medicines.

I think that some illnesses don't get enough treatment . . . probably in part due to what is called ageism. You say to yourself, What good will it do? Why add more medication? Is it worth optimising treatment? (doctor 5, geriatrician).

Finally, most doctors, two nurses, and both observers identified difficulties in sharing treatment decisions between prescribers. This was for two reasons. Firstly, doctors were reluctant to interfere with treatment delivered by a colleague.

A patient had heart failure, NYHA [New York Heart Association] stage II. I asked the house officer why she was not getting an ACE inhibitor. He answered: "In fact ACE inhibitors are a first choice in heart failure and this patient is not getting them, but she is under the care of a cardiologist, so I'm not going to change the treatment" (observer 2).

Secondly, two doctors acknowledged that information transferred to general practitioners could be limited by fear of offending them with comments on inappropriate prescribing.

Just yesterday I saw a patient whose general practitioner had prescribed metoclopramide, although she has very severe Parkinson's disease. Well I can't really write in the letter that . . . We're always afraid of offending (doctor 2, geriatrician).

Processes leading to appropriate medicines use

Besides the identification of processes underlying inappropriate use of medicines, participants and observers described several factors that acted as a stimulus for treatment review.

A first stimulus to review treatment was the perceived excessive number of medicines taken by the patient. Patients were often thought to take excessive numbers of medicines. This was mentioned by four doctors, two pharmacists, and one observer.

We often say among ourselves, "More than five, that's too many." When we exceed five medicines then one has to think, Is that really justified? (doctor 4, geriatrician).

The identification of drug related problems by other members of the multidisciplinary team and subsequent communication to the prescriber also helped to optimise treatment.

For example, a patient that the physiotherapist gets to stand up, he could walk with his Rolator [walking frame with wheels], but then they had to add melperone [a neuroleptic with cardiovascular and central nervous system side effects], and he can't stand up any more. The physiotherapist will talk to the doctor and might ask if it could be linked to a change in his medication (nurse 2).

When nurses find our tablets too big, for example . . . they ask me to find something else because it will never go down (doctor 3, house officer).

One doctor, one nurse, and one observer reported that a move from a curative to a palliative approach was an opportunity to reflect on the objectives of therapy and change treatment.

Sometimes people have taken 10 medicines while they were in curative care, and gradually they move on to palliative care. Then we must reconsider all the prescriptions, drug by drug, saying: OK, what's the goal? To improve your comfort? Well, this medicine will make you feel more comfortable; we can stop this other one (doctor 5, geriatrician).

Finally, several doctors and pharmacists perceived that the input of geriatricians was valuable to counteract the "one size fits all" approach. Observed events confirmed this.

When I see a patient who is on prazepam, for example [a benzodiazepine to be avoided in elderly people because of its long half life], well, I often ask for a review of the prescription, and to see if it wouldn't be more appropriate to select a drug with a shorter half life, for example (doctor 2, geriatrician).

Discussion

Reliance on general acute care and short term treatment, passive attitudes towards learning, and paternalism can all lead to inappropriate use of medicines in elderly people. We analysed data from the perspectives of professionals and patients (theory and data triangulation), using a combination of methods (methodological triangulation).[10]

Reliance on general acute care and short term treatment

Considerations relating to the treatment of chronic conditions relating to treatment are sometimes overlooked, one reason being the nature of an acute care setting. Though this is a worldwide issue,[11] this is the first report of occurrence on wards for care of the elderly. Such considerations did not seem to apply to events of overt polymedication or of palliative care. Another reason was the limited transfer of information on treatment between primary and secondary care. This highlights the importance of improving continuity of care.[12] It contrasts with the reported benefit of oral communication in the multidisciplinary team for care of the elderly. Another issue, which is also worldwide, was the lack of adequate training of doctors in prescribing for geriatric patients.[13]

Passive attitude towards achieving learning outcomes

Previous work found that "lack of knowledge" and "lack of time" contribute to suboptimal prescribing.[14 15] This was often cited by participants in our study. We have also identified new explanatory factors behind these rather descriptive terms: doctors anticipated inefficiency in accessing information about medicines and junior doctors had a passive attitude towards learning. This is worrying because most prescribing errors are made by junior medical staff.[16]

Paternalistic decision making

Paternalism may lead to inappropriate use of medicines. Provision of information should be tailored to individual needs.[17] This reinforces the importance of patient empowerment.[18] Similarly to findings from other settings, some patients wanted information but the doctor did not realise this or thought the patients did not need to know or would not understand.[19]

Ageism can be viewed as a form of paternalism. Together with "acute care" reasons, it led to events of underuse. However, there may be other reasons for undertreatment. Common explanatory themes in the literature are conceptualisation of illness and ageing, socioeconomic factors, allocation of resources, and provision of information.[20]

Finally, the findings show that decision making is further complicated because it often involves more than one prescriber.[18] The reluctance to interfere with treatment prescribed by a colleague was, interestingly, not reported in previous qualitative studies on appropriateness of medicines use. A similar issue, however, was raised in a quantitative study.[21]

Weaknesses

Generalisability is an issue because our study involved a limited number of respondents in a limited number of hospitals. A comparison of the results with previous qualitative studies (cumulative validation) showed that some factors had often been identified in other settings, while others had not. For the latter factors we do not know whether they are specific to the local or national setting from which the sample was drawn.

We cannot exclude the occurrence of a researcher-respondent interaction (Hawthorne effect) during interviews and observations. This was minimised by presenting research objectives in a constructive way and by using a disguised observation technique. Most interviewees were not reluctant to talk about problems, and the presence of observers was well accepted. It is possible, however, that healthcare professionals paid more attention to medicines when observers were present.[22]

Conclusions and implications

Elderly people often have several chronic conditions and need several medicines, are often admitted to hospital, and need regular review of treatment.[1] Optimising use of medicines throughout a hospital stay is therefore highly relevant to this population.

We identified several factors contributing to inappropriate medicines use. Some have been described in previous studies (reliance on general acute care, paternalistic doctor-patient relationship), while others are rather new (factors relating to the learning attitude and to relationships between prescribers). Strategies for improvement should include approaches such as developing incentives for considerations relative to the treatment of chronic conditions and for active learning in geriatrics by junior doctors[23 24]; developing systems for reliable transfer of information; and increasing involvement of patients and encouraging constructive communication between prescribers. The input of geriatricians, as well as active multidisciplinary communication, should be encouraged. It might be interesting to study to what extent collaboration with clinical pharmacists could help overcome some of the barriers described.

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Contributors: AS and CS had the idea for the study. AS, VL, CS, and SD designed the study. CS advised on recruitment. AS recruited and interviewed healthcare professionals. AS and VL developed the coding

What is already known on this topic

Quantitative studies have identified problems in the use of medicines for elderly patients, including inappropriate prescribing, counselling of patients, and transfer of information between primary and secondary care

There is limited qualitative data on the processes underlying inappropriate use of medicines in older inpatients

What this study adds

Reliance on general acute care and short term treatment, passive attitudes towards achieving learning outcomes, and paternalistic decision making contribute to inappropriate use of medicines in elderly patients

The input of geriatricians and communication between members of a multidisciplinary geriatric team contributed to a better use of medicines

framework. All authors helped to analyse and interpret the data. AS and VL wrote the paper, and all authors revised it. AS is guarantor.

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Ethical approval: The present study was part of a global project approved by the local ethical committee. The overall project was approved by the Belgian National Foundation for Scientific Research and by the PhD university research committee.

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Supplementary material: Details of the research process, interview schedules and observation grid (available at www.bmj.com)

1. Details of the research process

1.1. Data analysis

All interviews were taped and transcribed verbatim. All transcripts were entered into QSR NVivo® (version 1.2) for support in coding and analysis. Analysis was performed using the principles of grounded theory, and using an inductive approach combining biomedical and sociological perspectives. This balanced approach was felt to be the best approach, considering that the main objective of the study was to contribute to a better understanding of medicines use in the elderly.
AS (a clinical pharmacist) and VL (a sociologist) started the analysis with open inductive coding, through an intense line-by-line reading of transcripts of interviews with two doctors, one nurse and one pharmacist. Data collection and analysis continued simultaneously, and observations took place while the analysis of interviews with HCPs was in process. Finer coding was applied as more data were coded and analysed. Throughout the analysis, AS and VL wrote memos to store ideas, insights, and interpretations. This was essential in the development of analytical ideas.
The provisional coding scheme generated by AS and VL was discussed with other members of the research team, after independent reading of a sample of transcripts. Some codes were refined, and researchers moved to axial coding, looking for relationships between categories, and then to selective coding. Researchers searched for elements in the data that seemed to contradict the emerging explanation of the phenomena under study. Analysis was enhanced by constant comparison between interview and observation data, looking for deviant cases, and by comparison with available research in this field.

Findings were further validated by sending all participants (HCPs) a summary of the results and asking them to report any disagreement. None disagreed on the categories as they were presented, but the majority added comments on the perceived relative importance in everyday practice (eg by saying that it occurred inconstantly, or that in contrast it was a very important factor). We did not supply them to patients because the findings as they were presented were obtained several months after focus groups were conducted, and it seemed difficult to ask patients' views on something that happened several months before.

Besides the inductive analysis described above, researchers had defined in advance descriptive codes to facilitate text retrieval and comparisons during analysis. These codes were: step of the medication use process (prescribing, patient counselling, information transfer); perceived appropriateness (appropriate, difficult-inappropriate).

AS coded all transcripts, using inductive and descriptive categories. A second pharmacist, not involved in the rest of the study, coded two transcripts to check for reliability. Calculated Cohen's kappas were 0.87, 0.60 and 0.54 for nodes relating to activity, perceived appropriateness, and influencing factor respectively. Since the third value was not satisfactory, these subnodes were redefined and all material was subsequently recoded.
The data from focus groups were used to compare patients' accounts to providers' account. The data set did not enable researchers to perform an inductive approach on this.
The quotes presented in the article were chosen for representativeness, and further checked by external reviewers for relevance and understanding.

1.2. Roles of the researchers

None of the persons collecting the data were involved in patient care, to limit the risk of researcher-respondent interaction. One member of the research team (AS) was involved in data collection (all interviews with HCPs and one set of observations) and data analysis. Other persons involved in data analysis were not involved in data collection and vice-versa, because it was not feasible or unsuitable. All members of the research team were involved in data analysis, and they represented different disciplines (geriatrics, pharmacy, pharmacology and social sciences). This helped to prevent personal or disciplinary biases of a single researcher from excessively influencing the findings.

1.3. Process for informed consent

For semi-structured interviews with HCPs, each potential participant was contacted by telephone or by electronic mail. The researcher introduced herself as a pharmacist doing a research project whose aim was to collect HCPs' views on the use of medicines in their practice. All agreed to participate (i.e. we had a 100% acceptance rate), and an interview time and date was arranged. They all received a letter providing further details about the project, assuring them of confidentiality and asking for written consent (see supplemental file). No financial incentive was offered.
For focus groups with patients, after identification of eligible participants with the medical team, AS had a first contact with each patient in his/her room. She presented herself as a person doing research on the use of medicines in elderly patients, and explained that we were interested in their views on treatment changes and information received. She also explained the modalities of the group discussion. Each patient received a personalised letter with additional details but no agreement was sought at that time. AS came back the following day to ask whether they agreed to participate. The acceptance rate was 95%. No financial incentive was offered.

Anonymity was assured to all participants in the information letter. No names of persons or institutions were transcribed and participants were identified by numbers only. When using quotes for illustration of the results, researchers removed each piece of talk that could lead to an identification of the person or institution.

2. Interview guides and examples of interview questions

Note to readers: all questionnaires were developed and piloted in the French language. Interview guides and questions have been translated for illustration purposes only.

2.1. Semi-structured interviews with health care professionals

A. Interview guide

1° Introduction

- Personal experience in geriatrics, and roles/responsibilities with regard to medicines use
- Definition of appropriate medicines use

2° Detailed questioning on the following domains of medicines use

- prescription and follow-up
- patient counselling
- transfer of information to the general practitioner

For each domain, discuss the following:

  - description of activities
  - perceived quality in practice; difficulties encountered (encourage examples)*
  - reasons for difficulties/ inappropriateness
  - approaches for optimisation

3° Miscellaneous (years of experience in geriatrics, years of practice under current position, postgraduate training in geriatrics)

B. Examples of interview questions

- [After defining appropriate medicines use] What is the situation like in your daily practice? (positive, negative perceptions)
- Which difficulties do you face in the prescription of medicines (/follow-up) for elderly patients admitted on your unit?
- Many scientific publications have looked at the use of medicines in elderly patients, and some of them highlighted that medicines use is often suboptimal. What do you think? What does it mean to you?

- Do you think that medicines tend to be misused (/overused, /underused) ? Overused? Misused? Can you give examples from your practice ?
- What are the reasons for this? Why does this happen? Can you explain the reasons why this happens?

2.2. Focus groups with inpatients

A. Interview guide

1° Introduction (opening questions)

- Roundtable; names and origin

2° Treatment changes

- Description (introductory question)
- Positive experience, advantages
- Difficulties, discomfort, annoyance
- Optimisation (suggestions)

3° Information received

- Description
- Satisfaction / Difficulties
- Optimisation (suggestions)

4° Discharge

- Fear, difficulties
- Optimisation

5° Ending questions

B. Examples of interview questions (key questions)

- Let's talk about the changes that have been made during your stay here with regard to your medicines.
- What makes you happy about it?
- What makes you unhappy? What bothers you?
- Which difficulties have you encountered?

- Tell me about the last time somebody told you something about your medicines
- What did this person tell you? Are you satisfied? If not, why?
- What else would you like to know about your medicines?

3.2.

Implementation of ward-based clinical pharmacy services in Belgium – Description of the impact on a geriatric unit

Spinewine A, Dhillon S, Mallet L, Tulkens PM, Wilmotte L, Swine C

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INTERNATIONAL REPORTS

Implementation of Ward-Based Clinical Pharmacy Services in Belgium—Description of the Impact on a Geriatric Unit

Anne Spinewine, Soraya Dhillon, Louise Mallet, Paul M Tulkens, Léon Wilmotte, and Christian Swine

BACKGROUND: Patient-centered clinical pharmacy services are still poorly developed in Europe, despite their demonstrated advantages in North America and the UK. Reporting European pilot experiences is, therefore, important to assess the usefulness of clinical pharmacy services in this specific context.

OBJECTIVE: To report the results of the first implementation of Belgian clinical pharmacy services targeting patients at high risk of drug-related problems.

METHODS: An intervention study was conducted by a trained clinical pharmacist providing pharmaceutical care to 101 patients (mean age 82.2 y; mean ± SD number of prescribed drugs 7.8 ± 3.5) admitted to an acute geriatric unit, over a 7 month period. All interventions to optimize prescribing, and their acceptance, were recorded. An external panel (2 geriatricians, 1 clinical pharmacist) assessed the interventions' clinical significance. Persistence of interventions after discharge was assessed through telephone calls.

RESULTS: A total of 1066 interventions were made over the 7 month period. The most frequent drug-related problems underlying interventions were: underuse (15.9%), wrong dose (11.9%), inappropriate duration of therapy (9.7%), and inappropriate choice of medicine (9.6%). The most prevalent consequences were to discontinue a drug (24.5%), add a drug (18.6%), and change dosage (13.7%). Acceptance rate by physicians was 87.8%. Among interventions with clinical impact, 68.3% and 28.6% had moderate and major clinical significance, respectively. Persistence of chronic treatment changes 3 months after discharge was 84%.

CONCLUSIONS: Involving a trained clinical pharmacist in a geriatric team led to clinically relevant and well-accepted optimization of medicine use. This initiative may be a springboard for further development of clinical pharmacy services.

KEY WORDS: Belgium; clinical pharmacy; drug-related problems; frail elderly; pharmaceutical care.

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Improving patient safety is an important priority for any healthcare system. This involves reducing adverse drug events (ADEs) and optimizing the safe and effective use of medicines. Clinical pharmacy services are patient-oriented services developed to promote the rational use of medicines and, more specifically, to maximize therapeutic effect, minimize risk, minimize cost, and respect patient choice.[1] To achieve this, clinical pharmacists can obtain medication histories, perform medication reviews, attend ward rounds, provide recommendations on drug selection and follow-up, and provide counseling to patients and providers. The positive impact of clinical pharmacy services (or pharmaceutical care services) on clinical, economic, and humanistic outcomes has been demonstrated in numerous publications in North America and the UK.[2,3] Despite this, there is much inter- and intracountry variability in the practice of clinical pharmacy, which is still in the early stages in most European countries. Leblanc and Dasta[4] highlighted that, to ease the development of clinical pharmacy services and demonstrate their value, hospital pharmacists should report their experiences in international journals.

In Belgium, hospital pharmacists spend limited time on clinical tasks.[5,6] However, for many years there has been a desire to develop clinical pharmacy services, and a legal framework has been in place since 1991 (through the definition of the clinical tasks of hospital pharmacists in a Royal Decree). Barriers to the implementation of clinical pharmacy services have been the lack of specific training for pharmacists, the limited pharmacy manpower, the ab-

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sence of financial support, and the fear of poor acceptance from healthcare professionals.[5] Several factors, however, have been identified as driving forces for the implementation of clinical pharmacy services. These include the national and local willingness to improve the quality of drug use and reduce costs as well as a government-planned limitation of the number of practicing physicians.[6] It is in this context that clinical pharmacy education and practice have been developed by a joint effort of our university and university-based teaching hospitals, and a first pilot intervention study has been undertaken in one of the affiliated teaching hospitals.

An important aspect of strategic planning for implementing clinical pharmacy services is to target patients at high risk for ADEs, because they are more likely to benefit. Elderly patients are among these, because of multiple comorbidities, multiple medication use, altered pharmacokinetics and pharmacodynamics, and frequent inappropriate prescribing.[7] Suboptimal prescribing and ADEs/adverse drug reactions (ADRs) can occur on admission to the hospital,[8] during hospital stay,[9] and after discharge.[10] Only a few North American studies have evaluated the impact of multidisciplinary teams that included clinical pharmacists on drug-related outcomes for elderly inpatients.[11,12] Their applicability to European settings, in which clinical pharmacy is developing, is not established.

This article reports the results of the first intervention study performed by a clinical pharmacist providing pharmaceutical care on the geriatric unit of a university hospital. It describes the characteristics of interventions made by the clinical pharmacist, measures their acceptance by prescribers and their clinical significance, and measures their persistence after discharge. This is part of a larger program whose goal is to determine the feasibility of providing clinical pharmacy services to identify the driving forces and barriers for implementation.

Methods

DEVELOPMENT OF CLINICAL PHARMACY

Clinical pharmacy practice and education were created at our university in 2003, through a joint initiative of the faculty of medicine and the affiliated teaching hospitals. The present implementation relies on a new teaching program for hospital pharmacists, consisting of a certificate degree (90 h) and a Masters degree (1 y) in clinical pharmacy and a PhD program for research in clinical pharmacy (www.md.ucl.ac.be/pharma/cfcl/intro.htm). This provided the conceptual and scientific support to enable studies such as this one.

When the project started in 2002, Belgian physicians and pharmacists were not unfamiliar with the concept of clinical pharmacy and its usefulness in terms of improved use of drugs, mainly because of previous contacts with colleagues in North America and the UK. However, its effective implementation had not yet been initiated due to doubts about its feasibility in the national context.

To address this issue and to maximize the chances of success in launching a pilot program, a coordinated action was set up at the level of our institution. Its objectives were to identify the favorable and limiting factors relevant to the local situation[5]; to clearly explain the project and its advantages to all interested parties, without concealing the expected difficulties; and to establish an agenda for the implementation of the necessary changes in both the teaching programs (for undergraduate, postgraduate, and PhD students) and the hospital pharmacy. In this process, critical questions were raised. The answers given were based on a balance between what clinical pharmacy/pharmaceutical care should be and the local constraints or experience. Appendices I and II summarize the important aspects of the implementation process, which may be of interest to pharmacists willing to develop clinical pharmacy services in other countries.

SETTING

The study took place between November 2003 and May 2004 in the geriatric unit (27 beds) of a 350-bed teaching hospital in Belgium. The unit admits frail patients 70 years of age and older who present with typical acute geriatric problems. Patients are cared for by a multidisciplinary team of 2 geriatricians, 2 physicians who specialize in hospital care, nurses, 2 physiotherapists, a social worker, a psychologist, and an occupational therapist. Medical care, rehabilitation, and discharge planning are provided.

All patients admitted to the unit during the study period were eligible for inclusion in the study. Exclusion criteria were the presence of terminal illness; refusal to participate; length of stay 48 hours or less; inability of the pharmacist to perform an abstracted chart within 3 days of admission, due to time constraints; and inclusion during a previous admission. The ethics committee of the institution approved the study protocol. Informed written consent was obtained from each participant, or from a relative or caregiver if the patient was unable to give consent (eg, if the patient was experiencing severe cognitive impairment).

INTERVENTION

The intervention consisted of a clinical pharmacist providing pharmaceutical care from admission to discharge (Figure 1). The pharmacist had a postgraduate degree in clinical pharmacy and previous experience in geriatrics. The pharmacist was present in the geriatric unit 4 days a week, participated in medical and multidisciplinary rounds, had direct contact with patients and caregivers, and had access to the complete medical record, including biologic data and results of diagnostic tests. For each patient, the clinical pharmacist performed a medication history on admission and prepared an abstracted patient record with demographic, clinical, and pharmaceutical data. The appropriateness of treatment was then analyzed and a pharmaceutical care plan was prepared.[13,14] When an opportunity for optimization was identified, on admission or at any time during the hospital stay, the clinical pharmacist intervened. Interventions could occur during rounds or through discussions outside of the scheduled rounds time. They could pertain to acute or chronic medicines, and to medicines prescribed on a regular or as-needed basis. Each intervention was made orally. The pharmacist provided written information when judged necessary or when requested by the prescriber. The pharmacist also answered questions asked by other healthcare professionals about medications. At discharge, the clinical pharmacist provided treatment change information to the patient or caregiver and the general practitioner. A written plan (including names of drugs, indications, dosages and forms, frequency and time of administration, modalities of administration, list of drugs discontinued and reason) was given to the patient or caregiver, together with oral explanations. For the general practitioner, at the end of each discharge letter prepared by the physician, the pharmacist added a section titled, "Reasons for changes in medications and recommendations for follow-up." Its content was approved by the physician in charge.

DATA COLLECTION

The clinical pharmacist recorded each intervention, using a form developed during the pilot phase. The pilot program was conducted over 2 weeks, in a convenience sample of 20 inpatients, to test the feasibility and reliability of data collection. An intervention was defined as a recommendation made by the clinical pharmacist to a healthcare professional, pertaining to drug therapy, which aimed to improve the quality of medication use. Interventions could be initiated by the pharmacist or by another healthcare professional who asked a question of the clinical pharmacist. Patient counseling and medication histories were not recorded as interventions.

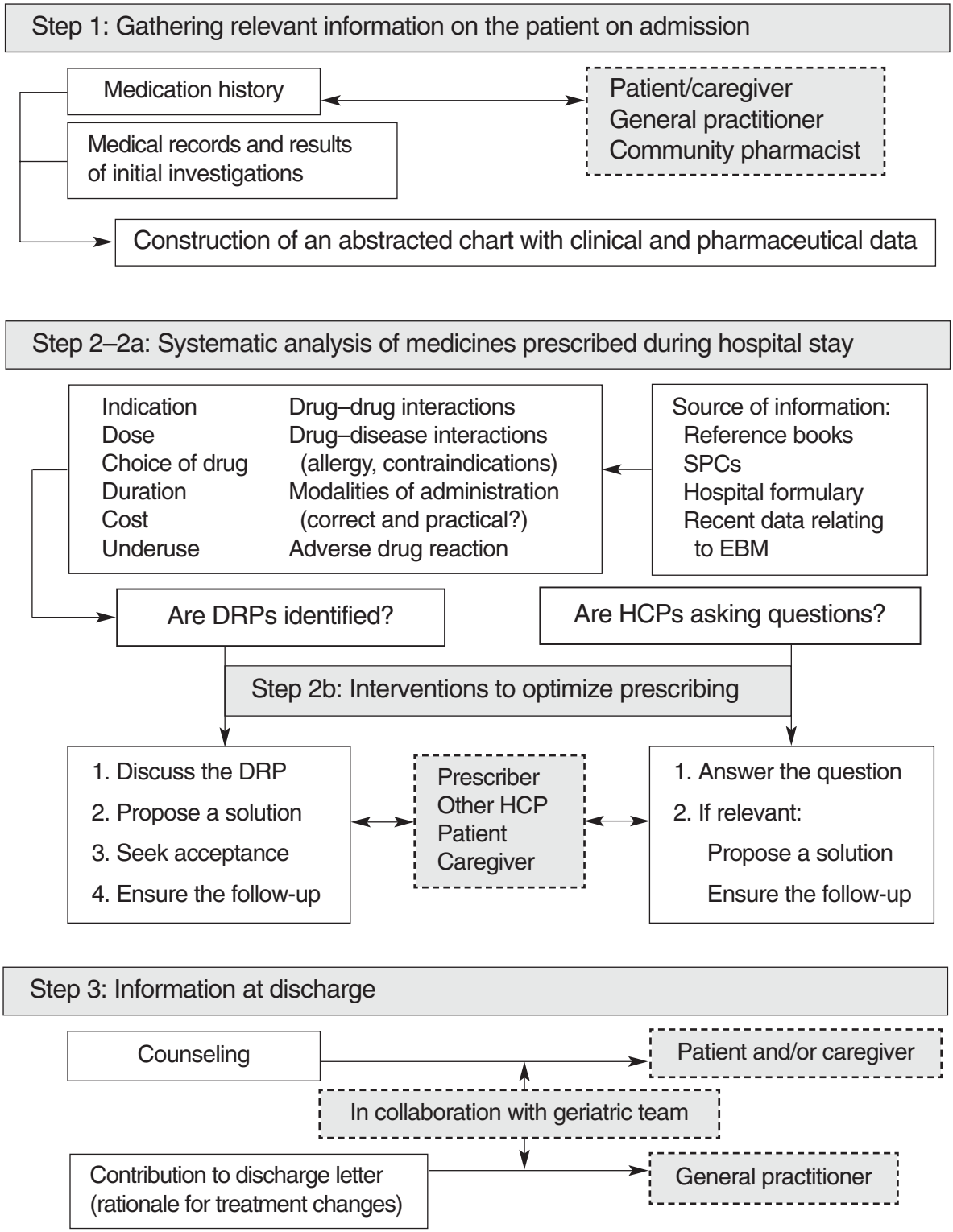

Figure 1. Pharmaceutical care process used in the study. Gray dotted boxes represent persons with whom the clinical pharmacist collaborated. DRP = drug-related problem; EBM = evidence-based medicine; HCP = healthcare professional; SPC = summary of product characteristics.

The following information was recorded on the form: (1) type of healthcare professional eliciting the intervention (ie, clinical pharmacist or other healthcare professional upon request); (2) healthcare professional to whom the pharmacist made the recommendation; (3) underlying drug-related problem (DRP), 17 categories; (4) type of intervention, 13 categories; (5) drug involved (Anatomical Therapeutic Chemical [ATC] code)[15]; (6) description of intervention and outcome, as measured for short-term effects and as anticipated for long-term effects; and (7) acceptance. We defined a DRP as an event or circumstance involving drug therapy that actually or potentially interferes with desired health outcomes.[16] The classification systems for DRPs and types of interventions were based on previous classifications and on pilot work.[14,16,17]

CLINICAL SIGNIFICANCE

All interventions that had potential clinical impact on the efficacy or safety of treatment (excluding those with impact exclusively on cost or compliance) and that were subsequently accepted by healthcare professionals were validated by an expert panel. The panel consisted of 2 Belgian geriatricians and one visiting Canadian clinical pharmacist with expertise in geriatrics and knowledge of the local setting. None was involved in the care of patients included in the study. To rate interventions, the experts used a scale developed according to previous scales (minor: no benefit or minor benefit, depending on professional interpretation; moderate: recommendation that brings care to a more acceptable and appropriate level of practice or that may prevent an ADE of moderate importance; major: intervention may prevent serious morbidity, including readmission, serious organ dysfunction, serious ADE; extreme: life saving; deleterious: may lead to adverse outcome).[18,19] Written instructions and examples from pilot work were provided. Panelists first rated each intervention individually, and then met to compare their ratings. When individual ratings differed, the panel discussed them to reach a consensus for each intervention.

PERSISTENCE OF INTERVENTIONS AFTER DISCHARGE

For interventions related to chronic treatments, we recorded whether the treatment change initiated by the pharmacist and carried out in the hospital was still in application 3 months after discharge. This was done because quantitative evidence indicates that treatment changes are frequent after discharge.[20] All patients were followed up 1 and 3 months after discharge, through telephone calls performed by 2 trained hospital pharmacists who had not been involved in the rest of the study. The questionnaire was developed by one pharmacist and by the main researcher and was pilot tested with 5 patients to check for appropriate questioning and understanding. Data were provided by the person preparing medications (patient or caregiver), and included medicines taken after discharge.

DATA ANALYSIS

Analysis was performed using SPSS (Statistical Package for Social Sciences, version 11.0). Descriptive statistics were used for characterizing interventions. Interrater reliability for classifying DRPs and types of interventions was checked. Two clinical pharmacists coded 33 interventions made during the pilot study. Cohen's kappa[21] was 0.87 for the underlying DRP and 0.96 for the type of intervention, indicating good agreement.

Results

CHARACTERISTICS OF PATIENTS

The clinical pharmacist provided pharmaceutical care to 101 patients; 73% were female, 72% were living in the community, and 36% had received previous geriatric care. Their mean (± SD) age was 82.2 (± 6.9) years. The average number of drugs prescribed on a regular schedule, per patient, was 7.8 (± 3.5) and the average number of daily doses was 9.8 (± 4.7). Mean length of stay was 19.7 (± 12.1) days.

CHARACTERISTICS OF INTERVENTIONS

The pharmacist made 1066 drug-related interventions. The person who initiated the intervention (ie, identified a DRP and made a recommendation to resolve the problem) was the clinical pharmacist in 84.9% (n = 905) of cases and another healthcare professional in 15.1% (n = 161) of cases (ie, the intervention was initiated when another healthcare professional asked the pharmacist a question and the pharmacist made a recommendation). This represents a mean of 8.9 interventions per patient (median 8) initiated by the pharmacist and 1.6 interventions per patient (median 1) initiated by another healthcare professional. Table 1 summarizes the main characteristics of all interventions made. A total of 87.8% of all interventions were fully accepted and 7.2% were partially accepted by physicians. The most common classes of drugs (ATC level 2) were antithrombotic agents (B01; 9.1% of all interventions), psycholeptics (N05—including antipsychotics, anxiolytics, hypnotics, sedatives; 8.8%), psychoanaleptics (N06—including antidepressants, antidementia drugs; 8.2%), analgesics (N02; 6.9%), and drugs for obstructive airway diseases (R03; 6.6%). There were no major differences in the characteristics of interventions initiated by the pharmacist versus interventions initiated by another healthcare professional.

CLINICAL SIGNIFICANCE

The external panel assessed the clinical significance of 700 interventions; 366 interventions were excluded because they had no direct clinical impact (Table 2). Individual ratings differed for two-thirds of evaluations, and discrepancies originated equally from the 3 panelists. After discussion and consensus, there was a mean of 4.7 ± 3.8 (median 4) moderate interventions and 1.9 ± 2.1 (median 1) major interventions per patient. Examples are provided in Table 3. The results were similar for interventions initiated by the pharmacist or by another healthcare professional.

PERSISTENCE OF INTERVENTIONS AFTER DISCHARGE

Three months after discharge, 88% of patients could be reached to obtain follow-up data on the persistence of interventions relating to the treatment of chronic conditions (missing data were related to various types of DRPs and treatment changes). For moderate and major chronic interventions, 83.8% and 85.4% of treatment changes persisted

3 months after discharge, respectively. The majority of treatment changes that had not been followed up were not systematically associated to specific drugs of DRPs.

Discussion

Our study reports the development of patient-centered clinical pharmacy services. A structured process was followed that included a reflection on international experiences as well as focusing special attention on local and national considerations and taking advantage of local driving forces. Several barriers initially thought to limit the development of clinical pharmacy services, such as poor acceptance from healthcare professionals, lack of training, and insufficient hospital–faculty collaboration, were overcome. In addition, careful documentation of impact was done, through the combination of practice and research activities.

To our knowledge, this is the first study to report involvement of a clinical pharmacist in acute patient care in Belgium, and it is one of the first international reports on the

Table 1. Characteristics of Interventions (N = 1066) Made by the Clinical Pharmacist

Drug-Related Problem	Interventions, n (%)	Drugs Most Often Involved
Underuse	169 (15.9)	calcium/vitamin D, antithrombotics, analgesics
Wrong dose	127 (11.9)	antibiotics, psycholeptics,[a] psychoanaleptics,[a] ACE inhibitors, ARAs
Inappropriate duration of therapy	103 (9.7)	psycholeptics, heparins, antiasthmatics, antibiotics
Inappropriate choice of medicine	102 (9.6)	psycholeptics, psychoanaleptics, analgesics
No valid indication	74 (6.9)	antithrombotics, antacids, antiulcer drugs
No specific problem[b]	72 (6.8)	psychoanaleptics, psycholeptics, ACE inhibitors, ARAs, hypolipemics
Inappropriate modalities of administration[c]	65 (6.1)	analgesics, antibiotics, psychoanaleptics, antiasthmatics
Adverse drug reaction[d] suspected or confirmed	57 (5.3)	psychoanaleptics, diuretics, analgesics
Error in medication history	55 (5.2)	psychoanaleptics
Inappropriate follow-up	41 (3.8)	antianemics, cardiac therapy (digoxin)
Prescription writing error	36 (3.4)	psycholeptics
Drug–disease interaction (including allergy)	35 (3.3)	β-blockers, ACE inhibitors, ARAs, bisphosphonates, psychoanaleptics
Duplication	34 (3.2)	psycholeptics, antiasthmatics
Less costly alternative	32 (3.0)	miscellaneous
Modalities of administration not practical for the patient	26 (2.4)	miscellaneous
Drug–drug interaction	24 (2.3)	antithrombotics
Other	14 (1.3)	miscellaneous

ACE = angiotensin-converting enzyme; ARA = angiotensin receptor antagonist.
[a]Psycholeptics include antipsychotics, anxiolytics, hypnotics, and sedatives; psychoanaleptics include antidepressants and antidementia drugs.
[b]No underlying drug-related problem; for example, when physicians asked a question without the presence of a drug-related problem for a specific patient.
[c]Modalities of administration include frequency of administration, time, route, and formulation.
[d]An adverse drug reaction was defined as a noxious and unintended reaction to a drug that occurred at doses normally used in humans, that could not be related to another drug-related problem.

Table 2. Type, Acceptance Rate, and Clinical Importance of Interventions Made

		Acceptance Rate (%)			Clinical Importance (%)[a]				
Intervention Type	n (%)	Full	Partial[b]	Rejected	Minor	Moderate	Major	Extreme	Deleterious
Discontinue drug	261 (24.5)	87.4	6.5	6.1	3.9	63.3	31.4	1.4	0
Add a new drug	198 (18.6)	88.9	6.1	5.1	1.2	66.7	31.5	0	0.6
Change dose	146 (13.7)	92.5	3.4	4.1	2.4	57.7	39.8	0	0
Educate/inform healthcare professional	107 (10.0)	96.8	3.2	0	NA	NA	NA	NA	NA
Switch to other drug	95 (8.9)	76.8	10.5	12.6	1.8	75.0	23.2	0	0
Other	259 (24.3)	85.7	10.8	3.5	2.2	84.4	13.3	0	0
TOTAL	1066 (100)	87.8	7.2	5.0	2.6	68.3	28.6	0.4	0.1

NA = not applicable (ie, clinical importance not assessed by the external panel because the intervention was not initiated by the clinical pharmacist, and/or because it did not lead to direct change in the treatment of a specific patient).
[a]N = 700 interventions (the external panel assessed the clinical significance of 700 interventions; the remaining 366 were excluded because they had no direct clinical impact).
[b]Advice accepted but not acted upon, or partially acted upon.

involvement of clinical pharmacists in the care of acutely ill, frail, elderly patients. We found that the clinical pharmacist, through the provision of pharmaceutical care, was able to propose a large number of interventions relating to a wide variety of DRPs and drugs. The majority of these interventions were accepted and were deemed clinically relevant.

Several reasons may have accounted for the high acceptance rate of interventions (Table 4); these could be considered for developing additional clinical pharmacy services in Belgium and abroad. The clinical pharmacist used a structured approach to provide pharmaceutical care.[13,14] Furthermore, the communication between the clinical pharmacist and the physician (as well as other healthcare professionals) may have been critical. Previous studies reported acceptance rates that varied from less than 50% to more than 90%.[22,23] A low value of 47.5% was observed in a European study, in which the authors stated that there was a lack of communication and an insufficient multidisciplinary approach.[22] Higher values (67–81%) were reported in a North American study in which the pharmacist met with the physician to discuss DRPs.[23] In our study, the pharmacist was part of the multidisciplinary team, and there was direct contact between the pharmacist and the prescribers. The fact that most interventions persisted after discharge is also encouraging. To our knowledge, as of November 1, 2005, that kind of measure has rarely been reported.

A comparison of the characteristics of our interventions with data from the literature gives external validity to the results. First, the most frequent DRPs underlying the interventions (Table 1) fit prevalent types of inappropriate prescribing in the elderly population. This emphasizes the relevance of our interventions. For example, observational studies have identified high levels of undermedicating for the treatment of osteoporosis,[24] for the prevention of thromboembolic diseases,[25] and for pain control.[26] Underdosing of angiotensin-converting enzyme inhibitors is frequent,[27] as is inappropriate use of psychotropic drugs.[28] In a study describing DRPs in 827 patients hospitalized in Norway (mean age, 71.7 y), the number of DRPs per patient was lower than in our study, but the drugs most often involved for each type of DRP were similar to those in our results.[29] Second, the drugs most commonly involved in interventions in our study (ie, antithrombotic agents, psycholeptics, psychoanaleptics, analgesics) frequently lead to ADEs/ADRs in the elderly.[11,30] Therefore. the clinical pharmacist has probably helped improve patient safety through the prevention or resolution of frequent ADEs.

The external validation of the clinical importance of interventions, by Belgian and foreign experts, further strengthens the results. Direct comparison with other studies is difficult, however, for several reasons. First, the definitions of minor versus moderate versus major interventions vary from one study to another. Second, the clinical importance of a single intervention made for an adult versus that made for a frail older patient may be different, because the risk and seriousness of ADEs is higher in the latter group. Hence, the age and frailty of the population should be taken into consideration when assessing clinical importance. This was done by having experts in geriatrics on the panel.

Our study has several limitations. First, it represents interventions made by a single clinical pharmacist working on one geriatric unit, raising the issue of generalizability. Such a limited pilot study was, however, essential in our context, and we believe that it will lead the way for generalization of clinical pharmacy services delivered by other

Table 3. Examples of Interventions Initiated by the Clinical Pharmacist

Interventions of moderate clinical importance
Drug-related problem: zopiclone was started the day after admission for insomnia; 2 weeks later, the patient was about to be discharged and was sleeping well, but was at risk of falling.
Intervention: discontinue zopiclone and explain the rationale to the patient (treatment must be short term, no need for it at home, and risk of adverse effects, including falls).
Drug-related problem: 2 antihistamines (hydroxyzine and cetirizine) prescribed by general practitioner for pruritus; both prescriptions rewritten in the hospital.
Intervention: duplication of treatment; little benefit, but increased risks of adverse effects. Discontinue hydroxyzine (more anticholinergic and sedative effects than with cetirizine) and monitor for symptoms of pruritus.
Interventions of major clinical importance
Drug-related problem: nausea reported; digoxin dose increased 3 days prior.
Intervention: check electrocardiogram and digoxin blood level; discontinue or decrease dose if intoxication confirmed (note: intoxication was confirmed).
Drug-related problem: patient with diabetes and peripheral arterial disease; no cardiovascular prophylaxis and no contraindication.
Intervention: start aspirin 100 mg/day.

Table 4. Factors Likely to Have Contributed to Successful Implementation

Before the study
hospital and ward managers open to collaboration
close collaboration with the hospital pharmacy department
willingness to target patients at high risk of adverse drug events
needs identification through qualitative analysis
objectives of the study well defined and communicated to healthcare professionals
During the study
presence of pharmacist on a regular basis (0.8 full-time equivalent)
structured process for pharmacist to evaluate patient
pharmacist with adequate training in clinical pharmacy/pharmacotherapy in the elderly population
direct contact with members of the multidisciplinary team, patients, and caregivers
close collaboration with hospital pharmacy department

pharmacists, on other units, and with other physicians. In fact, the pharmaceutical care model described here is now being replicated in other units in our institution, and a full-time position for a clinical pharmacist has been created. Second, we did not address the pharmacoeconomic aspects of the intervention, although we are aware that these will be essential to justify further development of clinical pharmacy. Third, from a research perspective, measuring pharmacists' interventions is only an indirect measure of the impact on the quality of medicines use. Further work should address the impact of the intervention on direct measures of prescribing appropriateness and/or on actual ADEs.

Conclusions

Patient-centered clinical pharmacy services aim to promote a rational use of medicines. This practice is well developed in North America and the UK. Our study shows that it is possible to implement new ward-based clinical pharmacy services in Europe, using a structured approach. In addition, our study provides new data on the impact of pharmaceutical care in a population for which limited international data are available, namely, frail elderly inpatients. Most interventions made by the clinical pharmacist were accepted by healthcare professionals, were deemed clinically relevant by external experts, and the improvements made were largely maintained after discharge. Attention paid to key factors required for success in developing clinical pharmacy services may have significantly contributed to the results.

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Appendix I. Steps in the Implementation of Ward-Based Clinical Pharmacy Services

A. Preparing the hospital pharmacy
- Make sure that hospital pharmacists agree on the willingness to change practice; define the objectives and the means.
- Optimize the distribution and administrative tasks.
- Identify the training needs of hospital pharmacists and the needs relative to medicine information resources and skills.

B. Preparing the key persons at the hospital level
- Sensitize the hospital board managers and the medical therapeutic committee to the willingness to change; agree on the objectives and methods of the pilot project.

C. Developing a comprehensive but realistic academic teaching program
- Identify the training needs of hospital pharmacists, and implement relevant changes at each educational level (undergraduate, postgraduate, research programs).

D. Launching pilot ward-based clinical pharmacy projects
- Define 1 or 2 wards on which 1 or 2 clinical pharmacists can start.
- Establish a first contact with the key persons of the ward (main doctor and main nurse) and agree on the objectives and method of the project.
- Reflect on the pilot experience at regular intervals with the key persons involved, and perform a detailed evaluation at the end of the pilot phase.

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EXTRACTO

TRASFONDO: Los servicios farmacéuticos clínicos centrados en el paciente todavía están pobremente desarrollados en Europa a pesar de que sus ventajas han sido demostradas en la América del Norte y el Reino Unido. El reportar experiencias de programas piloto europeos es por lo tanto importante para la evaluación de la utilidad de los servicios de farmacia clínica en este contexto en específico.

OBJETIVO: Reportar los resultados de la primera implementación de servicios farmacéuticos clínicos belgas teniendo como objeto pacientes en alto riesgo de problemas relacionados a fármacos.

MÉTODOS: Un estudio de intervención realizado por un farmacéutico clínico adiestrado proveyendo cuidado farmacéutico a 101 pacientes (edad promedio 82.2 años; número promedio de fármacos prescritos 7.8 ± 3.5) admitidos a una unidad de cuidado geriátrico agudo por un período de 7 meses. Todas las intervenciones para hacer óptima la prescripción y su aceptación fueron documentadas. Un panel externo (dos geriatras y un farmacéutico clínico) evaluaron su importancia clínica. La perseverancia de las intervenciones después del paciente haber sido dado de alta fue evaluada a través de llamadas telefónicas.

RESULTADOS: Se realizó un total de 1066 intervenciones durante el período de 7 meses. Los problemas relacionados a fármacos más

Appendix II. Important Questions Raised During the Implementation Process

1. What is the value of considering the North American/UK experience? Should we attempt to replicate it?
   In our case, the experience of North America and the UK was highly valuable, but we did not simply replicate it. International experts participated and/or gave advice for the implementation process. In parallel, several Belgian pharmacists were trained abroad. This enabled us to clearly define the potential models of clinical pharmacy/pharmaceutical care practice and education and objectively inform the decision-making persons about the respective successes and failures of the North American/UK models. None of them, however, entirely match the local needs. The driving forces were not the same, and the baseline education programs and skills of graduated Belgian pharmacists were also quite different from those in the US or UK. The model that we developed, therefore, took account of these baseline differences.
2. Should clinical pharmacists be distinct from hospital pharmacists?
   This "distinct model," which is most frequently encountered in the US, was considered unacceptable by Belgian hospital pharmacists, who wanted to be the future clinical pharmacists (as in the UK and Canadian models). In our present model, clinical pharmacists are, therefore, hospital pharmacists who acquire an additional certificate or Masters degree in clinical pharmacy. They are able to perform clinical and nonclinical tasks.
3. What were the respective roles of faculty members and of hospital pharmacists?
   Responsibilities were shared. Faculty members were responsible mainly for creating the necessary educational programs, and for defining the pilot projects linked to PhD research programs. Hospital pharmacists oversaw the implementation of the pilot projects within the hospital setting, managed the contacts and exchanges with healthcare providers at all levels, and ensured that the activities of the clinical pharmacists in the hospital were made with the full respect of ethical and medical requirements with which they are familiar. A close faculty–hospital collaboration has been essential to the present success of our implementation.
4. Should the activities of the clinical pharmacists be linked to research activities?
   This was considered a major requirement for successful implementation in a university teaching hospital. Our present model encompasses clinical pharmacists seeking a PhD degree (4- to 5-year program with presentation of a full dissertation and publications in peer-reviewed international journals) and clinical pharmacists with more limited research activities but who must, nevertheless, contribute to the development of research in clinical pharmacy.
5. Should pharmacoeconomy be an important part in the development of clinical pharmacy?
   In contrast to the prevailing situation in the US, most clinical and pharmaceutical activities are still performed under a fee-for-service structure in Belgium. Drug savings were, therefore, not perceived as critical and could even be counterproductive as far as hospital pharmacies and pharmaceutical industries are concerned. This situation is, however, under reevaluation as financing based on diagnosis-related group is being implemented. Clinical pharmacists may, therefore, play an additional important role in the near future to support this.

frecuentes justificando intervenciones fueron: menos uso (15.9%), dosis incorrecta (11.9%), duración de la terapia inadecuada (9.7%) y selección del medicamento inadecuada (9.6%). Las consecuencias más frecuentes fueron: descontinuar un fármaco (24.5%), añadir un fármaco (18.6%) y cambiar la dosis (13.7%). El nivel de aceptación por los médicos fue de 87.8%. Entre las intervenciones con impacto clínico, 68.3% tuvieron significado clínico moderado y 28.6% mayor impacto. La perseverancia de cambios en tratamiento crónico tres meses después del paciente ser dado de alta fue 84%.

CONCLUSIONES: El envolvimiento de un farmacéutico clínico adiestrado en un equipo geriátrico llevó a hacer óptimo el uso de medicamentos de forma relevante clínicamente y bien aceptada. Esta iniciativa puede servir de impulso para el desarrollo adicional de servicios farmacéuticos clínicos.

Brenda R Morand

RÉSUMÉ

OBJECTIF: Présenter les résultats d'une première étude de services pharmaceutiques cliniques en Belgique; étude effectuée auprès d'une population âgée à haut risque de problèmes reliés à la pharmacothérapie.

MÉTHODES: Une étude d'intervention a été réalisée pendant une période de 7 mois. Durant cette période, une pharmacienne clinicienne a prodigué des soins pharmaceutiques chez 101 patients (moyenne d'âge de 82.2 ans et nombre moyen de médicaments prescrits 7.8 ± 3.5) admis à l'unité de gériatrie aiguë. Toutes les interventions pour optimiser la prescription et leurs acceptations ont été documentées. Un panel externe (2 gériatres et une pharmacienne clinicienne avec une expertise en gériatrie) ont évalué l'importance clinique des interventions. Le suivi des recommandations au congé a été effectué via des appels téléphoniques.

RÉSULTATS: Un nombre de 1066 interventions a été effectué pendant une période de 7 mois. Les problèmes reliés à la pharmacothérapie les plus fréquemment rencontrés étaient: sous utilisation (15.9%); dose inappropriée ou incorrecte (11.9%), durée de traitement inappropriée (9.7%) et choix inapproprié de médicaments (9.6%). Les modifications dans les prescriptions étaient les suivantes: cesser un médicament (24.5%); ajouter un médicament (18.6%) ou modifier une posologie (13.7%). Le pourcentage d'acceptation des recommandations par les médecins était de 87.8%. Parmi les interventions avec impact clinique, 68.3% et 28.6% avaient une importance clinique de modérée à majeure respectivement. Le suivi des recommandations trois mois suite au congé du patient était de 84%.

CONCLUSIONS: L'implication d'un pharmacien clinicien au sein d'une équipe gériatrique a permis d'optimiser l'utilisation des médicaments Cette initiative pourrait servir de tremplin pour permettre le développement d'autres services cliniques.

Louise Mallet

3.3.

Impact of pharmaceutical care on the quality of medicines use

3.3.1.

Medication Appropriateness Index: Reliability and recommendations for future use

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Spinewine A, Dumont C, Mallet L, Swine C.

MEDICATION APPROPRIATENESS INDEX: RELIABILITY AND RECOMMENDATIONS FOR FUTURE USE

To the Editor: The Medication Appropriateness Index (MAI) measures the appropriateness of prescribing for elderly patients, using 10 criteria for each medication prescribed. For each criterion, the evaluator rates whether the medication is appropriate, marginally appropriate, or inappropriate. Support is provided through explicit definitions and instructions.[1] The MAI has been used in observational and interventional studies.[2–6] Its feasibility, content validity, predictive validity, and reliability have been demonstrated in ambulatory settings.[1,7–10] Its limitations are that reliability was lower when assessed by researchers different from the authors[9,10] and that the original instrument does not address some areas (drug allergy, adverse drug reactions, compliance). We wanted to assess the reliability of the MAI for elderly patients hospitalized on a Belgian geriatric unit. Professionals with expertise in geriatrics but practicing on different sites were involved. Similar to previous research,[9] this study proceeded in two phases. First, the MAI was translated into French and piloted by a clinical pharmacist on 10 patients. Following discussions with another clinical pharmacist and a geriatrician, clarifications were introduced in the instructions. Second, interrater reliability between a clinical pharmacist (AS) and a geriatrician (CD) was checked, using 113 drugs prescribed to 16 patients at discharge (69% female, mean age 79.6, mean number of prescribed drugs on admission 6.2). The raters used an abstracted patient chart compounded by the clinical pharmacist (using data from the medical record and patient interview and from contact with the general practitioner or the community pharmacist if needed). Both raters performed the evaluations independently and then met to compare their ratings. Discrepancies were discussed, and raters were allowed to change their ratings to reach a consensus. Table 1 summarizes the results of agreement before and after discussion. Overall agreement was good and improved after discussion. Agreement on interactions was unsatisfactory before discussion between raters. Insufficient or unclear instructions in the MAI were found to be an important source of discrepancies. Based on this and on previous similar experience,[8–10] the following suggestions that might enhance the validity and reliability of the instrument are made.

General suggestions:

Add examples of appropriate, moderately appropriate, and inappropriate prescribing that are relevant to the geriatric population.

Define "moderately appropriate" for all criteria.

Consider how compliance could be accounted for, for example with regard to choice (e.g., is the choice appropriate in a patient unwilling to take his or her medicines) or to practical directions (e.g., evidence that the patient does not take the medication).

Suggestions specific to individual criteria:

- Indication:
  Add instruction that "global status" should be taken into account (e.g., vitamin D in a patient with previous fractures but in palliative care is not always a valid indication).
- Choice:
  Clarify how to cope with cases in which choice is inappropriate because of drug–drug or drug–disease interactions (e.g., use of alendronate in a patient with severe esophagitis; is it considered inappropriate in terms of choice and/or of drug–disease interaction?).
- Dosage:
  When a dose has been recently modified but consequences are not yet measurable, specify that clinical judgment should be used instead of the evaluation tool provided in the instrument.

Replace the 1997 Beers list with the 2003 updated list.

- Modalities correct
  The directions (regarding food and time of administration) provided for a limited number of drugs should be completed to include directions for additional drugs commonly prescribed in geriatrics.
- Modalities practical
  Take into account the information provided to the patient to ensure adequate intake of the medication; give inappropriate ratings when written instructions for a new medicine with specific modalities of administration (e.g., bisphosphonates) are not provided.
- Drug–drug and drug–disease interactions
  Further investigate interrater reliability, because low prevalence precluded a complete analysis in previous reports,[1,8,10] and prevalence was higher in the current study, but initial reliability was unsatisfactory.

Review the modifications proposed previously,[8,9] and agree on the definition to use in each setting.

Update the list of drug–disease interactions provided in the instrument. (Some may not be clinically relevant anymore.)

Include allergy as a drug–disease interaction.

- Duration
  Add specific instructions for drugs that are progressively withdrawn.

Table 1. Interrater Reliability Between a Clinical Pharmacist and a Geriatrician (n = 113 Drugs Prescribed to 16 Patients at Hospital Discharge)

Parameter	A	B	C	D	Positive Predictive Value	Negative Predictive Value	Kappa*
Before discussion between raters							
Indication	104	6	0	3	0.97	0.5	0.48
Effectiveness	93	6	2	12	0.96	0.75	0.71
Dosage	90	6	6	11	0.93	0.65	0.58
Correct directions	92	5	3	13	0.96	0.76	0.72
Practical directions	94	7	4	8	0.94	0.59	0.54
Drug–drug interaction	91	16	4	2	0.90	0.20	0.09
Drug–disease interaction	86	19	2	6	0.89	0.36	0.29
Duplication	106	0	0	7	1.00	1.00	1.00
Duration	94	5	1	13	0.97	0.81	0.78
Overall†	49	11	4	49	0.87	0.87	0.74
After discussion between raters							
Indication	106	1	0	6	1.00	0.92	0.92
Effectiveness	94	2	1	16	0.98	0.91	0.90
Dosage	92	1	3	17	0.98	0.89	0.87
Correct directions	95	0	2	16	0.99	0.94	0.93
Practical directions	97	4	1	11	0.97	0.81	0.79
Drug–drug interaction	95	10	0	8	0.95	0.62	0.57
Drug–disease interaction	92	8	0	13	0.96	0.76	0.73
Duplication	106	0	0	7	1.00	1.00	1.00
Duration	95	1	0	17	0.99	0.97	0.97
Overall†	50	7	2	54	0.92	0.92	0.84

Note: Cost (10th criterion) was not included in the analysis, because an explicit source for comparing the costs of drugs in Belgium was used instead.
*A kappa statistic of 0.40–0.75 denotes good interrater reliability, and a kappa value > 0.75 denotes excellent reproducibility.
†Drug's overall appropriateness (inappropriate if $\geq$ 1 of the 10 items were rated as inappropriate).
A = appropriate according to both raters; B = appropriate according to clinical pharmacist, inappropriate according to geriatrician; C = appropriate according to geriatrician, inappropriate according to clinical pharmacist; D = inappropriate according to both raters.

Consider giving (moderately) inappropriate rating for short-term treatments for which no indication on the end of treatment has been provided in the letter or to the patient.

In conclusion, even though perfect interrater agreement is illusory, additional instructions and examples could improve the validity and reliability of the instrument. Researchers with previous experience with the MAI could discuss this.

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3.3.2.

Effect of pharmaceutical care provided with acute geriatric care to improve the quality of medicines use in elderly inpatients: a randomised controlled trial

Submission in process

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Abstract

Background: Despite compelling evidence that the use of medicines is often inappropriate in elderly inpatients, limited data exist on the effectiveness of optimization strategies.

Objective: To evaluate the impact of pharmaceutical care provided in addition to acute geriatric care on the appropriateness of prescribing.

Design: Randomized, controlled trial, with the patient as unit of randomization.

Setting: Acute geriatric unit.

Patients: 203 patients aged 70 and older.

Measurements: Appropriateness of prescribing on admission, at discharge, and 3 months after discharge, using the MAI (Medication Appropriateness Index), Beers criteria, and underuse ACOVE (Assessing Care Of Vulnerable Elders) criteria; mortality, readmission and emergency visits up to 12 months after discharge.

Intervention: Pharmaceutical care provided from admission to discharge by a specialist clinical pharmacist who had direct contacts with the geriatric team and patients.

Results: Intervention patients were significantly more likely than control patients to have an improvement in the MAI and in the ACOVE underuse criteria from admission to discharge (OR 9.1, 95% CI 4.2-21.6 and OR 6.1, 95% CI 2.2-17.0 respectively). Both the control and intervention groups had comparable improvements in the Beers criteria. Most improvements in the Beers and ACOVE criteria were maintained after discharge. A trend toward improved clinical outcomes one year after discharge was observed.

Conclusions: Pharmaceutical care provided in the context of acute geriatric care improved the appropriate use of medicines both during the hospital stay and after discharge. This approach has the potential to minimize risk and to improve patient outcomes.

Introduction

Inappropriate use of medicines in elderly patients is a major concern to clinicians and public health authorities (1;2). Drug-related problems are implicated in 10 to 30% of hospital admissions in the elderly (3-6). Moreover, adverse drug reactions occur during hospital stay in up to 50% of these patients (6). A recent study found that 42% of elderly inpatients were prescribed at least one drug without valid indication, and that dosage or duration was inadequate in about half of these patients (7). Conversely, medicines for the treatment of conditions such as heart failure or osteoporosis remain underused in 20% to 70% of patients (8). Furthermore, medication errors are frequently made during transition between acute and post-acute care, partly due to incomplete discharge instructions (9).

While geriatric evaluation and management (GEM) programs have been shown to decrease mortality and to improve functional status in hospital and around discharge (10), their impact on the quality of drug use has been less studied. Early studies reported some impact on limited aspects of overuse or misuse (11;12). A more recent evaluation showed that inpatient geriatric care significantly reduces suboptimal prescribing (13). Improvements were, however, only partially maintained after discharge, and the added value of clinical pharmacists in the GEM team was not evaluated.

Involving pharmacist in drug therapy is nowadays largely perceived as an effective mean to improve patient care (14). Most pharmacist-based intervention studies with elderly persons, however, have been performed in primary care (15). The few published studies with inpatients carry two limitations: (a) outcome measures were incomplete with respect to overuse/misuse, and did not include underuse (12;16), (b) the intervention concerned limited aspects of pharmaceutical care, such as discharge planning (11;16). In the present study, we used a prospective, randomized design to examine the impact of pharmaceutical care provided in addition to acute GEM care on the appropriateness of prescribing for elderly patients during admission and after discharge.

Methods

Setting

The study was conducted at the acute GEM unit of a University teaching hospital (Mont-Godinne, Yvoir, Belgium). The unit has 27 beds and admits patients aged 70 years and older who present with acute geriatric problems. Patients are cared for by a multidisciplinary team composed of two geriatricians (with training in geriatric pharmacotherapy), two residents (rotating twice a year), nurses, two physiotherapists, a social worker, a psychologist and an occupational therapist. Medical care, rehabilitation and discharge planning are provided. Usual length of stay is 20 days.

Patients

We evaluated all patients admitted on the unit between November 2003 and May 2004 for eligibility. Exclusion criteria were: patients with a terminal illness and a life expectancy of less than 3 months; refusal to participate; expected length of stay ≤48 hours; for time reasons, pharmacist unable to perform an abstracted chart within three days of admission; patient transferred from another acute unit where he/she had been cared for by geriatrician(s); inclusion during previous admission.

Randomization

Patients were randomized to receive GEM care (control group) or pharmaceutical care in addition to GEM care (intervention group). Randomization was alternate and stratified for age (< or ≥ 85), number of prescribed medicines (< or ≥ 5), and identity of the resident in charge of the patient. A pharmacist external to the main study checked inclusion criteria and assigned participants to their groups. Because of the nature of the project, the physicians were not blinded to group assignment.

Ethical Considerations

The Ethics Committee of the Institution approved the study protocol. Informed written consent was obtained from each participant (or from a relative if the patient was unable to give consent). The absence of pharmaceutical care in the control group was considered acceptable because clinical pharmacy is not yet widely implemented in Europe, and was not part of the standard of care in the Institution.

Baseline Data Collection

The clinical pharmacist performed a medical record review and an interview with each patient/caregiver to determine demographic characteristics, clinical status, and medications. The Charlson comorbidity score was calculated (17). Cognitive impairment was defined as a diagnosis of dementia or the identification of cognitive problems without dementia. Patients without confusion or severe dementia were asked to rate their global health status on a 5-point Likert scale.

Intervention

The intervention consisted of a clinical pharmacist providing pharmaceutical care from admission to discharge according to a validated scheme described in details elsewhere (18). Briefly, the clinical pharmacist (AS) performed a medication history on admission, and prepared a patient record with clinical and pharmaceutical data. The appropriateness of treatment was analyzed, and a pharmaceutical care plan was prepared. Whenever an opportunity for optimization was identified, the clinical pharmacist discussed that opportunity with the prescriber, who could accept or reject the intervention. At discharge, the clinical pharmacist provided written and oral information on treatment changes to the patient/caregiver, as well as written information to the general practitioner.

Primary Outcome Measure

Appropriateness of prescribing was measured on admission and at discharge. A combination of three measures that encompassed overuse, misuse and underuse was used (table 1).
First, the Medication Appropriateness Index (MAI) was selected because it is currently the most comprehensive instrument to evaluate appropriateness. The MAI consists of 10 criteria. For each criterion, the evaluator rates whether the particular medication is appropriate, marginally appropriate, or inappropriate (19). The ratings generate weighted scores that serve as summary measures of prescribing appropriateness (0-18 per drug; higher scores equal greater degrees of inappropriateness) (20). The instrument was tested before the study, and we found good inter-rater reliability, after making minor modifications to improve clarity and understanding (overall kappa value = 0.84) (21). The clinical pharmacist evaluated the prescribing of all regularly scheduled medications at baseline (in a blinded way, using the list of medications prescribed on the first day of admission) and then at discharge. Discharge evaluations were unblinded, but a comparison with ratings by a blinded clinical pharmacist for a sample of 15 patients showed that there was no bias toward more favorable/unfavorable ratings for intervention/control patients, respectively.
Second, the use of drugs that should be avoided in the elderly was assessed using the 1997 Beers criteria (22), and selecting eight (classes of) drugs from the original list based on their inclusion in the hospital formulary. This measure was selected in addition to the MAI to enable comparisons with

published data. In addition, we looked at the use of benzodiazepines (which is a major concern in Belgium) in patients with at least one fall in the previous six months, as proposed in the most recent Beers criteria (23).

Third, seven Assessing Care Of the Elderly (ACOVE) criteria relative to underuse were selected because the MAI does not detect underuse, and because high levels of underuse were identified in previous studies (9). The ACOVE criteria are process measures of quality of care for vulnerable elders (24). Underuse indicators are expressed as follows: if there is a certain condition, then the patient should receive a certain drug, unless contraindicated. We developed additional instructions on the contra-indications (available upon request). These were based on previous publications (25-27) and on minor adaptations related to local considerations. An inappropriate rating was given if (i) the patient had the condition of interest and no contra-indication to receive the medication, but did not receive it; (ii) the patient had the condition of interest and received the medication but had a contra-indication to receive the drug. Two blinded pharmacists independently performed all Beers and ACOVE measures. When ratings differed, they reexamined and discussed the data to reach a consensus. Appropriateness at baseline was based on the drugs that the patient was taking the day before admission, and using the data from the medication history done by the clinical pharmacist. They also recorded whether medication improvements made during admission were maintained after discharge (see below).

Secondary Outcome Measures

Because polymedication is not a valid measure of appropriate prescribing, a measure of unnecessary drug use was used instead (defined as patients who received an inappropriate rating for indication, efficacy, or therapeutic duplication with the MAI) (28). Prevalence was evaluated on admission and at discharge.

Additional outcome measures were collected after discharge. All patients were followed up one month, three months and one year post-discharge, through telephone calls performed by two trained hospital pharmacists who were blinded to group assignment. The questionnaire was developed by one of these two pharmacists (SA, see Acknowledgment) and by the main researcher (AS). Data, which were provided by the person preparing the medications (patient/caregiver), included the following: mortality, readmission or visit to an emergency department (double-checked with the hospital record when applicable), medications taken, satisfaction with the information received on medications during admission (1-month post-discharge, using the following scale: satisfied, moderately satisfied, not satisfied).

Contamination (Educational Bias)

Because the same physicians were caring for control and intervention patients, contamination of control patients was possible. To assess this bias, we applied the Beers and ACOVE criteria to a random sample of 90 patients admitted on the unit one year before the study (November 2002 – May 2003). This sample is called here the "historical control group". The MAI could not be applied because of the insufficient data in the medical record. Patients were excluded if a discharge letter was lacking, if information was missing about the drugs taken, or if the patient died before discharge.

Statistical Analysis

A sample size of 90 patients per group was required, in order to have 80% power to detect a 20% absolute improvement in ACOVE and Beers criteria, at a two-sided 0.05 significance level, and assuming a response rate of 0.2 in the control group. Twenty-eight patients per group would provide 90% power to detect an effect size of 0.9 on the MAI (29). The sample size was finally set to 100 patients per group to account for loss of participants due to dropout and death.
Study groups at baseline were compared using chi-square or Fisher exact test for categorical variables, Student t-test for normally distributed continuous variables, and Wilcoxon rank sum test for non-normally distributed variables. Baseline and discharge ratings were compared within groups, using non-parametric related sample tests. A Pearson's chi-squared test was used to detect a significant difference between the probabilities of improvement of the MAI score in the control and intervention groups. When conditioning on a baseline categorical covariate was required, the Cochran-Mantel-Haenzsel (CMH) test was used. The homogeneity of the (log) odds ratios across strata assumed by the CMH test was checked using the Breslow-Day test. These procedures were applied to detect an improvement of (i) the Beers criteria conditionally on an age indicator, and (ii) the ACOVE criteria conditionally on the number of conditions with omitted drug on admission. When necessary, a Fisher exact test was preferred to the Pearson's chi-squared test in sparse contingency tables. Similar results (available upon request) were obtained by using singular logistic regression (to compare the proportion of patients with at least one improvement) and t test and Wilcoxon rank-sum test (to compare mean differences on admission -vs- discharge between control and intervention groups). In each test, we considered statistical significance to be at a level of 0.05. Statistical analyses were performed using SPSS Statistical Software 13.0.

Results

Patient Characteristics

Figure 1 summarizes the flow of patients entered in the study and analyzed for the primary outcome measures. No significant differences were present in the characteristics of patients at baseline (table 2). The percentage of patients for which data were available after discharge were as follows: at one month: 98% of control and 99% of intervention patients for clinical data, 84% and 83% for pharmaceutical data, respectively. At three months, these percentages were 96% and 98%, and 86% and 85%, respectively. At 12 months: 92% and 93% for clinical data, respectively.

Appropriateness Of Prescribing

Medication Appropriateness Index

Almost 60% of prescriptions had at least one inappropriate rating at baseline. Intervention patients were significantly more likely to have an improvement in their summated MAI score than were control patients (OR 9.1, 95% CI 4.2-21.6, $p<0.0001$ – table3b). Intervention patients had highly significant improvements in MAI scores (table 3a), as well as important improvements in each individual criterion (table 4). In contrast, for control patients, improvements were smaller, and two individual criteria (modalities practical, and cost) did not improve (table 4).

Drugs-to-avoid In The Elderly

About 30% of patients were taking at least one drug-to-avoid on admission. Long-acting benzodiazepines and dipyridamole accounted for 65% of cases. Both groups had similar improvement from admission to discharge (table 3). For the benzodiazepine : fall criteria, there was a higher absolute decrease in prescribing for intervention patients (the difference between groups was, however, not significant). This was secondary to an increase in new users in the control group (3.4% intervention patients, 12.7% of control patients, $p=0.097$), whereas discontinuation was similar in both groups (15.5% vs 15.9%, respectively).

ACOVE Criteria Of Underuse

Seventy-eight percent of patients were eligible for at least one indicator. More than 50% of patients had at least one inappropriate rating at baseline. When controlling for the baseline level of underuse, intervention patients were six times more likely than control patients to have at least one improvement (OR 6.1, 95% CI 2.2-17.0) (table 3b).

Persistence Of Improvements After Discharge

Among patients with an improvement in the Beers or ACOVE criteria, three months after discharge this improvement was maintained equally or more often in the intervention group as compared to the control group: (a) Beers drugs (improvement maintained in 94% of intervention vs 86% of control cases); (b) benzodiazepine in patient with previous fall (86% vs 56%, respectively); (c) underuse (87% vs 87%). The differences were not significant.

Secondary Outcome Measures

At least one unnecessary drug use was prescribed to 84.4% of both control and intervention patients on admission. At discharge, unnecessary drug use was still detected in 77.8% of control patients, in contrast to 37.5% of intervention patients (figure 2).

One year after discharge there was a trend towards reduced death rate (22.5% of intervention vs 30.1% of control patients), similar readmission rate (32.6% vs 33.7%, respectively) and reduced ermergency visits (7.9% vs 12.0%, respectively). One month after discharge, there was a trend toward higher satisfaction with information received on medicines in the intervention group (80.0% of intervention patients versus 60.9% of control patients were satisfied, p=0.1).

Assessment of Educational Bias

The baseline characteristics of the historical control group did not differ significantly from that of control and intervention patients. There was a trend towards higher improvements in the control than in the historical control group for Beers criteria (p=0.41, table 3). When the analysis was restricted to patients with at least one Beers' drug on admission (n=63), improvements were significantly higher in the control than in the intervention group (p=0.035). There was no evidence of contamination for the ACOVE criteria.

Discussion

This study demonstrates that adding pharmaceutical care to a GEM program substantially reduces overuse, misuse, and underuse of medicines in elderly inpatients. The robustness and usability of our data stems from (i) the use of a randomized controlled design, (ii) the combination of three validated instruments to document overuse, misuse, and underuse, (iii) the representativeness of the study population with respect to patients commonly seen on GEM wards; (iv) the limited number of patients lost to follow-up.

The most significant finding is that pharmaceutical care led to marked improvements in the MAI and the ACOVE scores. The reasons underlying the success of the intervention are probably that (i) a structured and comprehensive approach towards treatment review was taken, (ii) the intervention addressed several factors responsible for inappropriateness (30), (iii) there was direct contact between the pharmacist and the multidisciplinary team, with the pharmacist present when prescribing decisions were made. The latter is consistent with previous studies that reported only moderate impact when direct involvement of the pharmacist in daily practice was limited (11).

Two pharmaceutical care studies reported comparable improvements in MAI scores but neither had a control group (31;32). Other controlled studies involving collaborative approaches reported significant but lower improvements in MAI scores (13;16;29), but the baseline MAI scores were lower than in our study. The use of the MAI questions by the pharmacist to review prescribing in the present study was probably an important determinant in a better identification of opportunities for optimization. Therefore, the systematic use of this approach should perhaps be part of routine practice in drug regimen review.

Our study is one of the first to show that pharmaceutical care can substantially improve underprescribing. Underuse of medicines in the elderly is indeed prevalent (8;33-36) and linked to increased morbidity/mortality, but there is scarce data on approaches for improvement (14;32;37).
In contrast to the definite improvement in the MAI and underuse criteria, pharmaceutical care appeared not to improve the drug-to-avoid criteria. As in other studies, prescribing drugs from the Beers' list was frequent at baseline (38-40), but was substantially decreased at discharge in both groups. In our study, this decrease, however, was larger than reported in previous studies (13;41-43) and in the historical control group. We ascribe this result to contamination since (i) the study was not blinded; and (ii) identifying "bad drugs" and discontinuing them is easier (and more prone to contamination) than identifying and resolving problems related to underuse, indication, or dosage. A low impact was achieved for the benzodiazepine:fall criteria. This could be related to the known difficulty in discontinuing these drugs (44-46).

The prevalence of unnecessary drug use on admission was alarming, and the intervention lowered that burden. The inclusion of inappropriate choice of drug in this measure (in addition to inappropriate indication and duplication) is questionable, and could overestimate the true rate of unnecessary drugs. It is nevertheless a better quality measure than polymedication data.
Finally, two rewarding observation were that (i) most improvements were maintained after discharge, a point rarely documented so far, and (ii) there was a trend toward improvements in clinical outcomes in the intervention group.

Our study has limitations. First, generalization is an issue because the intervention was provided by one clinical pharmacist on a single unit. The time required to apply the measures of appropriateness (and more specifically the MAI) would compromise the feasibility of a multi-center study. Yet, the intervention could be replicated elsewhere, provided that a similar pharmaceutical care model is followed. Second, the study was not designed to detect an impact on clinical outcomes. Third, we did not evaluate whether the intervention improved compliance and quality of life, and decreased adverse drug events (but pharmacist's interventions potentially decreased the risk of adverse events (18)). Further work on the pharmacoeconomic benefit of the intervention is also needed.

In conclusion, this study shows that the prescribing of medicines in frail elderly patients can be substantially improved during hospital admission, with persistent effects after discharge, when a clinical pharmacist plays a proactive and structured role in drug treatment review within the context of a GEM program. Combined efforts are necessary to improve the care of patients with complex drug regimens, multiple comorbidities, and other risk factors for drug-related morbidities.

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Tables

Table 1: Criteria of appropriateness of prescribing used in the study

1. Medication Appropriateness Index (20-22)

→ 10 questions per drug:

1.1. Is there an indication for the drug? (weight: 3 if inappropriate)

1.2. Is the medication effective for the condition? (weight: 3)

1.3. Is the dosage correct? (weight: 2)

1.4. Are the directions correct? (weight: 2)

1.5. Are the directions practical? (weight: 1)

1.6. Are there clinically significant drug-drug interactions? (weight: 2)

1.7. Are there clinically significant drug-disease/condition interactions? (weight: 2)

1.8. Is there unnecessary duplication with other drugs? (weight: 1)

1.9. Is the duration of therapy acceptable? (weight: 1)

1.10. Is this drug the least expensive alternative compared with others of equal utility? (weight: 1)

→ Calculation of a weighted summated score per drug (0-18) and per patient

Note: For each criterion, the index has operational definitions, explicit instructions, and examples, and the evaluator rates whether the particular medication is appropriate, moderately appropriate, or inappropriate.

2. Prescription of drugs to avoid in the elderly (23-24)

2.1. Independent of diagnoses (Beers 1997) – prescription of any of the following:

Dipyridamole	Propoxyphen
Long-acting benzodiazepines	Amitriptyline
Anticholinergic anti-histamines	Indomethacin
Ergot mesyloids	Oxybutinin

2.2. Dependent of diagnoses

Benzodiazepine in patients with at least one fall in the previous six months

3. Underuse of medicines for selected conditions (ACOVE criteria)

(IF the patient has a certain condition, THEN he should receive a drug, UNLESS contra-indicated) (25)

Condition	Drug
3.1. Ischemic cardiomyopathy	Aspirin
3.2. Diabetes	Aspirin
3.3. Atrial fibrillation	Aspirin / anticoagulant
3.4. Osteoporosis / fracture	Bisphosphonate, calcium, vitaminD
3.5. Heart failure (with ejection fraction < 40%)	β-blocker
3.6. Heart failure (with ejection fraction < 40%)	ACE-I
3.7. Myocardial infarction	β -blocker

Abbreviations: ACE-I: angiotensin converting enzyme inhibitor; ACOVE: Assessing Care Of the Vulnerable Elders; MAI: Medication Appropriateness Index

Table 2: Patient characteristics

Variable	Control (n=90)	Intervention (n=96)	p value
Demographic			
Age, mean ± SD, y	81.9 ± 6.2	82.4 ± 6.9	0.618
Female, %	66.7	71.9	0.525
Community-dwelling, %	66.7	71.9	0.525
Living alone, %	24.7	26.0	0.867
Clinical and functional status			
Charlson comorbidity score, mean ± SD	2.0 ± 1.5	2.0 ± 1.6	0.819
Cognitive impairment, %	46.7	43.8	0.768
≥ 1 fall within previous 6 months, %	74.4	70.2	0.608
≥ 1 hospital admission within previous 6 months, %	31.1	36.5	0.535
Support for ≥1 ADL, %	56.7	59.4	0.653
Self-rated health, %	(n=61)	(n=57)	
- Good to excellent	32.8	42.1	0.578
- Fair	57.4	49.1	
- Poor	9.8	8.8	
Pharmaceutical data			
No of prescribed drugs, mean ± SD	7.3 (3.3)	7.9 (3.5)	0.278
No of daily administrations, mean ± SD	9.7 (4.8)	10.0 (4.7)	0.705

Abbreviations: ADL: activities of daily living; SD: standard deviation

Table 3a: Changes in appropriateness of prescribing from admission to discharge

	Historical control group (n=90) *			Control group (n=90)			Intervention group (n=96)		
	Baseline	Discharge	p†	Baseline	Discharge	p†	Baseline	Discharge	p†
Medication Appropriateness Index									
Mean MAI score per drug (0-18) (SD)‡	NE	NE		3.2 (2.1)	2.7 (1.6)	0.020	3.2 (2.1)	0.9 (1.0)	<0.001
Mean summated patient score (SD)	NE	NE		21.2 (14.3)	19.3 (12.5)	0.362	24.1 (17.0)	7.1 (7.5)	<0.001
Drug- to-avoid (Beers)									
Mean no of inappropriate drugs per patient (SD)	0.38 (0.53)	0.13 (0.37)	<0.001	0.44 (0.69)	0.04 (0.21)	<0.001	0.29 (0.56)	0.03 (0.17)	<0.001
Patients with ≥1 inappropriate drug, %	35.6%	12.2%	<0.001	34.4%	4.4%	<0.001	25.0%	3.1%	<0.001
Patients taking a BZD among patients with previous fall, %	NE	NE		65.1%	60.3%	0.629	58.6%	44.8%	0.021
Underuse (ACOVE criteria)									
Mean no of inappropriate ratings per patient (SD)	0.76 (0.87)	0.57 (0.78)	0.002	0.92 (0.95)	0.63 (0.81)	0.002	0.75 (0.89)	0.17 (0.43)	<0.001
Patients with ≥1 inappropriate rating, %	55.6%	43.3%	0.007	58.9%	44.4%	0.015	50.0%	14.6%	<0.001

Abbreviations: BZD: benzodiazepine; MAI: Medication Appropriateness Index; NE: not evaluated because lack of data to perform the MAI, or unreliable data on previous falls; SD: standard deviation.

* Random sample of patients admitted on the unit one year before the study period.

†2-sided p values when comparing baseline and discharge scores, using the Wilcoxon Signed Ranks Test for continuous data and the McNemar test for categorical data.

‡ The average MAI score per drug on admission or discharge was gotten by dividing total score on admission by the number of drugs evaluated on admission or discharge.

Table 3b: Odds ratio for improvements from admission to discharge in the intervention group as compared to the control group

	OR	95% CI
≥1-point improvement in the summated MAI patient score	9.1	4.2 - 21.6
≥1 improvement in the number of drugs to avoid (Beers)	0.6	0.3 - 1.1
≥1 improvement in the number of inappropriate ACOVE criteria of underuse*	6.1	2.2 - 17.0

Abbreviations: CI: confidence interval; MAI: Medication Appropriateness Index; NS: Not significant; OR: odds ratio.

* Conditionally on the number of conditions with omitted drug on admission.

Table 4: Percentage of drugs with inappropriate ratings on admission and at discharge in the control and intervention groups, using the Medication Appropriateness Index

MAI criteria	Control		Intervention	
	Baseline (n=633) %	Discharge (n=654) %	Baseline (n=728) %	Discharge (n=766) %
Indication	9.8	7.5	12.1	2.6
Choice	23.2	18.5	25.4	6.1
Dosage	28.0	25.1	26.5	6.8
Modalities correct	19.3	17.9	17.6	8.1
Modalities practical	15.0	16.8	17.3	3.3
Drug-drug interactions	7.4	6.7	7.3	1.3
Drug-disease interactions	18.8	15.4	18.1	4.6
Duplication	3.0	2.3	5.2	1.0
Duration	16.7	13.8	20.5	6.1
Cost	23.2	25.8	23.1	10.7
Overall †	59.9	64.5	59.8	27.3

* Comparison of baseline and discharge ratings used 2-sided p values estimated with the Fisher exact test for categorical variables.

† Inappropriate rating in at least 1 of the 10 criteria.

Figures

Figure 1: Flow of patients through the trial

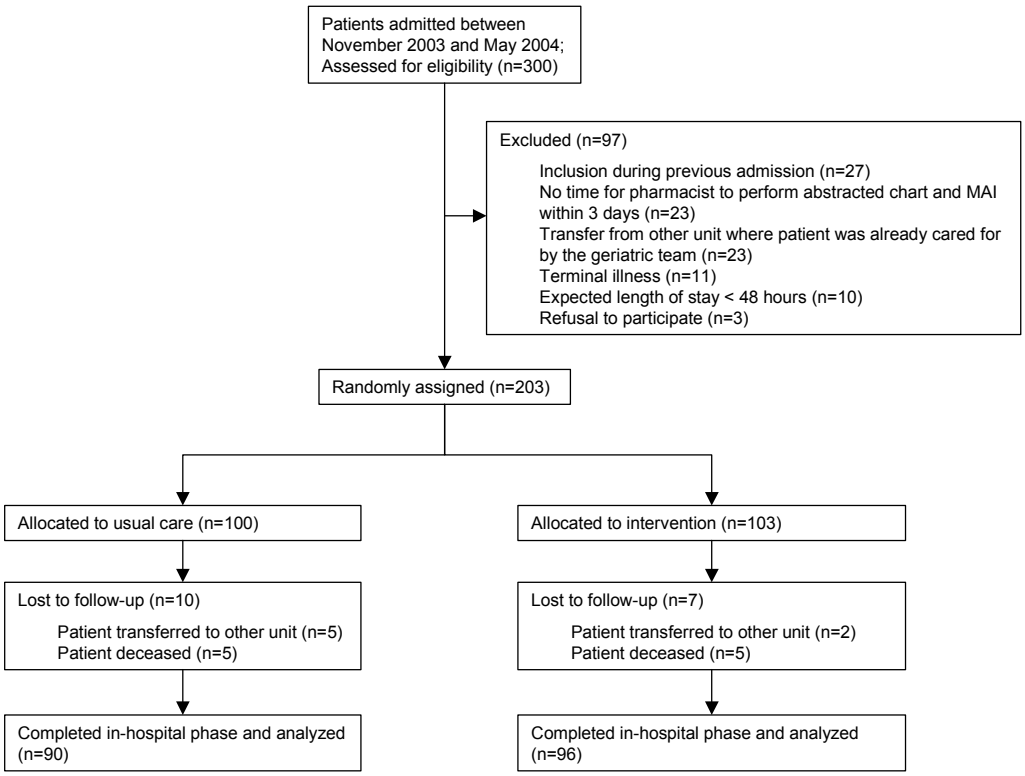
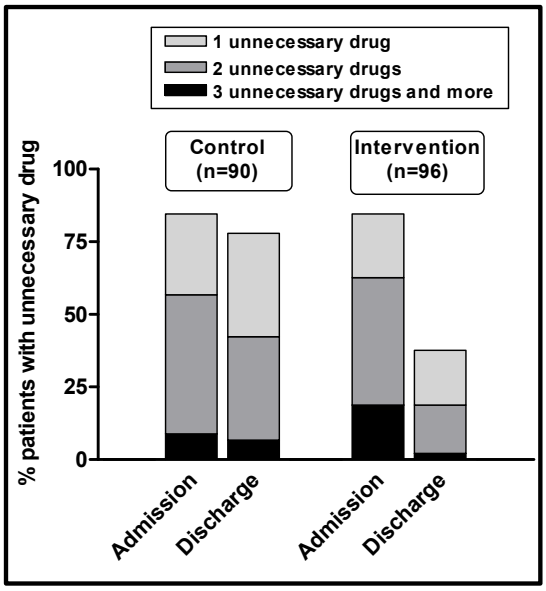


Figure 2: Unnecessary drug use on admission and at discharge



3.3.3.

Additional data

A. Could the clinical pharmacist be replaced by a computerised prescribing system?

B. Drug-induced lithium intoxication: a case report.
Journal of the American Geriatrics Society 2005; 53: 360-361
Spinewine A, Schoevaerdts D, Mwenge GB, Swine C, Dive A.

A. Could pharmacist's interventions be replaced by a computerised prescribing system?

Introduction

Computerised prescription order entry (CPOE) refers to a variety of computer-based systems that share common features of automating the medication ordering process, which work to ensure standardized, legible, and complete orders. Similarly, a clinical decision support system (CDSS) is a software program that matches patient data with a computerized knowledge base to generate patient-specific assessments or recommendations that are then presented to health care providers for consideration.[1] The CDSS therefore crosses the boundary of patient-specific and knowledge-based information.[2] The intent is not to have the system think for the physician, but rather for it to handle certain rote functions, so that the physician can focus on overall diagnostic and treatment plans and on communicating effectively with patients.[3]

Computerisation of ordering improves safety in several ways: firstly, all orders are structured, so that they must include a dose, route and frequency; secondly, they are legible and the order can be identified in all instances; thirdly, information can be provided to the prescriber during the process; and fourthly, all orders can be checked for a number of problems including allergies, drug interactions, overly high doses, drug-laboratory problems, and whether the dose is appropriate for the patient' liver and kidney function.[4] The literature supports CPOE/CDSS's beneficial effect in improving prescribing practices, and reducing the frequency of a range of medication errors, including serious errors with the potential for harm.[3;5] However, not all systems are equal, and the ability to add CDS to a CPOE system is critical.[6;7] A recent study found that high rates of ADEs may continue to occur after implementation of CPOE and related computerised medication systems that lack decision support for drug selection, dosing, and monitoring.[8] In addition, other recent studies found that errors can be generated by the system.[8-11]

We recently conducted a randomised controlled trial to evaluate the impact of pharmaceutical care on the quality of medicines use. A clinical pharmacist worked at an acute geriatric ward of a teaching hospital where CPOE was not implemented. The intervention was highly successful. However, it was rather resource-consuming (0.8 full-time equivalent), and did not benefit other wards of the hospital. The question was raised as whether a CPOE system could be similarly effective to identify prescription errors. Our objective was, therefore, to quantify the percentage and types of drug-related problems (DRPs) identified by the clinical pharmacist, that would have been detected by a CPOE system.

Methods

Data from a randomised controlled trial of pharmaceutical care provided in the context of acute geriatric care were used. All interventions that were initiated by the clinical pharmacist for patients in the intervention group (n=905) were evaluated to determine the likelihood (likely, possibly, unlikely) that the underlying DRP would have been detected by a CPOE system. The classification was similar to that used by Bobb et al.[12] DRPs were classified as "possibly detectable" by the CPOE system when optional non-automated features of the CPOE system could be used by the prescriber (eg use of a protocol, use of laboratory data visible on the screen, etc). The CPOE system implemented at another teaching hospital (affiliated to the same university) was used as a reference. This system had the core characteristics of a CPOE system, and had limited decision support features (screen for drug-drug interactions, and maximum doses for commonly prescribed drugs).

The classification (likely, possibly, or unlikely detectable) and analysis were made by a clinical pharmacist external to the main study, and with good knowledge of the CPOE system. When necessary (for example for drug interactions problems), the pharmacist entered the prescription in the system to check whether the DRP was detected. A double check was made by the same person for all evaluations, and by another pharmacist for the first 50 cases (agreement was good).

Results

Table 1 summarizes the detection rate by type of DRP. The DRPs most likely to be detected by the CPOE system were prescription-writing error (82% were always detected), inappropriate formulation (33%), duplication (31%), and drug-drug interactions (27%). In contrast, underuse, error in medication history, inappropriate follow-up, and adverse drug reactions were never detected by the system. Table 2 shows the detection rate classified by clinical importance of interventions. Major and extreme interventions were not more likely to be detected by the system than less important interventions.

Table 1: Detection rate of drug-related problems (that were identified by a clinical pharmacist) by a computerised-order entry system

Category of DRP identified by the clinical pharmacist (no)	DRP detected by the CPOE system (%)			Comments
	Never	Possibly	Always	
Underuse (166)	100	0	0	Never detected because no link with past medical history
Inappropriate duration (100)	90	10	0	"Possibly detected": the prescriber can specify the date of the end of treatment, on its own, or by using protocols.
Inappropriate choice (83)	95	5	0	"Possibly detected": possibility to access the therapeutic formulary of the hospital or specific protocols, with guidance on choice of drugs.
No valid indication (72)	89	11	0	"Possibly detected": Laboratory values appear below the prescription data on the screen, and direct comparison can enable the identification of no valid indication; reimbursement criteria for specific medicines can also appear .
Dose too low (67)	90	9	2	For most frequently prescribed medicines, minimum and maximum dose range are pre-specified. Laboratory values visible on the screen can also help to detect inappropriate doses.
Dose too high (52)	67	33	0	Same as above
Error in medication history (46)	100	0	0	
Inappropriate follow-up (41)	100	0	0	
Adverse drug reaction (39)	100	0	0	
Prescription-writing error (34)	18	0	82	Detected if the name of the medicine does not exist. Lack of dose or formulation is not allowed by the system.
Duplication (32)	69	0	31	Detected if same ATC class (fourth level)
Less costly alternative (29)	35	66	0	"Possibly detected": a warning message appears when medicines out of the formulary are prescribed; this message can be bypassed by senior doctors.
Drug-disease interaction (28)	93	7	0	Some diseases can be selected by the doctor, and drug-disease interactions can subsequently be detected, but disease selection is hardly ever made. Laboratory values on the screen can also help to detect interactions.
Inappropriate frequency/ time of administration (28)	93	0	7	The prescription order cannot be proceeded if this information is not entered.
Inappropriate route (20)	90	5	5	Existing routes are proposed to the prescriber
Modalities not practical for the patient (19)	95	0	5	In some cases the system detects tablets that cannot be split
Drug-drug interaction (15)	73	0	27	Severe interactions are detected (Delphi 1996)
Inappropriate formulation (12)	67	0	33	In some cases detects tablets that cannot be split.
Other (12)	75	0	25	
No specific problem (7)	86	0	14	
Allergy (3)	100	0	0	
Total (905)	**86.5**	**7.4**	**6.1**	

Abbreviations: CPOE: computerised prescription order entry; DRP: drug-related problem

Table 2: Detection rate of drug-related problems by a computerised-order entry system, classified by clinical significance of the problem

Clinical significance of the problem* (no)	DRP detected by the CPOE system (%)		
	Never	Possibly	Always
Minor (17)	100	0	0
Moderate (463)	87	7	6
Major (191)	90	5	6
Extreme (3)	100	0	0
Deleterious (1)	100	0	0
Total (675)*	88.3	5.8	5.9

* Determined by an expert panel of geriatricians and specialist clinical pharmacists. Intervention with no direct clinical impact were not evaluated by the panel.

Discussion

The results show that only a minority of DRPs detected by the clinical pharmacist would have been detected by the CPOE system. More importantly, major DRPs were not more likely to be detected than DRPs of moderate clinical importance.

Two main comments arise from these results. First, the detection rate may have been low because the "decision support" component of the system was limited. The CPOE system did not have the capability of taking the patient's pathophysiological status and medication conditions into account to present the physician with a recommendation of what to prescribe. This hypothesis corroborates previous findings that the addition of a CDSS to a CPOE system is essential.[6] In addition, it is surprising that only 27% of drug-drug interactions that were picked-up by the clinical pharmacist would have been detected by the computer. This illustrates that the sensitivity of the drug interaction database is not satisfactory.

Second, these results show that a computer interface cannot replace a human specialist component. Other researchers came to similar conclusions, although differences in study design preclude direct comparison of data. For example, Bobb et al identified that 30% of clinically significant prescribing errors detected by clinical pharmacists were likely preventable through CPOE.[12] In addition, Fair and Pane found that the implementation of a CPOE system generated new types of errors necessitating pharmacist interventions.[13]

Although these results clearly demonstrate that clinical pharmacists bring added value to quality of medicines use in comparison to CPOE, our data could be analysed further to find out whether the performance of the system could be improved through relatively simple modifications.

For example, the specificity and sensitivity of drug interactions alerts could be revised. This would save time for clinical pharmacists to concentrate on DRPs that are not detectable by a CPOE system.

The present work has limitations. First, the results cannot be generalised to other CPOE systems, and certainly not to CPOE with advanced decision support features. Second, the study design did not enable us to identify if CPOE generated new types of errors. Third, the main weakness of this study is that we used an indirect measure of the relative impact of pharmaceutical care versus CPOE. We did not evaluate if the computer would have detected DRPs that the clinical pharmacist had not identified. This is possible, but probably of limited importance, because the pharmaceutical care process was highly structured and comprehensive. However, the CPOE system could have detected other potential DRPs that had no or little clinical relevance. In fact, the literature clearly describes that owing to lack of specificity of the alerts, warnings may appear far too frequently, leading prescribers to ignore alerts altogether.[14]

In conclusion, a CPOE system with limited clinical decision support can identify only a minority of DRPs detected by a clinical pharmacist. The same observation applies to the subgroup of DRPs of major clinical importance. The added value of clinical pharmacists in the identification and resolution of these problems is substantial.

Acknowledgments

Stephanie Pirlot did the major part of the data collection and analysis. This was done in the context of her Masters in clinical pharmacy (DES en pharmacie hospitalière clinique, UCL, 2004-2005).

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B. Drug-induced lithium intoxication: a case report

DRUG-INDUCED LITHIUM INTOXICATION: A CASE REPORT

To the Editor: In their recent observation study, Juurlink et al. reported that the risk of lithium toxicity dramatically increased within a month of initiating treatment with a loop diuretic or an angiotensin-converting enzyme (ACE) inhibitor.[1] Besides pharmacokinetic drug interactions, interactions with psychotropic medications have been attributed to pharmacodynamic mechanisms.[2] We report a case of hospital admission for lithium toxicity secondary to drug interactions.

CASE REPORT

A 74-year-old woman was referred to us for a 3-week history of functional decline, lethargy, confusion, diarrhea, tremor, and dysarthria. Medical history included bipolar disorder, type II diabetes mellitus, hypertension, and ischemic heart disease. Medications on admission were lithium (250 mg three times daily), escitalopram (10 mg daily), levomepromazine (6.25 mg daily), lormetazepam (2 mg daily), metformin (850 mg three times a day), repaglinide (1 mg twice daily), lisinopril (30 mg daily), irbesartan (300 mg daily), furosemide (30 mg daily), and spironolactone (50 mg daily).

On admission, the patient was drowsy and confused. Glasgow Coma Scale was 12 of 15. Neurological examination showed dysarthria but no focal neurological deficits. Lithemia was 2.3 mEq/L (therapeutic range 0.6–1.2 mEq/L). Other investigations, including laboratory tests, computed tomography scan, and electroencephalogram, were not contributive. Serum creatinine was 161 μmol/L with an estimated clearance of 34 mL/min, secondary to dehydration.

Three months before admission, lisinopril dosage had been increased from 20 mg to 30 mg daily and irbesartan added for hypertension. Seven weeks before admission, spironolactone had been added. In addition, dexetimide 0.50 mg (a centrally acting anticholinergic drug licensed for the treatment of neuroleptic-induced extrapyramidal symptoms) had been recently added for worsening tremor, but no improvement was observed. Confusion had increased, and the drug was discontinued.

On admission, lithium was withdrawn, as were diuretics, levomepromazine, and escitalopram. Risperidone (0.25 mg twice daily) was added, but neurological status deteriorated with increased agitation, although the lithium level had fallen to 1.2 mEq/L on the fourth day after admission. Upon consultation, the clinical pharmacist proposed stopping potentially interacting drugs (lisinopril, irbesartan, risperidone) to accelerate lithium excretion and to eliminate neurotoxic symptoms. The patient was simultaneously transferred to the intensive care unit because of apathy and oliguria. Rehydration and withdrawal of interacting drugs led to substantial neurological improvement. The patient was discharged 2 weeks later on carbamazepine for maintenance treatment of bipolar syndrome. Two months later, the patient remains stable.

DISCUSSION

Risk factors for lithium toxicity include age-related altered pharmacokinetics, polypharmacy, and renal impairment. This case highlights the importance of stopping the causal drug but also drugs that may delay lithium elimination or worsen neurotoxic effects. Several drugs may have played a role in lithium intoxication. ACE inhibitors enhance the tubular reabsorption of lithium, and diuretics promote renal sodium wasting. They increase the risk of hospital admission for lithium toxicity.[1] The outcome of concurrent use of lithium and spironolactone remains unclear.[2,3] The addition of an angiotensin-II receptor antagonist (irbesartan) several weeks before admission may have contributed to lithium intoxication. The three case reports with candesartan, losartan, and valsartan that have been published indicate that intoxication can take several weeks to develop fully.[3] The mechanism of interaction is probably at least partially similar to that with ACE inhibitors. Finally, escitalopram and levomepromazine used with lithium may have increased the tremor associated with these drugs used alone.[4] It is also possible that a neurotoxic reaction occurred after the addition of risperidone. A similar observation has previously been reported.[3]

The equilibration of lithium between plasma and brain is extremely slow. Understanding this delay better enables the clinician to care for patients with lithium toxicity. Because clearance from the plasma is much faster than from the brain, it is not uncommon for patients who have presented with chronic lithium toxicity to still have signs of neurological toxicity when lithium concentrations have fallen into or below the therapeutic range.[5] This was the case here.

Inadequate monitoring of drug therapy can lead to a phenomenon called the "prescribing cascade."[6] The "prescribing cascade" begins when an adverse drug reaction is misinterpreted as a new medical condition. Another drug is then prescribed, and the patient is placed at risk of developing additional adverse effects. Dexetimide was added for worsening tremor probably secondary to lithium overdosage unrecognized at that time. This led to worsening neurological status. Geriatricians should be aware that a delay of several weeks between the addition of a new drug and lithium intoxication is possible.[2] Lithemia and clinical signs of overdosage should be monitored accordingly.

This case also illustrates that the contribution of clinical pharmacists is valuable in reducing drug-related morbidity and optimizing drug therapy.[7]

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4.

Discussion and perspectives

Improving the quality of care is a priority to public health authorities worldwide, and optimising the quality of use of medicines has always been an important component of quality initiatives. Among the numerous approaches that have been implemented over the last 30 years to improve medicines use in acute care, the involvement of clinical pharmacists was advocated in the US and the UK, and it was shown to be effective in decreasing medication errors, improving patient care, and decreasing costs. When we started our Doctoral work, clinical pharmacy services were almost inexistent in Belgium and in Europe,[1;2] although the results of pilot experiences were increasingly being reported. An analysis of the Belgian situation in 2001 showed that there were real opportunities to implement clinical pharmacy services, and that barriers for implementation could be overcome. The present work aimed – through a pilot experience – to assess the impact of clinical pharmacists providing pharmaceutical care to inpatients on the quality of use of medicines. Elderly patients were targeted for this pilot experience, mainly because these patients are at increased risk of DRPs.

4.1. Principal findings of this work

When evaluating our work as a whole, several important and new findings can be identified.

First, quantitative as well as qualitative findings unambiguously show that there is an important need for improvement in the quality of medicines use in elderly patients in Belgium. This applies to elderly patients while they are in acute care, as well as in transition between acute and chronic care. It is also potentially applicable to outpatients, as reflected by the high levels of inappropriateness of prescribing just before admission.

Second, the qualitative approach gave insight into the causes of inappropriate use of medicines, a perspective that had not been addressed in this population in the past. The causes are multifactorial and occur at several levels: the prescriber (e.g. prescription not adapted to frail geriatric patients, passive attitude toward learning), communication between the prescriber and the patient or other HCPs (e.g. lack of shared-decision making), and the system of healthcare (e.g. unreliable transfer of information between settings of care). These findings are important to design adequate optimisation strategies.

Third, for the first time in Belgium, we demonstrated that the implementation of clinical pharmacy and the provision of pharmaceutical care is feasible. What is more, this new pharmaceutical practice is very well accepted by other HCPs and by patients. The cautious preparation phase, that included attention to driving forces and barriers, probably contributed to the success of this implementation.

Fourth, the randomised controlled trial provides robust evidence that clinical pharmacy can substantially improve the quality of medicines use during hospital stay for geriatric patients. Furthermore, the majority of improvements are maintained after discharge, and there is a trend

towards improved clinical outcomes. This intervention cannot be subordinated to that of a computerised prescribing system.

In the remaining of the discussion, we will discuss the internal validity of the results, as well as their limitations. Then, we will argue on the added value of this work to the body of current knowledge, both from international and Belgian perspectives. Finally, the main perspectives for further work will be discussed.

4.2. Are the results valid?

This question is essential. To answer it, it is necessary to first address the validity of the global approach, to then appraise the quality of the sample, the robustness of the intervention, and the validity of the selected outcome measures and analytical methods.

The sequential approach of first evaluating the baseline level of appropriateness (in order to identify the needs for optimisation) and subsequently measuring the impact of an optimisation approach was adequate.[3] Even though the approach selected (i.e. clinical pharmacy) had been defined in advance, it enabled us to better identify what the opportunities for optimisation were, and to adapt our intervention to these needs. In addition, this project was designed so as to address the regularly quoted limitation that "pilot experiences in clinical pharmacy frequently lack robust design to evaluate their impact",[4] and that "they are not enough reported in the literature".[1]

The intervention provided was robust in several ways. As mentioned earlier, the intervention took into account several factors underlying inappropriateness (for example it encouraged an increased communication with the patient and the general practitioner). The clinical pharmacist was fully integrated in the multidisciplinary geriatric team, which facilitated interactions with other members and with patients. The intervention also embraced the core evidence-based clinical pharmacy activities described by Bond (activities selected based on favourable associations with mortality rate, drug costs, total cost of care, length of hospital stay, and medication errors): drug information, adverse drug reaction management, drug protocol management, medical rounds, and admission drug histories.[5] Finally, the intervention was precisely defined and structured, and this will facilitate its generalisability to other situations.

The rationale for targeting elderly patients has been explained at the beginning of this manuscript. The high susceptibility of this population to DRPs was certainly a good selection criteria, and high-risk situations (patients, units, drugs) should be targeted in further pilot studies. The

increasing proportion of elderly patients in our society also broadens the potential applicability of the present intervention.

With regard to the qualitative study, internal validity stems from (i) the inclusion of participants with different backgrounds – patients' voices were also elicited, and this was important – and of members of the research team; (ii) the combination of different data collection methods (i.e. interviews, focus groups, and observations); (iii) the analytical approach that included an inductive approach, attention to reliability in coding, and use of a qualitative software to support in coding and analysis. These considerations are all included in recent recommendations for robust qualitative research.[6-8]

The intervention study went far beyond a simple description of clinical pharmacist's interventions to resolve DRPs. An external panel validated the clinical relevance of these interventions, and this probably strengthens our credibility toward other physicians and hospital managers. Yet, the major strength comes from the comparison with a control group, and from the use of three validated measures of prescribing appropriateness that encompassed the three domains of suboptimal prescribing. In that regard we seized the opportunity that a control group without any pharmacist input was considered ethical in the Belgian context, which is no longer the case in the US or the UK, for example. The potential for contamination of prescribers was inevitable (randomisation at the ward level was not feasible), but we addressed that issue through the use of a historical control group.

Internal validity in the methods and analyses – as described above – were a prerequisite to claim that the results are valid. Validity of the results is further increased by the fact that (i) the clinical pharmacy intervention was compared to a gold standard, namely multidisciplinary geriatric care, and (ii) the results are unambiguous. It is also important to note that they largely corroborate the results of previous international studies These considerations open up interesting perspectives that will be discussed later.

Inevitably, our work has **limitations**. Although we believe that they do not invalidate our findings, they need to be addressed.

Lack of generalisability is probably one of the two main limitations of both the qualitative and quantitative studies. With regard to our qualitative study, the issue could be resolved by conducting a large survey on the importance of factors underlying inappropriateness, using questionnaires that would be inspired by the findings of the qualitative study. But this might be difficult to conduct, and the results of a Belgian survey could not be generalised to other countries. With regard to the quantitative study, although we are relatively confident that there is a need to optimise the use of

medicines in other situations (units, hospitals,…),[9-12] generalisability of the impact of the intervention cannot be claimed. Generalisability could have been improved by conducting a multicenter study (and so would have the power of the study). However, this was considered inappropriate in the context of a pilot implementation phase. This option will certainly be discussed in the near future.

The second main limitation is that cost-effectiveness was not addressed. The main focus of our project was quality, and we did not prospectively measure economic outcomes. Considering economics will be essential to justify further development of clinical pharmacy activities (see perspectives).

The RCT had other limitations. Sample size calculation was based on published data and not on local data, and sample size was too small to detect an impact on secondary outcome measures (clinical outcomes, benzodiazepines in patients with previous falls). The clinical meaning of the significant improvements in appropriateness of prescribing remains unknown. Finally, interesting outcome measures such as ADEs, quality-of-life, compliance, were not collected, mainly due to human resource constraints. We are progressively increasing our research team and broadening our competences, and this will enable us to perform additional measurements in the future. Quality-of-life is certainly a crucial outcome measure. Previous studies similar to ours did not find an impact on quality-of-life, when using the SF-36.[13-15] This instrument may not be sensitive enough to detect changes in health status that are attributable to pharmacist interventions. Disease-specific instruments, or pharmaceutical-therapy related instruments might be more sensitive, and could be used in the future.

Finally, from a global perspective, this work mainly focused on prescribing issues for individual patients, and did not look at other important areas of medicines use, such as medication errors, patient safety, access, and other public health issues.

4.3. What is the added value of this work to the body of current knowledge?

From an international perspective, our work could be viewed as “one more study to show that inappropriate prescribing in elderly patients is prevalent”, and “one more study to show that pharmaceutical care is effective to decrease DRPs[e]”. Our results, indeed, largely corroborate those of dozens of previous investigators. Yet we are convinced that our findings can be interesting for these investigators in several ways.

First, the qualitative approach in acute geriatric care was new. The results reinforce the importance of issues that have not been adequately addressed so far, such as shared decision-making and education in geriatric pharmacotherapy. Other factors that we identified have been rarely described in the literature, such as passive attitude towards learning, and difficulties in communication between

[e] DRPs can be due to both appropriate prescribing (e.g. in the case of an ADR that is predictable but not preventable) and inappropriate prescribing (e.g. inappropriate dosing leading to a preventable ADE)

prescribers. We do not know whether these are cultural factors specific to our country or not, but they certainly deserve further consideration.
Second, we have provided additional data on the reliability of the MAI. Published studies on reliability were rarely performed by researchers different from the authors of the instrument, and were not realised in acute care settings.
Third, although there have been many publications on approaches for improvement in medicines use in elderly patients, few were conducted in acute care. Only one recent study used a combination of validated measures of over-, mis-, and under-prescribing to evaluate the impact of GEM care, but the relative impact of clinical pharmacists was not assessed.[16] Our RCT, therefore, provides new data on the impact of pharmaceutical care in that population.
Finally, the vast majority of current data on prevalence of inappropriate use of medicines in elderly patients comes from non-European countries (US, Canada, Australia), and the few European studies focused mainly on the Beers' criteria. Similarly, there is a lack of European data on the impact of pharmaceutical care. The present work is one contribution to fill these gaps.

The added value of this work for Belgium is clear. It is the first pilot pharmaceutical care study in our country, and it provides (i) robust research findings demonstrating that there is a need for it, that it is feasible and effective, as well as (ii) information on strategic planning for implementation. These data should be an important contribution to convince hospital pharmacists, prescribers, and managers that pharmaceutical care is worth further development.

4.4. Perspectives

The present work generates perspectives in three different domains: use of medicines in geriatrics, further development of clinical pharmacy in Belgian hospitals, and development of pharmaceutical care activities for geriatric outpatients.

4.4.1. Use of medicines in geriatrics

With regard to the use of medicines in geriatrics, it is clear that the data from the RCT could be further exploited. We could first attempt to examine characteristics associated with inappropriate prescribing (such as the number of prescription drugs, self-reported health, cognitive impairment, residence before admission, etc). The results could be compared to that of previous authors,[17-24] and used to target the patients at higher risk. In a second time, we could evaluate if patients with an adverse clinical outcome (death or readmission) had higher levels of inappropriate prescribing at discharge. This would give us

data on predictive validity, for which there is inconclusive evidence. Yet, an increased sample size will be needed to have sufficient power.

In addition, our results on the most frequent types of interventions that were initiated by the clinical pharmacists could be used to implement of (i) educational-type interventions (interactive single or group sessions), or (ii) decision-support tools for CPOE systems, and their impact should be evaluated in prospective studies. Several examples of similar interventions that were reported in the literature could inform the design of a future study.[25;26]

To better understand the complexity of use of medicines in geriatrics, and based on our data on patients' perspectives, we could further investigate the concept of "patient attachment to their medicines"/ "patient reluctance to treatment changes". This concept is linked to that of shared-decision making, which has gained increasing interest over the last few years.[27-29] In our study, patient reluctance toward treatment changes was anticipated by most HCPs, but patients did not really express such a resistance. In addition, discontinuation of benzodiazepines was more successful in the intervention group, in which the clinical pharmacist paid special attention to reach an agreement with the patient on discontinuation, than was seen in the control group. Previous studies found that patient resistance might be part of a negotiation process rather than a final stance,[30] and that using a shared-decision making instrument could facilitate agreement with treatment goals and plans.[31] The research questions, therefore, could be the following: Patient reluctance is a major issue for HCPs, but does it really occur from the patient's perspective? Could increased sharing of treatment decisions lower this problem and eventually improve patient outcome? The case of benzodiazepine prescribing could be used, because (1) our data show that the prevalence of use in patients with a previous fall is alarming, and seems to be higher than in other countries,[32] and (2) because this class of drugs increases the risk of physical disability in community-dwelling older adults.[33]

4.4.2. Further development of clinical pharmacy in Belgian hospitals

Four years have passed since this project was designed and accepted. While it was a "risky bet" at that time, there are now good and exciting perspectives for clinical pharmacy in Belgium. To gain full recognition and to move from small pilot clinical pharmacy services to widely established services, two elements will, in our opinion, be essential.

The first challenge will be to demonstrate that the positive impact on the quality of use of medicines is generalisable to other populations (including other types of patients, other acute wards, other hospitals) and other clinical pharmacists. There are preliminary Belgian data suggesting that clinical pharmacists can optimise, in our national environment, the use of medicines for patients in intensive care, internal medicine, paediatrics, geriatrics, surgical orthopaedic wards, or for patients receiving antibiotics.[34] Recent experiences in non-teaching hospitals (mainly psychiatric hospitals) have also been reported.[34] Pharmacists and investigators involved in these projects could join their efforts, and a

multicentre study could be designed (discussions are ongoing in this context). We believe that it important, for such a study, that (i) clinical pharmacist are in direct contact with the rest of the medical team, with patients and carers, (ii) have access to patient records, (iii) follow a structured approach to identify and resolve drug-related problems. These characteristics are indeed essential components of successful interventions.[35-39]

The second and major challenge will be to justify the cost-effectiveness of pharmaceutical care. In fact, without well-documented evaluations of the economic impact of clinical pharmacy services, successful expansion is unlikely.[40] Ideally, the impact on direct costs as well as on indirect costs should be considered, but these evaluations may be difficult to perform. It would be possible to use the data from our RCT to compare the cost of drugs for patients in the control and intervention group, and add the cost to provide the service for intervention patients. However, most benefits of clinical pharmacist's interventions are not reflected into costs of drugs. There is another – and more attractive – perspective to demonstrate the economic impact. From July 2006, there will be a shift in drug financing policy in hospitals, from a retrospective system to a prospective payment system based on diagnosis-related groups. It is likely that hospitals will struggle to change doctors' habits, and to make them prescribe cheaper drugs than they are used to. Concentrating only on drug acquisition costs, however, may lead to suboptimal treatments, which will not only create medical problems, but will also cause additional financial burden (because of the necessity to readjust the therapy, and perhaps also of facing litigation issues). Several hospital managers have already envisioned that clinical pharmacists could play a great role to apply this new system – and therefore to decrease costs – while ensuring appropriate quality. A collaboration with the socio-economic department of the School of Public Health is being considered. The idea is, with the support of their comprehensive database, to study how clinical pharmacy activities can improve drug expenses so as to be as closely as possible in line with prospective payments, without reducing quality. Further discussions and pilot work involving experts in this domain will be necessary to progress on this perspective.

In parallel to the above challenges, chief pharmacists will have to be able to present strategic development plans to their hospital managers. These plans will define which patients or units should be targeted first, how many pharmacists will be needed (considering that one pharmacist per ward is ideal but not reasonable at this stage), and how the services will be evaluated. Such a plan has already been discussed at Saint-Luc teaching hospital, and by the end of the year a new position should be created, and implementation of pharmaceutical care on a paediatric unit will be tested and the results will be compared to that of other units. Another option that could be considered to increase clinical pharmacy positions is to give additional responsibilities to pharmacy assistants with regard to the preparation and dispensing of drugs, so that the pharmacists themselves will have more time for pharmaceutical care. Finally, further work is needed to develop educational programs for clinical pharmacists, and to gain accreditation at the national level.

4.4.3. Education

Further development of patient-centred clinical pharmacy services in Belgium requires that pharmacists with adequate competences are available. The School of Pharmacy at our university is well conscious that the educational programs need to be adapted in order to improve the knowledge and skills of pharmacists in pharmaceutical care. Toward this end, several measures have been taken in the last few years at both the undergraduate (e.g. taught courses in pharmacotherapy, and workshops on patient cases) and postgraduate (i.e. new Certificate and Masters in clinical pharmacy) levels. In the near future, we will need to evaluate if the objectives are met, and to proceed with further adaptations. Other objectives will be that similar measures are taken by the other Belgian universities in Belgium, and that continuing education programs are adapted. These initiatives are currently in progress.

The results of the qualitative study suggest (and confirm data from other sources) that doctors and nurses lack knowledge and skills in the appropriate use of medicines. At the undergraduate level, the amount of time devoted to teaching therapeutics is far too limited, and should be extended. The same observation applies to postgraduate training. Clinical pharmacists have a great opportunity to teach HCPs while they are on the ward. In addition, clinical pharmacists could be involved in formal teaching on therapeutics for medical students, as it is the case in other countries. Before this, it is necessary that the Faculties of Medicine acknowledge that therapeutic teaching should be increased, and take appropriate measures to enable this. We are progressively involved in postgraduate training for general practitioners, and also in the implementation of joined courses on therapeutics for pharmacy and medical students. This latter initiative is promising, and a direct contact between pharmacists and prescribers is probably essential to improve communication between practising doctors and pharmacists.

4.4.4. Development of pharmaceutical care activities for geriatric outpatients

Our data showed that over-, mis-, and under-prescribing of chronic medications was prevalent in elderly patients admitted to hospital. A subanalysis of the data (unpublished) revealed that the clinical pharmacist made 2.3 ± 1.6 interventions per patient that were related to chronic treatment and that could have been made before the acute condition developed. It is, therefore, very likely that elderly patients (including nursing home patients) could benefit from clinical pharmacy services in the outpatient setting. This has been largely demonstrated in other countries.[41] Preliminary considerations should address what would be the most adequate intervention (eg individual or group academic detailing with GPs and/or nurses, individual treatment reviews with general practitioners), and how barriers for implementation (e.g. access to patient data, limited presence of GPs, motivation) could be overcome.

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