Summary
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Solving drug related problems in older patients with polypharmacy discharged from hospital

Chapter 1 is a general introduction to the subject of this doctoral thesis which concerns the identification and prevention of DRP in older patients using multiple drugs for the treatment of a chronic disease (polypharmacy). DRP are circumstances or events related to (long term) drug treatment which are known to interfere with desired health outcomes and increase the risk of further morbidity and hospitalisation. They include prescription errors, unwanted pharmacological effects including those caused by metabolic alterations, non-adherence and inefficacy of treatment. In the case of older patients, polypharmacy, intentional or unintentional non-adherence to treatment, hospitalisation and hospital discharge are major risk factors associated with the occurrence of DRP. DRP can be prevented by applying a variety of measures like the use of checklists and protocols to support the selection of appropriate medication, discharge planning medication reconciliation, individual dose packaging and patient counselling. In contrast to these separate measures, the clinical medication review (CMR) is a comprehensive intervention that can be used to prevent, identify and resolve possible DRP. Critical to the CMR is the input of the patient and the cooperation between pharmacist and GP. The medication used by the patient is reviewed in the context of the condition of the patient and the way how patients organize the use of medication in their lives. The primary objective of the thesis was to study the effects of a CMR by community pharmacists on the occurrence of DRP among older patients with polypharmacy discharged from the hospital by means of a randomized controlled intervention study (RCIS). For this purpose a practical medication review tool was developed. A checklist listing medication-related DRP commonly associated with the medication of older patients with chronic diseases and a structured interview script to identify DRP experienced by patients and their causes, were two essential elements of the tool. The subsequent chapters describe the development of the medication review tool and its use in the RCIS. In addition, the effect of the review on health care utilization and associated costs with a focus on rehospitalisation was investigated.

Chapter 2 describes the results of an observational study in which specific prescriber- and patient-related DRP of older patients with polypharmacy discharged from hospital were investigated. For this purpose pharmacists conducted a medication review using a checklist listing specific prescriber-related DRP and whereas DRP experienced by patients were identified by means of a semi-structured interview. Determinants associated with the occurrence of DRP of this patient group were also investigated. This study showed that DRP occur frequently among older patients with polypharmacy discharged from hospital. The number of drugs used was significantly associated with the number of DRP. Moreover, patients with type 2 diabetes mellitus had significantly
more DRP than those without the disease whereas patients discharged from the pulmonary departments also had more DRP than those discharged from other departments. Using the checklist most frequently observed prescriber-related DRP included the absence of a prescription with a clear indication present, an unnecessarily long duration of treatment, an incorrect drug choice, a dose that was too low and drug-drug interactions. The most common patient-related DRP identified were side effects and a lack of knowledge on the purpose and use of the medication.

Chapter 3 concerns the design of the randomized controlled intervention study (RCIS). The RCIS comprises a control group and an intervention group. Patients, aged over 60 years, discharged from general and academic hospitals, using five or more prescription drugs for the treatment of a chronic disease participated in the study. Participating pharmacies were electronically randomized as a control or intervention pharmacy. DRP of patients of control and intervention pharmacists were assessed at baseline and at 12 months by two clinical pharmacologists. Pharmacy technicians were instructed to interview and counsel patients at discharge, after three, six and nine months. The counselling sessions are based on the cognitive behaviour treatment principles. Patients adherence towards drug use was determined using the Medication Adherence Report Scale (MARS). Linear regression analysis was performed to analyze the effect of the CMR on the occurrence of DRP. Subgroup analyses were used to investigate the effectiveness of the intervention in specific patient groups. Primary outcome measures were the difference in occurrence of DRP between the intervention and control groups and adherence with drug use. Secondary endpoints were attitude towards drug use, incidence of re-hospitalisations as the result of DRP, functional status of the patient, quality of life and the cost-effectiveness of the intervention. Health care costs made by the patient were assessed using monthly costs calendars.

Chapter 4 and 5 present the results of the RCIS on the effect of a CMR on the occurrence of DRP among older patients with polypharmacy discharged from hospital. The methods and results are discussed in more detail in chapter 5.

The CMR consists of a medication and treatment analysis by a community pharmacists and patient interview by pharmacy technicians. The results of RCIS show that both medication analysis and patient interview resulted in a significant reduction of DRP. In particular the DRP ‘no drug but clear indication’ and ‘fear of adverse effects’ were reduced. The beneficial effect of the CMR was more pronounced in patients with heart failure or hypertension.

Chapter 6 concerns the development of a practicable, structured and comprehensive tool for pharmacists and GP to conduct a CMR. The tool is based on the most frequently occurring chronic diseases in older patients in the Netherlands and the medicines most frequently used in the treatment of these disorders. The tool was developed on the basis of treatment guidelines literature.
data on DRP and the expertise of an expert panel comprising clinical pharmacologists, geriatricians, GP and pharmacists. The perspective of the patient was addressed by including DRP related to treatment effects experienced by the patient. For the identification of these DRP a script of a semi-structured interview was developed. The tool was optimized and validated by means of a content validity procedure consisting of a consensus review by an expert panel, subsequent testing in an RCIS, and a second round of expert evaluation to address shortcomings observed in the RCIS. Eventually the tool developed consisted of 126 DRP divided by 20 sections according to physiological systems and diseases, and includes a semi-structured interview script for a patient interview.

Chapter 7 provides the results of a descriptive study on the beliefs, satisfaction with information received about medication and self-reported adherence of older patients with polypharmacy after hospital discharge. Data were derived from questionnaires sent to the patients after hospital discharge. The results of the study showed that patients had strong beliefs about the necessity of using their medication and were less concerned about the potential risks of medication use. They had fewer negative beliefs about their medicines being addictive, but had more negative beliefs about doctors overusing medicines. All patients were satisfied with the information they received about their drugs. The study showed that emphasizing the importance of using drugs for the patients’ health and reducing negative beliefs about drugs being overused by doctors, increases the adherence to medication of older patients with polypharmacy after hospital discharge.

Chapter 8 investigates the effect of CMR on health care utilization and investigates whether CMR is a cost effective method to reduce DRPs in patients using a combination of drugs for the treatment of a chronic disorders who are discharged from a hospital. The data for this cost-effectiveness study were collected as part of the RCIS. The clinical outcome measure of this study was the number of DRP and health care utilization. Data on health care use was assessed from a societal perspective using monthly costs calendars in which costs were prospectively determined by the patient. Resources included in the calendars were visits to the GP, medical specialist, and physiotherapist, visits at home by a GP, use of home care and rehospitalisation. The use of informal care such as from neighbours, family and friends was also included in the calendars. A CMR in this group of older patients led to a non-significant reduction in DRPs and higher health care use. The number of re-hospitalizations was significantly higher after CMR. The mean number of days of readmission was also higher in patients in the intervention group. The intervention proved not cost-effective in this population of highly vulnerable patients.

Chapter 9 provides the general discussion of this thesis. In line with literature data, the results of the RCIS show that a CMR is effective in reducing DRP of older patients with polypharmacy
discharged from hospital. The issue of cost-effectiveness might be addressed by developing interventions specifically aimed at the reduction of re-hospitalization of high risk patients. Implications, limitations and future directions are discussed.