Effect of a Pharmacist Conducted Clinical Medication Review in Older Patients Discharged From the Hospital

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Detailed research paper of Chapter 4
Abstract

Background
Drug related problems (DRP) are common among older patients who are discharged from the hospital and use several drugs. Few interventions were reported to decrease DRP in older people discharged from the hospital. We therefore studied the effect of clinical medication review (CMR) by community pharmacists on the occurrence of DRP in older persons.

Methods
A randomized controlled study involving 340 patients. Community pharmacists were randomized to a control and an intervention group. Intervention pharmacists were instructed to perform a CMR, which include a medication analysis, treatment analysis, patient interview and counseling among patients aged over 60 years, using at least five chronic drugs and discharged from the hospital. Pharmacy technicians interviewed control and intervention patients in order to identify patient-perceived DRP at baseline. Intervention patients were counseled at discharge, after three, six and nine months. DRP in patients of control and intervention pharmacists were measured at baseline and at 12 months by two clinical pharmacologists.

Results
CMR resulted in a significant reduction of DRP. In particular, DRP such as no drug but clear indication and fear for side effects were significantly more reduced in the intervention group. Subgroup analyses showed that the reduction of DRP identified with medication analysis was significantly more pronounced among patients with hypertension (p= 0.011) and heart failure (p= 0.001).

Conclusion
The present study showed that pharmacist-led CMR is an effective method to reduce DRP among older patients discharged from the hospital.
Introduction

Older patients with chronic diseases for which they often use several drugs are at high risk of experiencing drug-related problems (DRP). Examples of DRP are contra-indications, interactions, adverse drug reactions and inefficacy of treatment and may result in hospitalizations, morbidity, mortality and increased health care utilization. As such, hospitalizations and discharge from the hospital lead to an increased risk of DRP. During hospital admission, often several changes in the drug regimen are introduced. After discharge from the hospital patients often do not know which drugs have to be taken. It was shown that one in five patients experience an adverse event after transition from hospital to home. Half of adverse drug events seem preventable or ameliorable. Frequently occurring DRP can be due to lack of knowledge of drugs and non-adherence and discontinuation with drug treatment, DRP which also may be inter-related. Prescription errors such as dosage problems and incorrect drug choice can also be the cause of DRP. In addition, interactions and contra-indications are common DRP which may also be prescription related.

Several interventions aimed at improving the quality of the pharmacotherapy of patients discharged from the hospital have been described in the literature. These interventions included medication reconciliation and discharge planning. Telephone interview and home visits were also used to identify and resolve DRP experienced by patients after discharge. These interventions resulted in a reduction of adverse drug events and improvement of patients’ drug knowledge and compliance.

Clinical medication review (CMR), which consists of the assessment of medicines prescribed, extraction of information from the medical records and patient counseling, has been introduced as a successful intervention to improve medication safety. CMR, using information from medical records and patient interview, was effective in identifying and resolving pharmaceutical care issues. In an RCT involving patients over 65 using at least five drugs, CMR reduced inappropriate prescribing and adverse events. We found one RCT showing that CMR reduced the occurrence of adverse events among elderly discharged from hospital. Another study demonstrated that CMR improved medication appropriateness among patients discharged from the hospital.

To our knowledge, studies on the effects of CMR among older patients discharged from the hospital on all types of DRP are not available. We therefore studied the effect of medication analysis, treatment analysis, patient interview and counseling by community pharmacists and pharmacy technicians on the occurrence of DRP among older patients discharged from the hospital.
Methods

Setting and participants
The study was designed as a randomized, controlled, intervention study. The design of the study has been described in detail previously and will be described here in brief\textsuperscript{23}. After approval from the ethical committee of the VU University Medical Center several community pharmacies in the Netherlands were asked to participate in the study. A total of 24 community pharmacists agreed to participate in the study. Each pharmacy was instructed to include between 15 and 20 patients who were discharged from the hospital. The pharmacist determined whether a patient was eligible to participate in the study on the basis of the medication used by the patients. Patients 60 years or older using at least five prescribed drugs and discharged from the hospital were eligible to participate in the study. Patients discharged both from a psychiatric or oncology department were excluded, as well as patients discharged to a nursing home. Patients needed to understand the Dutch language. Those who consented were included in the study.

Randomization
In the Netherlands general practitioners and pharmacists are organized in PharmacoTherapeutic Audit Meetings (PTAMs). Within a PTAM 3 pharmacists were potentially eligible for the study of which 2 agreed to participate. Through cluster randomized on the level of PTAM twelve control and twelve intervention pharmacies were randomized. After randomization seven pharmacies were excluded from the study, before the start of the inclusion of patients, because of lack of time of the pharmacists. This study is based on nine intervention pharmacies and eight control pharmacies (Figure 1.).

Intervention
Intervention pharmacists were instructed to perform a CMR, which included a medication analysis, treatment analysis, patient interview and counseling, among elderly discharged from the hospital. To support the CMR, we developed a tool including a checklist of commonly occurring DRP and a semi-structured patient interview script. Development and Testing of the tool have been described elsewhere\textsuperscript{24}. Medication records kept in the electronic pharmacy administration and information systems of the participating pharmacies (PAIS) listing all drugs prescribed and dispensed during the 6 months preceding the date of discharge were printed. PAIS were also used for the identification of possible drug-drug interactions. The semi structured patient interview script was used to identify DRP experienced by patients like ineffectiveness of treatment, side effects, and fear of side effects. In addition, general practitioners were contacted for information about the chronic diseases of each patient. The interventions could include interventions towards prescriber, and towards a pharma-
cist intervention such as dosage change, and practical instructions. The interview and counseling sessions were performed by pharmacy technicians. They were instructed to interview and counsel patients at discharge, after three, six and nine months. The patients were interviewed in the pharmacy, or when unable to visit the pharmacy, at home. During these interviews and counseling sessions potential DRP experienced by the patient after discharge were addressed. Patients were asked about the effects and side effects of their medication. Furthermore, patients were asked whether they were aware of the effects of their medication and whether they experienced side effects.

**Control group**
Control pharmacies provided usual care according to the Dutch Pharmacy Standard. Prescriptions are routinely checked for drug interactions and contraindications by the pharmacy computer system (PAIS)\textsuperscript{23}. Data on medication use was retrieved from the PAIS and general practitioners were contacted for information about the chronic diseases of each patient. Control patients were visited once by a researcher of the study and interviewed about possible DRP experienced after discharge from the hospital. After one year, the drugs used by the patients were assessed again on potentially DRP.

**Outcome measure**
The primary outcome measure in this study is the effect of CMR on the occurrence of DRP of older patients discharged from the hospital. DRP identified with use of the medication analysis in patients of control and intervention pharmacists were measured at baseline and at twelve months by two clinical pharmacologists. Each clinical pharmacologist independently assessed the DRP for each patient, after which the results were compared and differences reconciled. DRP were categorized according to a number of key items using the Pharmaceutical Care Network Europe classification scheme (Table 1)\textsuperscript{25}. During these measurements, the two clinical pharmacologists were blinded. The patient information on drug use did not include a pharmacy number, which could demonstrate that a certain patient belonged to an intervention or a control pharmacy.

**Statistical analysis**
A flow chart is used presenting participants who had a final medication analysis or interview. Differences between responders and non-responders were compared. Baseline characteristics are presented as percentages, means ± SD and interquartile range. The proportion of patients in whom the number of DRP was decreased, unchanged or increased after twelve months, in the control and intervention group, was calculated. Differences between groups were statistically tested using the chi-square test with linear-by-linear association. Linear-by-linear association was used because the change of DRP between baseline and follow-up are ordinal variables.
After determining that the variables were normally distributed, a linear regression analysis was performed using the change in total DRP between baseline and follow-up as the dependent variable. Models were adjusted for age, gender and total number of drugs used in model 1 and in addition adjusted for baseline DRP in model 2. Possible effect modifiers such as age, gender and number of drugs used by the patient that may have interacted with the intervention were analyzed and showed no significant results. In addition, subgroup analyses were made to investigate whether patients in the intervention group, discharged from different departments or with a specific chronic disease, had less DRP after one year, also adjusted for age, gender, number of drugs used, pharmacist level and baseline DRP.

Results

Adaptations to the intervention in practice

As described in the method section, community pharmacies and pharmacy technicians would perform the CMR: the medication analysis, treatment analysis and patient interview and counseling. However, it was not possible for all community pharmacists to perform the CMR as intended, because they experienced a lack of time or there were insufficient pharmacy technicians available. The CMR was therefore mainly performed by two clinical pharmacologists, who identified the DRP for the intervention pharmacies, contacted if needed the GP and contacted the patient if changes in the medication regimen needed to be made.

In addition, patient-perceived DRP at baseline were identified with the use of an interview by the researchers of the study. The counseling of patients was performed by the researchers of the study.

Participants

A total of 489 patients were eligible and 340 patients agreed to participate. Of the 149 patients who refused participation, 121 patients reported to be too ill and 32 patients had no time to participate in the interview. Age and the percentage females among responders and nonresponders were similar. Non responders were slightly older than responders, but the difference was not significant. The mean age and percentage of females among nonresponders and responders was 75.4 ± 8.7 and 78.1 ± 9.0 years and 54% and 48% respectively. A total of 180 patients in the intervention group and 160 patients in the control group completed the baseline interview and review, as shown in Table 1. The number of DRP was identified during the interviews at baseline. In the control group the number of DRP at baseline DRP identified during the interview was significantly lower. After a follow-up of 12 months, there were patients who did not have an interview or DRP assessment with the clinical pharmacologists for various reasons.
Figure 1. Consort (Consolidated Standards of Reporting Trials) flow diagram. + indicates that the pharmacist completed the medication analysis or patient interview after follow up.
– indicates that the pharmacists did not complete the medication analysis or patient interview.
Effect on the occurrence of DRP

The total number of DRP identified by means of review of medication analysis and the patient interview were 253 and 437 in the control group and 271 and 689 in the intervention group respectively. The mean number of DRP identified with the medication analysis at baseline decreased in the intervention group from 1.51 to 1.37 per patient. In the control group, the number of DRP increased from 1.58 to 1.62 DRP. The mean number of DRP per patient identified with the patient interview in the intervention group decreased from 3.88 to 2.33 DRP. In the control group, the mean number of DRP increased from 2.73 to 2.80.

Table 2 shows the proportion of patients in whom the type of DRP was increased, unchanged and decreased after the intervention in the intervention group and in the control group. The proportion of patients with a change of DRP, identified with the medication analysis and the patient interview in the intervention group was significantly different from the control group (p=0.011) and (p=0.023), respectively. In the intervention group, the proportion of patients with a DRP was reduced after twelve months. For the specific DRP, the proportion of patients in whom the number of the DRP, no drug but clear indication and the DRP, fear of side effects, was increased, unchanged or decreased in the intervention group was significantly different from the control group. In the intervention group, the proportion of patients with these DRP was lower.

Regression and subgroup analyses

Table 3 shows the results of the linear regression analysis. In model 1 the difference in the occurrence of DRP between baseline and after follow-up, adjusted for age, gender and number of drugs are presented. The analysis showed that both medication analysis and patient interview resulted in a significant reduction of DRP.

In model 2 the differences in the occurrence of DRP were adjusted for age, gender, number of drugs and the total DRP identified at baseline. This shows that medication analysis resulted in a statistically significant reduction of DRP after adjustment for baseline DRP. The reduction of DRP identified with the patient interview was not statistically significant.

Subgroup analyses showed that the reduction of DRP identified with medication analysis was significantly more pronounced among patients with hypertension (p= 0.011) and heart failure (p= 0.001). The reduction of DRP identified with patient interview was significantly more pronounced among patients with hypertension (p=0.035). The hospital departments from which patients were discharged did not influence the reduction of DRP.
Table 1. Baseline characteristics of patients included in the study.

<table>
<thead>
<tr>
<th></th>
<th>Intervention group (n=180)</th>
<th>Control group (n=160)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of women (%)</td>
<td>89 (49.45%)</td>
<td>94 (58.8%)</td>
</tr>
<tr>
<td>Age in years, mean ± SD (range)</td>
<td>76.01 ± 8.6 (59-95)</td>
<td>74.75 ± 8.7 (60-94)</td>
</tr>
<tr>
<td>Chronic diseases, mean ± SD (range)</td>
<td>2.7 ± 1.3 (1-7)</td>
<td>3.3 ± 1.7 (1-9)</td>
</tr>
<tr>
<td>Number of drugs, mean ± SD (range)</td>
<td>8.9 ± 2.9 (4-22)</td>
<td>8.3 ± 2.9 (4-24)</td>
</tr>
<tr>
<td>Total DRP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medication analysis</td>
<td>271</td>
<td>253</td>
</tr>
<tr>
<td>Patient interview</td>
<td>689</td>
<td>437*</td>
</tr>
</tbody>
</table>

*a= P<0.01 student t-test

Table 2. Proportion of patients with an increased, unchanged or decreased number of DRP after follow-up in the intervention and control groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Increased/Unchanged/Decreased,%*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention</td>
</tr>
<tr>
<td>Medication analysis</td>
<td></td>
</tr>
<tr>
<td>Total DRP’s</td>
<td>8.4/69.0/22.6</td>
</tr>
<tr>
<td>Interactions</td>
<td>2.6/88.4/9.0</td>
</tr>
<tr>
<td>No drugs prescribed but clear indication</td>
<td>6.4/83.2/10.3</td>
</tr>
<tr>
<td>Dose too low</td>
<td>1.9/96.1/1.9</td>
</tr>
<tr>
<td>No clear indication of drug use</td>
<td>0.0/ 99.4/0.6</td>
</tr>
<tr>
<td>Unnecessarily long duration of treatment</td>
<td>4.5/89.7/5.8</td>
</tr>
<tr>
<td>Incorrect drug choice</td>
<td>1.3/94.8/3.9</td>
</tr>
<tr>
<td>Double medication</td>
<td>0.0/97.4/2.6</td>
</tr>
<tr>
<td>Contra-indication</td>
<td>0.0/99.4/0.6</td>
</tr>
<tr>
<td>Patient interview</td>
<td></td>
</tr>
<tr>
<td>Total DRP’s</td>
<td>23.5/20.6/55.9</td>
</tr>
<tr>
<td>No knowledge of drugs used</td>
<td>18.3/48.9/32.5</td>
</tr>
<tr>
<td>Ineffectiveness</td>
<td>0.7/95.7/3.5</td>
</tr>
<tr>
<td>Adverse effects</td>
<td>12.0/52.5/35.4</td>
</tr>
<tr>
<td>Not satisfied with medication</td>
<td>9.9/74.5/17.1</td>
</tr>
<tr>
<td>Fear of adverse effects</td>
<td>5.7/78.0/16.3</td>
</tr>
</tbody>
</table>

Abbreviation: DRP, drug-related problems

*) Percentage of patients in which DRP are increased/unchanged/decreased.

**) P < .05, X² using linear by linear association
**Table 3.** Regression analysis of differences between baseline and follow-up DRP using difference total DRP identified with medication analysis and patient interview as dependent variable.

<table>
<thead>
<tr>
<th>Dependent variable</th>
<th>B (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Model 1</strong></td>
<td></td>
</tr>
<tr>
<td>CMR adjusted for age/gender/number drugs used</td>
<td></td>
</tr>
<tr>
<td>Difference total DRP medication analyses</td>
<td>0.221 (0.043 to 0.398)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Difference total DRP patient interview</td>
<td>1.227 (0.191 to 2.263)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td><strong>Model 2</strong></td>
<td></td>
</tr>
<tr>
<td>CMR adjusted for age/gender/number drugs used and baseline DRP</td>
<td></td>
</tr>
<tr>
<td>Difference total DRP medication analyses</td>
<td>0.231 (0.068 to 0.394)&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Difference total DRP patient interview</td>
<td>0.722 (-0.086 to 1.531)</td>
</tr>
</tbody>
</table>

Abbreviations: DRP, drug-related problems CMR, clinical medication review
95% CI = 95 percent confidence interval
a = p< 0.05
b = p< 0.01

**Discussion**

The present study demonstrated that CMR is an effective method to reduce DRP among older patients discharged from the hospital. The proportion of DRP among patients was reduced. The intervention was more effective among patients discharged from the hospital with heart failure or hypertension.

Several studies showed that CMR, including medication analysis, treatment analysis and patient interview, is an effective method to identify and to resolve existing DRP. However, it should be noted that, in contrast to our study, these studies did not investigate the effects of medication review on the actual occurrence of DRP. In addition, these studies did not include patients discharged from the hospital, and had a shorter follow-up period of their study patients. Krska et al. showed that in particular “the specific DRP, clear indication but no drugs” was considerably resolved by clinically trained pharmacists who had reviewed the drug therapy of older patients. This finding was consistent with the results of our study.

Two studies investigated the effects of CMR among older patients discharged from the hospital. CMR, patient counseling and telephone follow-up reduced the rate of side effects. In contrast to our study, the effect on other DRP than side effects was not studied. Another study showed that CMR resulted in an improvement in prescribing appropriateness. Particularly, problems concerning the dosage of the drugs were reduced. In contrast to our study, their study was focused on improvement in physician prescribing. Neither of these studies analyzed the effect of CMR on all specific problems or described the effect of CMR on specific patient-perceived DRP after hospital discharge.
Our study also showed that CMR and patient counseling resulted in a reduction of patients’ fear of side effects. This is important, because fear of side effects has been shown as a risk factor for non-compliance. We also found that CMR resulted in a more pronounced reduction of DRP in patients with heart failure or hypertension even after adjustment for the number of prescriptions. Some strengths and limitations of the study have to be addressed. The method used to identify the drug problems was validated. The checklist used was developed on the basis of extensive literature search and validated with a Delphi procedure with experts in the field.

There were patients who did not have a follow-up CMR or interview because they were deceased or were placed in a nursing home during the research period. However, we were able to include a large number of patients. This enabled us to demonstrate the effectiveness of combined CMR and patient counseling in this group of patients. A large number of pharmacies participated in the study and patients were discharged from both non-academic and academic hospitals. The results are therefore representative for the population of older patients discharged from hospital and using multiple drugs.

Despite the randomization procedure, DRP identified at baseline with use of the patient interview were significantly higher in the intervention group than in the control group. We adjusted for this difference in our analyses.

Community pharmacies knew whether they were randomized to the intervention or control pharmacies. Control pharmacists could have become more conscious of the possibility of DRP in their patients, thereby becoming more observant and active in resolving DRP. This may have led to an underestimation of the effect of CMR on the occurrence of DRP.

In conclusion, the present study showed that pharmacist-led CMR is an effective method to reduce DRP among elderly discharged from the hospital. In particular, patients with heart failure or hypertension had a pronounced reduction of DRP after a CMR.

Based on our results in this study we recommend pharmacists to consider the implementation of CMR including both medication analysis and patient interview in their daily practice.
Reference List

2. Frazier SC. Health outcomes and polypharmacy in elderly individuals: an integrated literature review. J Gerontol Nurs 2005 September;31(9):4-11.


