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Repeat Prescribing

Scale, Problems and Quality Management in Ambulatory Care Patients

Peter A.G.M. De Smet[1,2] and *Maaike Dautzenberg*[3]

1 Scientific Institute Dutch Pharmacists, The Hague, The Netherlands
2 Department of Clinical Pharmacy, University Medical Centre St Radboud, Nijmegen, The Netherlands
3 Centre for Quality of Care Research, University of Nijmegen, Nijmegen, The Netherlands

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Abstract

The reported scale of repeat prescriptions ranges from 29% to 75% of all items prescribed, depending on the definition of repeat prescribing and other variables. It is likely that a substantial part of repeat prescribing by general practitioners (GPs) occurs without direct doctor-patient contact. While this reduces the workload for the GP and is convenient for the patient, it does not provide the adequate control that is needed to ensure that every repeat prescription is still appropriate, effective and well tolerated, and that it is still being viewed upon and taken by the patient as intended. Infrequent therapy reviews may lead to failure to prevent, identify and solve drug-related problems and drug wastage, and may, thereby, have a negative impact on the effectiveness, safety or cost of the medications prescribed.

Studies evaluating the repeat prescribing process have shown that GPs and medical practices vary widely in their degree of administrative and clinical control of repeat prescriptions. Contrary to the opinion that GPs cannot change prescribing behaviour when the prescription is initiated by a medical specialist, GPs have their own responsibility for controlling the repeats of such prescriptions.

Intervention studies suggest that a medication review by a pharmacist can help to reduce drug-related problems with repeat prescriptions, and the effectiveness of the intervention may be increased by combining the medication review with a consultation of the patient's medical records and a patient interview. In several studies, such an intervention was relatively inexpensive and, therefore, feasible. However, these conclusions should be viewed with appropriate caution because a number of caveats pertain. There is still no evidence that these types of intervention improve health-related quality of life or reduce healthcare cost, and so far only a few trials have produced any evidence of clinical improvement. As implicit and explicit screening criteria have their own benefits and limitations, a combined application may offer a more thorough assessment but may also be more complex and time consuming.

Further studies on the development and evaluation of repeat prescription management models are needed, preferably focussing on improving clinical, humanistic and economic outcomes. New studies should investigate the effects of: different types of interventions; different organisational models; different target populations; and selecting and training different types of healthcare professionals. Future studies should also assess whether results are sustained, the optimal time interval between reviews of repeat prescriptions, and the possibilities offered by new computerised support technologies.

Improvement of repeat prescribing may be a major issue for practice management, because of its potential implications for the quality and cost of drug treatments. Traditional management of repeat prescribing has been criticised for its lack of structural periodic controls, resulting in failure to identify in a systematic way issues that compromise the appropriateness, effectiveness and/or safety of a given drug treatment. Improvements in this domain may be needed, because the condition of the individual patient and therapeutic insights are both subject to potential change.

The objective of this review is the provision of in-depth insight into this matter by surveying successively, on the basis of original research literature, the following aspects of repeat prescribing in ambulatory care patients:

- definition and scale of repeat prescribing;
- problems with repeat prescribing and areas for improvement;
- characteristics and results of intervention studies;
- conclusions and recommendations for future research.

1. Methods of Review

To find the pertinent literature, Medline was consulted through PubMed (entry date up to July 2003). Since the MeSH database of PubMed did not provide any useful MeSH term for repeat or refill prescribing, the primary search strategy consisted of the following free text search: (repeat or refill*) and (prescri* or medication* or "drug therapy"). As the continuous evolution of pharmacotherapeutic insights and the introduction of computerised support have substantially changed drug prescribing and dispensing practices in the past decades, references published more than 10 years ago were considered to have no major practical relevance. They were excluded by limiting the search to publication date from 1993 to 2003.

To be eligible for inclusion in this review, the retrieved references had to present original research data on the scale, problems and/or quality management of repeat prescribing in general in ambulatory care patients. Studies were excluded if they focused on an institutionalised care setting (e.g. a hospital setting[1] or nursing home[2]), on a specific diagnosis or drug group (e.g. lipid-lowering drugs[3]), or on a

nonclinical aspect (e.g. prescribing cost[4]). Studies were also excluded when the presentation of data was insufficiently clear (e.g. inadequate description of results[5]) or when they had been published in a language other than English, German or French.

Additional references were retrieved by carrying out the following secondary search strategies:

- announcements of two intervention studies found through the primary search strategy[6,7] were followed up by searching Medline for references presenting the results of these studies;
- the reference lists of major references found through the primary search strategy were hand searched for earlier pertinent references;
- since the latter search yielded several references published in two non-Medline journals (the *International Journal of Pharmacy Practice* and *Pharmaceutical Journal*), online volumes on the websites of these journals were also screened. The contents of the *International Journal of Pharmacy Practice* (http://www.pharmj.com/IJPP/IJPPIndex.html) were hand searched from March 1997 (volume 5, number 1) to June 2003 (volume 11, number 2), while the *Pharmaceutical Journal* (http://www.pharmj.com/) was computer searched from 18 September 1999 (volume 263, page 403) to 28 June 2003 (volume 270, page 912) for original papers or reviews on 'repeat or refill';
- as the intervention studies retrieved through the primary and secondary search strategies usually comprised a medication review and were often targeted at patients on polypharmacy, Medline was also searched for: ("drug utilisation review"[MeSH] or "polypharmacy"[MeSH]) and ("clinical trial"[publication type] or intervention*).

Pertinent references were selected if they adequately described original research data on the quality management of long-term prescriptions in general in ambulatory care patients. The exclusion criteria that were used in the primary search strategy were also applied in the secondary search strategies.

2. Definition and Scale of Repeat Prescribing

2.1 Definition of Repeat Prescribing

In its literal sense, repeat prescribing involves the issuing of any subsequent prescription within a given period, whether it is accompanied by a consultation or not. However, some authors like to reserve the term for prescriptions that have been issued without direct doctor-patient contact, because they are concerned that prescribing without a consultation may affect the medical quality of the prescription.[8-11] Others prefer to define repeat prescriptions as prescriptions that have been printed by a practice computer with the aid of a repeat prescribing program. This latter definition does not differentiate whether prescriptions are printed during a consultation or not, so it does not help to distinguish which patients have been reviewed clinically. However, it has the advantage of being practical and simple to use in analyses and comparisons of computerised patient data (e.g. to audit the impact of changes in practice policy).[12,13]

For the purposes of this review, we included all relevant data on the scale of repeat prescribing, irrespective of the definition used. However, given the impact that the definition can have on interpreting the data, we have consistently noted the definitions used.

2.2 Scale of Repeat Prescribing

Measured scales of repeat prescribing depend on numerous factors, such as: the inclusion or exclusion of telephone consultations, intermittent drug therapies (e.g. for eczema) and non-drug items (e.g. dressings); the study population, study period and number and nature of practices involved; and the method of data collection.[12,13] An important factor is the definition of repeat prescribing employed (see section 2.1).

General studies on the scale of repeat prescribing are summarised in table I.[8,9,12,14-16] Because of the lack of a common definition of repeat prescribing and other variables, reported figures on the scale of

Table I. General studies on the scale of repeat prescribing[a]

Study (year)	Setting (study period)	Definition of repeat prescription	Proportion (%) of repeat prescribing in		Effect of age on proportion of repeat prescribing	Drug groups with highest repeat percentage
			prescribed items	prescribed cost		
Rokstad and Straand[14] (1997)	149–153 GPs, Norway (November 1988 [149 GPs] and November 1989 [153 GPs])	Repeat prescription with or without direct contact (defined as face-to-face contact)	55 (61.5% of which were issued during indirect contacts by telephone, letter or through messenger)	NR	≥65 years: 72% of items prescribed in subgroup analysis[17]	CNS drugs Cardiovascular drugs
National Audit Office[8] (1993)	Two GP practices, UK (April 1991–March 1992)	Prescription issued without consultation	66	79	NR	Cardiovascular drugs (93%) Immunosuppressive drugs (88%) Respiratory drugs (79%) CNS drugs (75%) Endocrine drugs (73%)
Purves and Kennedy[9] (1994)	Seven GP practices, UK (February 1993 – final month not specified)	Prescription issued without consultation	65	75	NR for total study population	NR for total study population
Davidson et al.[15] (1997)	Six GP practices, UK (October 1992–December 1992)	Self-determined by participating GPs	29	32	NR	NR
Harris and Dajda[12] (1996)	115 GP practices, UK (January 1993–December 1993)	Printed by practice computer from repeat prescribing program	75	81	Determined as % of patients receiving repeat prescriptions within the relevant patient population: 25–34 years: 40% 35–44 years: 39% 45–54 years: 48% 55–64 years: 61% 65–74 years: 77% 75–84 years: 92% ≥85 years: 94%	Hypnosedative barbiturates (99%) Cardiac glycosides (98%) Antiparkinsonian drugs (98%) Antidiabetic drugs (98%) Thyroid drugs (98%) Lipid-lowering drugs (97%) Antiepileptic drugs (97%) Antigout drugs (97%)
Feely et al.[16] (1999)	92 GPs, Ireland (period not specified)	Any repeat prescription	51	NR	NR	NR

a Studies focusing on single GP practices or special populations (e.g. users of one or only a few specific drug groups) have been excluded.

GP = general practitioner; **NR** = not reported.

repeat prescribing ranged from 29% of all items prescribed (accounting for 32% of the total cost of prescribed drugs)[15] to 75% of prescribed items (accounting for 81% of the total cost of prescribed drugs).[12] In a Norwegian study, 61.5% of the repeat prescriptions generated by general practitioners (GPs) were issued without face-to-face contact.[14] In two UK studies that defined repeat prescribing as that which occurred without consultation, repeat prescription rates were approximately 65%.[8,9] Although these studies were based on older data and might, therefore, no longer accurately reflect the present situation, it is likely that a substantial part of repeat prescribing by GPs still occurs without a consultation.

Repeat prescribing increased with the age of the patients in the two studies that reported on the effect of age.[12,17] In the largest UK study, effects of sex were slight and there were no major differences between fundholding and non-fundholding practices, or between dispensing and non-dispensing practices.[12]

3. Problems with Repeat Prescribing and Areas for Improvement

3.1 Prescribing without Consultation

Doctors usually have to authorise every prescription because they are legally responsible for prescription writing. In daily practice, there may be a large difference between the authorisation of a prescription during a consultation and that of a repeat prescription without any direct patient contact. The latter often takes place between finishing surgery and going on home visits, when the doctor may not have the time or opportunity to review the patient's prescription requirements. Yet such a review can be relevant, since professional therapeutic insights, the beliefs and behaviour of patients, and the course of illness are all subject to potential change. Therefore, it has been argued time and again that adequate control of repeat prescriptions is needed to ensure that each drug prescribed is still appropriate, effective and well tolerated, and that it is still being viewed upon and taken by the patient as intended.[8,11,18] Infrequent therapy reviews may lead to failure to prevent, identify and solve drug-related problems and drug wastage and may, thereby, have a negative impact on the effectiveness, safety and/or cost of the medications prescribed.

Potential problems that may be reduced or avoided by adequate clinical and administrative control of long-term drug therapies include the following.

1. Incorrect prescribing: inappropriate drugs and unnecessary polypharmacy (e.g. unnecessary addition of another drug to combat the adverse effects of an already used drug); overprescribing or underprescribing; inappropriate duration of therapy (too short or too long); and/or insufficient attention to drug safety (e.g. no follow-up of potentially relevant drug interactions or adverse effects).
2. Incorrect usage by the patient: inadequate compliance to prescribed drug regimens (overuse or underuse); and/or discontinuation of drug therapy without consulting the prescriber.
3. Suboptimal cost effectiveness: unnecessary waste of money (e.g. drugs more expensive than needed, continued prescribing when patient no longer compliant or drug no longer needed, use of higher doses than necessary).

Practice computer systems may help to reduce such risks (e.g. by producing warning signals when inappropriate drugs are selected or when patients return too late for a refill), but also create a new concern about repeat prescribing. When repeat prescriptions are printed by the computer in large batches, it is unlikely that the doctor will spend much time thinking critically about each prescription.[12]

In contrast to the risks of repeat prescribing without a consultation are the benefits of a reduced workload for the GP and convenience for the patient (easy access and saving of time). It has been estimated that an average five partner GP practice in the UK would have to employ an additional doctor if all repeat prescribing was replaced with doctor visits.[8,19] In other words, intensifying the control of repeat prescriptions requires extra time and money. This raises the critical issue whether such control can be realised in a cost-effective way, that is,

whether the costs are outweighed by a reduction in clinical problems and economic waste.

3.2 Detailed Evaluations of Repeat Prescribing

Few studies have investigated the repeat prescribing process in detail on a larger scale. Zermansky[11] evaluated the management of repeat prescriptions (defined as those issued without a consultation) in 50 GP practices in the UK. For the purpose of the study, repeat prescribing was divided into the following subdomains.

- Production: receiving the requests and producing the prescriptions.
- Administrative control: authorisation check (are all repeats authorised by the doctor?); compliance check (which patients are overusing/underusing their medication?); setting of review date (does each patient have a clear indicator of when therapy should be reviewed?); and flagging (does each patient due for review come to the GP's attention?).
- Clinical control: clinical authorisation (clinical decision to confer repeat status for the drug or drugs); and clinical review (is the treatment periodically reviewed to assess whether the prescribed drugs are still effective, well tolerated and still needed, or whether they should be changed or stopped?).

The element of production was not studied. Administrative control was assessed by a subjective scoring system based on observation and a semi-structured interview. The extent and quality of administrative control varied greatly between practices, but some individual practices scored well, demonstrating that good control can be achieved. The area in which practices performed least well was the compliance check, which often resulted from a failure of the practice computer to provide warnings of early or late requests.

Clinical control was evaluated by examining 556 repeat prescriptions for anti-ulcer drugs, hypnosedatives or anxiolytics, and NSAIDs. In 56% of the cases, there was no evidence in the patient's file that a doctor had authorised a repeat status. For 66% of the repeat prescriptions there was no evidence that a periodic review had taken place in the past 2 years. A subjective impression was that reviews tended to focus on drugs being taken for the condition for which the patient was seen and that conditions not presented at the time were often ignored.[11]

McGavock et al.[20] evaluated the extent to which 57 non-dispensing GP practices in Northern Ireland had adopted procedures for repeat prescribing management by means of a semi-structured interview supplemented by prescribing and cost data. They constructed a scoring system of indicators for this purpose, which were partially based on procedural recommendations by a National Audit Office report on repeat prescribing[8] and partially generated by themselves (see table II).

Although an evaluation by self-report carries the risk that suboptimal practices may be under-reported, a substantial proportion of the GPs in the McGavock et al. study indicated that they did not routinely carry out recommended quality assurance procedures.[20] While two practices achieved a score of 24 out of a maximum score of 26, five practices scored <12. The potential of practice computers for improving management was often not realised.[20] The doctors reported reasonable compliance with five of the seven patient-centred aspects that should be considered, according to the National Audit Office,[8] when long-term medication is reviewed. However, they did not usually inquire about the taking of other conventional or unconventional medicines, or invite the patient to ask questions about the medicine(s) at review consultations.

Mean intervals between review consultations varied with drug category (e.g. 1.7 months for antidepressants, 6.2 months for cardiac drugs and 11.3 months for antiepileptic drugs).[20] There was a wide variation in reviewing policies between practices. Most doctors commented that special clinics (e.g. for patients with asthma or diabetes) allowed a more structured review of patients on long-term medication. Two GPs stated that they always checked hospital prescriptions for errors and to see whether there were any therapeutically important differences

Table II. Evaluation of repeat prescribing management in 57 general practices in Northern Ireland (reproduced from McGavock et al.,[20] with permission of the *British Journal of General Practice*)

Domain and questions	Responses (% of all practices)		
Before signing repeats, does GP[a]	**Always/usually**		**Not routinely**
consult patient's records?	27 (47)		30 (53)
check quantity and dosage?	55 (96)		2 (4)
enter exact dosage instructions?	39 (68)		18 (32)
check when patient's last review was?	33 (58)		22 (39)
check number of repeats since last review?	40 (70)		16 (28)
Is the computer used to:	**Always/usually**	**Sometimes**	**Never**
issue repeat prescriptions?	46 (81)	4 (7)	3 (5)
monitor compliance (check on early/late repeats)	41 (72)	3 (5)	9 (16)
Do GPs with more advanced software (n = 23) know if this software can:	**Yes**		**No**
embargo issue of repeats after a set number?	19		4
if yes, is this facility used?	3		16
generate review invitations letters?	15		8
if yes, is this facility used?	8		7
check for drug interactions?	11		12
if yes, is this facility used?	1		10
Are special clinics offered to certain patients (e.g. asthmatic, diabetic)	43 (75)		14 (25)
Are there arrangements with community pharmacists and nursing/ residential homes for repeats[a]	48 (84)		9 (16)
Is there a policy for high cost drugs?	34 (60)		23 (40)
Does the GP change hospital-initiated prescriptions to a generic?	48 (84)		9 (16)
Does GP ask at review consultation if patient[a]	**Usually**	**Occasionally**	**Rarely/never**
is still taking the medicine(s)?	39 (68)	14 (25)	4 (7)
can remember the dosage(s)?	24 (42)	27 (47)	6 (11)
notices any benefit from the medicine(s)?	33 (58)	20 (35)	4 (7)
is experiencing any side effect?	33 (58)	20 (35)	5 (9)
is taking other medicines (old, OTC, herbal)?	5 (9)	26 (46)	26 (46)
remembers what the medicines are for?	14 (25)	35 (61)	7 (12)
has anything to ask about the medicine(s)?	8 (14)	17 (30)	31 (54)

a Procedures recommended in a report by the National Audit Office.[8]

GP = general practitioner; **OTC** = over the counter.

between a patient's previous maintenance therapy and what had been recommended.

Fundholding practices used more advanced computer software and a much higher proportion reported running special clinics and having formal policies for high cost drugs. The economic advantage was confirmed by an analysis of cost data from a prescription pricing database. In one survey month (most probably in 1996), the mean prescribing cost per 1000 patients was £5929 for fundholders, which was significantly lower than the £10 485 for non-fundholders. Likewise, fundholders had a significantly lower prescribing frequency in that month than non-fundholders (727 vs 1317 per 1000 patients).

3.3 Specialist-Initiated Drug Treatments

A special feature of repeat prescribing in general practice is that GPs frequently continue drug therapies that have been initiated by medical specialists. In one UK study, prescriptions initiated by hospital-based specialists were responsible for 20% of the volume and 29% of the drug cost of repeat prescribing by GPs.[9] In another UK study, 44% of the drugs for acid peptic disorders, 17% of the NSAIDs and

10% of the hypnosedatives and anxiolytics in general practice had been initiated by a hospital-based specialist.[11]

In Ireland, patients who hold medical cards must get their prescriptions written by a GP, whether the primary prescribing decision is made by the GP or by a hospital-based specialist. Since certain specialist-initiated medications are expensive, these prescriptions can be responsible for a disproportionately high percentage of the GP's prescription costs.[21] In a study involving 92 Irish GPs, hospital-based specialists initiated about 28% of all GP prescriptions, and the cost of these prescriptions was substantially higher than the cost of GP-initiated prescriptions.[16]

GPs often indicate that they have no control over the prescribing of specialist-initiated medications and that they cannot change that part of their prescribing behaviour. This view is open to question, because patients may use the same medication for a long period of time and, especially when they consult different doctors, there is a risk of physicians losing track of prescriptions and not knowing what their colleagues have prescribed. In the UK study[11] which documented that 44% of the drugs for acid peptic disorders in general practice were specialist initiated, 20 of 68 patients (29%) with a specialist-initiated drug regimen did not have any indication (not even in a specialist letter) why the drug was started, nor a diagnosis that might explain it. The GPs had authorised a repeat regimen without recording (and perhaps without knowing) the reason for use. Three of these patients had been on the drug for more than 5 years.

The problem of specialist letters that do not always provide sufficient information for the GP was also highlighted by a study in Northern Ireland.[22] This study examined specialist letters regarding 173 patients who were on a specialist-initiated drug treatment that required regular monitoring. The majority of letters (74.6%) did not state who was to be responsible for ongoing monitoring (the GP or the specialist) and only 17% indicated that there was a risk associated with the drug or that it should be routinely monitored.

These examples make it clear that GPs have their own responsibility when issuing repeat prescriptions. They should know which specialist-initiated drug treatments require monitoring and should record who is responsible for such monitoring. GPs should also check which patients have been removed from any contact with their initial prescriber and bring the prescriptions of these patients under their own control.[21,23]

4. Intervention Studies

4.1 Basic Characteristics and Overview of Results

The methods of review outlined in section 1 yielded 31 references describing 22 intervention studies.[10,13,18,19,24-50]

The setting of these studies varied considerably; for example, from single GP practices[13,30,37] to a combination of 87 clinical pharmacists working in nine different outpatient clinics of medical veteran centres.[38,39] Obviously, findings in one particular setting cannot be extrapolated to another setting without due caution.[35,51]

Target populations ranged from general populations on at least one repeat prescription to patients who had been referred, were of older age and/or were taking a minimum number of different medications. So far, there have been no studies that compared the effects of the same intervention strategy in different target populations.

In one study, the intervention programme started with an online drug utilisation review using explicit criteria to identify potentially inappropriate drug use.[34] The pros and cons of this type of intervention are discussed in section 4.3. However, in most studies the intervention consisted of a pharmacist-conducted medication review with or without consulting medical records and with or without conducting one or more patient interviews.

Several studies provided evidence to suggest that the effectiveness of a pharmacist's medication review can be increased by combining it with a patient interview and/or a consultation of the patient's medical record.[30,36-38,44] In one study, the longer the

contact was between clinical pharmacist and patient, the more problems were identified and resolved. In addition, personal contact identified and resolved more problems than contacts by telephone.[38] In another study, clinically trained pharmacists identified 52% of the detected drug-related problems by looking at prescription records, 29% by interviewing patients at home and 18% by reviewing medical notes.[44] A third study found that 73% of the identified problems were recognised only through a patient interview.[36] Evidence that the quality of a pharmacist-conducted medication review increases as the pharmacist's access to complete patient information increases also comes from a US study of paper cases.[52]

The intervention pharmacist was sometimes a community pharmacist (without or with preparatory training, which may have influenced the selection of problems)[18,19,35] and sometimes a clinical pharmacist (who was defined in a UK study as a pharmacist with relevant hospital experience and a postgraduate diploma in clinical pharmacy).[30] There are no studies that have directly compared interventions of different types of pharmacists, but there is a recent study in which the performance of a trained community pharmacist was compared with that of trained GPs and nurses. GP reviews resulted in significantly more changes to prescribed drug therapy and monitoring than pharmacist and nurse reviews.[49] So far, this study has only been published as a non-peer-reviewed abstract, which does not make clear whether case allocation to the different professions was randomised in an appropriate way.

Intervention pharmacists usually provided feedback on the results of the medication review to the prescribing physician and/or patient. This feedback ranged from the provision of written recommendations to the physician[44] to personal contacts with the physician and the patient.[31,36] Such differences in feedback may have influenced the study results because, in general, passive approaches to change prescribing behaviour (e.g. mailing materials) are unlikely to be effective, whereas active feedback strategies (e.g. one or more personal meetings of a trained educator with the prescriber) can be effective under certain circumstances.[53,54]

The results of intervention studies have been measured and presented in divergent ways so that a plea for standardisation of the outcome assessment and reporting of studies on repeat prescription management is in order. Costs were often measured, but several studies focused on medication cost rather than total healthcare cost (e.g. physician visits, laboratory monitoring, emergency room visits, hospital days). Some studies regarded the provision of drug therapy education to the patient as an outcome,[27,31,38] whereas other studies only measured actual prescription changes and/or rate and acceptance of pharmacist's recommendations by prescribing physicians.

In many studies, the results of the intervention were interpreted by the same pharmacist who had carried out the intervention. This entanglement of different roles may have led to an overestimation of the effectiveness of the intervention. For this reason, some studies applied an external panel for verifying the validity or relevance of the pharmacist's recommendations,[13,30,35] and two randomised controlled trials used a blinded reviewer for the assessment of outcomes.[27,42]

Drug-related issues were identified by the reviewing pharmacists in percentages ranging from 12% in a general patient population receiving repeat prescriptions[18] to 100% in elderly patients with at least two chronic disease states and taking four or more medicines.[44] In the intervention studies, prescribing physicians agreed with 58–96% of the recommendations made by the intervention pharmacists[19,44] and acted on 32–86% of the received recommendations.[13,19] Most of the GPs responding to questionnaires found the pharmacist's interventions useful or somewhat useful and indicated that this service should continue, although sometimes with the proviso that the service should be modified.[10,31,32,36] In some studies, patients expressed a similar positive view.[30,32,36,49]

In one study, reassessment of the study population after 6 months showed that 64% of the initial intervention effects had been sustained.[30] In an-

other study, 90% of recommendations made by a clinical pharmacist remained implemented until the end of the study (i.e. up to 1 year after the patient interview).[47] In studies evaluating repetitive reviews in the same patients, consecutive reviews continued to bring drug-related problems to light.[13,24,44,48] Sometimes later reviews gave similar yields as the initial review,[13] but in other studies the yield of a second review was smaller.[44,48] In one of these latter studies, clinically trained pharmacists initially identified 1206 pharmaceutical care issues in 168 patients; 3 months later, 208 care issues remained but 86 new care issues had emerged.[44] Such findings open the possibility that patients on repeat prescriptions are not necessarily as static as they might seem to be, and that it may, therefore, be useful to review their medications periodically rather than as a once-only service.

Eight of the 22 studies were uncontrolled studies[10,19,24,26,30,34,35,49] and 14 studies were randomised controlled trials.[13,18,25,27-29,31-33,36-48,50] As the absence of a control group entails the risk of overestimating the effect size of the intervention,[55] the next section focuses on the results of the randomised controlled trials.

4.2 Focus on Randomised Controlled Intervention Trials

Details of the randomised controlled trials are provided in table III. Overall, ten of the 14 trials showed at least one significant positive difference between intervention group and control group, but a breakdown in individual parameters shows a rather mixed picture of results as summarised in the following points; where results are described as negative, intervention produced no significant positive effect in the trial.

- Resolution of pharmaceutical care issues: four positive trials.[13,27,33,44] In six other trials there was also a substantial positive effect on pharmaceutical care issues in the intervention group, but these trials did not assess or report the care issues in the control group.[31,38,42,43,45,50]
- Medication compliance: one positive trial[37] and three negative trials.[25,27,31] In another trial, there was a significant difference between intervention and control patients with respect to the identification of compliance problems (9.5% vs 2.5%).[18]
- Appropriate prescribing score: one positive trial[27] with respect to score; one negative trial[43] with respect to within-group change in score.
- Adverse effects score or symptoms: one negative trial with respect to number of adverse events;[27] one positive trial[36] and two negative trials[25,31] with respect to within-group change in adverse effects score or symptoms.
- Health-related quality of life (HR-QOL; as measured by the 36-Item Health Survey [SF-36]): three negative trials[27,40,50] with respect to SF-36 score; one negative trial[44] with respect to change in SF-36 score.
- Healthcare consumption: four negative trials[18,27,45,50] with respect to total consumption; one negative trial[44] with respect to change in consumption.
- Death rate: two negative trials.[18,45]
- Number of medications/medication units per patient: one positive trial[18] and three negative trials[27,42,50] with respect to total number; three positive trials[25,37,45] and two negative trials[31,43] with respect to within-group change in number.
- Medication cost per patient: two negative trials[42,50] with respect to total cost; two positive trials[25,45] and three negative trials[31,36,44] with respect to within-group change in medication cost. In another trial (which comprised monthly checks on stockpiling), 66% of the intervention patients did not require their full quota of prescribed medications, representing 18% of the total prescription costs (estimated annual medication cost avoidance of £43 per patient; year of values not specified).[18]
- Healthcare cost: two negative trials[27,50] with respect to total cost; two negative trials[36,39] with respect to change in cost.

In view of the various caveats expressed in the previous section (section 4.1), these results should be considered with appropriate caution. Additional caveats are that the trials may not always have been adequately powered to detect relevant differences

Table III. Randomised controlled trials of the benefits of a medication review of long-term prescriptions in general or elderly outpatient populations, alone or in combination with a patient (pt) interview and/or medical record review[ab]

Study (year)	Setting (start of study period)	Target population	Number included (withdrawals)	Intervention programme	Results		Additional comments
					general	clinical/humanistic/ economic[c]	
Hanlon et al.[27-29] (1996, 1998)	One ambulatory care department of general medicine clinic for veterans, US (1991)	Pts ≥65y with ≥5 long-term medications	208 (36)	Review of medications and medical record plus pt interview by one clinical pharmacist during all scheduled visits. Personal and written feedback to pt and physician	After 12mo, significant difference showing improvement of inappropriate prescribing score between intervention and control pts (decrease 28% vs 5%). No significant differences in medication compliance, drug knowledge, no. of medications or pt satisfaction. Physicians were receptive to recommendations by clinical pharmacist and enacted recommended changes in intervention group more often than independent changes in control group (55% vs 20%). Enactment was predicted by the type of drug therapy recommendation	After 12mo, no significant differences between intervention and control pts in HR-QOL (SF-36), experiences of adverse drug events (30% vs 40%; p = 0.19), healthcare consumption, or total healthcare costs. Total cost of clinical pharmacist intervention averaged $US120 per pt per year[29]	Rigourous design (e.g. validated outcome measures and blinded assessment of outcomes). Pharmacist spent more time with pts than with physicians (40 vs 16 min at baseline and 5 vs 4 min at follow-up contacts)[29]
Jameson et al.[25] (1995)	One primary care practice, US (June 1991)	Pts with ≥2 of the following criteria: ≥5 medications, ≥12 doses/day; ≥4 medication changes in previous year; >3 concurrent diseases; history of drug noncompliance; drug treatment requiring therapeutic monitoring	64 (8)	Chart review and pt interview by clinical pharmacist. Personal feedback to physician and pt	After 6mo, significant differences between intervention and control pts with respect to change in no. of medications/medication units, but nonsignificant difference with respect to change in understanding and compliance score	After 6mo, significant difference between intervention and control pts with respect to change in medication cost but nonsignificant difference with respect to change in adverse effects score	Pilot study retrieved via larger follow-up study[36]

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Table III. Contd

Study (year)	Setting (start of study period)	Target population	Number included (withdrawals)	Intervention programme	Results		Additional comments
					general	clinical/humanistic/ economic[c]	
Grymonpre et al.[31] (2001)	One community-based health clinic for the elderly, Canada (May 1993)	Pts ≥65y using ≥2 medications	135 (21)	Home inventory of medications and problems conducted by trained staff/ volunteers and blindly repeated after 6mo Inventories of intervention pts reviewed by trained/supervised pharmacist. Personal and written feedback to pt and written feedback to physician	After 6mo, 230/794 (29%) of DRPs identified by intervention pharmacist in 56 of the 69 intervention pts available for follow-up had been fully or partially resolved After 6mo, no differences between intervention and control pts with respect to changes in no. of prescribed medications, drug knowledge, or medication compliance 35/57 (61%) prescribers who received feedback responded to physician survey; 23 (66%) stated that they would make one or more changes to the drug regimen and 29 (83%) rated service as somewhat/very useful	After 6mo, no differences between intervention and control pts with respect to changes in symptoms reported or cost of prescribed medications	Inventories of control pts reviewed by different pharmacist but this assessment of DRPs in control group was not reported
Sellors et al.[42] (2001)	Four family medical practices, Canada (February 1995)	Pts aged ≥65y taking ≥4 medications	132 (11)	Medication review, medical chart consultation and pt interview by one trained community pharmacist. Personal and written feedback to physicians	119/153 recommendations (78%) for 62 of 66 (94%) intervention pts fully or partially implemented by physician. After 6mo, no significant difference in no. of medications/ medication units between intervention and control group	After 6mo, no significant difference in mean daily medication costs between intervention and control pts	No assessment of DRPs in control group Pilot study retrieved via larger follow-up study[50]

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Table III. Contd

Study (year)	Setting (start of study period)	Target population	Number included (withdrawals)	Intervention programme	Results		Additional comments
					general	clinical/humanistic/ economic[c]	
Bond et al.[18] (2000)	19 GP practices (71 GPs) and 62 community pharmacists, UK (summer 1995)	Pts on one or more repeat medication(s)	3074	Monthly dispensing with protocolled check on DRPs (e.g. stockpiling, compliance problems) by community pharmacists without special training	Potential DRPs identified in 12% of intervention pts; duplication with problems identified from pt notes was rare Significant differences between intervention and control pts with respect to identification of compliance problems (9.5% vs 2.5%) and median no. of prescribed medications Information on problems welcomed by GPs[32]	No significant differences between intervention and control pts with respect to death rate or healthcare utilisation. 66% of intervention pts did not require full quota of prescribed medications, representing 18% of total prescribed costs (with estimated annual cost avoidance of £43 per pt; year of values not stated)	Feedback to GPs not well defined Unit of analysis error (randomisation per GP practice, analysis per pt)
Mackie et al.[33] (1999)	Six GP practices, UK (September 1995)	Pts ≥20y receiving ≥4 repeat prescriptions	1677[d]	Review of medication record and medical record plus pt interview by pharmacist. Unspecified feedback to physician	Of 3889 PCIs identified, 2481 were considered clinical and 1408 administrative. In the intervention group (n = 921), physicians agreed fully or partially with 95% of 2064 recommendations. After 6–12mo, 264 (13%) of these PCIs remained in the intervention group compared with 1198/1825 (66%) in the control group (n = 752)	Not reported	Only available as an abstract
Granås and Bates[13] (1999)	One GP practice (2 GPs) and one community pharmacist, UK (November 1995)	Pts receiving repeat prescriptions with ≥3 items	285 receiving 511 repeat prescriptions[e]	Medication review and medical record review by community pharmacist. Personal feedback to physician	DRPs identified for 187/511 (37%) repeat prescriptions (comprising 3018 items). No decline in DRP ratio when pts received more than one prescription review GPs agreed to action on 77/90 (85%) DRPs in 248 intervention repeat prescriptions and routinely identified and actioned on 11/86 (13%) DRPs in 252 control repeat prescriptions	Not reported	It was often difficult to find enough timeslots for GP/pharmacist meetings

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Table III. Contd

Study (year)	Setting (start of study period)	Target population	Number included (withdrawals)	Intervention programme	Results		Additional comments
					general	clinical/humanistic/ economic[c]	
Jameson and VanNoord[36] (2001)	Four large primary care practice groups (133 physicians), US (June 1996)	Pts >5y with ≥50 prescriptions in preceding year, which corresponded with ≥5 long-term medications in all cases	340 (72)	Chart review, medication review and pt interview by clinical pharmacist. Personal feedback to physician and pt	70% of pts and 76% of physicians believed that intervention was beneficial	After 6mo, significant difference between intervention and control pts with respect to change in adverse effects score, but no significant differences with respect to changes in medication cost or total medical cost	
Lowe et al.[37] (2000)	One GP practice, UK (not specified)	Elderly pts taking ≥3 medications	161 (9)	Medication review and pt interview at home by clinical pharmacist to identify problems, rationalise medication regimens and resolve packaging difficulties. Second home visit to provide education	Changes to medication regimens in 47% of intervention pts (resulting in significant fall in no. of medications). Compliance (measured by tablet count 3 wks after second visit) was 91% in intervention group and 79.5% in control group	Not reported	Feedback to prescriber not well described
IMPROVE study[38,39] (2000)	Nine outpatient clinics in medical centres for veteran pts, US (not specified)	Veteran pts meeting ≥3 of the following criteria: ≥5 drugs; ≥12 doses/day; ≥4 drug changes in previous year; ≥3 concurrent diseases; history of drug noncompliance; drug treatment requiring therapeutic monitoring	1054 (123)	Medication review and pt interview by clinical pharmacists, followed by monitoring and additional contacts with pt Collaboration between pharmacists and physicians was variable	Of 3048 DRPs identified in 1855 contacts with 523 intervention pts, 2109 (69%) were rated as resolved. Most commonly addressed problems (after need for education) were 'needed drug not received' (16%) and 'not taking drug as described' (14%)[38] No difference in pt satisfaction between intervention and control pts[39]	No clinically meaningful difference between intervention and control pts in HR-QOL score (SF-36)[40] Mean increase in total healthcare cost nonsignificantly lower in intervention group than in controls ($US1020 vs $US1313; p = 0.06; year of values not stated)[39]	No assessment of DRPs in control group More intervention pts lost to follow-up (15%) than control pts (9%) Results may have been affected by organisational changes during study (e.g. release of many disease management guidelines)

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Table III. Contd

Study (year)	Setting (start of study period)	Target population	Number included (withdrawals)	Intervention programme	Results		Additional comments
					general	clinical/humanistic/ economic[c]	
Allard et al.[43] (2001)	One town, Canada (not specified)	Pts >75y with no/ positive response to questionnaire that screened risk of functional decline and with >3 medications per day	266 (23)	Home inventory of medications by nurse, followed by medication review with access to diagnoses by two physicians, one pharmacist and one nurse (in case conference). Written feedback to physician	Prescribing physicians accepted 37/147 (25%) recommendations for 80 intervention pts with case conference review After 12mo, no significant differences between intervention and control pts with respect to change in mean no. of medications or change in mean no. of potentially inappropriate prescriptions (−0.24 vs −0.15); change was −0.31 in 80 intervention pts with case conference review	Intervention was considered inexpensive ($Can70 per pt; year of values not stated)	Only 80 of the 136 intervention pts actually received case conference review
Krska et al.[44] (2001)	Six general practices, UK (not specified)	Pts ≥65y with ≥4 repeat prescriptions and ≥2 chronic diseases	381 (49)	Review of medical notes and medication records by clinically trained pharmacists, followed by home interviews of all pts. Written feedback to physician	After 3mo, 998/1206 (83%) of PCIs in intervention pts had wholly or partially resolved compared with 569/1380 (41%) in control pts; there were 86 new PCIs in intervention pts and 92 new PCIs in control pts GPs agreed with 1155/1206 (96%) of the PCIs identified in intervention pts	After 3mo, no significant differences between intervention and control pts with respect to changes in HR-QOL (SF-36), medication cost or healthcare consumption	52% of the PCIs were identified from prescriptions, 29% by pt interview and 18% by medical note review

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Table III. Contd

Study (year)	Setting (start of study period)	Target population	Number included (withdrawals)	Intervention programme	Results		Additional comments
					general	clinical/humanistic/ economic[c]	
Zermansky et al.[45-47] (2001, 2002)	Four general practices, UK (June 1999)	Pts ≥65y with one or more repeat prescriptions	1188 (57)	Review of medical record and medication record plus pt interview by clinical pharmacist. Personal feedback to pt and physician	After 12mo, significant difference between intervention and control pts with respect to change in no. of repeat medications per pt After 12mo, pharmacist had reviewed 97% of intervention pts; GPs reviewed 44% of control pts. Pharmacist made interventions/ recommendations in 44% of the pt reviews and dealt with 65% of 603 interventions/recommendations without needing to consult the GP. GPs accepted 179/208 (86%) recommendations for which their permission was sought	After 12mo, significant difference between intervention and control pts with respect to change in repeat medication cost, but not with respect to death rate or healthcare consumption Repeat medication cost saving outweighed review cost of £7 per pt (1998 values) [for average review of 20 min]	Second review 18mo after first review led to interventions in 52% of 50 pts compared with 62% at first review[48]
Sellors et al.[50] (2003)	24 clusters (each comprising 2 family physicians and 1 community pharmacist), Canada (August 1999)	Pts ≥65y taking ≥5 medications daily	889 (101)	Medication review and pt interview by trained community pharmacists. Personal and written feedback to physician	After 5mo, 608/1093 (56%) of pharmacists' recommendations for 344/431 (80%) intervention pts were fully or partially implemented by physician. After 5mo, no significant difference in no. of medication/medication units between intervention and control groups	After 5mo, no statistically significant difference between intervention and control pts with respect to HR-QOL score (SF-36), healthcare use, medication cost or total healthcare cost	Randomisation per cluster Family physician as unit of analysis No assessment of DRPs in control group Study retrieved from Medline via an accompanying editorial[56]

a See section 1 for the criteria for exclusion of studies.

b Unless stated otherwise, randomisation was per pt.

c The years of value were not specified in the original articles, but are assumed to be those of the study period (see table II).

d Four of the pts were excluded from the control group because they needed immediate attention.

e Eleven of the pts were excluded because they needed immediate attention.

DRP = drug-related problem; **GP** = general practitioner; **HR-QOL** = health-related quality of life; **IMPROVE** = Impact of Managed Pharmaceutical Care on Resource Utilization and Outcomes in Veterans Affairs Medical Centers; **min** = minutes; **mo** = months; **PCI** = pharmaceutical care issue; **SF-36** = Medical Outcomes Study 36-Item Health Survey; **wks** = weeks; **y** = years.

with respect to particular outcomes,[27,43-45] and that most trials randomised patients instead of practices, thereby introducing a risk of the so-called Hawthorne effect, which may occur when intervention and control patients are treated by the same physicians.[57]

Overall, the results suggest that the interventions helped to resolve pharmaceutical care issues, that is, they helped to identify, resolve and prevent potential or actual drug-related problems.[58] In one trial, a medication review and education programme by a home-visiting clinical pharmacist gave a compliance (measured by tablet count 3 weeks after second visit) of 91% in the intervention group compared with 79.5% in controls.[37] The pharmacist could not predict which patients would need help from a review of case notes alone. Many patients did not comply with their medication for a variety of reasons, and the pharmacist was able to negotiate medications regimens with the patient and doctor after having identified these reasons.

Effects on HR-QOL, death rate, healthcare consumption or total healthcare cost have not been observed, and in most studies the clinical outcomes of the intervention remained unclear. In one trial (in which a community pharmacist reviewed the medications and medical records of GP patients on repeat prescriptions with three or more items, without interviewing the patients), an external GP panel rated 1/19 (5.3%) of the interventions as interventions that resulted or potentially resulted in clinical improvement in patient care.[13]

Actual clinical improvements have only rarely been reported.

- In one trial, 54% of the intervention patients showed a clinically relevant improvement in adverse effects score, which was significantly better than the 38% improvement in control patients.[36]
- In the Impact of Managed Pharmaceutical Care on Resource Utilization and Outcomes in Veterans Affairs Medical Centers (IMPROVE) trial, subanalysis of the patients with dyslipidaemia showed that the lipid values of intervention patients improved significantly more than those of controls.[41]
- In a third trial (one of the most rigourous trials performed so far), a clinical pharmacist significantly reduced inappropriate prescribing in elderly outpatients receiving polypharmacy.[27] Although the trial design did not focus on clinical outcomes, further analysis found that worse inappropriate prescribing scores were significantly associated with more unscheduled ambulatory or emergency care visits and with inadequate blood pressure control.[59]

Only some of the trials showed a positive effect on the number of medications/medication units and/or medication cost. However, the lack of such effects does not necessarily represent a negative result, because the addition of a missing essential drug may be as important as the discontinuation of an inappropriate or superfluous drug. In the most recent trial that failed to find any effect on number of medication units or medication cost, the most commonly identified drug-related problem was that the patient was not receiving a required drug (28% of all drug-related problems).[50]

Five studies measured the variable intervention cost per patient (derived from the average time that the intervention pharmacist or intervention team actually spent per patient) and found that the intervention was relatively inexpensive and, therefore, feasible: $US84 in a US trial in 1991,[29] $Can70 to $US85 in three Canadian trials[42,43,50] and £7 in a UK trial (which was outweighed by a monthly medication cost saving of £4.70 per patient [based on December 1998 values]).[45]

4.3 Implicit versus Explicit Screening Criteria

Most of the published intervention studies seem to have applied implicit screening criteria. An illustrative example is the set of general questions in the last section of table II, which a healthcare provider can ask when reviewing the medications of an individual patient.[8,20]

However, one of the uncontrolled studies depended completely on explicit screening criteria. It used a computerised drug utilisation review based on 11

predefined criteria to identify potentially inappropriate drug use in elderly patients. Online screening resulted in computer alerts that triggered telephone calls to the prescribing physicians by pharmacists with training in geriatrics. The overall rate of change resulting from the pharmacists' recommendations was 24%. One screening criterion (use of β-adrenoceptor antagonists in patients with chronic obstructive pulmonary disease) showed a rate of change that was equal to the expected baseline rate of 2%, but all other screening criteria had significantly greater rates of change, varying from 7% (for NSAIDs in patients with peptic ulcer disease) to 40% (for benzodiazepine hypnosedatives with a long elimination half-life).[34]

Generally speaking, implicit screening criteria allow a full and flexible clinical judgement of individual drug treatments, which can also detect problems that are not prespecified. However, implicit screening methods depend heavily on the knowledge, experience and skills of the individual reviewer. It can be difficult to apply them consistently and to measure outcomes in a valid and reliable way.[60] This is well illustrated by a US study which found substantial intra-rater reliability but poor inter-rater reliability among a sample of drug utilisation reviewing pharmacists and physicians.[61] In contrast, explicit screening criteria have the advantages that they can be reliably based on literature review and expert consensus, that they can identify and prioritise problems in a consistent way and that they can be easily incorporated in medical practice computer systems (see table IV for examples). However, explicit screening methods also have the disadvantage of an inflexible approach, which leaves insufficient room for individual differences between patients and can, thereby, lead to false-positive signals. Furthermore, explicit screening methods will miss any drug-related problem that has not been prespecified and will, therefore, fail to provide a full assessment of the patient.[60] In addition, computerised screening programmes based on explicit criteria should only be introduced in daily practice after their clinical usefulness has been carefully validated.[62,63]

As implicit and explicit screening criteria have their own benefits and limitations, a combined application may offer a more thorough assessment than each approach separately. However, such a combined approach is typically more complex and time consuming to administer and might, therefore, be less feasible and sustainable in daily practice.[60]

5. Conclusions and Recommendations for Future Research

It is likely that repeat prescribing without consultation occurs on a large scale and that this entails risks of incorrect prescribing, incorrect drug usage and insufficient cost effectiveness. Most of the available intervention studies suggest that a medication review by a pharmacist can help to identify and reduce some of these prescribing defects, and there is evidence to suggest that the effectiveness of medication review may be increased by combining it with a consultation of the patient's medical records and a patient interview. In several studies, such an intervention was relatively inexpensive and, therefore, feasible. However, these conclusions should be viewed with appropriate caution, because a number of caveats pertain. There is still no evidence that these types of intervention improve HR-QOL or reduce healthcare cost, and so far only a few trials have produced any evidence of clinical improvement.

Further well designed studies to develop and evaluate repeat prescription management models are needed. Such studies would preferably be targeted at the improvement of clinical, humanistic and economic outcomes. When direct measurement of these outcomes is not feasible, validated surrogate markers for these outcomes should be applied. New studies should compare different organisational models, and they should make clear how results can be affected by selecting different target populations or by selecting and training different healthcare professionals in different ways. Future studies should also show whether different types of interventions produce different effects, whether the results are sustained and which time intervals for review should be adopted when repeat prescriptions are assessed on a

Table IV. Examples of warning signals concerning potential drug- or therapy-related problems that can be generated by medical practice or pharmacy computer systems to support the medication review of patients on repeat prescriptions

Domain	Examples
Appropriateness of medication	Various medications are considered inappropriate for use in the elderly.[64,65] For instance, glibenclamide (glyburide) should preferably be avoided in this age group because its long duration of action increases the risk of severe hypoglycaemia[66,67] In the future, it may well become possible to predict inefficacy or toxicity of various drugs on the basis of pharmacogenetic determinations[68-70]
Dosage regimens	Elderly patients may need reduced drug dosages compared with younger adults.[71] This is particularly relevant for drugs with a narrow therapeutic index, such as lithium[72] and digoxin[73] Dosage regimens can also be adjusted on the basis of data on renal function[74] or genotyping of cytochrome P450 enzyme systems[69,75]
Duration of treatment	Medications should be prescribed for neither too short nor too long a duration. For instance, repeating antibacterial prescriptions for a lower respiratory tract infection should be the exception rather than the rule in general practice.[76] On the other hand, patients with major depression should receive antidepressant treatment for at least 3–6 months after an initial response to decrease the risk of relapse or recurrence[77,78]
Contraindications and precautions	When diagnostic information is available in the computer system, alerts can be generated concerning medications that should not or only cautiously be prescribed to patients with that diagnosis.[64] In the case of repeat prescribing, alerts are particularly useful for relative contraindications which are not strictly forbidden but require careful follow-up to avoid adverse consequences. When clinical information is not available (e.g. because only dispensing data are recorded), certain concurrently used drugs may serve as a surrogate marker of a disease state (e.g. ischaemic heart disease can be identified by looking at nitrate prescriptions)[79]
Drug interactions	Computerised screening of prescriptions can help to recognise potentially relevant drug interactions.[80,81] In the case of repeat prescribing, alerts are particularly useful for combinations of drugs that interact but are not strictly forbidden but do require careful follow-up to avoid adverse consequences
Overtreatment	New medications may have been added to an existing drug regimen to combat an adverse drug reaction. It is then preferable to evaluate whether the causative agent can be withdrawn or substituted with another medication. For instance, when hyperuricaemia has developed in a hypertensive patient on hydrochlorothiazide, the addition of allopurinol can be prevented or reversed by changing the diuretic agent to another type of antihypertensive, such as an ACE inhibitor[82,83]
Duplication of drugs	Unnecessary duplications in drug treatment (different brands of the same drug or different drugs from the same therapeutic class) should be avoided.[83,84] For instance, the concurrent use of more than one NSAID may increase the risk of gastroduodenal toxicity[85]
Duplication of adverse effects	When possible, combination of medications with anticholinergic adverse effects should be avoided, especially in elderly people.[86] The same applies to combinations of medications with sedative adverse effects
Undertreatment	Treatment with acetylsalicylic acid (aspirin) should be considered in patients with angina pectoris.[87,88] Similarly, bisphosphonate treatment should be considered in patients on high daily doses of corticosteroids[89]
Overuse of medication	Overuse of inhaled β-agonists by patients with asthma should be evaluated, especially when this is accompanied by underuse of corticosteroids.[90-92] Migraine prophylaxis should be considered when a triptan derivative appears to be used for more than three attacks per month[93]
Underuse of medication	Dispensing records can identify patients with gaps in their long-term medication supply that are suggestive of underuse[94,95]
Discontinuation of medication	Medications intended for long-term therapy (e.g. antihypertensive agents) may have been discontinued by the patient without consulting the prescriber[96,97]
Less expensive equivalent medication available	The clinical rules for safe generic substitution and its economic benefits are well documented.[98,99] Therapeutic interchange may also be considered, but establishing therapeutic equivalence within drug classes is much more complex than it is for generic substitution[100,101]

repeated basis. Finally, new studies should explore the possibilities and added value of new technologies, such as the application of computerised support systems.

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Correspondence and offprints: *Peter A.G.M. De Smet*, Institute Dutch Pharmacists, Alexanderstraat 11, 2514 JL The Hague, The Netherlands.
E-mail: pdesmet@winap.nl