Determinants of pharmacists' interventions linked to prescription processing

• Marnix P.D. Westein, Ron M.C. Herings and Hubert G.M. Leufkens

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Marnix P.D. Westein, Ron M.C. Herings and
Hubert G.M. Leufkens (correspondence)**:** Department of Pharmacoepidemiology and Pharmacotherapy, Utrecht Institute for Pharmaceutical Sciences (UIPS), PO Box 80 082, 3508 TB Utrecht, The Netherlands
(E-mail: H.G.M.Leufkens@pharm.uu.nl)

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Abstract
Aim of study: The role of pharmacists in today's healthcare is changing rapidly. As they are close to the prescribing process, pharmacists are in the position to identify and adjust prescribing errors before dispensing. The objective of this study was to identify relevant determinants of interventions directly linked to prescription processing in community pharmacy.
Methods: As part of a yearly continuing education programme, all community pharmacies in the region of 'Zeeland' (N=23) in the south-west of The Netherlands kept detailed records of all interventions directly linked to prescription processing during one week in May 1998. For every patient involved in an intervention, a control-patient was matched on pharmacy practice, date, gender and age.
Results: A total of 39,357 prescriptions were evaluated by the 23 pharmacies during the one-week intervention programme. Out of these, one out of 10 resulted into an intervention. Being a first prescription in a new treatment episode was found to be a significant determinant (OR 1.75, 95 CI% 1.18-2.33). Variables reflecting drug therapy complexity (> 3 prescribers, > 15 prescriptions in 3 months before, > 3 different medications) showed all ORs higher than 1.00, but not significant. When looking at the individual drug categories, anti-infectives, respiratory drugs and cardiovascular medicines came out as important drug classes for intervention risk. We could not find any association between the number of signals per pharmacy and the number of interventions.
Conclusion: The 'whistle-blower'- model of pharmacy based interventions is a valid one but needs a targeted and integral way of implemented thinking and use of information technology. In such an environment, interventions are a logical step of in-process quality control in the drug usage system.

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Introduction
The role of pharmacists in today's healthcare is changing rapidly. The government, insurers and the public are increasingly demanding for evidence based pharmaceutical services [1,2]. For this reason pharmacists are concentrating creating added value in their role as 'guardians' of drug therapy, by means of contributing to rational prescribing policies, adjusting prescribing errors and improving patient compliance [3-5]. Under the umbrella of what we call today 'pharmaceutical care', various strategies have been developed to improve drug taking behaviour and patient outcomes [2]. Still, it has been estimated that less than 60% of patients who are receiving drug treatment have a favourable outcome (effectiveness, no drug-related problems) [6]. In addition, 2,9% to 14,2% of all emergency department visits have been reported to be drug-related [7,8]. These problems can be either due to inappropriate therapy decisions, abuse, adverse effects, drug interactions or patient non-compliance.

As they are close to the prescribing process, pharmacists are in the position to identify and adjust prescribing errors before dispensing. Various studies have quantified the number of pharmacy based interventions. Most short-term studies (1-2 weeks of observation) report frequencies of around one out of 100 prescriptions leading to a pharmacy-based intervention [9-12]. Recently, Hawksworth et al. presented data from a 12 months' study on clinical pharmacy interventions in the UK, and reported an average frequency of 0.89% interventions of dispensed items [13]. This study also concluded based on a clinical panel judgement, that in 0.12% of dispenses, pharmacy interventions might have prevented hospital admission.

Thus, there is reasonable consistency, both in short term and long term studies, about the overall incidence of interventions during the prescription dispensing process. However, most studies have found considerable variation in the incidence of interventions per individual pharmacy [9,10,12], that not could be explained by pharmacy characteristics as prescription volume and the like. So far little work has been done to evaluate patient and medication characteristics as determinants of interventions linked to prescription processing. In addition, the influence of computerized medication surveillance systems, which are the backbone of modern pharmaceutical care, on intervention rates is in need of investigation. The objective of this case-control study was to identify relevant factors leading to an intervention during filling prescriptions in community pharmacy.

Methods
As part of a yearly continuing education programme, all community pharmacies in the region of 'Zealand' (N=23) in the South-west of The Netherlands kept detailed records of all interventions directly linked to prescription processing during one week in May 1998. Standardised intervention log-forms were used to collect clinical and other relevant data. For every patient involved in an intervention (case), a control-patient was matched from the same pharmacy practice, with a prescription on the same day, same gender and same age (five years. Interventions were defined as 'any action taken by a pharmacist that lead to clarification or change of a prescription'. This varied from the correction of patient information to therapeutical changes. From each patient involved in an intervention, the medication history going back three months before the event of the intervention was collected. This information was used to calculate odds ratios to estimate the association between various prescribing variables and the occurrence of an intervention. Multiple interventions on a single prescription order were noted on a single intervention log-

form, and treated as one intervention. Both new and refill prescriptions were included for analysis. Generic substitutions were excluded, because many Dutch pharmacists have made agreements and contracts with their insurers and physicians regarding substitution policies. In the third quarter of 1998, one out of two prescriptions dispensed in the region of Zealand was generic. Non-drug prescriptions like needles or incontinence materials were also included because, although rare, prescribing errors do happen with these prescription orders. The total number of warning-signals each medication surveillance system generated was noted together with the total number of prescriptions processed in each pharmacy practice. Physicians in the study region were not informed by purpose of the intervention programme.

Interventions were classified according to the scheme of Rupp et al. (12). An extra category was added to include deviations on earlier prescriptions: [1] Errors of omission: prescription can not be dispensed without further clarification. [2] Errors of commission: prescription is not appropriate according to current standards of care or can possibly cause complications. [3] Deviation: prescription was unintendently different from an earlier prescription with the same indication. [4] Drug interactions: drug-drug interactions (pharmacokinetic and pharmacodynamic), allergies, and sensitivities. [5] Other reasons: unnecessary prescription, increasing patient compliance, problems with financial compensation by the insurance company. Statistical analysis included various univariate approaches and conditional logistic regression in order to evaluate the individual contribution of the co-variates to the event of an intervention linked to prescription processing in the pharmacy. Odds-ratio's were calculated for the following variables: first prescription, general practice physician or specialist, drug categories, number of prescribers associated with the patient, number of prescriptions filled in the 3 months before the event.

Results

A total of 39,357 prescriptions were evaluated by the 23 pharmacies during the one-week intervention programme. Out of these, 337 resulted into an intervention (average: 0.86%, range 0.13% to 1.94%). All pharmacy practices showed more than one intervention, with a maximum of 52 during the five-day evaluation programme. The majority of patients with an intervention-prescription was female (66,2%). When looking at the age of patients, the largest proportion of interventions was found in the elderly (older than 65 years) (41,8%). The medication history showed that patients with a tagged intervention had a slightly higher use of prescription drugs, although this was not significant.

In Table 1 a listing of the interventions according to the categories of Rupp is presented.

More than one out of three interventions could be categorised as 'Errors of commission' (37.1%), in these cases pharmacists found the pharmaceutical therapy to be suboptimal. The second largest class 'Errors of omission', constituted 24.3% of all interventions. In contrast to the other interventions, these prescriptions could not have been dispensed without further clarification. In 60 cases (17.8%) prescription orders deviated from an earlier prescription in continued chronic therapy. This did not only include dose/regimen and drug formulation changes, but also the drug substance itself (2.4%). 16.3% of all interventions had been made because of the risk of an interaction. This could be either an interaction between two different drugs or a suspected contraindication due to disease or allergy. In 57.0% (192) of cases a change or clarification concerning dosage, use, dosage form or amount supplied was judged as appropriate by the pharmacists before dispensing was allowed. Pharmacists changed the medication before dispensing in 71 cases (21.1%). Clarification of use with co-medication was needed in 27 cases (8.0%), while stopping of co-medication was needed in 13 cases (3.9%). The prescription order was cancelled in 17 cases (5.0%), mostly because the patient still had medication in stock and needed no new prescription at that time. Patient information needed to be clarified or changed in 17 cases (5.0%).

In Table 2 a selection of possible determinants of an intervention are listed according to the odds-ratios for the occurrence of an intervention. Being a first prescription in a new treatment episode was found to be a significant determinant (OR 1.75, 95% CI 1.18-2.33). Variables reflecting drug therapy complexity (> 3 prescribers, > 15 prescriptions in 3 months before, > 3 different medications) showed all ORs higher than 1.00, but not significant. When looking at the individual drug categories, anti-infectives, respiratory drugs and cardiovascular medicines came out as important drug classes for intervention risk, although the sample size was a limitation in assessing statistical significance. The odds-ratio of two for anti-infectives was mostly due to drug-interactions, i.e. interactions with metal-ions (Mg, Ca, Fe and Al). The odds-ratio for respiratory drugs was 1.71. The most common reason for this intervention was an unintended deviation of

Table 1 *Listing of nature of 337 interventions according to classification of Rupp [12]*

Reason for intervention	*%*
Errors of commission	37.1
Errors of omission	24.3
Deviation	17.8
Drug interactions	16.3
Other	4.5
Total	100.0

Table 2 *Determinants of pharmacy-based interventions*

Determinant	*OR (95% CI)*
First prescription	1.75 (1.18-2.33)
Specialist prescription	1.21 (0.69-1.72)
>3 prescribers	1.75 (0.51-2.99)
>15 pres in 3 months before	1.60 (0.80-2.40)
>3 different medications	1.48 (0.98-1.99)
Antibiotics	2.00 (0.90-3.10)
Respiratory drugs	1.71 (0.85-2.57)
Cardiovascular drugs	1.40 (0.81-1.98)

an earlier prescription for treating the same condition. In Figure 1, the number of interventions per pharmacy against the number of computerised medication surveillance signals per pharmacy during the 'intervention week' is plotted, showing no direct association.

Discussion and conclusions

In one out of hundred prescriptions, a pharmacy-based intervention in the prescription process was needed. This rate is comparable to incidences of other previously conducted studies [9,12,13]. The occurrence of an intervention was associated to being a first prescription for a new therapy and being a patient with complex therapy patterns. The association found with individual drug classes was not significant, probably due to small sample sized and needs further clarification. When looking at the drugs involved in interventions, the drug category most frequently associated with interventions was the group of anti-infectives. Other studies have also named this group as being commonly involved in problematic prescription orders [9-11]. In this study the most common reason for an intervention concerning anti-infectives was a problem with drug-interactions. Other factors that seem to enhance the risk of prescribing errors are the need to calculate drug doses for certain medicines and difficulties with drug- and prescribing nomenclature (e.g. retard and non-retard).

This study confirms that community pharmacists are able to identify inappropriate prescriptions and to 'intervene' accordingly. However, as far as we can judge based on our data, there is not a clear and systematic approach in how to implement a 'guardian of therapy'-model for preventing patient harm and lack of benefit in intervening in the prescription process. Such a model should be integrated in a clear co-operation and communication system with the prescriber, where there are clear rules and agreement of who is doing what, under which conditions and responsibilities [2,3]. Rupp et al. examined patient and prescribers' characteristics of pharmacy based interventions and found that both the professional education of the prescriber, and the way by which prescribers and pharmacists communicate about drug prescribing, were strong determinants of the risk of a prescribing error [12]. Also hand written prescriptions were associated with significantly more problems, a finding also confirmed by a study by de Jong who found that hand written prescriptions were linked to the need of pharmacy interventions [14]. With the rise of computerised prescribing and printed prescriptions this problem will probably be soon of the past.

Hawksworth et al. found an inverse link between prescription volume and the number of prescriptions and they suggested that pharmacy work load could jeopardise the pharmacists ability to perform interventions appropriately [13]. Although our data show a similar slight suggestion of such a trend, the main conclusion we would like to draw from the data on volume adjusted number of interventions is the enormous variation per individual pharmacy. These vary from 0.13 to 1.94, average 0.86 and SD 0.49. A direct link to the computerised medication surveillance systems most pharmacies are equipped with, would be a logical scenario to explain such variance. Signals based on peer reviewed and internationally accepted listings of unwanted interactions, contra-indications and the like, are currently available in virtually all practices in The Netherlands, as they were in the study region. Though, we could not find any association between the number of signals per pharmacy and the number of interventions. During the intervention-week, individual pharmacies encountered between 303 and 1,673 computer driven medication surveillance signals (on average 41% of all prescriptions). Overall, only about 2% of the surveillance signals lead to an intervention. Clearly, the impact of medication surveillance signals on the occurrence of an intervention needs further research.

Important limitations of this study were the small sample size and the short period of observation. Future research should cope with these issues, although the one year-study of Hawksworth came to a similar estimate of intervention incidences as the short-term studies did [13]. Another concern is bias. In some cases the formulation of the term 'intervention' could have caused a selection bias, because - as mentioned before by Smith, et al. (10) - some pharmacists tend to selectively report only important interventions. This effect is probably partly responsible for the variance of interventions between individual pharmacies. The influence on the total number of interventions is counterweighted by the fact that other pharmacists tend possibly to increase their intervention activities during the week of study. The problem with this type of study remains that there is no feasible way of determining the number of potential interventions that have been missed by pharmacists and should have been recognised. Moreover, the clinical significance of interventions needs to be addressed in future work on the subject.

Ensuring optimal drug therapy is a multidisciplinary effort of physicians, pharmacists and other health professionals. From both an effectiveness and a safety point of view, there is a clear need to encompass such an effort [15]. Pharmacists are able to improve medication regimens, but at the moment a fully systematic approach is lacking. The model of the pharmacist as a 'guardian of drug therapy' is still a valid one but needs a targeted and integral way of implemented thinking and use of information technology [3,16]. In such an environment, interventions are a logical step of in-process quality control in the drug usage system. At the moment, another much more extensive study on interventions in Dutch pharmacy practice is underway and the results of this study are due to be presented [17].

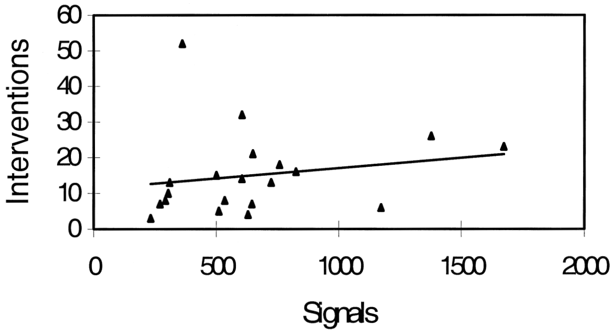

Figure 1.
Number of interventions against the number of medication surveillance signals during the one-week intervention period per individual pharmacy

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