Summary
In chapter 1 (the general introduction) the subject of inappropriate prescribing, inappropriate medication use and clinical medication reviews (CMR) is introduced. A CMR is an intervention that aims to reduce inappropriate prescribing and medication use. Three important gaps in the literature for CMRs are introduced: the lack of clinical effectiveness, the best target group for CMRs and patient participation. The implementation of CMRs in primary care settings in The Netherlands and worldwide poses some important feasibility challenges.

Furthermore, the rationale and outline of the thesis was presented in this chapter, in which we aimed to answer the following research questions:

1. What is known in the literature about ways of patients participation in the medication review process and its effects on the outcomes of a medication review?
2. Can patient participation in medication reviews be achieved via a questionnaire instead of an interview?
3. What is the (cost)-effectiveness of an optimized clinical medication review on quality of life and geriatric problems in comparison with usual care, in older patients with geriatric problems presented in general practice?
4. What is the implementation fidelity of optimized clinical medication reviews in the setting of general practice?

Chapter 2 includes a systematic literature review to answer the first research question. We systematically searched and reviewed the literature on the subjects of patient participation and medication reviews. In total, 37 studies with a variety of study designs met the inclusion criteria. In all studies patient participation in medication reviews was limited to the level of information giving by the patient to the professional, mainly on actual drug use. The effects of patient participation were not frequently studied and poorly described. We found some evidence that involving patients in medication reviews might result in a better identification of drug related problems (DRPs) as well as improved knowledge and patient satisfaction. However, no evidence on patients’ health outcomes was found.
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In chapter 3, we described the development of a patient questionnaire as preparation for a CMR and an agreement study in 97 older community-dwelling patients to answer the second research question. In this study the agreement between patient information on actual medication use and occurrence of DRPs obtained with a questionnaire was compared with information obtained during an interview at home. Of all medications used, almost 90% was reported identically in the questionnaire and the interview. However, agreement for the complete medication list was only found for 45% of the patients. With respect to DRP level, agreement between questionnaire and interview amounted to 75%. The number of medications and DRPs reported in the interview was higher than in the questionnaire. Agreement tended to be lower in vulnerable patients characterized by ≥4 chronic diseases, patients using ≥10 medications and those with a low health literacy. Taking the limitations into account, a questionnaire seems a suitable tool for medication reviews that may replace an interview for most patients.

In chapter 4, we describe the design of the Opti-Med intervention, a cluster randomised controlled trial (RCT). The aim was to include 500 patients, 250 in each arm from 20 general practices. The Opti-Med intervention was designed as an innovative intervention applying an optimally facilitated, prepared and structured problem-oriented CMR, with the specific objective to tackle the most important obstacles for large scale implementation of CMRs.

In chapter 5, the results concerning the effectiveness of the Opti-Med intervention have been presented to answer the third research question. In total, 518 older patients from 22 general practices who consulted their general practitioner for a geriatric problem were included. No significant differences between the intervention and control group and over time were found for the primary outcome measures (quality of life and geriatric problems), and for two secondary outcome measures: medication satisfaction and adherence. The percentage of solved DRPs after six months was significantly different between the intervention and the control group. The Opti-Med intervention resulted in 22% more solved DRPs compared to usual care. However, the higher percentage of solved DRPs in the intervention group did not result in effects on the patients’ health.
In chapter 6, the cost-effectiveness study of the Opti-Med intervention, which was performed alongside the Opti-Med effectiveness study, has been presented, to answer the third research question. Total societal costs in the intervention group were €684 higher than in the control group, but this difference was not statistically significant (95% CI -1142 ; 2387). Cost-effectiveness acceptability curves showed that for solved DRPs, the probability of the intervention being cost-effective reached 0.95 at a WTP of €2100 per solved DRP. For all other outcomes (quality-adjusted life years (QALYs), quality of life and changes in geriatric problems), the probability was low at all willingness-to-pay (WTP) values (i.e. range 0.25 ; 0.49). Optimized CMRs were not considered cost-effective compared to usual care.

In chapter 7, we described a quantitative and qualitative process evaluation alongside the Opti-Med effectiveness study according to the Conceptual Framework for Implementation Fidelity, to answer the last research question. Adherence to the intervention and moderating factors for implementation fidelity were evaluated per key intervention component. Some elements, such as patient selection and preparation of the medication analyses were carried out by the researchers instead of the practice nurses. Cooperation between expert teams’ members (physician and pharmacist) and the use of an online decision-support medication evaluation tool facilitated implementation. Barriers for implementation were time constraints in daily practice, software difficulties with patient selection and incompleteness of medical files. The total time investment of healthcare professionals for the Opti-Med intervention was on average 94 minutes per patient. Overall, the implementation fidelity was moderate to high for all key intervention components. The absence of effectiveness of the intervention with respect to its primary outcomes could not be explained by insufficient implementation fidelity.

In chapter 8 (general discussion) I reflect on all the findings in the light of the current evidence and clinical practice. The most important methodological considerations and possible explanations for the absence of effectiveness and cost-effectiveness are discussed. They range from the definition of the target group, the implementation fidelity, the selection of outcome measures to the duration of the follow-up period. In spite of a moderate to good implementation fidelity, the Opti-Med CMRs were not effective for health outcomes and also not cost-effective as compared to usual care. There seems to be a mismatch in the evidence for the effectiveness on patient’s health outcomes and the current practice to conduct mandatory CMRs in The Netherlands as well as in many other developed countries. With the current approach, a CMR has developed into an inefficient tool. First, before proceeding further a high-risk target group that benefits most from CMRs in terms of health outcomes should be identified.
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