Nature, frequency and determinants of prescription modifications in Dutch community pharmacies

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Aims To examine the nature, frequency and determinants of prescription modifications in Dutch community pharmacies.

Methods A prospective case-control study comparing modified prescriptions with nonmodified prescriptions was carried out in 141 Dutch community pharmacies. 2014 modified prescriptions (cases), collected in the selected pharmacies on a predetermined day in a specific period (25th February until 12th March 1999) and 2581 nonmodified prescriptions (controls) randomly selected on the same day were studied. The nature and frequency of prescription modifications and patient, drug and prescriber related determinants for a modified prescription were assessed.

Results The overall incidence of prescription modifications was 4.3%, with a mean of 14.3 modifications per pharmacy per day. For prescription only medicines (POM) the incidence was 4.9%. The majority of POM modifications concerned a clarification (71.8%). In 22.2% a prescription could potentially have had clinical consequences when not altered; in more than half of the latter it concerned a dose error (13.7% of all cases). POM prescriptions of patients of 40–65 years had a significantly lower chance of modification compared with those of younger people (OR = 0.74 [0.64–0.86]). With respect to medication-class, we found a higher chance of POM modifications in the respiratory domain (OR = 1.48 [1.23-1.79]) and a decreased chance for nervous system POMs (OR = 0.71 [0.61–0.83]). With regard to prescriber-related determinants modifications were found three times more often in non printed prescriptions than in printed ones (OR = 3.30 [2.90-3.75]). Compared with prescriptions by the patient's own GP, prescriptions of specialists (OR = 1.82 [1.57-2.11]), other GP's (OR = 1.49 [1.02-2.17]) and other prescribers such as dentists and midwives (OR = 1.95 [1.06-3.57]) gave a higher probability of prescription modifications. When a GP had no on-line access to the computer of the pharmacy the chance of a modification was also higher (OR = 1.61 [1.33-1.94]). Multivariate analysis revealed that a nonprinted prescription was the strongest independent determinant of prescription modifications (OR = 3.32 [2.87-3.84]), remaining so after adjustment for GP computer link to the pharmacy and for type of prescriber.

Conclusions At least 30% of Dutch community pharmacies corrected 2.8 POM prescriptions per pharmacy per working day, which could potentially have had clinical consequences if not altered. If the study sample is representative for The Netherlands, Dutch community pharmacies correct a total of approximately 4400 of these prescriptions per working day. Using computerized systems to generate prescriptions is an important strategy to reduce the incidence of prescription errors.

Keywords: clinical pharmacy, community pharmacy services, drug-related problems, evaluation studies, interventions, medication errors, pharmacists, prescriptions

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Introduction

The management of patient health care can be compromised by drug-related morbidity and mortality, which in their turn can be the result of prescription errors [1]. Community pharmacies can contribute to a reduction of potentially harmful prescription errors. A recent UK study of 1503 pharmacy interventions on 201 000 items dispensed (0.75%) estimated that between 71 and 483 interventions (0.04–0.24% of all items) could have prevented harm, whilst 19–242 interventions (0.01–0.12%) might have prevented a drug-related hospital admission [2]. Moreover, 748 interventions (0.37%) had the potential to improve clinical outcome and could have saved a visit to or by the general practitioner.

We were interested in the contribution of Dutch community pharmacies to the timely detection of prescription errors, particularly because they have used computerized medication surveillance for about two decades [3]. We were also interested in the determinants of prescription modifications accomplished by community pharmacies, because better insight into the determinants of such prescription modifications may lead to improved or new strategies to reduce prescription errors. The impact of the basic characteristics of the prescription, the patient and the prescriber on prescription modifications for outpatients have not been extensively evaluated in previous studies. Therefore, we have carried out a large-scale study to investigate the frequency, nature and determinants of prescription modifications in Dutch community pharmacies.

Methods

Setting and design

In January 1999 all Dutch community pharmacies ($n = 1571$) were invited to participate in the study by a letter and by a notice in the Dutch pharmaceutical journal. From 470 community pharmacies, that reacted positively within 3 weeks, 188 (40%) were randomly selected. There were 36 nonresponders (mainly because of lack of time and/or personnel or because they had forgotten about it) and 152 responders. Of the latter, 11 pharmacies had to be excluded, because they had not adhered to the study protocol, which left 141 pharmacies (9% of all Dutch pharmacies) that could be enrolled in our evaluation.

All participating pharmacies received a pretested study protocol and three types of registration forms for the documentation of modified prescriptions (cases), non-modified prescriptions (controls) and basic characteristics of the pharmacy on the day of the study. The protocol advised contact with a telephone help desk in case of any uncertainty. Each participating pharmacy had to collect all modified prescriptions (cases) during one predetermined day between February 25 and March 12, 1999. On the same day they had to collect at random an equal number of nonmodified prescriptions (controls). After selection of cases and controls the pharmacists had to fill in a registration form for each case and each control.

Selection of cases

All prescriptions for medicines and other health care products (e.g. dressings, incontinence materials, syringes and needles) that were offered on the predetermined day to the community pharmacy by the patient, or by fax or telephone had to be included. Cases were all prescriptions that were modified by the pharmacy on that particular day (even if actual dispensing took place on another day). Reasons for including a prescription modification as a case were defined in the protocol and in the registration form for cases. If there were two or more reasons for modifying a prescription the pharmacist had to select the one he/she considered most relevant. The protocol excluded the following modifications because of their lack of potential impact on patient care: address incorrect or absent, no or incorrect insurance data, incorrect package size, product not in stock, unit of dosage or package specified incorrectly (e.g. ml instead of g), generic substitution and legal requirements (e.g. for narcotic drugs). During the data management process we divided the nature of prescription modifications into three groups. In the first group a clarification was needed to carry out the prescription order. In most cases an essential administrative feature of the prescription was missing or obviously incorrect. In fact the pharmacy could not have dispensed the drug without clarification. In the second group for items identified as 'Correction prescription error' the prescription was administratively correct, but could potentially have had clinical consequences if not altered. Those identified as 'wrong dose' is an important example, for which there are several reasons, like too high/low dose according to standard references or in conflict with the patient's own records. The third group included reasons for modification not covered by the first two categories.

Selection of controls

The pharmacists had to provide an equal number of nonmodified prescriptions (controls) by selecting this number at random from a box containing all prescriptions of the same day.

Validation of the cases

To control for the reliability of the registered data pharmacists were asked to send in the registration forms as

well as relevant copies of the prescriptions and 6 month medication records of the patients concerned. This information was stripped of personal data. Incorrect data in the registration form when compared with the copies of the prescription and/or medication record could lead to an alteration in the final form registered by the research team. For these reasons various cases were excluded from the study. Where double or triple reasons for modification were given, the one considered most relevant was selected so that only one modification per prescription was counted.

Classification of prescriptions

Following Dutch reimbursement regulations items prescribed were classified as prescription only medicines (POM), prescribed OTC medicines (such as paracetamol and miconazole), and nonmedicines (such as dressings, incontinence materials, syringes and needles). The number of prescribed OTC medicines were too small to be worth analysing. All medicines were classified into therapeutic groups using the Anatomical Therapeutic Chemical (ATC) classification of the WHO Collaborating Centre for Drug Statistics Methodology [4].

Analysis

After inspection, data from the registration forms were entered in a Microsoft Access database and statistically analysed using SPSS version 9.0. Logistic regression analysis was used to estimate the association between characteristics and modification of a prescription.

Results

The characteristics of the enrolled pharmacies were comparable with the characteristics of all Dutch community pharmacies in the study period. However, the number of pharmacy assistants in the participating pharmacies was somewhat lower than that in the average Dutch pharmacy, leading to a slightly increased workload per individual (Table 1).

There was a large variation in the total number of prescriptions per pharmacy, which probably reflects the fact that both small and very large pharmacies were involved in our study.

On the study day, the overall incidence of modifications by the community pharmacies was 4.3% (2014 cases of 47 374 prescriptions) (Table 2). The number of modifications per pharmacy varied from 0 to 100 with a mean of 14.3 prescription modifications per pharmacy. The incidence of modifications for prescription only medicines was 4.9% compared to only 1.4% of the prescriptions for nonmedicines. Modifications of POM prescriptions were most frequently found in the following therapeutic domains: nervous system (ATC group N), respiratory system (R), alimentary tract and metabolism (A), and cardiovascular system (C) (Table 3a).

Table 1 Characteristics of the selected pharmacies.

Characteristics	*Pharmacies (n,%)*	*Range*	*Mean (s.d.)*	*Mean data of Dutch pharmacies (n = 1571)*[1]
Urbanization level[2]				
No urbanization	12 (8.5%)			9.4%
Little urbanization	31 (22.0%)			21.7%
Moderate urbanization	37 (26.2%)			22.4%
Strong urbanization	37 (26.2%)			25.8%
Very strong urbanization	24 (17.0%)			20.7%
Prescription characteristics				
Number of prescriptions per day		42–998	336.0 (140.5)	322.5
Number of POM prescriptions per day*		34–609	259.8 (99.8)	256.1
Personnel characteristics				
Number of pharmacists		0.0–4.0	1.3 (0.5)	1.55
Number of assistants		1.0–9.5	4.7 (1.6)	5.85
Number of personnel[3]		2.0–13.5	6.0 (1.9)	7.40
Workload assistants[4]		30.9–162.0	73.0 (22.4)	55.1
Workload personnel		19.6–105.2	55.9 (15.4)	43.6

[1]data obtained from SFK (Stichting Farmaceutische Kengetallen = Foundation for Pharmaceutical Statistics, The Hague) concerning the first quarter of 1999.
[2]this measure of urbanization is used by the Central Bureau of Statistics (CBS) in the Netherlands and by SFK as well [22].
[3]personnel = number of pharmacists plus number of pharmacy assistants.
[4]workload assistants = number of prescriptions per assistant per day.
*POM = prescription only medicine(s).

In 219 cases (12.2%), the modification of a POM prescription was triggered by a signal of the computerized medication surveillance system of the pharmacy concerning a change in therapeutic regimen (e.g. different strength or dose), a potential drug–drug interaction, contraindication or double medication (combination of two medicines with the same or similar ingredient). More than half of the problems concerning POM prescriptions (51.2%) were solved by communication with the patient or his representative, and the same was found for nonmedicines (52.7%). In 282 cases (15.6%), the pharmacy consulted the prescriber about a POM prescription, but the prescriber was contacted less often for nonmedicines (7.5%). Contacts with the prescriber's assistant were similar for POM prescriptions (4.9%) and for prescription modifications of nonmedicines (5.5%) (Table 3b).

In Table 4 the nature of the prescription modifications is summarized. The majority (1294; 71.8%) of the reasons for the 1802 POM modifications concerned the clarification of an insufficiently specified prescription (e.g. dose not specified, insufficient patient data, wrong strength or strength not specified), whereas in 400 cases (22.2%) a prescription error was corrected that might have had clinical consequences ('Correction Prescription Error'). Dose corrections were more prevalent in this latter group (13.7%) than other interventions, such as for a drug–drug interaction, contraindication or double medication (8.5%). In Table 5 we present some individual examples of modifications of POM.

In our analysis of determinants, we focused on modifications of POM prescriptions, since these form the most important group (Table 6). Of the patient-related factors, gender was not significant, but patients of 40–65 years had a lower rate of modifications than younger people (OR = 0.74 [0.64–0.86]). With respect to drug-related factors, we found a higher frequency of POM modifications in the respiratory domain (OR = 1.48 [1.23-1.79]), while a decreased frequency was observed for nervous system POMs (OR = 0.71 [0.61–0.83]). There was no difference between initial and refill prescriptions for POMs, but when a nonmedicine was prescribed for the first time the chance of a modification was much higher than when it was refilled (OR = 3.75 [2.07-6.80]).

With regard to prescriber-related determinants modifications were found three times more often in hand written prescriptions than in computer printed ones (OR = 3.30 [2.90-3.75]). Compared with prescriptions of the patient's own GP, those of specialists (OR = 1.82 [1.57-2.11]), other GPs (OR = 1.49 [1.02-2.17]) and other prescribers such as dentists and midwives (OR = 1.95 [1.06-3.57]) had a higher rate of prescription modifications. When a GP had no on-line access to the computer of the pharmacy, i.e. to the actual medication record of the patient, the chance of a modification was significantly higher (OR = 1.61 [1.33-1.94]).

Multivariate analysis revealed that a hand written (nonprinted) prescription remained a strong independent determinant of prescription modifications (OR = 3.32 [2.87-3.84]) after adjustment for GP computer link to the pharmacy and for type of prescriber. Conversely, the association between a GP computer link to the pharmacy and a prescription modification as well as the association between type of prescriber and a prescription modification disappeared after adjustment for nonprinted prescription.

Table 2 Incidence of prescription modifications.

	Total number	*Number of cases*	*Incidence*
All prescriptions	47374	2014	4.3%
POM prescriptions	36625	1802	4.9%
Non-medicine prescriptions	10298	146	1.4%

Table 3a Characteristics of the modified prescriptions (cases): the distribution of ATC classes.

	POM prescriptions (n,%)
ATC class Nervous system	311 (17.3%)
ATC class Respiratory system	252 (14.0%)
ATC class Alimentary tract and metabolism	227 (12.6%)
ATC class Cardiovascular system	216 (12.0%)
Other ATC classes	796 (44.2%)

Discussion

In this study we found an average modification of 14.3 prescriptions per day per pharmacy. The majority of

Table 3b Characteristics of the modified prescriptions (cases): share of computer signals and consultations.

	POM prescriptions (n,%)	*Non-medicine prescriptions* (n,%)
Modifications based upon a computer signal	219 (12.2%)	
Modifications after consultation with prescriber	282 (15.6%)	11 (7.5%)
Modifications after consultation with the prescriber's assistant	88 (4.9%)	8 (5.5%)
Modifications after consultation with patient or representative	924 (51.2%)	77 (52.7%)

Table 4 Nature of prescription modifications in Dutch community pharmacies.

Description	*Prescription only medicines* (n,%) (n = *1802*)	*Non-medicines* (n,%) (n = *146*)
Clarification needed	1294 (71.8)	141 (96.6)
Dose not specified (including use known)	409 (22.7)	
No or insufficient patient data	348 (19.3)	8 (5.5)
Name or use of nonmedicine wrong or insufficiently specified		127 (87.0)
Wrong strength (mostly nonexisting or incorrect)	125 (6.9)	
Strength not specified	122 (6.8)	
Wrong dosage form	110 (6.1)	
Number of tablets, capsules, etc. not specified or incorrect	53 (2.9)	5 (3.4)
Medicine, strength or dosage form not on the market	43 (2.4)	1 (0.7)
Dosage form not specified	37 (2.1)	
Prescription not dispensed (patient still has enough supply)	34 (1.9)	
Medicine not specified	5 (0.3)	
Dosage form insufficiently specified	8 (0.4)	
Correction prescription error	400 (22.2)	
Wrong dose	246 (13.7)	
Wrong medicine	45 (2.5)	
Wrong patient data	42 (2.3)	
Interaction with other medicines (one prescriber involved)	11 (0.6)	
Contraindication allergy	11 (0.6)	
Other contraindications	9 (0.5)	
Medicine obsolete	8 (0.4)	
Double medication * (one prescriber involved)	9 (0.5)	
Double medication * (two prescribers involved)	9 (0.5)	
Interaction with other medicines (two prescribers involved)	4 (0.2)	
Too prolonged use of a medicine	3 (0.2)	
Too short period of use	2 (0.1)	
Contraindication pregnancy or lactation	1 (0.1)	
Other	108 (6.0)	5 (3.4)
Prescription not dispensed (other reason than enough patient's supply)	47 (2.6)	5 (3.4)
Various	61 (3.4)	

*double medication is a combination of the same substance or different substances from the same therapeutic group.

Table 5 Some examples of modifications of prescription only medicines (POM).

Sildenafil not dispensed because of interaction with isosorbide mononitrate and because of contraindication in angina pectoris.
Erythromycin changed to doxycycline because of interaction with cisapride.
Dexamethasone eye drops not dispensed and changed to hypromellose eye drops because of too prolonged use.
First prescription of itraconazole dispensed for 7 days instead of 3.5 days because of too short use.
Tablets with paracetamol (500 mg) + codeine (20 mg) not dispensed because of double medication with naproxen 500 mg and paracetamol 500 mg, prescribed by other doctor.
Capsules with paracetamol, dexchlorpheniramine and ephedrine changed to capsules with paracetamol and dexchlorpheniramine because of contraindication in hypertension.
Amoxicillin changed to clarithromycin because of hypersensitivity.

modifications (88.3%) involved prescription only medicines (POM), but the community pharmacies also intervened with prescriptions for other health care products (such as dressings and incontinence materials), although at a much lower rate (1.4% *vs* 4.9%).

We used a random sample from volunteering community pharmacies. These pharmacies represented 30% of all Dutch community pharmacies, but we did not find any major differences between the average enrolled pharmacy and the average Dutch community pharmacy (Table 1). We cannot exclude the possibility that the participating pharmacies were more active or had a more positive attitude towards the provision of professional services than pharmacies which did not volunteer for our study, either in general or on the predetermined, not blinded, study day [5]. To reduce the risk of overestimation, every reported

Table 6 Determinants of prescription modifications of prescription only medicines (POM) in Dutch community pharmacies.

Prescription characteristic	*Cases (n = 1802, 100%)*	*Controls (n = 2377, 100%)*	*OR[95% CI]*	*Reference*
Patient related				
Female	1080 (60.3%)	1490 (62.8%)	0.90 [0.80,1.02]	Male
Age: < 40 years	596 (33.2%)	702 (29.6%)	1.00	Age: < 40 years.
Age: 40–65 years	594 (33.1%)	943 (39.7%)	0.74 [0.64,0.86]	Age: < 40 years.
Age: > 65 years	606 (33.7%)	730 (30.7%)	0.98 [0.84,1.14]	Age: < 40 years.
Drug related				
ATC-code N	311 (17.3%)	539 (22.7%)	0.71 [0.61,0.83]	All but N
ATC-code R	252 (14.0%)	235 (9.9%)	1.48 [1.23,1.79]	All but R
ATC-code A	227 (12.6%)	258 (10.9%)	1.18 [0.98,1.43]	All but A
ATC-code C	216 (12.0%)	309 (13.0%)	0.91 [0.76,1.10]	All but C
First dispensing	598 (33.6%)	796 (33.6%)	1.00 [0.88,1.14].	Refill prescription
Prescriber related				
Non printed prescription	1070 (59.4%)	730 (30.7%)	3.30 [2.90,3.75]	Printed prescription
Specialist prescription	494 (27.5%)	418 (17.6%)	1.82 [1.57,2.11]	Own GP prescription
Other GP prescription	55 (3.1%)	57 (2.4%)	1.49 [1.02,2.17]	Own GP prescription
Other prescriber prescription	24 (1.3%)	19 (0.8%)	1.95 [1.06,3.57]	Own GP prescription
GP without computer link to pharmacy	1620 (89.9%)	2012 (84.6%)	1.61 [1.33,1.94]	GP with computer link to pharmacy

case was checked on the basis of anonymous copies of the original prescription and the medication record of the patient. Underestimation cannot be totally ruled out, because some interventions may not have reached us due to lack of time or inappropriate handling. Another limitation of our study was that it occurred in a short time and that it cannot predict seasonal variations (e.g. fluctuating prescription patterns of drugs such as antibiotics and antihistamines). Fluctuating patterns within a week were ruled out by assigning all days of the week equally in the study period.

It is difficult to interpret the large variation of numbers of modification between individual pharmacies as a quality indicator for pharmacy performance. For instance, a low number of interventions could signify a less perceptive pharmacy, but it could also reflect a very active pharmacy team which had already reduced the daily number of prescription errors by systematic feedback to individual prescribers [3, 6, 7]. The incidence of modifications may also be related to some of the determinants assessed in this study.

We intend to assess the potential clinical relevance of the POM modifications in depth by presenting representative samples to multidisciplinary rating panels [2, 8]. A preliminary estimate based on the nature of the 1802 POM modifications suggests that clarification was needed in 1294 cases (2.7% of all prescriptions), whereas 400 modifications (0.84%) concerned potentially relevant prescription errors (Table 4), a mean of 2.8 per pharmacy per day. This tentative crude intervention rate of 0.84% for real prescription errors lies in the same range as previously reported rates for community pharmacy interventions [2, 9]. Our findings only refer to actual modifications of the prescriptions presented on the study day as our protocol did not ask for the recording of other potentially relevant interventions, such as the modification or discontinuation of an already dispensed drug or an instruction to the patient to avoid certain drug problems. We know from our study that modifications of already dispensed drugs occur in daily practice, because our pharmacists submitted various examples as cases (even though our protocol excluded them). It is of interest that at least half of the prescription errors found were not the result of a medication surveillance signal from the pharmacy computer, but were corrected on the basis of another trigger. Further analysis of these modifications is warranted to find out whether and how current medication surveillance systems in Dutch pharmacies can be improved.

For nonmedicines the predominant reason for modification was inexact or incorrect specification of name or use. Problems in the pharmacy were significantly higher when a nonmedicine was prescribed for the first time, but the prescriber was not often contacted (7.5%). These findings may reflect a tendency among prescribers to leave details of nonmedicinal prescriptions to the professional judgement of the community pharmacist.

The chance of a POM modification was similar for young and old patients but reduced among the age group in-between (40–65 years). Whether this is related to differences in care, patient vulnerability and/or other causes requires further study. With respect to drug-related characteristics no difference in risk could be found between first-time and repeat prescriptions, indicating that the latter are still an important source of POM

prescription modifications [10, 11]. With respect to therapeutic groupings, we found a higher chance of modifications for respiratory medicines. One of the reasons may be that changes in dose and switching to another dosage form (i.e. inhaler) occurred relatively often in this group.

One of our most important findings is that the risk of a prescription modification was substantially lower, when the prescriber had used a printer to generate the prescription. The potential relevance of this result was highlighted by a recent US study, which identified illegible handwriting of doctors as a potential cause of fatal medication errors [12]. In The Netherlands, about 80% of the general practitioners are using a computer system to generate prescriptions, but medical specialists are still lagging behind in this respect [13]. A favourable impact of computerized physician order entry systems on medication errors has already been observed in a North American hospital setting [14, 15].

A final consideration is that our study focused on prescription errors that were detected in the community pharmacy before dispensing. Additional strategies are needed to reduce additional avoidable errors that continue to result in drug-related problems [16-19]. It should be kept in mind that drug-related problems are not limited to problems with dosage, adverse drug reactions and drug–drug interactions, but also comprise such problems as inappropriate drug selection, undertreatment, and drug use without valid indication [1]. It is therefore a promising development that an electronic prescription system is now issued to all general practitioners in The Netherlands [20], that is similar to the Prodigy system for general practitioners in the UK [21].

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