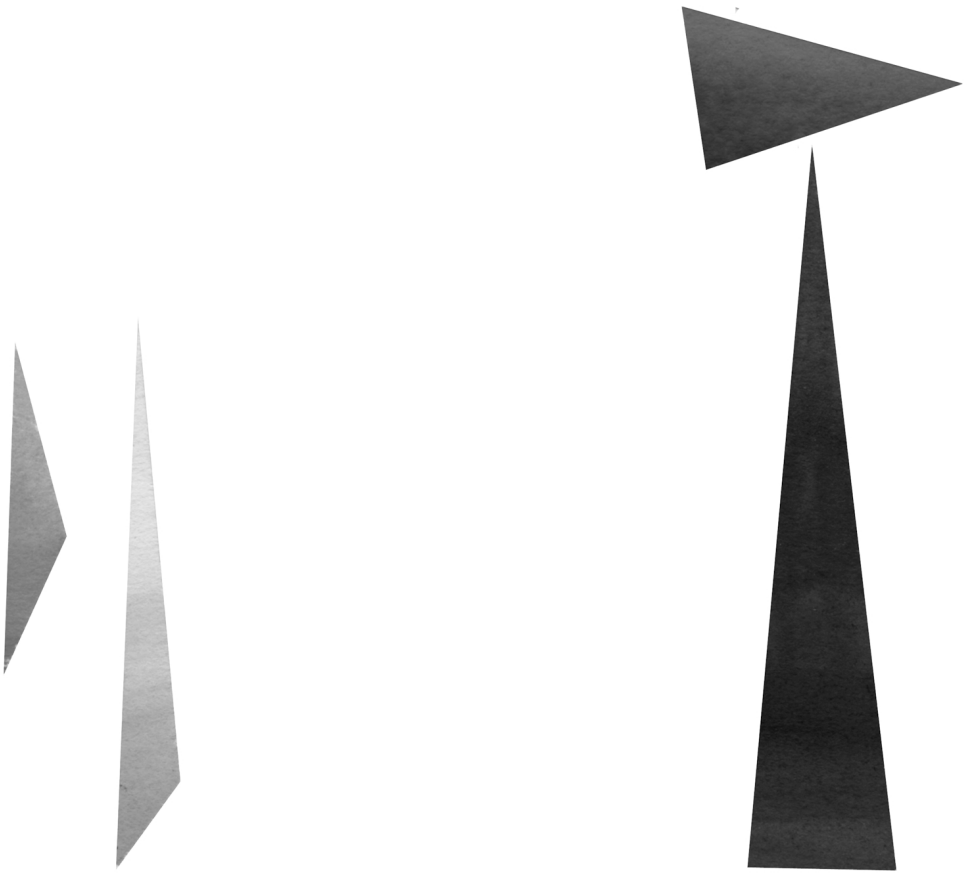
Chapter 4

THE PATIENT



4.1

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

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ABSTRACT

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 pre-determined day between 25 February and 12 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 non-intervention. Our analyses included 144 interventions from the first general assessment and a selection of 90 consistently positively rated 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 (POMs) 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 non-modified prescriptions that were collected from 141 Dutch community pharmacies on one predetermined day.[10] Of the total 2014 modified prescriptions collected, 400

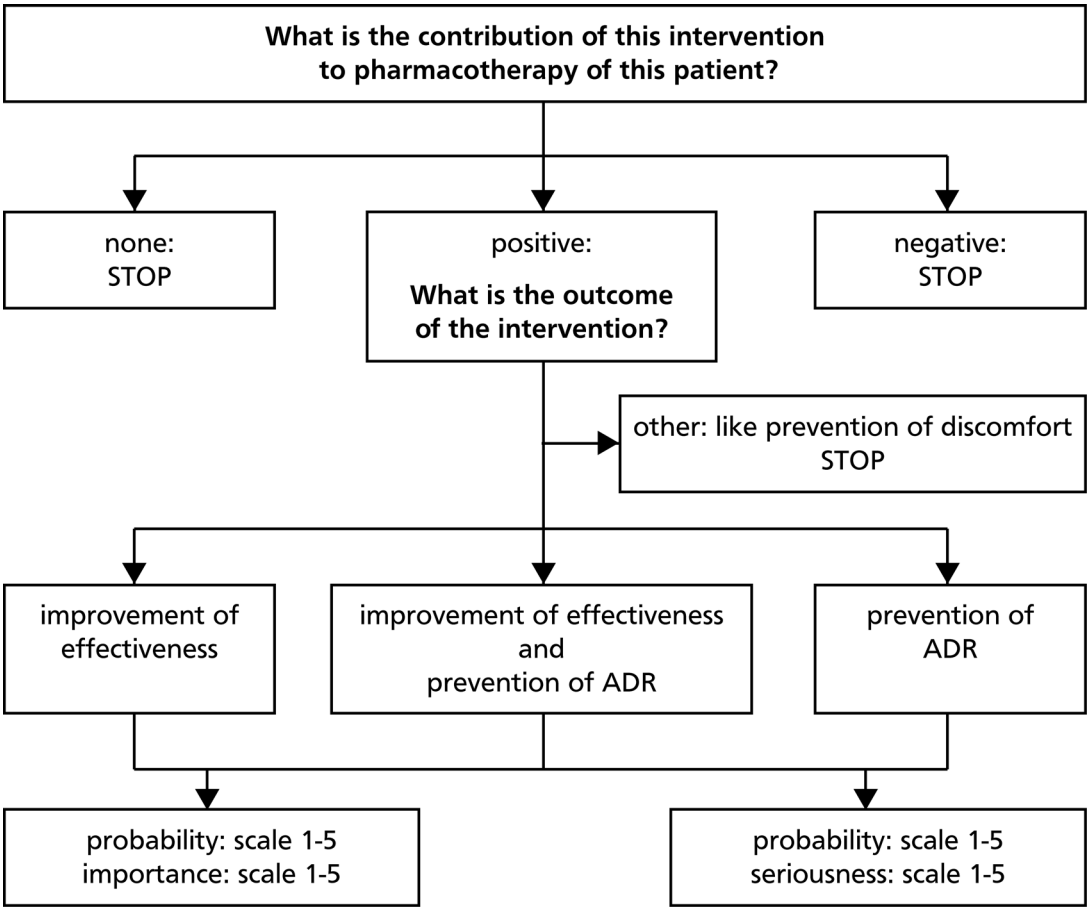
(22.2%) were considered to be corrections for errors related to several potential DRPs, namely wrong dose (n=246), wrong medicine (n=45), wrong patient data (n=42), interaction (n=15), contraindication (n=21), medicine obsolete (n=8), double medication (n=18) and duration of use (n=5). These modifications (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: community pharmacists, hospital pharmacists, general practitioners, specialists for internal diseases, or other non-practising medical/pharmaceutical experts. Each group had four members. 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 both category A and B and 46 other interventions to both category 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 pharmaco-therapy 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 seriousness. The algorithm used by reviewers for rating interventions is presented in Figure 1.

Figure 1: ALGORITHM REPRESENTING THE FLOW OF QUESTIONS FOR RATING INTERVENTIONS



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. Box 1 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).

Box 1: STUDY SELECTION PROCEDURES

1) **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 one negative against more than 88% positive ratings or unless there is just one negative and one 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.
   ⇓ 7 Interventions excluded because of insufficient ratings (<4).
5) **83** consistently positively judged interventions.
   ⇓ Visualisation in *Figure 2* of estimated impact per intervention stratified according to categories of DRP.

RESULTS

Nineteen of the 20 reviewers (response rate of 95%) returned our evaluation forms. All groups had participated with four members except for the group of internal medicine specialists (n=3). We received 71 evaluation forms instead of 72 from one internist. This means that every intervention was evaluated by ten or nine reviewers 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 with approximately three minutes 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% was 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 and the duration of use-category (93.3% and 100%, respectively).

Table 3 further categorizes reviewers' opinions as to the outcome of the consistently positively rated 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).

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[a]	(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%)

For the selection procedure of the judged interventions see the Methods section and/or Box 1.
a) 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 TO THE CONSISTENTLY POSITIVELY RATED GROUP AFTER SAMPLING AND AFTER SELECTION

Drug related problem category	Interventions before sampling	Interventions after sampling	Interventions after selection	Interventions after selection, adjusted
Total	**n=301 (100.0%)**	**n=144 (100.0%)**	**n=90 (100.0%)**	**n=178 (100.0%)**
Contraindication	23 (7.6%)	22 (15.3%)	17 (9.0%)	18 (10.0%)
Double medication[a]	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%)

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

Table 3: OPINION 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; 155 ratings)	1 (0.6%)	143 (92.3%)	4 (2.6%)	7 (4.5%)	0 (0.0%)
Double medication[a]	(n= 14; 126 ratings)	1 (0.8%)	76 (60.3%)	3 (2.4%)	45 (35.7%)	1 (0.8%)
Interaction	(n= 9; 78 ratings)	19 (24.4%)	55 (70.5%)	3 (3.8%)	1 (1.3%)	0 (0.0%)
Duration of use	(n= 3; 26 ratings)	9 (34.6%)	16 (61.5%)	0 (0.0%)	1 (3.8%)	0 (0.0%)
Medicine obsolete	(n= 3; 24 ratings)	7 (29.2%)	14 (58.3%)	1 (4.2%)	2 (8.3%)	0 (0.0%)
Wrong medicine	(n= 15; 125 ratings)	43 (34.4%)	19 (15.2%)	27 (21.6%)	31 (24.8%)	5 (4.0%)
Wrong dose	(n= 29; 245 ratings)	91 (37.1%)	107 (43.7%)	23 (9.4%)	24 (9.8%)	0 (0.0%)
All interventions	(n= 90; 779 ratings)	171 (22.0%)	430 (55.2%)	61 (7.8%)	111 (14.2%)	6 (0.8%)
All interventions adjusted for sampling	(n=301; 1521 ratings)	444 (29.2%)	758 (49.8%)	130 (8.6%)	183 (12.0%)	6 (0.4%)

For the selection procedure of the judged interventions see the Methods section and/or Box 1.
a) Double medication is a combination of the same substance or different substances from the same therapeutic group.

Table 4: SOME EXAMPLES OF INTERVENTIONS PRESENTED IN FIGURE 2

Coordinates[a]	DRP Category	Description of initial prescription	Outcome
3.7 – 4.4	Dosing	Woman; 1962; GP; ethinyl estradiol 1mg; 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 500mg; 1dd1; no. 15; first prescription.	Specialist consulted; amoxicillin 500mg; 3dd1; no. 15.
3.5 – 3.6	Dosing	Woman; 1913; GP; isosorbide dinitrate 5mg sublingual; 4-6dd1; repeat prescription.	Communication with patient; one tablet only when needed.
4.0 – 3.7	Contraindication	Woman; 1920; GP; amoxicillin 500mg; 3dd1; first prescription; penicillin intolerance.	Other GP consulted; ofloxacin 200mg.
4.2 – 3.1	Contraindication	Woman; 1923; GP; diclofenac 50mg; 3dd1; diclofenac intolerance.	Assistant GP consulted; tramadol 50mg; 3dd1.
3.8 – 3.8	Duration of use	Man; 1954; GP; itraconazole 100mg; 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 50mg and nitroglycerin spray.	GP consulted; not dispensed.
1.8 – 4.6	Interaction	Woman; 1950; GP; erythromycin 500mg; 4dd1; no 30; first prescription; in combination with cisapride.	GP consulted; doxycycline 100mg instead of erythromycin; first day two tablets, then 1dd1.
1.8 – 1.8	Double medication	Woman; 1950; GP; flunitrazepam 1mg; ante noctem 2; stock at home.	Pharmacist consulted; no dispensing.
1.5 – 1.5	Double medication	Woman; 1922; GP; amoxicillin 750mg; 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.

GP = **general practitioner**
a) Probability score – importance/seriousness score

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 2, 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 scores for importance/seriousness concerning two interactions and one duration of use intervention. Of the interaction interventions 50% (4 out of 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 2 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 in all Dutch pharmacies on one day. These interventions by pharmacists were not exclusively 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 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 2 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).

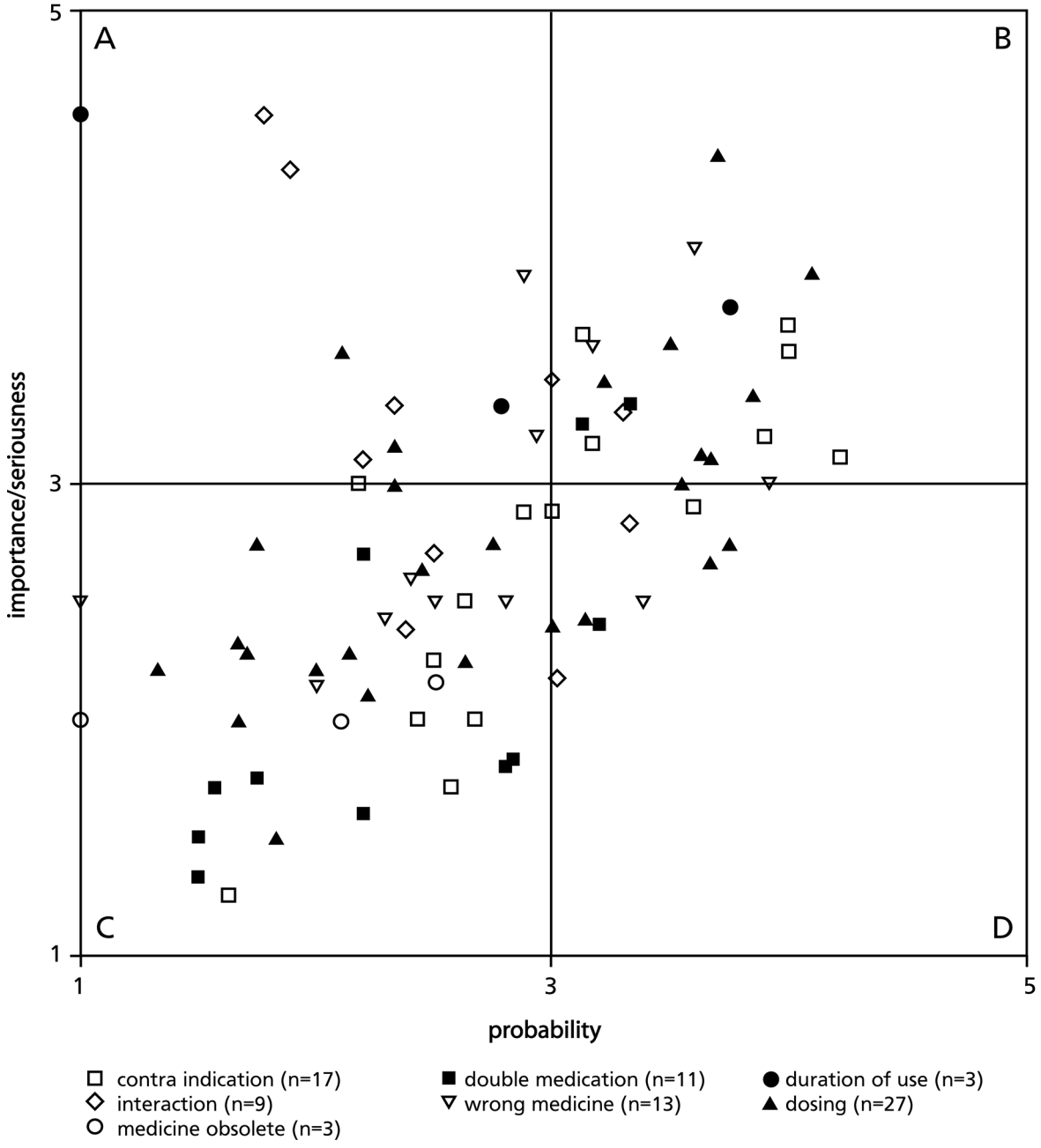
We found some interesting differences between the different DRP categories. The variety between the dosing problem interventions can be specified by the highest yield of negative judgements found in this group on the one hand (10.1%; Table 1), while on the other hand, 28.8% of these interventions received a relatively high impact score (quadrants A, B, and D in Figure 2). The dosing problems did not only concern overdoses or wrong doses, but also underdose 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 were found in the left upper quadrant A in Figure 2. This illustrates a relatively low probability but a high (and in some instances very high) importance/seriousness 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 2 were located in the right upper quadrant B, meaning a relatively high probability score and a high seriousness score (e.g. penicillin allergy).

Figure 2: THE AVERAGE ESTIMATED IMPACT OF 83 INTERVENTIONS



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 2. 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 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 2). 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 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 (general practitioners) 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 (non-practising 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%; non-practising 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 one 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 patient's health was likely to be significant in a substantial number of cases.

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4.2

Pharmacy shopping: determinants and the relation with heavy use of psychotropic drugs

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ABSTRACT

Aims

Discontinuity of care bears the risk of medication errors and poor clinical outcomes. Little is known about continuity of care related to pharmacies. The objective was to explore the prevalence and determinants of pharmacy shopping behaviour and, in addition, the association between shopping behaviour and heavy use of psychotropic drugs.

Methods

All beneficiaries from a Dutch health insurance pharmacy claims database who had visited two or more pharmacies in 2001 were indicated as 'shoppers' (n=45 805). A random sample was taken from all other beneficiaries who had received at least one prescription and these were indicated as 'non shoppers' (n=45 805). Shoppers were classified into three mutually exclusive categories (light, moderate, heavy). Gender, age, number of different type of prescribers, and number of different drugs dispensed, were investigated as determinants of shopping behaviour. We investigated the association between the use of any dispensing of ATC classes of drugs in 2001 and shopping behaviour. The association between shopping behaviour and the heavy use of (a combination of) categories of psychotropic drugs (hypnotics and anxiolytics, antidepressants, antipsychotics, and opioids) was examined. Heavy use was defined as the use of more than 365 Defined Daily Doses dispensed in 2001.

Results

Of all beneficiaries 10.8% were identified as shoppers, of which the vast majority (98.8%) could be described as 'light shoppers' and a small minority (0.2%) as 'heavy shoppers'. Female gender (OR_{adj} 1.2; 95%CI 1.1-1.2), younger age (≤40 yr) (OR_{adj} 1.7; 95%CI 1.7-1.8), the use of three or more different drugs (OR_{adj} 2.9; 95%CI 2.8-3.0) and visiting different kind of prescribers (OR_{adj} 2.4; 95%CI 2.4-2.5) were associated with shopping behaviour. Shoppers more frequently received at least one prescription for systemic anti-infectives (51.7% vs. 30.8%) and for nervous system drugs (46.2% vs. 29.3%). There was a clear association between the degree of shopping behaviour and heavy use of one or more categories of the psychotropic drugs. For example, between heavy shopping behaviour and the heavy use of hypnotics and anxiolytics (OR_{adj} 17.3; 95%CI 10.4-28.9), and the heavy use of opioids (OR_{adj} 19.4; 95%CI 4.3-87.8).

Conclusions

Pharmacy shopping behaviour is still limited in the Netherlands. However, it may put the patient at risk for unintentional problems, such as drug-drug interactions with systemic antibiotics and antimycotics. A relatively small proportion of patients exhibit possibly intentional shopping behaviour with psychotropic drugs, in particular related to the heavy use of hypnotics and anxiolytics. Linking pharmacy computer systems will signal and hopefully prevent most problems related to pharmacy shopping behaviour. Communicating with the patient may already reduce unintentional problems.

INTRODUCTION

Transition of patients across health care settings (e.g. from hospital to long-term care, from hospital to primary care or vice versa) as well as physician shopping (among others defined as the use of a second physician without referral from the first for a single episode of illness) have been associated with discontinuity of care.[1] Discontinuity of care bears the risk of medication errors and poor clinical outcomes.[2-5] Conversely, continuity of care has been associated in most but not all studies with improved preventive care, reduced hospitalization and lower costs.[2,3,6-14]

Continuity of care has been addressed especially from the perspective of general medical practice.[15] Little is still known about the relation between continuity of care from a community pharmacy perspective and clinical outcomes. Some studies have described pharmacists' provision of continuity of care for special groups of patients (e.g. HIV patients) or the provision of structures that support continuity of care across health care settings (e.g. transfer of information about drug use).[16-20] Discontinuity of pharmacy care may put the patient at risk for drug therapy related problems, since pharmacy shopping hampers adequate medication surveillance. Examples of such unintentional problems include unwanted duplicate medications, drug-disease interactions, drug intolerabilities (including allergies) and drug-drug interactions, but also conflicting information about drug use from different pharmacies, confusion between brand and generic names and incorrect quantities.[5,21] Medicine users may also intentionally visit different pharmacies because of certain drug related problems, such as heavy use and addiction. Prescription claims from more than five pharmacies in one quarter of a year have been reported as indicators of potential abuse or misuse of prescription drugs.[22]

As continuity of pharmacy care can be considered an important prerequisite for the clinical risk management of drug therapy related problems, we studied the prevalence and determinants of pharmacy shopping behaviour. Since physician shopping, in some instances described as prescription shopping, has been mainly associated with the heavy use of benzodiazepines and opioids, we additionally aimed to describe the association between pharmacy shopping behaviour and heavy use of psychotropic drugs.[23,24]

METHODS

Setting, study population and data collection

Data were obtained from the pharmacy claims database of a Dutch health insurance company ('O.W.M. Zorgverzekeraar Zorg en Zekerheid u.a.') concerning the year 2001. This health insurance company mainly proceeds in the western region between The Hague and Amsterdam, and can be described as relatively small (on average 448 392 beneficiaries in 2001).

The data obtained were related to the beneficiaries who were insured under the Social Health Insurance Act comprising all employees earning less than about 33 000 Euro per year, social security recipients and certain old-age groups. In 2001, about 65% of the Dutch population was insured under this law, against 94.8% (on average 425 061) within this insurance company.

Of all Social Health Insurance Act beneficiaries, 338 423 (79.6%) had at least one pharmacy claim during 2001. Of these, all patients visiting[a] two or more pharmacies in 2001 – thus having received at least two prescriptions in 2001 – were identified from the pharmacy claims database (n=45 805). These patients, with a certain degree of discontinuity of pharmacy care, were indicated as 'shoppers'. From all other beneficiaries who received at least one prescription and visited only one pharmacy during 2001, a random, numerically equivalent, sample was taken (n=45 805). These patients were indicated as 'non shoppers'.

For shoppers as well as non shoppers, data were obtained comprising age and gender. For each patient a medication history was collected covering information about all dispensed and (partially) reimbursed drugs during 2001, such as name, Anatomical Therapeutic Chemical (ATC) code, date of dispensing, dispensed amount, dosage regimen, type of prescriber, and the community pharmacy (anonymous, unique code) where the drug had been dispensed.

Classification of data

Determinants of pharmacy shopping behaviour

Although several measurement techniques have been used in the literature to define and study (dis)continuity of care, especially in general medical practice, we used a method tailored to the pharmacy setting.[6,15] Shoppers were classified into three mutually exclusive categories based upon (a) the number of visits to one or more pharmacies other than the main dispensing pharmacy (='elsewhere'), (b)

[a] This means that a visit was made to a pharmacy concluded by a dispensing and a pharmacy claim to the health insurance company based upon the dispensing.

the proportion of prescriptions dispensed in pharmacies elsewhere, and (c) the total number of prescriptions dispensed in pharmacies elsewhere (Table 1). Several characteristics were investigated as determinants of shopping behaviour: gender, age (four categories: 0-25; 26-40; 41-60; >60), the number of different type of prescribers (general practitioner (GP), specialist or other), and the number of different drugs (active substances) dispensed in 2001 (based upon ATC code-level 7; three categories: 0-2; 3-5; >5). In addition, we studied whether any dispensing in 2001 of the therapeutic groups of drugs in accordance with the ATC classification of the WHO Collaborating Centre for Drug Statistics Methodology (level 1), as well as subclasses of the Nervous System drugs (N category), was associated with shopping behaviour.

Table 1: CLASSIFICATION OF SHOPPING BEHAVIOUR

Description	Definition[a]	Number	(% of all shoppers)
Non shopper	patients who visited only one pharmacy	45 805	-
Light shopper	all patients who visited more than one pharmacy at least once, except for patients defined as heavy or moderate shoppers	45 252	98.8%
Moderate shopper	- number of pharmacies visited 3 or 4 AND - proportion of prescriptions elsewhere >10% AND - number of prescriptions elsewhere >10	458	1.0%
Heavy shopper	- number of pharmacies visited ≥5 AND - proportion of prescriptions elsewhere >10% AND - number of prescriptions elsewhere >10	95	0.2%

a) 'visited' means that a visit was made to a pharmacy concluded by a dispensing and a pharmacy claim to the health insurance company based upon the dispensing (see the method section).

Shopping behaviour and heavy use of psychotropic drugs

Partly based upon literature and based upon data analysed and presented in this study concerning the association between any dispensing of an ATC-group and shopping behaviour, we examined the association between shopping behaviour and the heavy use of specific psychotropic drugs.[23,24] Psychotropics comprised hypnotics and anxiolytics (including all benzodiazepine hypnotics and anxiolytics as well as zolpidem, zopiclon, chloral hydrate, buspiron and hydroxyzine; excluding clonazepam), antidepressants, antipsychotics (excluding lithium salts and prochlorperazine) and opioids (excluding codeine). Clonazepam was

excluded from analyses because it is mainly prescribed for epilepsy and restless legs. The relation between shopping behaviour and heavy use of more than one category of psychotropic drugs (hypnotics and anxiolytics, antidepressants, antipsychotics, and opioids) was investigated as well. Heavy use was defined as the use of more than 365 Defined Daily Doses (DDDs) dispensed in 2001, implying an average use of more than one DDD per day.

Data analysis

Data were analysed using standard descriptive data analysis (SPSS version 12.0). Logistic regression analysis was used to estimate the strength of the association between characteristics and pharmacy shopping behaviour and of the association between pharmacy shopping behaviour and the heavy use of several psychotropic drugs and expressed as odds ratios (OR) with 95% confidence intervals (CI).

RESULTS

Shopping behaviour

Of the Social Health Insurance Act beneficiaries of the health insurance company (on average n=425 061 in 2001), a total number of 45 805 patients (10.8%) were identified who had visited more than one pharmacy in 2001 on at least one occasion (Table 1). Of these, the vast majority (98.8%) could be described as 'light shoppers'. Most of these 'shopping' patients (86.4%) visited only one other pharmacy, 11.2% visited two and 2.4% three or more other pharmacies. Within the group of patients visiting only one other pharmacy, 63.4% visited the second pharmacy only once (data not shown). A small minority (0.2%) of the shoppers was classified as 'heavy shoppers'.

Table 2 shows the characteristics of the study population. Comparing all shoppers with non shoppers and adjusted for all included variables, female gender (OR_{adj} 1.2; 95%CI 1.1-1.2), younger age (≤40 yr) (OR_{adj} 1.7; 95%CI 1.7-1.8), the use of three or more different drugs (OR_{adj} 2.9; 95%CI 2.8-3.0) and different kind of prescribers (OR_{adj} 2.4; 95%CI 2.4-2.5) were associated with shopping behaviour.

Shoppers received more frequently at least one prescription for systemic anti-infectives (51.7% vs. 30.8%; OR 2.4; 95%CI 2.3-2.5) and for nervous system drugs (46.2% vs. 29.3%; OR 2.1; 95%CI 2.0-2.1) than non shoppers (Table 3). For the other ATC classes the differences were less clear. We especially found a strong association between any dispensing of nervous system drugs and heavy shopping (OR 16.7; 95%CI 9.1-30.5) as well as between any dispensing of

nervous system drugs and moderate shopping (OR 20.1; 95%CI 14.9-27.1). To some extent similar associations were also found for selected psychotropics, i.e. hypnotics and anxiolytics, antidepressants, antipsychotics and opioids.

Shopping behaviour and its relation with heavy use of psychotropic drugs

In the group of patients with any form of shopping behaviour, the prevalence of heavy use of hypnotics and anxiolytics was 2.8% compared to 1.4% in non shoppers (Table 4). The prevalence values concerning the heavy use of antidepressants were 2.6% and 1.2%, respectively. The prevalence of heavy use of antipsychotics was found to be relatively low both in non shoppers (0.2%) and in shoppers (0.3%). A low prevalence of heavy use was also found in the group of opioid users: 0.04% (non shoppers) versus 0.2% (shoppers).

Although the absolute prevalence of heavy use of the selected psychotropics was low, there was a clear association between the degree of shopping behaviour and heavy use of various psychotropic drugs. The association between heavy shopping behaviour and the heavy use of hypnotics and anxiolytics was OR_{adj} 17.3; 95%CI 10.4-28.9. A strong association was revealed between moderate and heavy shopping behaviour respectively and heavy use of opioids (OR_{adj} 14.9; 95%CI 7.0-31.7 and 19.4; 95%CI 4.3-87.8, respectively). Lower risks were found concerning the association between moderate shopping behaviour and heavy use of hypnotics and anxiolytics, moderate shopping behaviour or heavy shopping behaviour and heavy use antidepressants or antipsychotics.

In Table 5, patients with heavy use of either hypnotics and anxiolytics, antidepressants, antipsychotics or opioids (n=3507) are presented. Of this group 412 (11.7%) were overusing a combination of two or three of these groups of psychotropics. There was a clear association between the degree of shopping behaviour and heavy use of more than one category of these psychotropic drugs. For example, within the group of heavy shoppers 41.1% had heavy use of at least one of the defined categories of psychotropic drugs, whereas this was 2.5% in the group of non shoppers. After adjustment for all variables, the association between heavy shopping behaviour and the heavy use of two or three groups of psychotropic drugs was OR_{adj} 14.8; 95%CI 7.1-31.1, concerning moderate shopping behaviour it was OR_{adj} 7.4; 95%CI 4.7-11.8.

Table 2: CHARACTERISTICS OF THE STUDY POPULATION (n=91 610)

Characteristic	Number of patients (medicine users)			
	Non shoppers n=45 805 (100%)	Light shoppers n=45 252 (100%)	Moderate shoppers n=458 (100%)	Heavy shoppers n=95 (100%)
Female gender	28 116 (61.4%)	30 272 (66.9%)	322 (70.3%)	62 (65.3%)
Age (yr)				
mean (sd)	*41.8 (22.0)*	*41.1 (21.9)*	*57.6 (21.2)*	*39.6 (17.9)*
0–25	11 333 (24.7%)	10 803 (23.9%)	36 (7.9%)	18 (18.9%)
26–40	12 042 (26.3%)	14 362 (31.7%)	79 (17.2%)	40 (42.1%)
41–60	12 051 (26.3%)	10 543 (23.3%)	131 (28.6%)	25 (26.3%)
>60	10 379 (22.7%)	9 544 (21.1%)	212 (46.3%)	12 (12.6%)
Different type of prescribers (n)				
1	33 563 (73.3%)	21 431 (47.4%)	81 (17.7%)	16 (16.8%)
2	11 070 (24.2%)	19 835 (43.8%)	259 (56.6%)	46 (48.4%)
>2	1 172 (2.6%)	3 986 (8.8%)	118 (25.8%)	33 (34.7%)
Different drugs[a] (n)				
0–2	21 550 (47.0%)	9 444 (20.9%)	2 (0.4%)	4 (4.2%)
3–5	14 112 (30.8%)	16 973 (37.5%)	22 (4.8%)	14 (14.7%)
>5	10 143 (22.1%)	18 835 (41.6%)	434 (94.8%)	77 (81.1%)
Dispensed prescriptions (n)				
1–2	14 348 (31.3%)	3 161 (7.0%)	0 (0.0%)	0 (0.0%)
3–5	10 787 (23.5%)	10 747 (23.7%)	0 (0.0%)	0 (0.0%)
6–9	6 887 (15.0%)	9 138 (20.2%)	0 (0.0%)	0 (0.0%)
10–20	7 650 (16.7%)	11 105 (24.5%)	5 (1.1%)	7 (7.4%)
>20	6 133 (13.4%)	11 101 (24.5%)	453 (98.9%)	88 (92.6%)

a) active substances

Table 3: ASSOCIATION BETWEEN ANY DISPENSING OF GROUPS OF MEDICINES AND SHOPPING BEHAVIOUR

Group of medicines	Non shoppers n=45 805 (100%)	Light shoppers n=45 252 (100%)	Moderate shoppers n=458 (100%)	Heavy shoppers n=95 (100%)
Any dispensing of ATC-group				
Alimentary tract and metabolism (A)	10 787 (23.5%)	15 803 (34.9%)	329 (71.8%)	45 (47.4%)
Cardiovascular system (C)	9 939 (21.7%)	11 483 (25.4%)	268 (58.5%)	29 (30.5%)
Dermatologicals (D)	13 333 (29.1%)	17 050 (37.7%)	252 (55.0%)	45 (47.4%)
Genital-urinary system and sex hormones (G)	12 990 (28.4%)	16 831 (37.2%)	139 (30.3%)	40 (42.1%)
General anti-infectives for systemic use (J)	14 102 (30.8%)	23 330 (51.6%)	287 (62.7%)	60 (63.2%)
Musculoskeletal system (M)	11 988 (26.2%)	17 366 (38.4%)	220 (48.0%)	46 (48.4%)
Nervous system (N)	13 440 (29.3%)	20 690 (45.7%)	409 (89.3%)	83 (87.4%)
Respiratory system (R)	11 866 (25.9%)	16 160 (35.7%)	244 (53.3%)	55 (57.9%)
Any dispensing of specific psychotropic drugs				
Hypnotics and anxiolytics[a]	7 393 (16.1%)	12 156 (26.9%)	330 (72.1%)	72 (75.8%)
Antidepressants	2 968 (6.5%)	5 404 (11.9%)	165 (36.0%)	49 (51.6%)
Antipsychotics[b]	668 (1.5%)	1 446 (3.2%)	66 (14.4%)	23 (24.2%)
Opioids[c]	909 (2.0%)	2 669 (5.9%)	118 (25.8%)	22 (23.2%)

a) excluding clonazepam
b) excluding lithium and prochlorperazine
c) excluding codeine

Table 4: ASSOCIATION BETWEEN SHOPPING BEHAVIOUR AND HEAVY USE OF SELECTED PSYCHOTROPIC DRUGS

Category		No and normal use	Heavy use	OR (95%)	
		n (%)	n (%)	Crude	Adjusted[a]
Hypnotics and anxiolytics					
non shopper	n=45 805 (100%)	45 179 (98.6%)	626 (1.4%)	1 (reference)	1 (reference)
light shopper	n=45 252 (100%)	44 070 (97.4%)	1 182 (2.6%)	1.9 (1.8– 2.1)	1.4 (1.2– 1.5)
moderate shopper	n=458 (100%)	377 (82.3%)	81 (17.7%)	15.5 (12.0– 20.0)	4.7 (3.6– 6.1)
heavy shopper	n=95 (100%)	69 (72.6%)	26 (27.4%)	27.2 (17.2– 43.0)	17.3 (10.4–28.9)
Antidepressants					
non shopper	n=45 805 (100%)	45 266 (98.8%)	539 (1.2%)	1 (reference)	1 (reference)
light shopper	n=45 252 (100%)	44 141 (97.5%)	1 111 (2.5%)	2.1 (1.9– 2.3)	1.4 (1.2– 1.5)
moderate shopper	n=458 (100%)	415 (90.6%)	43 (9.4%)	8.7 (6.3– 12.0)	3.3 (2.4– 4.7)
heavy shopper	n=95 (100%)	76 (80.0%)	19 (20.0%)	21.0 (12.6– 35.0)	7.9 (4.7–13.4)
Antipsychotics					
non shopper	n=45 805 (100%)	45 735 (99.8%)	70 (0.2%)	1 (reference)	1 (reference)
light shopper	n=45 252 (100%)	45 127 (99.7%)	125 (0.3%)	1.8 (1.4– 2.4)	1.1 (0.8– 1.6)
moderate shopper	n=458 (100%)	451 (98.5%)	7 (1.5%)	10.1 (4.6– 22.2)	4.2 (1.8– 9.5)
heavy shopper	n=95 (100%)	93 (97.9%)	2 (2.1%)	14.1 (3.4– 58.1)	4.0 (0.9–17.2)
Opioids					
non shopper	n=45 805 (100%)	45 787 (100.0%)	18 (0.04%)	1 (reference)	1 (reference)
light shopper	n=45 252 (100%)	45 167 (99.8%)	85 (0.2%)	4.8 (2.9– 8.0)	2.8 (1.7– 4.8)
moderate shopper	n=458 (100%)	446 (97.4%)	12 (2.6%)	68.4 (32.8–142.9)	14.9 (7.0–31.7)
heavy shopper	n=95 (100%)	93 (97.9%)	2 (2.1%)	54.7 (12.5–239.1)	19.4 (4.3–87.8)

a) The association was adjusted for gender, age, number of different kind of prescribers, number of different drugs (ATC-level 7).

Table 5: RELATION BETWEEN SHOPPING BEHAVIOUR AND HEAVY USE OF ONE OR MORE CATEGORIES OF PSYCHOTROPIC DRUGS (HYPNOTICS AND ANXIOLYTICS, ANTIDEPRESSANTS, ANTIPSYCHOTICS AND OPIOIDS)

	Number	No heavy use	Heavy use of 1 category	Heavy use of 2 categories	Heavy use of 3 categories
Non shopper	45 805	44 654 (97.5%)	1 058 (2.3%)	84 (0.2%)	9 (0.02%)
Light shoppers	45 252	43 049 (95.1%)	1 919 (4.2%)	268 (0.6%)	16 (0.04%)
Moderate shoppers	458	344 (75.1%)	88 (19.2%)	23 (5.0%)	3 (0.7 %)
Heavy shoppers	95	56 (58.9%)	30 (31.6%)	8 (8.4%)	1 (1.1 %)

Heavy use of 4 categories of psychotropic drugs did not occur.

DISCUSSION

The prevalence of pharmacy shopping was rather low (10.8%) and occurred especially in women, younger people, people using a high number of different drugs and those having different kind of prescribers. The dispensing of any anti-infective drug was related to (light) shopping. Moderate and heavy shopping was clearly associated with the heavy use of one or more categories of psychotropic drugs.

This study confirms that Dutch patients are in general loyal to one pharmacy, leading to rather complete patient medication records.[25,26] This may be due to the fact that in the Dutch health care system, patients are historically closely linked to one pharmacist. This situation is different from several other countries, such as Canada, where 40% of elderly patients visit more than one pharmacy.[27] Our finding has been confirmed to some extent in a small Dutch survey in which less than 1% of the respondents stated to visit other pharmacies structurally.[28] In the same survey younger people reported to be more prone to pharmacy shopping, a confirmation of our finding as well. In the Netherlands, it is allowed to move around to seek medical treatment, especially outside office hours. Most shoppers visited only one other pharmacy. This 'light' shopping behaviour is probably at least partly related to required pharmaceutical (and medical) treatment outside office hours. Indicative for this explanation is our finding that there was a strong association between any dispensing of systemic antibiotics and antimycotics and shopping behaviour. These drugs are often needed in more or less acute situations occurring during evenings, nights and in the weekend.

Nevertheless, also light shopping behaviour may hamper adequate medication surveillance and put the patient at risk for unintentional drug therapy related problems, such as duplicate medications, drug-disease interactions and drug-drug interactions. Not surprisingly, it has already been reported that an increasing number of pharmacists involved in the dispensing of drugs, increases the risk of dispensing potentially inappropriate drug combinations.[21] In this respect, we may consider the strong association between any dispensing of systemic antibiotics and antimycotics and shopping behaviour as an indication for a possible high frequency of unintentional, but potentially harmful drug-drug interactions, in which antibiotics, particularly macrolides and fluoroquinolones, and several oral antimycotics, are involved.[29] This warrants further investigation in future studies.

A strong relation was found between pharmacy shopping behaviour, particularly moderate or heavy shopping behaviour, and heavy use of psychotropic drugs. To

our knowledge, the relation between shopping behaviour and heavy use of these medicines has been reported for physician shopping, but not yet for pharmacy shopping.[23,24]

We found a prevalence of 1.4% of patients with heavy use of hypnotics and anxiolytics in the non shopping category. Given the sampling strategy that we applied in our study design, this means that the prevalence of heavy use related to all non shopping beneficiaries was almost 1.1%. Assuming a similar prevalence for the other beneficiaries and extrapolating this figure to the average size of a Dutch pharmacy, each pharmacy would have about 88 non shopping patients with heavy use of hypnotics and anxiolytics. Although not the focus of our study, this considerable number has to be evaluated seriously by the responsible pharmacists and by community pharmacy in general. In the Netherlands, heavy use and addiction to medicines have especially been associated with the use of benzodiazepines.[30] We found a higher prevalence of heavy use of hypnotics and anxiolytics in patients with any form of shopping behaviour, on average 2.8%. For the Netherlands, this accounts for approximately 48 500 patients and 28 of such patients per pharmacy. For moderate and heavy shopping patients with heavy use of hypnotics and anxiolytics, the result is about 2.3 per pharmacy. Heavy shopping behaviour is a very strong determinant for heavy use of hypnotics and anxiolytics.

The prevalence of patients with heavy use of antidepressants was to some extent comparable to that of hypnotics and anxiolytics. Data from the Netherlands show that there has been a strong rise of antidepressant use from 1992 till 2004, among other things due to a longer duration of use.[31,32] In 2001 the total prevalence was found to be about 2.4%. Data of heavy use or misuse of antidepressants are unknown. The extent of shopping behaviour is a considerable determinant for the heavy use of antidepressants, and an even stronger one for the heavy use of hypnotics and anxiolytics.

The prevalence of antipsychotic use (excluding lithium) in the Netherlands increased 43% from 1994 till 2003, mainly based upon an increase of the duration of use of these agents. A prevalence of 0.47% was revealed.[33] Heavy use or misuse has not been described. In our study, data about heavy use of antipsychotics are presented for the first time. A less strong association was found between shopping behaviour categories and the heavy use of this group psychotropic drugs. Moreover, absolute numbers of shopping patients with heavy use of antipsychotics were low.

We found a strong association between the level of shopping behaviour and the heavy use of opioids. The absolute number, however, for moderate and heavy shopping patients with heavy use of opioids was low. Based upon our data, the extent of heavy use or misuse of opioid prescription medications in the Netherlands in general seems to be low. However, the use of opioids is strongly growing in the Netherlands, particularly concerning oxycodon prescriptions.[34] In the United States, there are multiple indicators that non-medical use of prescription opioids are on the rise. It is said, that these opioids, especially oxycodon, are abused to almost the same extent as cocaine, and perhaps heroin.[35,36] The growth of especially longitudinal use of these substances is understandable: people stay alive for a longer period of time since more cancer diseases are curable and, moreover, the use of opioids is not solely restricted to cancer therapy anymore.[37,38]

The first step to reduce discontinuity of care due to pharmacy shopping (which is frequently invisible in the pharmacy) is better detection. Asking the patient for actual medication use and diseases may help to detect unintentional drug therapy related problems, such as duplicate medications, drug-disease interactions and drug-drug interactions, for instance, those involving systemic antibiotics and antimycotics. In addition, patients should be encouraged to stick not only to a single primary care physician, but also to a single dispensing pharmacy. Tamblyn et al. found that the use of a single dispensing pharmacy lowered the risk of potentially inappropriate drug combinations.[21]

Intentional heavy use, however, such as the heavy use or misuse of psychotropic drugs, will probably not be found by communicating with these patients. To detect this type of problem, systems are needed which exchange information among pharmacists.[16] In the Netherlands, there is a tendency of locally and regionally clustering of pharmacy computer systems. The development of a nationwide system, coordinated by the Ministry of Health, is not expected to be finished within the next 2-3 years. In a recent Canadian study, primary care physicians believed that such an integrated system would improve continuity of care.[39]

Other more retrospective interventions may be added to these proactive interventions and prerequisites. Educational programmes designed to reduce inappropriate utilization of prescription drugs and aimed at patients and/or their physicians have shown some favourable impact.[22,40]

This study had several limitations. In studies like ours (over)dispensing claims are considered to be identical with the (over)use of medicines. It is known, however,

that psychotropic drugs are exchanged among drug abusers. Secondly, pharmacy shopping might have been underestimated. A prescription, in some instances, may not have been followed by a dispensing, because it was refused for some reasons, for instance, heavy use. Thirdly, pharmacy claims of a relatively small health insurance company were used. Although patients from rural as well as non-rural areas were included, over- or underestimation cannot be totally ruled out, because patients from the largest Dutch cities as well as those from areas with a low population density were underrepresented. In addition, we used only data from beneficiaries that were insured under the Social Health Insurance Act, which comprises a specific selection of the Dutch population with on average a lower socio-economic status. This could have led to overestimation. Moreover, we did not include the purchase of certain medications by the use of the Internet. This type of self-care could have occurred, but the extent to which Dutch people use Internet pharmacies is unknown. In the US, however, drug abusers of psychoactive prescription medications have turned increasingly to the Internet as community based efforts to curtail physician shopping have been expanded.[41] Over the counter drugs were not included in the database. Finally, our definition of heavy use was somewhat arbitrary but in line with definitions used in other studies.

CONCLUSIONS

Pharmacy shopping behaviour is still limited in the Netherlands. Female gender, younger age, using a high number of different drugs and having different kind of prescribers are the main determinants of pharmacy shopping behaviour. Even light shopping behaviour may put the patient at risk for intentional drug related problems (including heavy use which was the subject of our study) but also for unintentional drug therapy related problems, such as drug-drug interactions, for instance, with systemic antibiotics and antimycotics. Intentional shopping behaviour seems especially related to the heavy use of (several categories of) psychotropics. It was found that the higher the shopping category, the higher the chance of a heavy use of hypnotics and anxiolytics, opioids and to a lower extent antidepressants. Linking pharmacy computer systems, locally, regionally or preferably nationwide will signal and hopefully prevent most of the intentional and unintentional problems related to pharmacy shopping for prescription only medicines. Pending this development, communicating with the patient may

already reduce unintentional problems. Future research should focus on unintentional drug therapy related problems due to pharmacy shopping behaviour.

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