Chapter 8

Implications of a clinical medication review followed by a pharmaceutical care plan in primary care of elderly polypharmacy patients with a cardiovascular disorder

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Abstract

Background – To determine whether a clinical medication review followed by a pharmaceutical care plan decreases the number of potential drug-related problems and leads to a positive effect on relevant clinical and laboratory parameters for elderly cardiovascular patients with multiple drug use.

Methods – Elderly polypharmacy patients with a cardiovascular disorder were randomized into two groups. Intervention patients received a clinical medication review, followed by a pharmaceutical care plan developed in cooperation between these patients’ pharmacists and general practitioners (GPs), and agreed to by the patients. Control patients received care as usual. Patient data were collected at the start of the study (t=0) and after one-year follow-up (t=1). Two researchers independently coded the proposed interventions. Information on the interventions performed was collected retrospectively for the control-group patients. The primary outcome was a decrease in potential drug-related problems (DRPs) and pharmaceutical care issues (CIs). As secondary outcome, the effects on cardiovascular risk factors and safety parameters were measured. Statistical analyses were performed using SPSS 21, Mplus 7.1, and SAS 9.2. Differences in general patient characteristics were calculated using one-way ANOVA and Pearson Chi-square test. Multilevel analysis was used to analyze patient outcomes.

Results – Eight primary care settings resulted in a total of 512 patients. An average of 2.2 potential DRPs and pharmaceutical CIs were defined per patient in the intervention group. After one-year follow-up, 47.2% of potential DRPs and CIs were resolved. In total, 156 care interventions were proposed (0.9/patient), 108 of which were implemented after one-year follow-up (69.2%). For control-group patients, a total of 47 proposed care interventions were documented for 255 patients (0.2/patient); after one year, 43 had been implemented (91.5%). The study intervention (p<0.001) and the number of medicines used (p=0.030) had a significant effect on the number of interventions proposed. Small biochemical changes in cardiovascular risk factors did occur, but the differences were small and not considered clinically relevant.

Conclusion – The integrated use of a clinical medication review with a pharmaceutical care plan in a primary care setting supports the detection of and decrease in DRPs and pharmaceutical CIs in almost half of the patients. Its benefit in terms of control of cardiovascular risk factors and safety parameters was relatively low: in general, however, patients were already being well managed at baseline, with a low number of proposed care interventions in the control group. A clinical medication review followed by a pharmaceutical care plan is an extensive and time-consuming process; risk stratification might be necessary to decide which patients might benefit most from this type of intervention.


Introduction

Appropriate prescribing in elderly people needs more attention. The number of medications taken may affect the quality of prescribing and adherence in older persons. A regular medication review has the potential to improve pharmaceutical care in patients. This type of review is defined as “a structured, critical examination of a patient’s medicines with the objective of reaching an agreement with the patient about treatment, optimizing the impact of medicines, minimizing the number of medication-related problems and reducing waste.” Only a clinical medication review, including pharmacist, general practitioner (GP), and patient, can be expected to improve pharmaceutical care. In particular patient involvement is important both for the identification of drug-related problems (DRPs) and for the long-term success of the intervention performed.

Various medication review methods have been described. Clinical pharmacists are able to review care-home patients’ medication and make recommendations to GPs. These medication reviews, conducted by pharmacists, have been investigated in three studies in the Netherlands. A decrease in DRPs was shown after a pharmacist-conducted medication review of elderly patients receiving their medicines via automated dispensing machines. In a hospital setting, it was concluded that structured pharmaceutical care, according to a protocol, leads to more changes in drug therapy compared to care as usual. A clinical medication review intervention, including pharmacists, GPs, and patients, has demonstrated that such an intervention may prevent medication-related hospital admissions but without any statistically significant effect on the number of adverse drug events, quality of life, or survival. Assessment of a patients’ pharmacotherapy includes checking whether all indications are treated appropriately, whether the medication treatment is effective and safe, and whether a patient has adhered to the proposed therapy. Potential problems concerning pharmacotherapy can be defined as a potential DRP, based on the concept of Cipolle et al., or on the basis of a pharmaceutical care issue (CI). The literature defines different sub-groups of patients with known non-adherence and/or medication problems. The methods for enhancing medication safety in older persons may be directed towards aspects of specific types of drugs, such as anticholinergic drug burden, under-prescribing, or the use of the Medication Appropriateness Index, Beers criteria, or the STOPP and START criteria. Elderly patients with a cardiovascular disorder use multiple medicines that require regular monitoring using relevant clinical and laboratory parameters related to cardiovascular risk assessment (blood pressure and cholesterol levels) and safety (renal function and potassium). This patient population could benefit from a clinical medication review with adequate follow-up and was therefore chosen as our study population. We combined a clinical medication review with a web-based pharmaceutical care plan to facilitate integrated care and to systematically structure joint use of patients’ medical and pharmaceutical records and to document the integrated information and interventions for follow-up.

The main aim of this study is to determine whether a clinical medication review followed by a pharmaceutical care plan decreases potential DRPs and CIs, along with a positive effect on cardiovascular risk factors and safety parameters for elderly polypharmacy patients with a cardiovascular disorder.
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Methods

A randomized controlled trial was performed in the primary care setting of the Netherlands. Community pharmacists (n=500; 25% of all pharmacies in the Netherlands) were invited by letter to participate in the study. Pharmacies were randomly selected in an area defined by the sponsor of the study. After consenting, the pharmacists subsequently contacted the various GPs and asked for their participation. Good cooperation between pharmacists and GPs, and the willingness to share patient data were prerequisites. Participating pharmacies and GP practices were connected to a newly developed web-based pharmaceutical care plan (W-PCP) application. This web-based application uploaded all patient data from pharmacy and GP computer systems in order to combine information about diagnoses, medicines prescribed, and clinical and laboratory parameters in one patient file, accessible to both patient's pharmacist and GP. Elderly patients with polypharmacy, aged ≥ 60 years, and with a cardiovascular disorder were selected. Patients needed to be taking at least five medicines for chronic conditions, with at least one of these medicines prescribed for a cardiovascular disorder (ATC class C). Patients who did not speak the Dutch language or who were mentally impaired were excluded.

Patient inclusion transpired between August 2009 and June 2010. Patients were approached by letter. After informed consent, patients were randomized into an intervention or a control group. Randomization occurred based on unique patient identification numbers (IDs) in the pharmacy computer system (odd number: intervention group; even number: control group). Intervention-group patients received an invitation to consult their pharmacist for a clinical medication review. The pharmaceutical care plan was subsequently developed in cooperation between the patient’s pharmacist and GP, and agreed to by the patient. Each evaluation of the pharmaceutical care plan for intervention patients consisted of three components: (1) potential DRPs and CIs, (2) proposed care interventions to reach treatment goals, and (3) implemented care interventions. Patients from the control group received care as usual. All patients were followed-up for one year. The total study period per site was 18 months, with consultations and medication reviews performed during the first six months. The last data collection finished in December 2011.

An independent Ethics Committee (RTPO/Leeuwarden, the Netherlands) reviewed the study protocol. The protocol was graded as a clinical intervention study with no risk for patients. To guarantee patient privacy, patient data from the W-PCP were anonymized before the database was provided to the researchers. Forms containing patients’ names and addresses remained in the pharmacy and the researchers had no access to them.

Support

A learning module of the W-PCP application was provided by the researchers to all participating pharmacists and GPs. During the study period technical assistance was available. Before the start of the study, all participating pharmacists received a one-day training course on communication skills with GPs and patients. Additional written information about performing a clinical medication review was provided.
review was provided. During the study period, researchers visited study sites regularly in order to monitor the time schedule of the study and provide assistance.

Data collection
During the study period, patient data were uploaded regularly, depending upon patients’ consultations, and collected in the W-PCP application. Two measurements were performed, one at the beginning of the study (t=0) and one after one-year follow-up (t=1). Patient data consisted of general patient information (age, gender), episodes (ICPC-coded\textsuperscript{23}), medicines dispensed (ATC-coded\textsuperscript{22}), and clinical and laboratory parameters. Patient data was provided to the researchers in a database (Microsoft Access 2010).

The primary outcome of this study was a decrease in potential DRPs and CIs, expressed as a percentage of resolved DRPs and CIs. As a secondary outcome, the differences in clinical and laboratory parameters were measured. Pharmaceutical care plans consisted of “free text” entered by the healthcare providers. Two researchers (MG, author, and EM, not an author) coded all individual care plans independently. All codes were compared and inconsistencies discussed until agreement was reached. For control-group patients, information on care interventions was collected retrospectively.

Sample size calculation and analysis
Two sample size calculations were performed to determine the number of patients needed for both groups. Our main aim was to demonstrate a 25% decrease in potential DRPs and CIs. Based on a paired means power analysis using simulation and Wilcoxon signed-rank test using alpha=0.05 and a power of 0.80, we needed 13 patients per pharmacy in the intervention group. The second aim was to demonstrate a 10% improvement in clinical and laboratory parameters. Based on a two independent proportions power analysis using alpha = 0.05 and a power of 0.80, we needed 400 patients for each group. Our aim was to recruit patients from 10-12 study sites. Based on our second sample size calculation, and considering dropouts as a consequence of losses to follow-up, our aim was to include 100 patients per study site.

Statistical analyses were performed using SPSS 21, Mplus 7.1, and SAS 9.3. Differences in patient characteristics were calculated using one-way ANOVA and Pearson Chi-square test. Multilevel analysis was used to analyze the nesting structure. Effects of the study intervention on number of care interventions performed were analyzed using a two level Multilevel analysis with Poisson regression analysis, where patients (level 1) were nested within GPs (level 2). As model information, we used the Akaike Information Criteria (AIC) and the Bayesian Information Criteria (BIC) to compare the relative goodness-of-fit of the presented models. A model with a smaller information criterion fits better. Effect of the study intervention on clinical endpoints was analyzed using a three level Multilevel analysis, including measurements (t=0 and t=1) (level 1) nested within patients (level 2) and patients nested within GPs (level 3). Results were considered statistically significant at a significance level p < 0.05.
Results

In total, eight study sites recruited 512 patients: 248 in the intervention group and 264 in the control group. Overall inclusion rate for patients was 24.4%. Pharmacists and GPs did not manage to perform clinical medication reviews for all intervention patients during the study period due to time limitations. Therefore, 70 patients, originally randomized into the intervention group, were analyzed as a separate group since they did not receive any part of the intervention (Figure 1). Patient characteristics were comparable between groups (Table 1).

In total, 394 potentially harmful DRPs and CIs were defined for 178 intervention patients (2.2/patient). After one-year follow-up, 186 potential DRPs and CIs (47.2%) were resolved; 208 DRPs and CIs (1.2/patient) were not resolved or with unknown outcome from the available data. During the study period, 156 care interventions were proposed (0.9/patient) (range 0 – 5 per patient) of which 108 were implemented after one year (69.2%). Figure 2 shows the number of proposed and implemented care interventions per category. Most proposed care interventions were related to drug-taking/adherence, monitoring (e.g., additional clinical values), and unnecessary drug therapy. Categories

Figure 1. Flow diagram – patients.
### Table 1 – Patient characteristics (n=512) at time of inclusion (t=0).

<table>
<thead>
<tr>
<th></th>
<th>Intervention patients with intervention n=178</th>
<th>Intervention patients without intervention n=70</th>
<th>Control n=264</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Mean (SD))</td>
<td>(Mean (SD))</td>
<td>(Mean (SD))</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>72.5 (7.735)</td>
<td>71.8 (8.372)</td>
<td>73.1 (7.797)</td>
<td>0.433c</td>
</tr>
<tr>
<td>Gender, male (%)</td>
<td>46.1</td>
<td>52.9</td>
<td>47.3</td>
<td>0.622d</td>
</tr>
<tr>
<td># medicines&lt;sup&gt;a&lt;/sup&gt;</td>
<td>8.3 (2.721)</td>
<td>8.0 (3.277)</td>
<td>7.9 (2.926)</td>
<td>0.591e</td>
</tr>
<tr>
<td># episodes&lt;sup&gt;b&lt;/sup&gt;</td>
<td>14.6 (8.210)</td>
<td>14.3 (6.475)</td>
<td>14.8 (8.683)</td>
<td>0.891f</td>
</tr>
</tbody>
</table>

SD = Standard Deviation; # = number.

<sup>a</sup> ATC-coded<sup>22</sup>
<sup>b</sup> ICPC-coded<sup>23</sup>
<sup>c</sup> One-way ANOVA
<sup>d</sup> Pearson Chi-Square test

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**Figure 2.** Number of proposed and implemented interventions based on DRPs/CIs retrieved from the pharmaceutical care plan (n=178).

DRP = Drug Related Problem; CI = Care Issue.
with the most implemented interventions: unnecessary drug therapy (e.g., stop medicine) (91.7%), dosage too low (e.g., increase dosage) (90.0%), and dosage too high (e.g., decrease dosage) (80.0%). In the control group, a total of 47 proposed care interventions were documented for 255 patients (0.2/patient) (range 0 – 4 per patient). Information was missing for 9 patients. Of the 47 proposed care interventions, 43 were implemented after one year (91.5%).

Six different models analyzed the effect of the study intervention (model 1), age and gender (model 2), number of medicines (model 3), number of episodes (model 4), all independent variables (model 5), and the study intervention together with number of medicines (model 6). The study intervention and the number of medicines showed a significant effect on the number of care interventions proposed. Table 2 shows the effect of models 5 and 6. Looking at the differences between models 5 and 6, AIC and BIC were lower for model 6 and thus considered preferable. According to Raftery24 a difference of over 10 between the BIC of models 5 and 6 is associated as “very strong” evidence. Table 3 shows the effect of the study intervention on cardiovascular risk factors and safety parameters. Patients from the intervention group had a significantly decreased diastolic blood pressure after one-year follow-up (79.8 to 76.8 mmHg; p=0.008). HDL-cholesterol showed a small but significant increase in two groups (intervention patients with intervention: 1.29 to 1.37 mmol/L; p=0.021; intervention patients without intervention: 1.26 to 1.37 mmol/L; p=0.039). LDL-cholesterol showed a small but significant decrease in the control group (2.61 to 2.58 mmol/L; p=0.032). Other parameters showed no significant effect.

### Table 2 – Effect of independent variables on number of care interventions proposed (n=433 patients) (*sign. (P value < 0.05)).

<table>
<thead>
<tr>
<th></th>
<th>Estimate</th>
<th>SE</th>
<th>P value&lt;sup&gt;c&lt;/sup&gt;</th>
<th>Estimate</th>
<th>SE</th>
<th>P value&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study intervention</td>
<td>1.657</td>
<td>0.317</td>
<td>&lt; 0.001&lt;sup&gt;*&lt;/sup&gt;</td>
<td>1.662</td>
<td>0.317</td>
<td>&lt; 0.001&lt;sup&gt;*&lt;/sup&gt;</td>
</tr>
<tr>
<td>Age</td>
<td>0.005</td>
<td>0.013</td>
<td>0.723</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>-0.158</td>
<td>0.142</td>
<td>0.265</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td># medicines&lt;sup&gt;a&lt;/sup&gt;</td>
<td>0.045</td>
<td>0.023</td>
<td>0.049&lt;sup&gt;*&lt;/sup&gt;</td>
<td>0.055</td>
<td>0.025</td>
<td>0.030&lt;sup&gt;*&lt;/sup&gt;</td>
</tr>
<tr>
<td># episodes&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.018</td>
<td>0.012</td>
<td>0.121</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model fit information</td>
<td></td>
<td></td>
<td></td>
<td>AIC</td>
<td>715.8</td>
<td>714.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>BIC</td>
<td>748.4</td>
<td>734.6</td>
</tr>
</tbody>
</table>

SE = Standard Error; # = number; AIC = Akaike Information Criteria; BIC = Bayesian Information Criteria.
<sup>a</sup> ATC-coded<sup>22</sup>
<sup>b</sup> ICPC-coded<sup>23</sup>
<sup>c</sup> Multilevel Analysis
This study shows that a clinical medication review followed by a pharmaceutical care plan resolves almost 50% of potential harmful DPRs and CIs (1.0/patient). Differences in percentages of care interventions implemented were observed in different categories. Higher percentages were found for "easy to implement" interventions like stopping a medicine or adjusting a dosage. Interventions from other categories taking more time, for example, in the category "additional drug therapy required", were implemented less frequently. Per patient, an average of 2.2 potential harmful DRPs and CIs were formulated in the pharmaceutical care plan. This is less compared to other studies. In a similar study, 3.5 DRPs and CIs per patient were found\(^1\), and, after a medication review in patients using an automated drug-dispensing system, even a mean of 8.6 potential DRPs per patient was observed\(^2\). A reason for the lower number of DRPs and CIs in our study could be the fact that the patients seemed well monitored – looking at the initial clinical and laboratory values (Table 3) – and

### Table 3 – Clinical and laboratory parameters (mean) before study intervention (t=0) and after one-year follow-up (t=1) (* sign. (P value < 0.05)).

<table>
<thead>
<tr>
<th></th>
<th>Intervention patients With intervention</th>
<th>Intervention patients without intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>t=0</td>
<td>t=1</td>
<td>P value*</td>
</tr>
<tr>
<td>BPsystolic (mmHg)</td>
<td>143.7</td>
<td>142.3</td>
<td>0.502</td>
</tr>
<tr>
<td>BPdiastolic (mmHg)</td>
<td>79.8</td>
<td>76.8</td>
<td>0.008*</td>
</tr>
<tr>
<td>Serum LDL-chol. (mmol/L)</td>
<td>2.72</td>
<td>2.63</td>
<td>0.337</td>
</tr>
<tr>
<td>Serum HDL-chol. (mmol/L)</td>
<td>1.29</td>
<td>1.37</td>
<td>0.021*</td>
</tr>
<tr>
<td>Serum Chol. (mmol/L)</td>
<td>4.77</td>
<td>4.77</td>
<td>0.976</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>29.8</td>
<td>29.5</td>
<td>0.371</td>
</tr>
<tr>
<td>Blood Glucose (mmol/L)</td>
<td>6.42</td>
<td>6.56</td>
<td>0.460</td>
</tr>
<tr>
<td>HbA1c (mmol/mol)</td>
<td>6.25</td>
<td>6.35</td>
<td>0.213</td>
</tr>
<tr>
<td>Creatinine clearance (mL/min)</td>
<td>65.1</td>
<td>65.4</td>
<td>0.933</td>
</tr>
<tr>
<td>Serum Sodium (mmol/L)</td>
<td>139.7</td>
<td>139.9</td>
<td>0.575</td>
</tr>
<tr>
<td>Serum Potassium (mmol/L)</td>
<td>4.2</td>
<td>4.2</td>
<td>0.601</td>
</tr>
</tbody>
</table>

BP = Blood Pressure; BMI = Body Mass Index.
\(^*\) Multilevel Analysis.
this should be seen in the context of the very low incidence of proposed care interventions in the control group (0.2/patient).

Furthermore, less skill and experience in performing a clinical medication review on the part of primary healthcare providers could have influenced our findings. It is important to have a patient interview as part of the medication review process in order to define DRPs\(^4\). For this reason, pharmacists participating in our study received a one-day training course in communication skills and additional written information about how to perform a clinical medication review. More intensive training and experience might help pharmacists perform a clinical medication review better and so define more DRPs. Another reason could be a selection bias, because community pharmacists who had a good relationship with their GPs were recruited, which could have had a positive effect on the quality of medication therapy management. In addition, our study was conducted in regular pharmacies and thereby could reflect regular daily practice more than in studies that those studies entailing an extensive training course for pharmacists\(^11\) or with medication reviews performed by independent pharmacists with several years of experience in performing medication reviews\(^9\).

Data on interventions performed on control-group patients were collected retrospectively and included only those care interventions where the pharmaceutical care problem was actively documented as a potential DRP and/or CI. A change in medication without a specific documented reason was not included in our data. Therefore, these data might underestimate the number of care interventions for control-group patients and specifically proposed interventions that were not implemented. In daily practice, we expect that, when a pharmacist proposes an intervention to a patient’s GP, not all the proposed interventions will be actively documented in the patient file, especially when the GP and/or patient does not agree with the intervention. Many medication changes occur during a patient’s treatment, but the reason for a care intervention is not always documented. The second objective of our study, that related to the patient efficacy outcome in terms of improvement in cardiovascular risk factors, showed small biochemical changes. It should be noted that in our study baseline clinical and laboratory parameters already showed acceptable values, so the room for improvement was small. Biochemical changes did occur, including changes in HDL- and LDL-cholesterol, but differences were small and not considered clinically relevant. We performed this study in primary care settings with a certain level of cooperation between pharmacists and GPs, who more commonly discuss patient outcomes on a regular basis. Settings where cooperation is less common could show an increased improvement in parameters. In future studies the effects of level of cooperation between pharmacists and GPs on patient outcomes would be of interest.

One pharmacist voluntarily registered time spent per patient, indicating an average of 145 minutes per patient with the GP spending an average of 30 minutes per patient. Patient consultation took an average of 30-60 minutes/patient. This exemplifies the fact that our extensive study intervention takes up a lot of time for healthcare providers. The study protocol had some main requirements about performing the intervention and data collection (involvement of pharmacist, GP, and patient and the use of the W-PCP application), but organizational matters were not described in detail. It
was our intention to allow the practice setting to develop this, as was considered appropriate. Each site could decide how to plan patient consultations and discussions of the care plans by pharmacist and GP. The study sites were visited regularly to monitor the progress and quality of the study. The main reason for this approach was to have the participating healthcare providers (partly) involved in the implementation of the study and thereby more motivated to perform it. A second reason for this approach was to include the intervention in their daily routine, hoping the medication reviews would be continued after completion of the study. However, since the medication reviews took up a lot of time and reimbursement was not available outside the study setting, none of the study sites did continue with the medication reviews after the study was finished. Thus, reimbursement of these services is essential in order to implement clinical medication reviews and pharmaceutical care plans in daily practice. Moreover, tools need to be developed to document interventions and to monitor follow-up, which are easy to implement. These problems related to time, organization, and funding should be seen in the context of the small benefit obtained in terms of cardiovascular risk factors and safety parameters. We question therefore whether this intervention is actually necessary for all patients who fit our inclusion criteria. It might be more suitable for more complex patients with multiple potential DRPs at baseline. Age and number of medicines used are not enough to define patients suitable for a clinical medication review. Risk stratification might be necessary to decide which patients might benefit from a clinical medication review and which patients might benefit sufficiently from a medication review on a lower, more customary level. Dutch pharmacies all have access to an extensive computer system where automatic checks are performed on drug-drug interactions, contraindications, and duplicate medications. Figure 2 shows that these care issues did not occur in our study population. Instead, they are all dealt with during the daily dispensing of medicines, based on the principle that the pharmacist has approved all dispensed medications after consulting the patient or prescriber.

Limitations
A lower number of patients than needed for sufficient power in this study were recruited (512 vs. 800). It was hard for pharmacists to motivate GPs to participate in the trial. More than 25 pharmacists responded to our letter, but only eight actually decided to participate. Furthermore, during the study period it was hard for pharmacists and GPs to perform clinical medication reviews for all intervention patients due to limited time. As a consequence, 70 patients (28%) from the intervention group had not received any part of the intervention by the end of the study period. In the design of our web-based pharmaceutical care plan the decision was made to have “free text fields” for the care plans instead of pre-defined codes. The main reasons for this were so as not to bother healthcare providers too much with additional information to document, and to prevent differences in interpretation and coding by different healthcare providers. Therefore, information from the care plans was coded after the study period by the researchers. A total of thirty-six potential
harmful DRPs and CIs were not described properly and could not be coded. This might have created bias.

Conclusions
Healthcare providers sharing information electronically are capable of performing integrated care for their patients by conducting clinical medication reviews and developing pharmaceutical care plans. The importance of documenting patient care was demonstrated, even when interventions were proposed but not implemented. The integrated use of a clinical medication review with a pharmaceutical care plan supports detection and decreases DRPs and CIs. However, its benefit in terms of efficacy and safety parameters is relatively low in a primary, well-regulated, low-risk population. It might have been more efficient in terms of outcomes if a higher-risk target group had been selected.

Funding
For each patient in the intervention group the healthcare insurance company Menzis (Enschede, the Netherlands) provided a total amount of € 210 to reimburse pharmacists and GPs for their clinical medication review services.

Conflict of Interest
No conflicts of interest have been declared.

Acknowledgements
We thank all participating pharmacists, GPs, and patients for their collaboration in this study. We thank Eva Mulder, PharmD, for her help with the coding of the interventions in the individual care plans. We thank Geert van der Werf, PharmD, for his help during the study.
References


Chapter 8


