


Original Research

For which patient subgroups are there positive outcomes from a medication review? A systematic review

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Abstract

Background: A medication review is a possibility to assess and optimise a patient's medicine. A model that includes a medication review and a follow-up seem to provide the best results. However, it is not known whether specific subgroups of patients benefit more from a medication review than others.

Objective: This literature review summarises the evidence that is available on which patient subgroups exist positive outcomes from a medication review carried out in a primary care setting.

Methods: We performed a PICO analysis to identify keywords for setting, medication review and effect. We then conducted a search using the PubMed database (2004 to 2019) to identify studies relevant for our investigation. A screening process was carried out based on either title or abstract, and any study that matched the aim and inclusion criteria was included. All matching studies were obtained and read, and were included if they met predefined criteria such as study design, medication review and primary care. The studies were divided into subgroups. First, each subgroup was divided according to the studies' own definition. Secondly, each subgroup was allocated as either risk patients if the subgroup described a specific patient subgroup or risk medication, if the subgroup was defined as using a specific type of medication. This was done after discussion in the author group.

Results: 28 studies from a total of 935 studies were included. Identified studies were divided into either risk patients; frail, recently discharged or multimorbid patients, or risk medication; heart medication, antithrombotic medication, blood pressure lowering medication, antidiabetic medication, anti-Parkinson medication or medication increasing the risk of falls. The subgroups identified from a medication review in primary care were defined as being frail, recently discharged from hospital or multimorbid (risk patients), or defined as patients using anticoagulant or blood pressure lowering medication (risk medication). Most of the medication reviews in the studies that showed an economic effect included at least one follow-up and were delivered by a pharmacist.

Conclusions: The literature review demonstrates that medication reviews delivered by pharmacists to specific subgroups of patients are a way of optimising the economic effect of medication reviews in primary care. This is obtained by reducing health-related costs or the number of contacts with primary or secondary health care services.

Keywords

Pharmacists; Community Pharmacy Services; Drug Utilization Review; Multimorbidity; Frail Elderly; Outcome Assessment, Health Care; Systematic Reviews as Topic

INTRODUCTION

A medication review is a method to optimise the patient's treatment with medicine. Several different names and models of the service have been described, including Medication Review, Medicines Therapy Management, Drug Utilization Review and MedsCheck.^{1,6} They all consist of a medication reconciliation followed by identification of drug-related problems (DRP) and solutions to solve the DRP as defined by Pharmaceutical Care Network Europe (PCNE).² A medication review with the possibility to further support the patient's implementation of agreed solutions by conducting follow-up consultations has been shown to significantly improve economic, clinical and humanistic outcomes, e.g. adherence, clinical goals, health-related costs and health-related quality of life.^{1,7-13} In Denmark, the current medication review service is based on data and experience from several programmes: The Therapeutic

Outcome Monitoring Program, Safe and Effective Use of Medicines and the Pharmaceutical Care Model.^{8,12,14-17}

A recent medication review study from Denmark included 951 home-dwelling elderly people (>65 years of age) using five or more medications.^{18,19} It was carried out in 2016-2018 and evaluated the current medication review service equivalent to a type 2A medication review defined by PCNE.² In brief, community pharmacists in the Region of Southern Denmark conducted medication reviews identifying DRP to be discussed and solved in collaboration with the patient or referred to the patient's general practitioner (GP).^{19,20} One interesting result was that for 20 percent of the patients, no DRP were identified. This raised the question of how the criteria for inclusion of patients to receive a medication review could be optimised to target subgroups of patients who would benefit the most. Based on the data from our study and the above citations about medication review models that includes a medication review and a follow-up, we decided to conduct a systematic literature review. We wanted to investigate the effect of medication reviews delivered to specific subgroups of patients to identify whether the criteria for including patients for medication reviews could be optimised.^{1,7-16} We were particularly interested in studies reporting a positive economic outcome, such as a reduction in contacts

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to health care professionals, admission to hospital/care home, readmission or death after performing a medication review. This was to further investigate how health care resources can be spent in the most beneficial way for both patients and society.

METHODS

The authors identified appropriate keywords from a PICO analysis followed by a comprehensive literature search using the PubMed database (2004, -August 2019). The search period was limited to the past 15 years to focus on the most recent studies and delivery of defined medication reviews. The search strategy used the following keywords: (((("pharmacy" OR "general practice" OR "ambulatory care facility" OR "home care" OR "elderly home" OR "nursing home" OR "outpatients" OR) AND ("medication review" OR "medication therapy management" OR "medscheck" OR ("drug utilization review"[Mesh])) AND ("clinical outcomes" OR "clinical effect" OR "economic outcome" OR "humanistic outcome" OR "impact" OR "consequence")))). See Figure 1.

An initial screening of title or abstract was conducted by the first author with screening criteria agreed by the three authors. The initial screening included studies published in English and excluded studies if they were grey literature, conference proceedings or had not been performed in the primary health care sector (community pharmacy, general practice, health clinic, nursing home). A second round of screening included reading the abstracts and, if the abstracts were unclear, reading the full text for additional criteria about study design categorised as a randomised clinical study (RCT), controlled non-randomised study, cohort study or having data on economic, clinical or humanistic outcomes. The eligibility of full-text studies was assessed by the first author followed by the second author. Studies with a described medication review process similar or with reference to the Pharmaceutical Care Network Europe definition, medicines therapy management, drug utilization review or MedsCheck were included.²⁻⁶ All included studies were further quality assessed using the Joanna Briggs Institutes Checklist for RCT, cohort, quasi-experimental or case-control studies.²¹⁻²⁴ Any disagreement regarding the selection was resolved through discussion between the authors. Included articles were categorised in the following way: First, each study was divided into a subgroup according to the study's own definition. Secondly,

each subgroup was allocated as either risk patients, if the subgroup described a specific patient subgroup, or risk medication, if the subgroup was defined as using a specific type of medication. This was done after discussion in the author group.

For each study, the following details were identified and reported: year, country, study size (interventions/controls), setting, age group, residency, medication review model (as defined by PCNE), study design, study outcome measures and conclusions. Also, the PRISMA checklist was used throughout the reporting.²⁵

RESULTS

The search identified 935 potential studies, with 22 studies included from existing knowledge or dialogue with other researchers. The initial screening excluded 789 studies for these reasons: the setting was wrong, the service did not include medication reviews, or conference proceedings, grey literature, and language. From the remaining 146 studies a further 118 studies were excluded due to undefined patient group, outcome measure or study design, and 28 studies were retrieved. Quality assessment using the Joanna Briggs appraisal checklist showed that all studies could be included. The detailed method for randomisation was unclear for several studies. Also, blinding was not possible for several studies. One or more statements from the assessment checklist were either unclear or impossible to answer. However, an overall appraisal resulted in 28 included studies. An overview of the screening is presented in Figure 2. The 28 studies were categorised into two main patient groups categorised by either risk medication (n=11) or risk patients (n=17). One main group characterised by the type of risk medication was medication related to falls (n=1), heart medication (n=1), anticoagulation medication (n=2), blood pressure lowering medication (n=2), antidiabetic medication (n=3) and anti-Parkinson's medication (n=2). The other group characterised by risk patients were frail patients (n=7), recently discharged patients (n=3) or multimorbid patients (n=7). Online appendix gives an overview of all included studies, outcome measures and results for economic, clinical and humanistic outcomes.

Risks for medication

Starting with subgroups defined by a specific medication, only one study investigated medication related to the

	Setting	Intervention	Effect	Time
OR	pharmacy	medication review	clinical outcomes	2004- august 2019
	general practice	medication therapy management	clinical effect	
	ambulatory care facility	drug utilization review	humanistic outcome	
	home care	medscheck	economic outcome	
	elderly home		impact	
	nursing home		consequence	
	outpatients			

Figure 1. PICO analysis



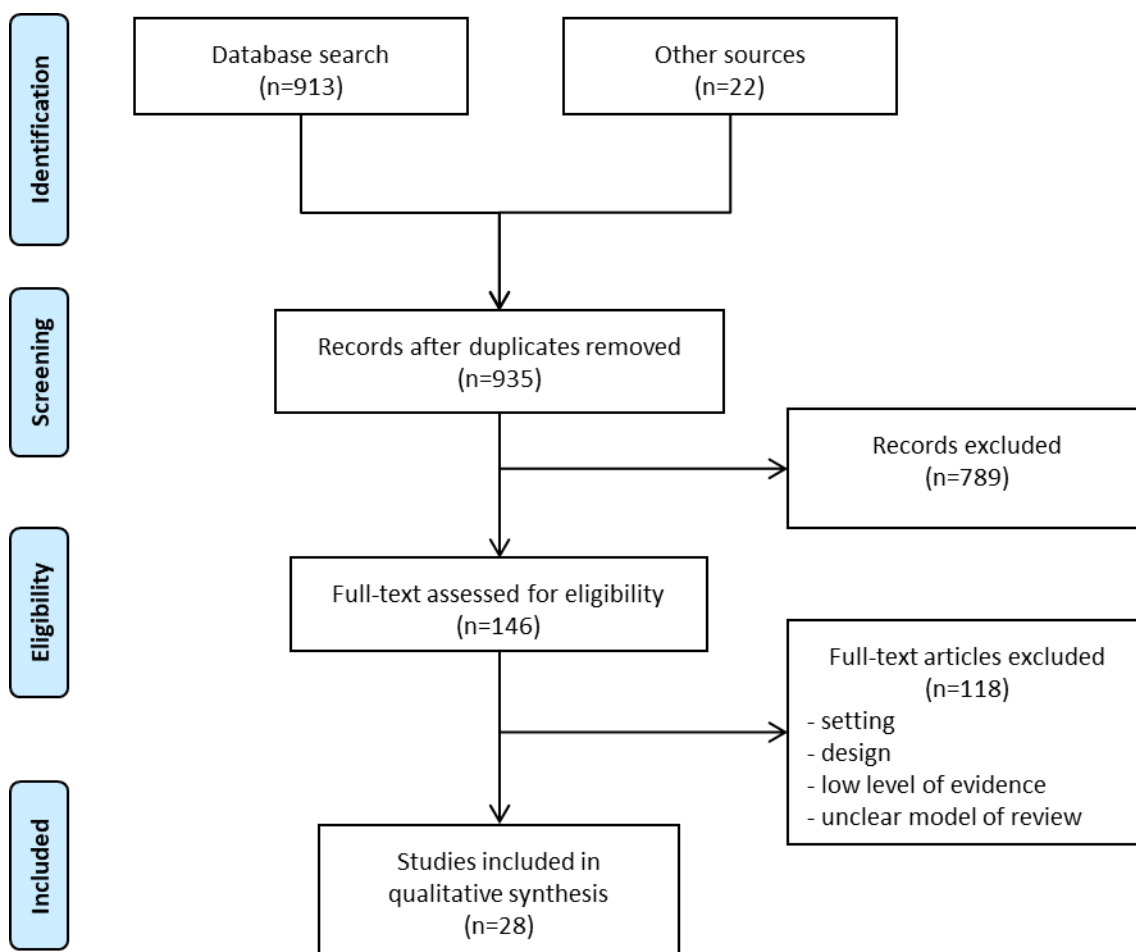


Figure 2. PRISMA flow chart

increased risk of falls.²⁶ The study cannot be considered representative for medication related to falls. However, the study showed a significant reduction in the use of medication related to falls. No overall difference in the number of falls was reported, nor was an economic evaluation provided.

In one study investigating the effect of medication review for a subgroup of elderly using at least one heart medication, no difference was reported for clinical outcomes.²⁷ The study cannot be considered representative for medication related to heart medication.

For anticoagulant medication two studies investigated the number of admissions to hospital or post-discharge haemorrhagic events, respectively.^{28,29} Both studies reported significant reductions for the outcome of either admissions or haemorrhagic events, demonstrating that patients using anticoagulant medication could benefit from a medication review.

Two studies investigated the effect of medication review for patients using medication for high blood pressure.^{30,31} Both studies reported significant improvement of blood pressure levels. One study also reported a significant reduction in health-related costs, suggesting that patients using medication for high blood pressure could benefit from a medication review.³⁰

A total of three studies reported data from patients using antidiabetic medication, with none of them providing an

economic evaluation.³²⁻³⁴ However, two studies reported a significant reduction in HbA1c.^{32,33} Two studies reported significant improvements of adherence in the intervention group.^{32,34}

Two studies investigated the effect of medication reviews for patients with Parkinson's disease.^{35,36} Foppa *et al.* reported significant reductions in non-motor related symptoms and improved HRQoL. Henrichsman *et al.* reported identification of clinically relevant DRP as well as significant improvements of scales specific to Parkinson's disease measuring levels of symptoms and disability. No economic evaluation was made for other studies.

With focus on patients receiving specific medication, a medication review can improve clinical and humanistic outcomes and reduce health-related costs. Particularly for the subgroups of patients receiving anticoagulant medication or blood pressure lowering medication the studies demonstrate significant positive economic effect. The medication reviews in the studies showing an economic effect were provided by a pharmacist with at least one follow-up. See Table 1 for a summary for each patient group.

Risks for patients

For subgroups based on patient characteristics, seven studies for frail patients were included.³⁷⁻⁴³ The group can be further divided into patients in care homes or home-dwelling.³⁷⁻⁴³ The three studies investigating the effect of

Table 1. Summary for subgroups of risk medication and risk patients and the effects of medication reviews.

	Studies (n=28)	Results
Risk medication		
Medication increasing risk of falls	1	Focus on medication increasing the risk of falls results in a significant reduction in the number of drugs, but no change in the number of falls
Heart medication	1	No effect on clinical outcomes
Anticoagulant medication	2	A significant reduction in likelihood of hospital admission
Blood pressure lowering medication	2	A significant improvement in blood pressure together with an economic advantage
Antidiabetic medication	3	A significant improvement of HbA1c and adherence. Economic outcomes were not measured.
Medication for Parkinson's Disease	2	A significant reduction in non-motor function related symptoms. Quality of life was improved.
Risk patients		
Frail patients	7	Overall increased deprescribing and improved adherence. Significant economic advantage for frail, home-dwelling patients.
Patients recently discharged from hospital	3	A significant reduction in the number of readmissions to hospital and the number of deaths
Patients with multimorbidity	7	An overall reduction in hospital admissions, visits to accident & emergency departments and improved adherence. A significant economic advantage.

medication review delivered to elderly people in care homes demonstrate that medication reviews can identify DRP, generate solutions in collaboration with other health professionals and facilitate deprescribing of inappropriate medication. The effect on economic outcomes was evaluated by two studies, with Zemansky *et al.* showing no difference in the cost of medication after medication review and Wouters *et al.* showing no difference for use of other health care professionals.^{37,41} The four remaining studies on frail patients that investigate the effect of medication review are on home-dwelling elderly people. The economic outcome was measured in three studies. Moore *et al.* analysed data from 2,250 patients from both intervention and control groups and reported a significant reduction in health care costs and the number of visits to the hospital and GP.³⁸ In contrast, Lenaghan *et al.* analysed data from 67 and 69 patients from the intervention and control group respectively and reported no difference for admissions to hospital.⁴⁰ Verdoorn *et al.* reported no significant differences for economic outcomes from 314 control- and 364 intervention patients.^{40,43}

Three studies investigated the effect of medication review delivered to patients recently discharged from hospital. All studies used an outcome measure related to readmission to hospital. The results are mixed with Lapointe-Shar *et al.* reporting a significantly larger reduction in readmission in the exposed group than Shaya *et al.* and Holland *et al.* reporting a significantly higher proportion of readmissions within the exposed group.⁴⁴⁻⁴⁶ An important note is that the study by Lapointe-Shaw, which showed an effect, is a retrospective cohort study based on data from a large group (n=67,163) of patients in both exposed and control groups, making the results very strong. Also, the Lapointe-Shaw study showed a significant reduction in the number of deaths in the exposed group.

The final patient group is characterised by multimorbid patients and includes seven studies.^{1,47-51} Two studies reported no differences between intervention and control groups for effects of medication review, and one study only reported data for humanistic outcomes, with increased knowledge and an increased feeling of safety.^{49,51,52} Three studies reported significant reductions in admissions to

hospital, and two studies reported a significant reduction in health-related costs.^{1,47,48,50}

For specific subgroups of risk patients, the results show that a medication review can have economic advantages, reduce admission to hospital and improve compliance. This is shown for frail patients, recently discharged patients and multimorbid patients. Different models of medication review were used in these studies. All studies, apart from one, reported that the medication reviews were delivered by a pharmacist, with the remaining study not reporting who did the review. For four of the six studies showing an explicit economic effect, the medication review has included at least one follow-up. For the studies delivered at care homes, in the group of frail patients, no positive economic effects, were reported.^{37,39,41} For two of three studies, medication reviews in care homes were obtained without interviewing the patient and no structured follow-up was described in the three studies.^{37,39} See Table 1 for a summary for each patient group.

Economic effect

For 17 of the included studies an economic outcome was measured.^{1,28-30,37,38,41-50} Nine studies report a positive economic effect with eight having a described procedure for follow-up on the medication review. Eight studies report no economic effect, with seven studies using a medication review model with follow-up.

DISCUSSION

Results from this review show how subgroups that either use risk medication or are risk patients can benefit from a medication review delivered by pharmacists in primary care, and how the medication reviews have a positive economic effect due to either reduced health-related costs or a reduction in the number of contacts with primary or secondary health care services. Medication reviews in the primary care setting delivered by a pharmacist to the subgroups using anticoagulant medication or blood pressure lowering medication, frail patients, recently discharged patients or multimorbid patients demonstrate the most convincing results for a positive economic effect. A common way of including patients for a medication review in primary care, e.g. at community pharmacies, has



so far been based on age, number of medications and perhaps residency. The results in this literature review show that dividing patients into subgroups based on characteristics of either medication or type of patient group can be a way forward to identify the eligible patients for a medication review in primary care. Another way to include patients who will benefit from a medication review is to use triage or screening before delivering a full medication review. A triage proposed by Messerli would acknowledge patients who comply and control their condition well and help focus resources on patients with greater needs.⁵³ The work to develop and test tool to identify the right pharmacy service for the right patient is on-going and was in 2019 one of the main workshops at the PCNE working conference in Holland.⁵⁴

A medication review with follow-up has shown to augment the impact of a medication review by supporting the patient and the suggested changes to their treatment.^{1,7} Considering a follow-up procedure detrimental for the effect of a medication review has not been proven from the studies included in this review. Follow-up procedures vary between studies with follow-up provided by community pharmacy or GP delivered either face to face or on the phone. No clear pattern was identified, suggesting that it is the contact between patient and healthcare professional that may support the implementation of changes in the treatment suggested through the medication review. A described follow-up procedure is not part of the definition for PCNE Medication Review or definitions for MTM, Drug Utilization Review or MedsCheck. The possibility for follow-up is often at the discretion of the pharmacist and has not been clearly defined.

The lack of studies conducting an economic evaluation makes it difficult to evaluate the possible economic benefits for e.g. patients using antidiabetic medication. The studies included in this review on patients who use antidiabetic medication reported significant clinical advantages that would conceivably give rise to also economic advantages, but the study did not measure economic outcomes. This possibility is further supported by the results from the Asheville project launched in 1997 for diabetes care that reported how long-term support with medication review and follow-up for patients with diabetes result in significant beneficial outcomes, both clinical and economic.⁹ Other patient subgroups, on whom no studies on economic effect or other effects have been carried out so far, could possibly benefit from a medication review delivered by a pharmacist in primary care, e.g. at a community pharmacy. Also a significant improvement of clinical parameters such as blood pressure, HbA1c, cholesterol, BMI etc. could lead to improvement of both economic and humanistic measures through slowing down progression of diseases and maintaining the patient's independence.

The definition of patient subgroups followed the way that the authors of the included studies had defined the subgroup. For instance, many of the patient groups are arguably "frail patients", but have not been included as such in this literature review, as we categorised the groups based on the studies' own definition of the patient group. An example is Shaya *et al.* which has as its aim to study

patients' discharge and not specifically the subgroup of patients.⁴⁵ Furthermore some of the other patient subgroups could be categorised in more than one group; e.g. a study with patients recently discharged from the hospital who all had diabetes.⁴⁵ These choices of categorising subgroups were made through discussion in the author group and based on the aim and categorisation of patient groups for each study.

A limitation of this literature review is that we only identified studies from the PubMed database and studies only available from other databases have been lost. Also, the search strategy was narrow resulting in exclusion of studies where the title did not reflect the actual aim of the study which means that some studies that fulfilled the inclusion criteria may have been missed in the search. Included studies had to specify a target group based on other parameters than age and number of medicines. The authors chose e.g. the search term 'humanistic outcome' and not more specific search terms as 'non-adherence' or 'quality of life', which could have resulted in lack of relevant studies.

A search period of 15 years was chosen as the development and delivery of medication review has become more standardised in recent years.

This literature review suggests that both the model of medication review and the target patient group are important when considering for whom and how a medication review can be a beneficial pharmaceutical care service delivered from e.g. the community pharmacy. To evaluate whether other patient subgroups than the ones identified in this review could also benefit from a medication review delivered by a pharmacist in primary care, more studies with an economic evaluation on other specific patient groups need to be conducted.

CONCLUSIONS

The literature review demonstrates that medication reviews delivered by pharmacists to specific subgroups of patients are one possibility of optimising the economic effect of medication reviews in primary care. This is obtained by reducing health-related costs or the number of contacts with primary or secondary health care services. The subgroups identified as having an economic effect from a medication review in primary care were defined by either being frail, recently discharged from hospital or multimorbid (risk patients), or defined by patients using anticoagulant or blood pressure lowering medication (risk medication). Most of the medication reviews in the studies showing an economic effect had at least one follow-up, and the medication reviews were delivered by a pharmacist.

CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest.

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