

Evaluation of the clinical value of pharmacists' modifications of prescription errors

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Aims

Our objective was to examine the clinical value of pharmacists' interventions to correct prescription errors.

Methods

In this study, we reviewed a random sample of prescriptions that had been modified in pharmacies. These prescriptions were collected on one predetermined day between 25th February and 12th March 1999 from 141 Dutch community pharmacies. Each prescription modification was evaluated by a panel of reviewers, including representatives of five groups of health care professionals. After generally rating each modification as positive, negative, or neutral, the reviewers assessed its outcome (in terms of prevention of an adverse drug reaction [ADR], an improvement in effectiveness, both, or other), the probability and importance of improvements in effectiveness and/or the probability and seriousness of an ADR in the case of a nonintervention. Our analyses included 144 interventions from the first general assessment and a selection of 90 consistently rated 'positive' interventions (from all assessments).

Results

On average, one in 200 prescriptions (0.49%) was found to have been positively modified by Dutch community pharmacists. About half of these interventions (49.8%) were aimed at preventing ADRs; 29.2% were rated as a positive modification in the effectiveness of pharmacotherapy and 8.6% affected both effectiveness and ADR. Reviewers' ratings varied widely between different categories of drug-related problems (DRPs). The impact of individual interventions ($n = 83$) varied, and for 53% of these interventions it was estimated to be relatively high.

Conclusions

Pharmacists' interventions led to modification of prescriptions for an array of DRPs. Such interventions can contribute positively to the quality of pharmacotherapy. By extrapolating our data, we estimated a daily occurrence of approximately 2700 positive interventions in all Dutch pharmacies (1.6 per pharmacy per day). Reviewers rated the impact of interventions on a patient's health as significant in a substantial number of cases.

Introduction

Since the 1990s, a growing awareness of medical and in particular drug related errors [1–3] has led to research of pharmacists' tactics for dealing with these errors. Several, mainly observational, studies describe and, to some extent, support the positive contribution of pharmacists in detecting and reducing the impact of drug-related problems (DRPs) [4–9].

In a previous report, we described the frequency, nature and determinants of prescriptions modified by pharmacists that were sampled on one working day from 141 Dutch community pharmacies [10]. We found that the overall incidence of modifications for prescription-only medicines (POM) was 4.9%. The problems could be divided into two main categories: unclear prescriptions (illegible or with omissions) (71.8%) and prescriptions with errors (22.2%). The incidence of POM-related modifications of errors ($n = 400$) was 0.84%, corresponding to an average of 2.8 modifications per pharmacy per day.

The assessment of the actual clinical value of these prescription-error modifications on an individual patient level can be challenging. One would ideally like to compare the outcomes of patients whose pharmacotherapy was modified to those for whom the prescription error was not modified, but of course this would be unethical. An alternative method is the use of multidisciplinary panels consisting of experienced medical and pharmaceutical professionals who judge the clinical value and, in some cases, the humanistic or economic value of the modified prescriptions [11]. Different parameters have been used for this purpose, including estimates of harm, adverse health outcomes of a DRP, evaluations of the intensity of health care needed (such as hospital admission) and finally evaluations of the effectiveness of the patient's therapeutic management [11–15]. Partly based on these studies, we developed a method using a multidisciplinary panel to discriminate between different categories of DRP and different outcomes of prescription modifications to assess the clinical value of pharmacists' interventions.

Methods

Setting and design

Our previous study was a comparison of modified and nonmodified prescriptions that were collected from 141 Dutch community pharmacies on one predetermined day [10]. Of the total 2014 modified prescriptions collected, 400 (22.2%) were considered to be corrections for errors related to several potential DRPs, namely wrong dose ($n = 246$), wrong medicine ($n = 45$), wrong patient data ($n = 42$), interaction ($n = 15$), contraindica-

tion ($n = 21$), medicine obsolete ($n = 8$), double medication ($n = 18$) and duration of use ($n = 5$). These modifications (or interventions) to prescription errors represent the domain for this study. We excluded 99 interventions because they could not be assessed according to this study methodology, e.g. wrong patient data as reason for intervention, insufficient data available or misclassification.

The majority ($n = 208$; 69.1%) of the selected interventions ($n = 301$) was attributed to wrong-dose interventions. In order to limit the number of cases to be reviewed and reduce the number of similar cases, we randomly selected 52 (25%) wrong-dose interventions. We included all other potentially relevant interventions ($n = 93$), with the exception of one randomly chosen intervention to make the total number of cases an even number.

Assessment of clinical value

Our panel comprised five groups of health care professionals. Each group had four members – a community pharmacist, hospital pharmacist, general practitioner, specialist for internal diseases, or other nonpractising medical/pharmaceutical experts. All panel members were experts in pharmacotherapy and drug use.

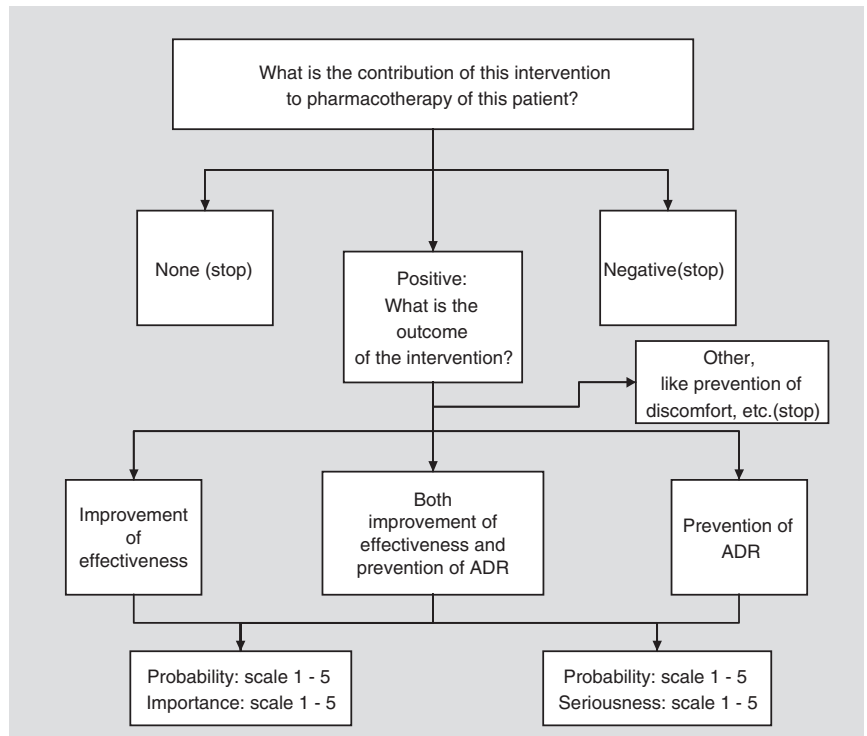
Each reviewer received 72 interventions for evaluation. Twenty-six wrong-dose interventions were randomly assigned to categories A and B and 46 other interventions to categories C and D. Each reviewer received A or B, and C or D. Within each group, the reviewers received another combination ($n = 4$). All reviewers evaluated their cases independently.

On an A4 page we presented an evaluation form and one intervention providing the following information: gender and age of the patient, the drug initially prescribed, type of prescriber, first use or repeat prescription, nature of DRP, person consulted, and the medicine ultimately dispensed. We asked reviewers to provide their opinions based upon their experience as a general practitioner, community pharmacist, or other. Additional guidance was provided concerning the necessity of conscientiously reading the forms, the use of literature, and requesting help or extra information on drug use.

Reviewers had to rate the contribution of each intervention on the pharmacotherapy of the patient as 'positive, negative or neutral'. In the event of a 'positive' rating, the reviewer had to gauge whether the intervention resulted in an improvement of effectiveness, prevention of an adverse drug reaction (ADR) or both. Finally, the judged improvement of effectiveness and/or prevention of ADR had to be rated on a five-point scale on two further points: probability and importance or

Figure 1

Algorithm representing the flow of questions for rating interventions



seriousness. The algorithm used by reviewers for rating interventions is presented in Figure 1.

Information on patient's disease status or other relevant clinical or private data (except for the prescription and the patient medication record) was not available, therefore the reviewers had to make the following three assumptions:

- the patient is reasonably normal; for instance, not an alcoholic;
- previous choice of (the combination of) the medicine(s) and its dosing was correct; and
- the patient complies with the text on the label.

A small number of questionnaires were returned to reviewers due to conflicting information and/or ratings.

Data analysis

After inspection, data from the evaluation forms were entered into a Microsoft Access database and statistically analysed using SPSS version 10.

Based upon the rating of the first elementary question as to the contribution of pharmacist's intervention to pharmacotherapy, the interventions that were most consistently rated as 'positive' ($n = 90$), were selected for further analysis. Figure 2 provides further information on the selection and exclusion of interventions in this study. The data derived from the selected 144 cases were adjusted for the sampling procedure ($n = 301$).

Results

Nineteen of the 20 reviewers (response rate of 95%) returned our evaluation forms. All groups had participated with four members except for one group of internal medicine specialists ($n = 3$). We received 71 evaluation forms instead of 72 from one internist. This means that 10 or nine reviewers evaluated every intervention except for one intervention, which was assessed by only eight reviewers. The reviewers spent on average 3.8 (1.5–9.0) hours for all 72 interventions, which corresponds to approximately 3 min per intervention. The mean number of interventions for which literature was required was 24 (33.3%).

Of all ratings ($n = 1367$), adjusted for sampling, 77.0% were judged positive with regard to the contribution of the intervention to the pharmacotherapy of that patient, including double medication interventions (93.7%), duration of use (89.7%), contraindication (88.0%) and interactions (79.7%) (Table 1). Interventions that were judged to have no or neutral contributions to the quality of the pharmacotherapy comprised 11.8% of the assessments. A relatively small percentage of ratings were negative (adjusted: 8.2%).

Subsequently, 90 interventions that were consistently judged as providing a positive contribution to pharmacotherapy were selected for further analysis (59.1%, after adjustment for sampling) (Table 2). The highest yields were found in the double medication-category

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1. Starting point: 400 interventions of pharmacies related to several drug related problems. [10]
 - Exclusion of 99 interventions because these interventions could not be assessed according to the proposed system in this study: wrong patient data as reason of intervention, insufficient data available, and misclassification.
 2. 301 Interventions to be examined.
 - At random exclusion of 156 'wrong dose' interventions and 1 'other' intervention.
 3. 144 Randomly selected interventions to be examined.
 - Randomly assignment of 26 'wrong dose'-interventions to both group A and B, 46 'other interventions' to both group C and D. Every reviewer received A or B, and C or D; this means 72 interventions to assess.
 - 1367 Ratings presented in **Table 1**.
 - Exclusion of 54 interventions with the following exclusion criteria:
 - One negative rating unless there is just 1 negative against more than 88% positive ratings or unless there is just one negative and 1 missing value against all other positive ratings.
 - No negative ratings but two or more "no contribution" ratings.
 4. 90 Consistently positively judged interventions.
 - Number of interventions in different stages of exclusion/inclusion presented in **Table 2**.
 - 779 Positive ratings presented in **Table 3**: the outcome of the intervention with respect to effectiveness improvement, ADR prevention and other.
 5. 83 Consistently positively judged interventions.
 - 7 Interventions (of 90) excluded because of insufficient ratings (< 4).
 - Visualisation in **Figure 3** of estimated impact per intervention stratified according to categories of DRP.
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Figure 2

Study selection procedures

and the duration of use-category (93.3% and 100%, respectively).

Table 3 further categorizes reviewers' opinions as to the outcome of the consistently positive pharmacy interventions. After adjustment for sampling, positive judgements were related to effectiveness of pharmacotherapy in 29.2% of the cases, 49.8% to ADRs and in 8.6% to both effectiveness and ADRs. Except for the wrong medicine category, prevention of ADRs was considered to be the most important outcome of pharmacist's intervention in all DRP groups. Contraindication interventions were almost exclusively related to ADRs. Wrong medicine interventions were mostly related to effectiveness (34.4%) or to both effectiveness and ADRs (21.6%). In 12.0% of all positive evaluations, there were other reasons judged as positive contributions by the pharmacy –32.3% concerned prevention of discomfort

for the patient, 23.1% prevention of cost and, remarkably, 3.8% prevention of ADR. There were also other reasons (9.2%) and reasons not specified (27.7%) (data not shown). The wrong medicine group (24.8%) and the double medication group (35.7%) yielded relatively high scores in this category of other reasons.

The impact of an intervention can be described as the product of the probability and seriousness of an ADR or as the product of the probability and importance of effectiveness improvement. In Figure 3, average ratings of these products per intervention are presented. This analysis could be made for only 83 interventions (92.2%) because of insufficient (less than four) ratings for seven interventions. Most interventions (47%) are situated in the left lower quadrant C followed by the right upper quadrant B (27.7%). The left upper quadrant A (14.5%) shows some interventions with very high

Table 1

The ratings ($n = 1367$) for all interventions ($n = 144$) by all reviewers ($n = 19$)*

| Drug related problem category | Positive contribution | No contribution | Negative contribution | Missed rating |
|---|-----------------------|-----------------|-----------------------|---------------|
| Contraindication ($n = 22$; 209 ratings) | 184 (88.0%) | 18 (8.6%) | 6 (2.9%) | 1 (0.5%) |
| Double medication** ($n = 15$; 142 ratings) | 133 (93.7%) | 4 (2.8%) | 3 (2.1%) | 2 (1.4%) |
| Interaction ($n = 14$; 133 ratings) | 106 (79.7%) | 22 (16.5%) | 3 (2.3%) | 2 (1.5%) |
| Duration of use ($n = 3$; 29 ratings) | 26 (89.7%) | 1 (3.4%) | 0 (0.0%) | 2 (6.9%) |
| Medicine obsolete ($n = 8$; 76 ratings) | 55 (72.4%) | 17 (22.4%) | 1 (1.3%) | 3 (3.9%) |
| Wrong medicine ($n = 30$; 284 ratings) | 215 (75.7%) | 38 (13.4%) | 21 (7.4%) | 10 (3.5%) |
| Wrong dose ($n = 52$; 494 ratings) | 368 (74.5%) | 59 (11.9%) | 50 (10.1%) | 17 (3.4%) |
| All interventions ($n = 144$; 1367 ratings) | 1087 (79.5%) | 159 (11.6%) | 84 (6.1%) | 37 (2.7%) |
| All interventions adjusted for sampling ($n = 301$; 2857 ratings) | 2199 (77.0%) | 337 (11.8%) | 234 (8.2%) | 88 (3.1%) |

*The judged interventions were selected from a sample of 301. With respect to the ratings, an adjustment had to be made for the group of wrong dose interventions ($\times 4$), the group of contraindication interventions ($+1$) and for all interventions. See the Methods section and/or Figure 2. **Double medication is a combination of the same substance or different substances from the same therapeutic group.

Table 2

The shift of interventions from the total group ($n = 301$) to the consistently positively rated group (second selection) after sampling and after selection*

| Drug related problem category | Number of interventions before sampling | Number of interventions after sampling | Number of interventions after second selection | Number of interventions after second selection, adjusted |
|-------------------------------|---|--|--|--|
| Contraindication | 23 (7.6%) | 22 (15.3%) | 17 (19.0%) | 18 (10.0%) |
| Double medication** | 15 (5.0%) | 15 (10.4%) | 14 (15.5%) | 14 (7.9%) |
| Interaction | 14 (4.7%) | 14 (9.7%) | 9 (10.0%) | 9 (5.1%) |
| Duration of use | 3 (1.0%) | 3 (2.1%) | 3 (3.3%) | 3 (1.7%) |
| Medicine obsolete | 8 (2.7%) | 8 (5.6%) | 3 (3.3%) | 3 (1.7%) |
| Wrong medicine | 30 (10.0%) | 30 (20.8%) | 15 (16.7%) | 15 (8.4%) |
| Wrong dose | 208 (69.1%) | 52 (36.1%) | 29 (32.2%) | 116 (65.2%) |
| Total | 301 (100.0%) | 144 (100.0%) | 90 (100.0%) | 178 (100.0%) |

*Not all data count for 100% because of rounding off. **Double medication is a combination of the same substance or different substances from the same therapeutic group.

scores for seriousness/importance concerning two interactions and one duration of use intervention. Of the interaction interventions 50% ($n = 8$) belong to this quadrant. The fewest interventions were found in the right lower quadrant D (10.8%), but all scores are quite close to the level of 50% importance/seriousness. Some examples of the interventions shown in Figure 3 are described in Table 4.

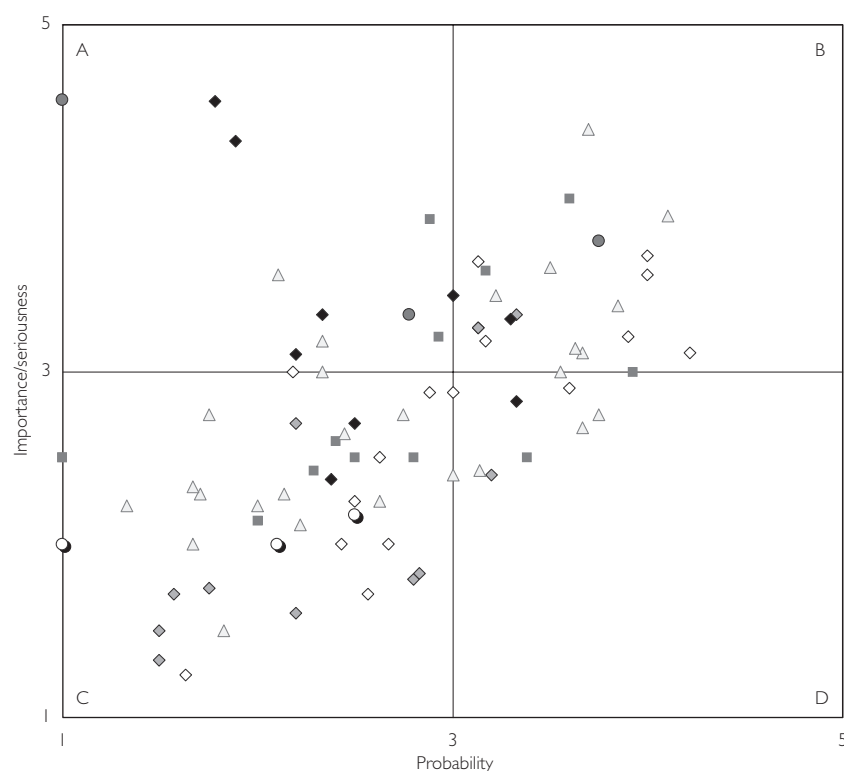
Discussion

Our study reports an incidence of 0.49% for prescription modifications by Dutch community pharmacists, which were consistently rated as positive by our expert review panel. This incidence would translate to about 1.6 interventions per pharmacy per day, or approximately 2700 interventions in all Dutch pharmacies on 1 day. These interventions by pharmacists were not exclusively

Table 3Opinion as to the outcome of the consistently positively judged pharmacy interventions ($n = 90$)*

| | Improvement of effectiveness | Prevention of ADR | Both effectiveness and ADR | Other outcome | Missed ratings |
|---|------------------------------|-------------------|----------------------------|---------------|----------------|
| Contraindication ($n = 17$) | 1 (0.6%) | 143 (92.3%) | 4 (2.6%) | 7 (4.5%) | 0 (0.0%) |
| Double medication ($n = 14$) | 1 (0.8%) | 76 (60.3%) | 3 (2.4%) | 45 (35.7%) | 1 (0.8%) |
| Interaction ($n = 9$) | 19 (24.4%) | 55 (70.5%) | 3 (3.8%) | 1 (1.3%) | 0 (0.0%) |
| Duration of use ($n = 3$) | 9 (34.6%) | 16 (61.5%) | 0 (0.0%) | 1 (3.8%) | 0 (0.0%) |
| Medicine obsolete ($n = 3$) | 7 (29.2%) | 14 (58.3%) | 1 (4.2%) | 2 (8.3%) | 0 (0.0%) |
| Wrong medicine ($n = 15$) | 43 (34.4%) | 19 (15.2%) | 27 (21.6%) | 31 (24.8%) | 5 (4.0%) |
| Wrong dose ($n = 29$) | 91 (37.1%) | 107 (43.7%) | 23 (9.4%) | 24 (9.8%) | 0 (0.0%) |
| All interventions ($n = 90$) | 171 (22.0%) | 430 (55.2%) | 61 (7.8%) | 111 (14.2%) | 6 (0.8%) |
| All interventions adjusted for sampling ($n = 301$) | 444 (29.2%) | 758 (49.8%) | 130 (8.6%) | 183 (12.0%) | 6 (0.4%) |

*The judged interventions were selected from a sample of 301. With respect to the ratings an adjustment had to be made for the group of wrong dose interventions ($\times 4$), the group of contraindication interventions ($+1$) and therefore for all interventions. See the Methods section and/or Figure 2.

**Figure 3**

The average estimated impact of 83 interventions. Contraindication ($n = 17$) (◇), double medication ($n = 11$) (◆), duration of use ($n = 3$) (●), interaction ($n = 9$) (■), wrong medicine ($n = 13$) (▲), dosing ($n = 27$) (△), medicine obsolete ($n = 3$) (○)

aimed at the prevention of ADRs (49.8%), but also at effectiveness of pharmacotherapy (29.2%) and both (8.6%). We found large differences with respect to judgements of interventions in different groups of DRPs. The impact of individual interventions ($n = 83$),

as perceived by the panel, varied greatly. For 53% of these interventions this impact was estimated as relatively high.

The incidence is comparable to those reported in other studies. In a UK-based study by Hawksworth

Table 4

Some examples of interventions presented in Figure 3

| Coordinates* | DRP Category | Description of initial prescription** | Outcome |
|--------------|-------------------|---|---|
| 3.7–4.4 | Dosing | Woman; 1962; GP; Ethinyl estradiol 1 mg; 1dd1; no. 5; first prescription. | GP consulted; Stediril D®; within 12 h two tablets, after 24 h again two tablets. |
| 4.1–3.9 | Dosing | Woman; 1969; specialist; Amoxicillin 500 mg; 1dd1; no. 15; first prescription. | Specialist consulted; Amoxicillin 500 mg; 3dd1; no 15. |
| 3.5–3.6 | Dosing | Woman; 1913; GP; Isosorbide dinitrate 5 mg sublingual; 4–6dd1; repeat prescription. | Communication with patient; one tablet only when needed. |
| 4.0–3.7 | Contraindication | Woman; 1920; GP; Amoxicillin 500 mg; 3dd1; first prescription; penicillin intolerance. | Other GP consulted; Ofloxacin 200 mg. |
| 4.2–3.1 | Contraindication | Woman; 1923; GP; Diclofenac 50 mg; 3dd1; Diclofenac intolerance. | Assistant GP consulted; Tramadol 50 mg; 3dd1. |
| 3.8–3.8 | Duration of use | Man; 1954; GP; Itraconazole 100 mg; 2dd1; no. 7. | GP consulted; 2dd1; no. 14. |
| 1.9–4.3 | Interaction | Man; 1943; GP; Sildenafil; first prescription; in combination with Isosorbide-5-mononitrate retard 50 mg + Nitroglycerin spray. | GP consulted; not dispensed. |
| 1.8–4.6 | Interaction | Woman; 1950; GP; Erythromycin 500 mg; 4dd1; no. 30; first prescription; in combination with Cisapride. | GP consulted; Doxycycline 100 mg instead of Erythromycin; first day two tablets, then 1dd1. |
| 1.8–1.8 | Double medication | Woman; 1950; GP; Flunitrazepam 1 mg; ante noctem 2; stock at home. | Pharmacist consulted; no dispensing. |
| 1.5–1.5 | Double medication | Woman; 1922; GP; Amoxicillin 750 mg; 2dd1; first prescription; already in use Ofloxacin 1dd1 (urologist). | Consultation assistant GP; no dispensing. |
| 1.0–2.0 | Obsolete | Woman; 1981; GP; ointment with combination of Hydrocortisone and Neomycin. | Pharmacist consulted; ointment with combination of hydrocortisone and tetracycline. |

*Probability score – seriousness/Importance score. **Interventions obtained in 1999.

et al., 49.8% of interventions were judged positively by a multidisciplinary but unspecified panel of reviewers, which corresponds to an incidence of 0.37% positively valued interventions [12]. In a US-based study using only three reviewers, Rupp revealed that 28.3% of the identified problems could have resulted in patient harm, implying toxic or side-effects, hypersensitivity and poor disease control, corresponding to an incidence of 0.54% [13]. The panel in Hawksworth's study related 48.7% of the interventions to improvement of effectiveness and 64.6% to harm prevention, presumably meaning that 13.3% were related to both [12]. In an Australian study, 41.0% of the pharmacy interventions were associated to a toxic or side-effect outcome, followed by 33.5% for inadequate control of the patient's condition [14]. Unlike these studies, we were also able to investigate

different groups of DRPs and to estimate the impact of individual interventions.

Figure 3 presents the variation of the impact between individual interventions of pharmacies, as estimated by our panel. The real impact of pharmacists' (non) interventions concerning different categories of DRPs has to be studied in other settings; for instance, by linking data concerning hospital admissions to confirmed DRPs, such as dosing problems or obsolete medicine. Juurlink *et al.* found that hospital admissions were associated with previous drug–drug interactions [15]. The variation of the estimated impact between individual interventions of pharmacies can be described as: the higher the probability rating for an intervention, the higher its importance, or seriousness, rating. There were just a few extreme results regarding assessment of the impact of the recorded interventions, which may be explained by

the fact that average data were used (i.e. regression to the mean in most cases).

We found some interesting differences between the different DRP categories. The variety between the dosing problem interventions can be specified by the highest yield of negative judgements found in this group on the one hand (10.1%, Table 1), while on the other hand, 28.8% of these interventions received a relatively high impact score (quadrants A, B, and D in Figure 3). The dosing problems did not only concern overdoses or wrong doses, but also underdosing as can be seen in Table 4.

Drug–drug interactions (DDIs) are generally well defined, i.e. most of the interventions are more or less well documented in literature [16–18]. In this study, DDIs were not all selected for the group of consistently positively estimated interventions [Table 2]. Although there was only a low yield of negative opinions (2.3%) there was a considerable share of neutral judgements (16.5%) (Table 1). Most of the consistently positively judged DDI interventions ($n = 4$) were found in the left upper quadrant A in Figure 3. This illustrates a relatively low probability but a high (and in some instances very high) seriousness/importance score. Likewise, by linking hospital admissions to previous DDIs, Juurlink *et al.* recently demonstrated the high seriousness factor related to DDIs [15].

For many of the contraindication interventions reviewers were strongly cautious (Table 2). More than 41% (seven out of 17) of the contraindication interventions shown in Figure 3 were located in the right upper quadrant, meaning a relatively high probability score and a high seriousness score (e.g. penicillin allergy).

A large contingent of ratings in the double medication group (35.7%) was not directly related to health issues such as ADR and effectiveness, but to prevention of discomfort and prevention of cost. The double medication issue was clearly interpreted as unpleasant for the patient, but apparently was not perceived as an immediate threat to the health status of the patient. This is illustrated by several individual cases in Figure 3. On the other hand, the duration of use interventions ($n = 3$) were highly estimated and mainly related to effectiveness improvement and prevention of ADR.

Despite the strong development of evidence-based medicine (EBM) during the last two decades, this study shows that interventions of pharmacists with respect to obsolete medicines were not highly estimated – a large number of exclusions (Table 2) and a relatively low impact score (Figure 3). An explanation may be found in the fact that the most important obsolete medicines have already been withdrawn from the

(Dutch) market. Interventions for wrong medicine showed a rather diffuse picture.

A number of limitations to this study should not be ignored. It should be noted that the presented incidence rates of modifications and consistently positively judged modifications in Dutch community pharmacies correspond to only a segment of community pharmacy interventions. For instance, we did not analyse modifications in the regimens of already used medicines, which may be the outcome of the same signal as, for example, a DDI. Furthermore, other interventions may have taken place without leading to a modification but to advice concerning proper use of the drug or a combination of drugs. There are also a few restrictions when comparing our results to the studies mentioned above. Hawksworth *et al.*, for instance, had a broader definition of intervention, which included enquiries by the pharmacist about the dose or the dose interval, recommendations concerning the monitoring of blood plasma parameters, and discussions with the prescriber about a patient's pharmacotherapy [12].

A large group of reviewers from different professional backgrounds was recruited to comply with the requirements based upon the literature [11] and our group of reviewers was favourable (large group; five different professions) to the above-mentioned studies [12–14]. For some questions, we investigated the inter-rater differences by using the kappa value [19], although we initially expected relatively low values based upon the literature [11, 14]. For our second question concerning the 90 selected interventions, the overall kappa value was moderate (0.49) with differences between the reviewer categories of 0.35 (GPs) to 0.58 (hospital pharmacists). For a combination of question one and two ($n = 90$), we found an overall kappa value of 0.40 and differences between the reviewer categories of 0.19 (internists) to 0.52 (nonpractising specialists).

Although the kappa value is the most preferable variable in describing inter-rater differences, the problem is that even in a simple situation with two categories, the same proportional agreement can lead to markedly different kappa values [20]. The higher the prevalence in one category (as in our case: positive judgement in question one, especially regarding the 90 selected cases), the higher the proportion of units for which agreement is expected by chance. Another important difficulty in the interpretation of these values occurs when several variables and subvariables are involved, as in our study [14, 20]. Perhaps more meaningful data are derived when the proportion of agreement overall and between the reviewer categories are considered. For instance, the mean percentage of positive evaluations (question 1,

$n = 90$) was overall 93.5% (variance = 0.6%) with differences between the reviewer categories of 89.3% (variance = 5.9%; internists) to 97.8% (variance = 1.1%; nonpractising professionals).

Our very strict second selection after the first general question excluding 54 interventions (out of 144) does not mean that the excluded interventions were overall poorly rated. We would like to emphasize that 18 (33.3%) of these exclusions received a 70–80% positive score. Furthermore, there were no interventions with 100% negative and/or neutral ratings. Only a small group of 10 interventions (6.9%) received less than 50% positive ratings, of which four received no negative ratings but especially 'neutral' ratings. We found three interventions that received more negative ratings than positive ones.

In conclusion, part of pharmacists' interventions included modifying prescriptions for an array of DRPs. A large panel of medico-pharmaceutical professionals consistently positively judged almost 60% of these modifications. According to this panel, at least 1.6 such interventions per pharmacy per day can contribute positively to patients' quality of pharmacotherapy. By extrapolating our data to all pharmacies in the Netherlands, this corresponds to approximately 2700 positive interventions in all Dutch pharmacies on 1 day. Community pharmacists may not only have avoided adverse drug reactions but also improved the effectiveness of pharmacotherapy. According to the expert panel, the impact of an intervention on a patient's health was likely to be significant in a substantial number of cases.

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