TRANSITIONAL PHARMACEUTICAL CARE FOR PATIENTS DISCHARGED FROM THE HOSPITAL

FATMA KARAPINAR

Transitional pharmaceutical care for patients discharged from the hospital

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Transitional pharmaceutical care for patients discharged from the hospital

Farmaceutische transitiezorg voor patiënten die met ontslag gaan uit het ziekenhuis (met een samenvatting in het Nederlands)

PROEFSCHRIFT

ter verkrijging van de graad van doctor aan de Universiteit Utrecht op gezag van de rector magnificus, prof.dr. G.J. van der Zwaan, ingevolge het besluit van het college voor promoties in het openbaar te verdedigen op woensdag 25 april 2012 des middags te 4.15 uur

door

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Dr. S.D. Borgsteede

Always do what you are afraid to do.

(Ralph Waldo Emerson: essayist and poet, 1803 –1882)

Arabic translation of quote and design by Everitte Barbee

CONTENTS

Even the longest journey must begin where you stand.

(Lao-tzu: Chinese philosopher, 604 BC - 531 BC, translation by Michael Moncur, 2004)

Arabic translation of quote and design by Everitte Barbee

PART

1

Introduction

PATIENT SAFETY

Today's healthcare context is highly complex. Care is often delivered in a fast-moving environment, involving many individual decisions and judgments by healthcare providers.[1] Ensuring the safety of everyone that comes into contact with health services is one of the most important challenges of healthcare today.[2,3] Patient safety is the absence of the potential for, or occurrence of, healthcare-associated injury to patients.[4] Healthcare-associated injury can be the result of healthcare providers not following the professional standards, shortcomings of the healthcare system and/or the patient's behaviour.[5] Current conceptual thinking on patient safety places the prime responsibility for medical errors on deficiencies in system design, organisation and operation rather than on individuals.[1,6] Patient safety is created by avoiding medical errors as well as taking action to prevent errors once occurred from causing injury.[4] There is a growing demand for improved safety in healthcare from patients, providers, insurers and regulators.[4]
Internationally, *adverse drug events* are among the most common adverse events reported.[7] According to the Institute of Medicine's report *"Preventing medication errors"* the average hospitalised patient is subject to at least one medication error per day.[8] Within two months after hospital discharge 49% of patients experienced at least one medication error.[8]
Several studies have shown that patient safety is also jeopardised in the Netherlands.[9-13] Lack of continuity between healthcare providers and settings and medication errors were similarly identified as important contributors.[8,14]

CONTINUITY OF CARE

The decentralised and fragmented nature of the healthcare delivery system contributes to discontinuity of care when patients see multiple healthcare providers, none of whom have access to complete information regarding the patient's healthcare status.[15-17] Therefore, each transition in the continuum of care will create an opportunity for adverse (drug) events.[6] Continuity of care is defined as the degree to which a series of discrete healthcare events is experienced as coherent and connected and consistent with the patient's medical needs and personal context.[18] Haggerty et al. have identified three distinct means of providing continuity (see Table 1): informational continuity, management continuity and relational continuity.[18] For patients, the experience of continuity is the perception that providers know what has happened before and that different providers agree on a management plan. For healthcare providers, the experience of continuity relates to their perception that they have sufficient knowledge and information about a

Table 1 Three types of continuity

Type	Explanation	Comment
Informational continuity	Use of information on past events and personal circumstances to make current care appropriate	Includes transfer of information regarding the medical condition and the patients' preferences or values
Management continuity	A consistent and coherent approach to the management of a health problem	Includes shared management plans, but also flexibility in adapting to changes in an individual's need
Relational continuity	An ongoing therapeutic relationship between a patient and one or more providers	Includes a consistent core of personnel to give patients a sense of predictability and coherence in their care

patient to best apply their professional competence and the confidence that their care inputs will be recognised and pursued by other providers.[18]

For continuity of pharmaceutical care information about the actual and past use of medicines is crucial in assessing the impact of medicines, in assisting in future decisions about care and in enabling safe transfer of care to another healthcare provider.[19] Remarkably, the intended medication regimen before, during and after a hospital stay often becomes a point of confusion for patients, clinicians and pharmacists.[20,21] At hospital admission the medication a patient actually should use and actually uses often is not clear.[22,23] During hospitalisation medication is changed regularly.[24-27] The patient and the next healthcare provider (e.g. community pharmacist, general practitioner) are not informed on reasons for changes and whether these changes should be maintained or not.[24,26]

It is estimated that 46% of all medication errors occur during the patient's admission or discharge from a clinical unit.[28] Poor communication and documentation of medical information has been cited as the main cause for these medication errors.[26,28,29]

The healthcare system is not equipped with one single healthcare professional who assumes full responsibility for the coordination of care across settings or care providers.[30,31] This lack of coordination and collaboration between inpatient and outpatient healthcare providers could have serious consequences as illustrated in box 1.

Box 1 One patient, many healthcare providers, many medication lists

Case 1: A 77-year old woman was seen by the renal-hypertension service, of which the physician advised the patient to reduce her daily dose of furosemide by 40 mg. Before this visit, her general practitioner had already decreased her daily dose from 80 to 40 mg, but this was not communicated to the renal-hypertension service. After receiving this service's latest advise (reduce by 40mg), she stopped taking her furosemide altogether. Subsequently, she developed shortness of breath, a 3.5-kg weight gain and increased swelling of her legs.[32]

Case 2: A patient using a statin was hospitalised three times for pancreatitis; the statin was discontinued in hospital but incorrectly restarted by the general practitioner after the first and second hospital discharge, leading to readmissions.[33]

TRANSITIONAL CARE

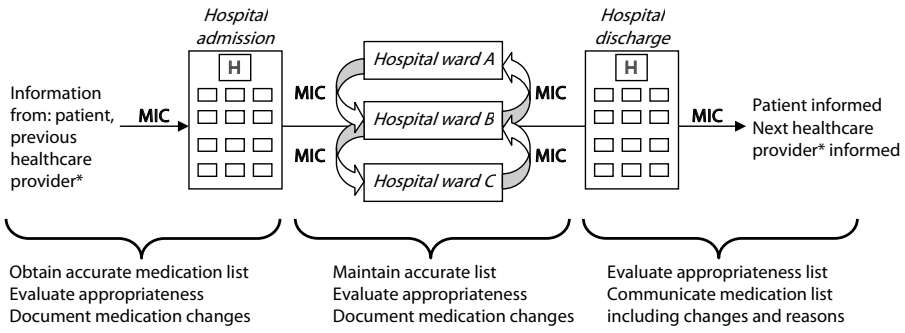
Several (inter)national programs have been developed to implement transitional care programs to ensure coordination and improve continuity of pharmaceutical care between healthcare settings.[19,34-41] As shown in Figure 1, conflicts between different sources of information need to be resolved and acted upon appropriately. Informational continuity regarding medication is needed at several transitions where responsibility for a patient is transferred between healthcare professionals (i.e. between several wards in the inpatient setting and at hospital admission and hospital discharge).[42,43]

A tool helping to ensure accurate informational continuity is medication reconciliation.[35,44] Medication reconciliation is defined as the process of creating the most accurate overview possible of all medicines a patient is taking — including drug name, dosage, frequency, and route — and comparing that overview against the physician's admission, transfer, and/or discharge orders, with the goal of providing correct medication to the patient at all transition points within the hospital.[35]

The medication reconciliation process involves four sequential steps.[35,36,44] First, in the *verification* step the current medication list is assembled by using one or more sources of information. Second, in the *clarification* step the medication and dosages are checked for appropriateness. In the third *reconciliation* step newly prescribed medicines are compared against the old ones and changes to pharmacotherapy are documented. In the final *transmission* step the updated and verified list is communicated to the next healthcare provider to improve the continuity of care.[44]

The implementation and use of medication reconciliation differs greatly between settings depending on the time and effort of healthcare providers.[29,31,45] In general, healthcare providers focus on obtaining a medication list to prevent discrepancies in medica-

Figure 1 The ideal medication informational continuity (MIC) from hospital admission to discharge



* In general, the next healthcare provider is the general practitioner and/or community pharmacist.

tion use between the primary and secondary care setting.[46] However, simply matching lists of medicines (i.e. the *verification* step) could lead to the persistence of inappropriate therapy. Medication reconciliation also requires the evaluation of the information on the list for appropriateness of the pharmacotherapy (i.e. the *clarification* and *reconciliation* step) and involving the patient and next healthcare provider in the continuation of the right pharmacotherapy (i.e. the *transmission* step).[35,36,47]

HOSPITAL DISCHARGE

Although all transition points are susceptible to medication errors, in this thesis the main focus is on the transition from hospital discharge to home. First, the discharge process receives low priority due to the many tasks of physicians and nurses. The financial pressure to fill beds as soon as they are empty works as a disincentive to give physicians the time needed to create and communicate an accurate medication overview.[48,49] Furthermore, the responsibilities regarding the elements of the discharge transition, such as informing the patient about discharge medication and communicating with the next healthcare providers, is frequently unclear.[48,49]

Second, the pharmacotherapy is regularly changed late in the hospitalisation, if not right at discharge.[26,48,50] While hospitalised, patients have little control over their medications. Yet, they are expected to assume immediate and often complete responsibility at discharge. Studies have shown that patients are incompletely informed on discharge medication.[51-53] Patient counselling at discharge, however, is essential to prepare patients to manage their medication at home and to inform them on the medication changes.[35,48,50]

Third, recent studies have shown that medication errors occur more frequently at hospital discharge.[54,55] For medication errors at hospital admission 51% were intercepted before reaching the patient. In contrast, only 28% of discharge errors were intercepted.[28]

Finally, hospital discharge is the last moment to check the medication as other healthcare providers may assume that medication is (un)intentionally adjusted in the hospital. To enhance continuity of pharmaceutical care, the next healthcare provider needs to be informed on the reasons for changes in the pharmacotherapy.[22,27,56,57] Studies have shown the possible consequences of inaccurate medication communication, for example the inappropriate restart of medication, that has been stopped during hospital admission due to adverse drug reactions.[58,59]

Although the described problems are alarming, these results are predictable. Most research funding, and thus, studies have focused on understanding disease biology and identifying effective therapies, whereas little research has looked into methods of delivering those therapies safely, effectively and efficiently.[4,60] Research into continuity of

pharmaceutical care is in a developing phase and more insight is needed for the following reasons. First, the studies performed, aiming to improve the transition from hospital discharge to home, differ greatly. A systematic review aggregating this evidence should make clear which components of discharge medication related interventions are effective in improving clinically relevant outcomes such as a decrease in hospital rehospitalisations.

Second, studies regarding discharge medication related interventions are mostly performed in the United States.[55,61-64] As the Dutch and European healthcare systems differ from the United States, it is not possible to extrapolate the results of these studies.

Third, guidelines stress the importance of collaborating with the patient and the general practitioner to improve continuity of care.[19,34-36] Implementing recommended strategies for good collaboration is likely to be more successful when these strategies match with the information needs of patients and general practitioners. Several studies have found that patients want basic information about medication, such as the names of the different drugs, dosing schedule and indication.[65,66] However, no study has explored the patient's needs of information about medication at hospital discharge. Limited (older) studies have shown that general practitioners want to be informed timely and want information regarding (the reason for) medication changes.[27,56,57,67] The new guidelines on safe information exchange and policy documents may have changed or increased the information need of general practitioners. So, new research is required.

Fourth, studies describe the importance of implementing medication reconciliation, but the method for the process differs greatly. The sources used for medication reconciliation (e.g. general practitioner, community pharmacy or hospital medication records) can vary and a lot of studies do not involve the patient.[55,62,67,68] The time spent on medication reconciliation differs also. The community pharmacist is not always adequately informed regarding the discharge medication. Two studies, in the outpatient and ambulatory setting, showed that patient counselling added in the identification and elimination of medication errors during medication reconciliation.[69,70] More research is needed to assess the exact contribution of patient counselling to the medication reconciliation process at discharge.[71] Reports provide limited insight on how time-consuming the complete medication reconciliation process is and what the associated labour costs are.[71-73] Furthermore, no studies have evaluated the effect of medication reconciliation on medication related costs after hospital discharge. Studies discuss that improving communication to the community pharmacy improves patient profiles and patient care after hospital discharge.[74-76] However, these studies do not focus on whether medication changes are made clear in community pharmacy records and whether all relevant information is documented (e.g. non-dispensed medication, over-the-counter drugs, allergies, contraindications).

Finally, studies tend to concentrate on a small part of the medication reconciliation process.[55,68,72,77] The effect of medication reconciliation and the economic consequences, after implementing all four steps, needs to be clarified. Economic analyses for different processes in medication reconciliation are lacking. Only, a model-based cost-effectiveness analysis of medication reconciliation at hospital admission is described in literature, which estimated that pharmacist-led medication reconciliation had a probability of being cost-effective of over 60%.[78]

OBJECTIVE OF THE THESIS

The objective of this thesis is to summarise existing evidence on transitional pharmaceutical care interventions and to develop and evaluate a transitional care program with respect to effects and costs.

OUTLINE OF THESIS

The research in this thesis is built upon gathering literature on possible pharmaceutical interventions at hospital discharge, exploring the informational need of patients and general practitioners about discharge medication, developing a transitional care program that includes medication reconciliation, collaborating with the next healthcare provider and finally evaluating the effect of the program.
This thesis consists of the following parts.

Part 2: Evidence on transitional pharmaceutical care interventions

Several reviews on improving the transition from hospital discharge to home have been performed.[79-83] No systematic review has described specifically the effect of interventions on medication. Therefore, the evidence in literature on the effectiveness of discharge medication related interventions and the different intervention components contributing to the effectiveness was summarised.

Part 3: Development of a transitional care program for hospitalised patients

To improve the medication information transfer from hospital discharge to the outpatient setting, the informational needs of general practitioners regarding discharge medication were investigated (Chapter 3.1). To involve the patient in the medication reconciliation process and support the development of patient counselling, the informational needs of patients regarding discharge medication were explored (Chapter 3.2).

The additional contribution of involving the patient was assessed through studying the influence of patient counselling on additional interventions during the medication reconciliation process (Chapter 3.3). To give insight in the labour costs and the medication costs after hospital discharge, the labour costs were compared to the medication cost savings after hospital discharge (Chapter 3.4).
Community pharmacists can act as the key performers of medication surveillance as they have access to medication ordered by multiple healthcare providers. In Chapter 3.5 the effect of instruction manuals on completeness of patient profiles in community pharmacies was explored. The instruction manuals specified how community pharmacies could document discharge medication related information in their patient profiles.

Part 4: Evaluation of a transitional care program for hospitalised patients

Medication reconciliation is complex and therefore studies need to give detailed insight in how the medication reconciliation is performed. In Chapter 4.1 the study protocol that was developed for the transitional care program COACH (Continuity Of Appropriate pharmacotherapy, patient Counselling and information transfer in Healthcare) is described.
Most studies on discharge medication related interventions are performed (partly) by pharmacists and concentrate on a small part of the medication reconciliation process.[55,61-63,68,77,84,85] In this thesis the effect of the COACH program that combined interventions and was performed by healthcare providers with a lower level of education was investigated. Rehospitalisations and secondary outcomes such as drug-related problems, patient's attitude towards medicines, adherence and patient's satisfaction were assessed (Chapter 4.2). Finally, in Chapter 4.3 a cost-effectiveness study is described. Total costs of the COACH program and usual care were compared.

Part 5: General discussion

In Part 5 the results of the different studies are discussed. Recommendations for further research and for improving continuity of care in daily practice are given.

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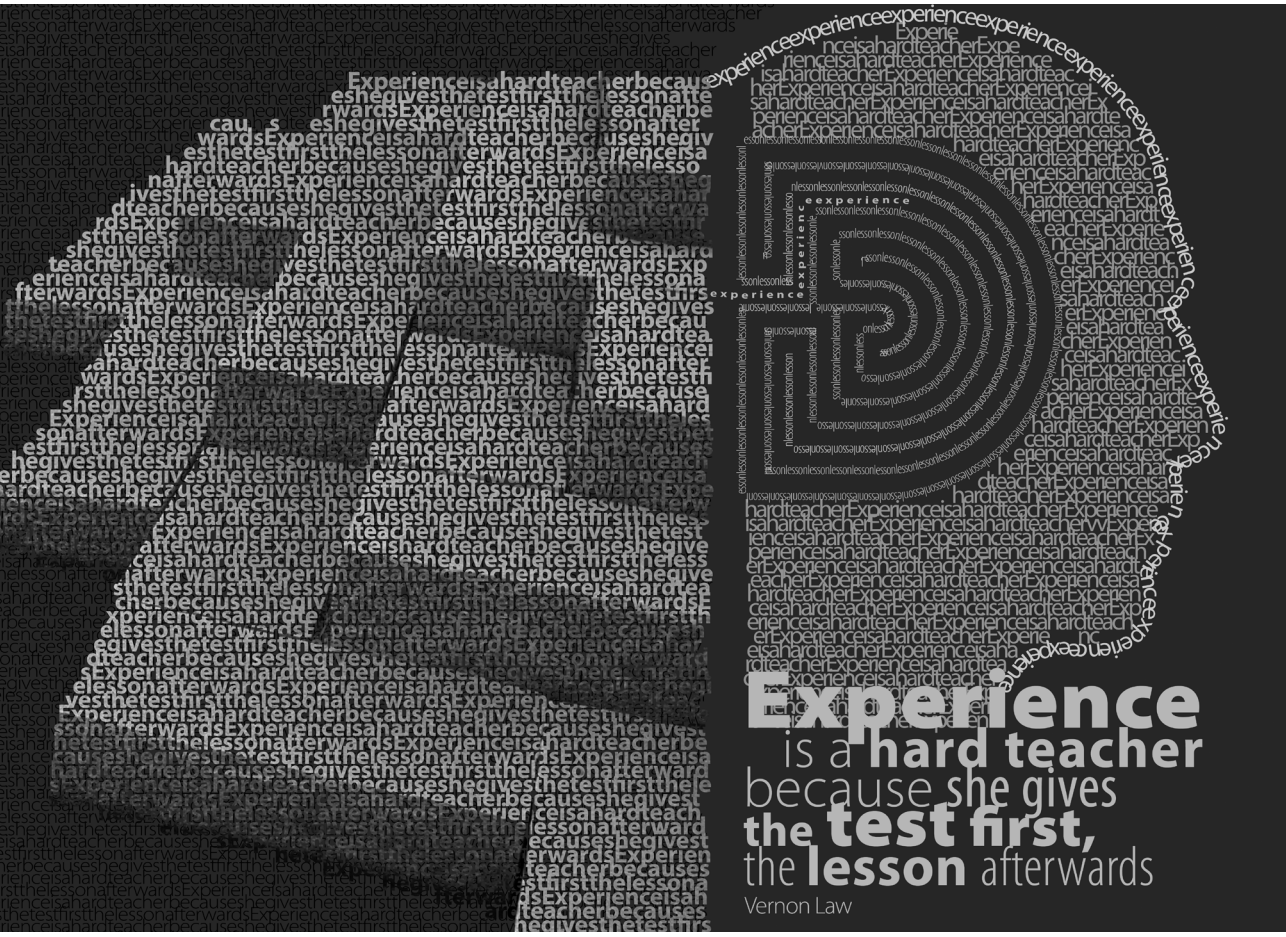

Experience is a hard teacher because she gives the test first, the lesson afterwards.

(Vernon Law: athlete, 1930)

Designed by Denis Tenev

PART

2

Evidence on transitional pharmaceutical care interventions

CHAPTER

2.1

Effectiveness of discharge medication related interventions. A systematic review.

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ABSTRACT

Background: No systematic review has focused on discharge medication related interventions (DMIs) aimed at improving continuity of care between the hospital and community setting. This study aimed to systematically review the evidence for the effectiveness of DMIs in order to reduce post-discharge medication problems in adult patients.

Methods: Multiple electronic bibliographic databases (until August 2010) were searched supplemented with hand searches of references. Independent assessors evaluated 6984 articles. Studies with a control group were included if the article involved a DMI performed around hospital discharge for adult patients discharged home. The outcomes hospital readmission rates (primary), health services use, mortality, medication knowledge, adherence, and drug-related problems (DRPs) were studied. Studies were categorised based on their characteristics (e.g. intervention components, methodological quality). Data were synthesised by use of narrative methods.

Results: Fifty-eight original articles met inclusion criteria. Studies described multicomponent and various interventions. Hospital readmissions (n=17) and health services use (n=10) were reduced in 18% and 40% of studies respectively. Mortality was not decreased (n=5). Medication knowledge (n=20) and adherence (n=20) was improved in 75% and 70% of studies respectively. Twenty-eight studies evaluated DRPs of which 26 were effective (93%). Larger sample sizes, in general, led more frequently to effective studies. Studies with good methodological quality tended to be more frequently effective for the outcomes readmission and knowledge.

Conclusions: DMIs were reported to be effective for process measures (knowledge, adherence and DRPs). A limited number of studies reported effectiveness on morbidity (readmission and health services use).

BACKGROUND

Patients are seen by an increasing number of healthcare providers in a wide variety of organisations and places, raising concerns about fragmentation of care.[1] In recent years the concept of continuity of care has received a lot of attention. Continuity is defined as the degree to which a series of discrete healthcare events is experienced as coherent and connected and consistent with the patient's medical needs and personal context.[1] Haggerty et al. have identified three distinct means of providing continuity: personal continuity (provision of care through an ongoing clinician-patient relationship), continuity of information (the use of information on past events and personal circumstances to make current care appropriate) and management continuity (a consistent and coherent approach to the management of a health problem).[1]

Continuity of care is especially important in the transition from hospital to home as this transition is known to have a high risk for errors.[2] Ineffective planning and coordination of care can contribute to the occurrence of adverse events and hospital readmissions.[2,3] Studies have found that 19%-23% of medical patients discharged from hospital experienced an adverse event within one month of discharge, of which many were preventable and the majority were related to medication.[3,4]

In order to prevent these adverse events and hospital readmissions, interventions aimed at improving the continuity of care have been developed. Proposed interventions are for example the reconciling of discharge prescriptions to obtain an accurate overview of the actual medication use of a patient, discharge counselling to prepare the patient to manage his/her medication at home and accurate communication to the next healthcare provider to make sure this provider can take over the care.[2,3,5,6]

Several reviews on improving the transition from hospital discharge to home have been performed.[7-16] Some of them were focusing on the effect of the healthcare provider on continuity of care.[7,13] Most reviews specifically looked at discharge programs in heart failure patients and implemented multi-faceted interventions.[7-11,13,14,16] In none of these systematic reviews the effect of interventions on medication has been described specifically. A Belgian report focused on medication related interventions but excluded older studies (published before 1995) and this report has not been published in a peer reviewed journal.[17] Many interventions have been developed and studied, which vary widely and mostly consists of several components. There is sparse evidence for which components are essential for success and what the most effective strategies have in common.

Therefore, we performed a systematic review aimed at analysing the evidence in literature on the effect of discharge medication related interventions (DMIs) on post-

discharge medication problems in adult patients discharged from hospital, and the different study characteristics contributing to the effectiveness.

METHODS

Search strategy

Discharge medication related interventions were defined as interventions performed around discharge by different healthcare professionals, explicitly targeted at continuity of pharmacotherapy or at preventing or diminishing problems with medication use after hospital discharge.

Electronic searches of the published literature were conducted in Medline, Embase and the Cochrane Library with the language restrictions English, Dutch, German and Turkish. Each electronic database was searched until August 2010 as far back as possible. The detailed search strategies can be found in Appendix A. The exact search strategy varied across databases, but was based on the same three combined components: related to an intervention around discharge, related to medication and related to the outcomes.

Studies were identified using a broad range of index terms and additional free text words in order to maximise the sensitivity of the retrieval. The search strategy was validated and fine-tuned by checking the indexing of 70 previously identified relevant articles which would be expected from an accurate search. The search that identified most of the earlier identified articles was eventually used.

Reference lists of relevant articles and reviews were checked, and citations of relevant articles were checked through the databases Web of Science and Scopus.

Study selection

All titles and abstracts retrieved by the literature search were reviewed by two of the three independent reviewers (FA/MR, FK). Full paper copies of articles were obtained and examined when the abstract and/or title provided insufficient information. Two of the reviewers (FA/MR, FK) independently assessed the articles for possible inclusion. All differences in assessment were resolved by discussion or with assistance from a third reviewer (PB or SB). If obvious duplicate papers were available, the information from these papers was combined.

Studies were included if they fulfilled all of the following criteria:

- The intervention described was in the period around discharge for patients discharged from hospital wards to home; the intervention was performed shortly before discharge (48h), at the time of discharge or within one month after discharge from the hospital.

- The outcome studied concerned one of the following items: hospital readmissions (primary outcome for this review), health services use post-discharge (e.g. general practitioner, emergency department visits), mortality, medication knowledge, medication adherence, drug-related problems (DRPs, e.g. medication errors, adverse drug effects, medication appropriateness) and costs of health services (if the study included the cost of the intervention).
- The intervention focused explicitly on medication so that the effect of a medication related intervention could be isolated; the medication related intervention should be mentioned in the abstract and/or objective. There should be an explanation in the method section of what was done (e.g. a description on which items a patient was counselled for).
- The article was a (randomised) controlled trial, a before-after study or a study with a historical control group.

Publications were excluded when:
- The DMI was not aimed at enhancing continuity of medication care around hospital discharge (e.g. studies that solely examine whether guidelines are followed up at hospital discharge, e.g. ACE-inhibitors prescribed for heart failure patients).
- The intervention described was aimed at one therapeutic group (e.g. enhancing adherence with statins prescribed at discharge).
- The study failed to report data on the patient level.
- The article involved psychiatric patients, paediatric patients or patients with cognitive malfunction.

Quality assessment

The methodological quality of all included studies was assessed by two of three reviewers (FK, MJ/SB) with the Amsterdam-Maastricht score list for (randomised) controlled trials and before/after studies (see Appendix B). This score list has been adapted by the Dutch Cochrane Centre to grade the internal validity of individual studies.[18] Uncertainty or disagreement about scoring articles with the list was resolved by discussion with another reviewer. Studies were not excluded based on the methodological quality. Instead, studies were classified as having a good methodological quality (4 or more positive items on the score list) or marginal methodological quality (<4 positive items on the score list). The reviewers were not blinded for information on authors, journal or institution.

Data extraction

Data from all included articles were extracted from relevant articles using a data extraction sheet in Excel 2003. The data extraction sheet was piloted on five randomly-selected

studies and further refined. The extraction was reviewed and confirmed by one other review author for 50% of the studies. As there were no major differences in judgments between the assessors, the other half of studies was not assessed. Data extraction included: study type and setting, study population, study methods, usual care, type of interventions, measurement methods, type of healthcare provider involved, outcome measures, primary outcome as stated by the authors or defined in the objective, results, periods of follow-up, conclusions and limitations. Information was literally extracted from the original manuscripts and missing information was scored as 'not reported'. Authors were contacted if further information or confirmation of data was required.

Data classification and analysis

Data were synthesised by use of narrative and tabular methods. The eligible studies were expected to differ substantially regarding patient population, intervention and measurements methods, rendering pooling of results inappropriate. Instead, different study characteristics of the included articles were classified and investigated. Study characteristics investigated were methodological quality, definition of primary outcome, number analysed (sample), intervention moment (before or after discharge or both), intervention type (educational, pharmacotherapy, transfer of information; see below), number of intervention types combined (e.g. one vs two intervention types), intervention performer (nurse, hospital physician, pharmacist, pharmacy technician and other) and number of professions performing the intervention.

Studies were primarily grouped by intervention type (see Table 1). Three main intervention types were categorised:

- *Patient educational (Ed)* interventions described cognitive strategies designed primarily to educate and motivate patients by instructions, based on the concept that patients who understand their condition and its treatment will be more informed, empowered and likely to adhere. Informational sessions could be individually, in a group setting or with family. Examples are face-to-face oral consultation, written consultation and audiovisual consultation.
- *Pharmacotherapy related (Ph)* interventions described interventions which were meant to minimise medication errors. Examples are reviewing or reconciling of medication, preventing drug-related problems and optimisation of polypharmacy.
- *Discharge information transfer to the next healthcare provider related (Dt)* interventions described interventions which were meant to inform the next healthcare provider on the discharge prescriptions. An example is communicating medication changes to the next healthcare provider.

Subsequently, the analysis was performed by comparing effective and ineffective interventions with respect to different study characteristics. Interventions were classified as effective or ineffective according to statistically significant changes in outcome mea-

sures. If studies did not report a p-value, but reported that their study was significant, the p-value was calculated. A $p<0.05$ was considered statistically significant. Significant combined outcomes (e.g. readmission and mortality reported as one result) were considered non-effective unless the separate outcomes were significant. If possible, relative risks were calculated, or if the paper reported an adjusted odds ratio, this value was reported.

Table 1 Classification of intervention types

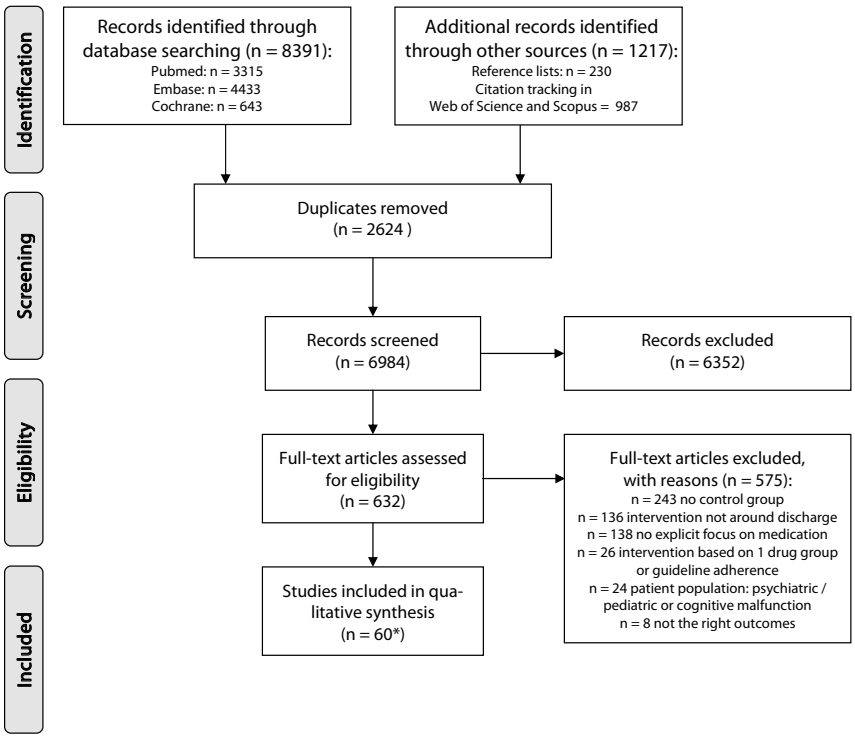
Type of interventions	Definition/explanation	Synonyms/examples
Patient educational interventions: patients received information, advice or guidance about their disease, medication purpose, medication names, treatment options, medication changes and reasons for changes, adherence, side effects, drug-related problems, storage of medication, how to arrange new supplies and what to do with missed doses.		
Verbal	Patients received verbal information	Discharge interview, patient interview, patient counselling, patient education
Written	Patients received written information	Medication sheet, medication report, information folders, booklets, written instructions, discharge summary
Audiovisual	Patients received audiovisual information	Video images, presentations
Promoting adherence aids	Tools given to the patient to enhance adherence of medication use	Pill sorter, medicine reminder devices, non-child resistant containers or larger bottles, self-administration during hospitalisation
Pharmacotherapy related interventions: adjustments in pharmacotherapy after checking medication lists to minimise discrepancies between and/or after optimising the pharmacotherapy to prevent drug-related problems.		
Discrepancies	Eliminating discrepancies between medication used before admission or in-hospital medication with the medication prescribed at discharge or post-discharge (through identifying an accurate and complete medication list)	Medication history taken, correction of discrepancies, transcription of discharge prescriptions
Review	Analysing the appropriateness of drug therapy and optimising the pharmacotherapy to prevent drug-related problems	Rationalisation of drug therapy, drug interactions, monitoring of therapy, simplification of therapy.
Discharge information transfer to next healthcare provider related interventions: informing the next healthcare provider on the discharge prescriptions by providing a list of medications, medication changes, reasons for changes, follow-up instructions to primary care caregivers (e.g. general practitioner, community pharmacy, community nurse).		
Verbal information	Verbal feedback to the next healthcare provider	Telephone call
Written information	Written information to the next healthcare provider	Discharge summary or prescriptions, discharge letter

RESULTS

A total of 9608 articles were identified in the initial search. After eliminating duplicates, 6984 articles were screened (see Figure 1) and 632 full-text articles were assessed for eligibility. A total of 575 articles were mainly excluded because the article did not have a control group or the described intervention was not performed around hospital discharge. A total of 60 articles were included in the review of which 58 were original articles and 2 were double-publications.

Of the 58 original articles 50% were (quasi-, cluster-) randomised controlled trials, 26% were (controlled) before-after studies and 24% were controlled clinical trials (see Table 2). Most studies were performed in the United Kingdom (38%), followed by the United States (24%) and Australia (16%). In 45% of studies ≤100 patients were analysed. The methodological quality of the studies was in general poor (78%, score <4). For

Figure 1 Flowchart of the inclusion process using the PRISMA 2009 guidelines[89]



* 58 original articles and 2 double-publications. Information from double-publications was combined.

Table 2 Characteristics of included studies and patient population

MQ of study	Study reference	Study characteristics				Patients		Characteristics study population			
		Design*	Country†	MQ‡ score	M§	Number analysed¶ I	C	Setting	Age (mean/range)	Gender (% men)	No. drugs at discharge (mean/range)
	Patient educational related interventions (E)										
Good MQ	Louis-Simonet 2004[45]	CBA	Switzerland	4	B	370	439	General internal medicine wards, university hospitals	63	50	5.2
	Manning 2007[46]	RCT	US	4	B	72	57	Medical units, academic medical center	68	50	9.4
Poor MQ	Baker 1991[39]	RCT	UK	3	B	49	52	Cardiology ward, hospital	52	63	3.4
	Edwards 1984[41]	RCT	UK	3	B	62	20	Acute medical wards, hospital	79	34	2.1
	Hawe 1990[42]	CCT	Australia	3	B	77	71	Elderly ward, hospital	69	42	3.6
	Johnston 1986[43]	RCT	UK	3	B	14	13	Medical wards, hospital	76	31	NR
	MacDonald 1977[61]	CCT	UK	3	B	105	60	Geriatric medicine ward, hospital	80	8	2.1
	Schneider 1993[30]	q-RCT	US	3	B	26	28	Cardiac nursing unit, medical center	72	50	6.0
	Al Rashed 2002[19]	c-RCT	UK	2	B	43	40	Elderly ward, hospital	81	57	7.1
	Baker 1984[40]	RCT	US	2	B	37	11	Medical/surgical ward, hospital	64	NR	3.4
	Cole 1971[58]	q-RCT	US	2	B	50	25	General hospital	18-80	NR	NR
	Raynor 1993[49]	RCT	UK	2	B	98	99	General medicine wards, general hospital	69	56	3.6
	Sherrard 2009[34]	RCT	Canada	2	A	137	143	Cardiac surgical wards, hospital	63	NR	NR
	Stitt 1979[51]	CCT	US	2	B	68	21	Medical/surgical/maternity wards, university hospital	47	31	NR
	Whyte 1994[55]	CCT	UK	2	B	24	24	Medical wards, hospital	61-95	NR	3.5
	Bjork Linne 1999[44]	RCT	Sweden	1	A	50	58	Heart failure ward, university hospital	70	64	NR
	Braun 2009[21]	q-RCT	Israel	1	A	153	156	Internal medicine ward, hospital	63	51	NR
	Esposito 1995[60]	RCT	US	1	B	23	19	Community medical centre, hospital	76	37	NR
	Strobach 2000/2001[52,53]	RCT	Germany	1	B	7	12	Internal medicine wards, university hospital	61	54	6.4
	Wolfe 1992[56]	CCT	US	1	B	18	20	Teaching and community hospital	74	42	4.6
	Kellaway 1979[25]	BAS	New Zealand	0	B	280	477	Acute general medical wards, hospital	NR	49	NR
	Sweeney 1989[62]	BAS	UK	0	B	29	39	Acute medical wards, general hospital	72	46	4.1

Table 2 Continued

MQ of study	Study reference	Study characteristics				Patients		Characteristics study population			
		Design*	Country†	MQ‡ score	M§	Number analysed¶ I	C	Setting	Age (mean/range)	Gender (% men)	No. drugs at discharge (mean/range)
	Patient educational and pharmacotherapy related interventions (E,P)										
Good MQ	Dudas 2001/2002[23,24]	RCT	US	4	A	110	111	General medical service, academic teaching hospital	55	47	NR
Poor MQ	Polack 2008[48]	RCT	Canada	3	A	4	10	University hospital	64	79	7.4
	Eurich 2001[70]	BAS	Canada	2	B	36	50	Acute care hospitals	69	56	NR
	Kramer 2007[26]	BAS	US	2	B	136	147	Adult general medical unit, medical center	65	50	7.1
	Begley 1997[37]	q-RCT	UK	1	A	61	129	Medical/surgical wards, hospitals	82	39	5.0
	Barret 2002[63]	BAS	UK	0	B	nr	nr	Diabetes/endocrine ward, hospital	NR	NR	NR
	Boorman 2000[65]	BAS	UK	0	B	102	187	Medical unit, general hospital	NR	NR	NR
	Patient educational and discharge information transfer related interventions (E,D)										
Good MQ	Sandler 1989[50]	q-RCT	UK	4	B	65	66	General medical ward, university hospital	62	62	3.9
	Stewart 1998[35]	RCT	Australia	4	C	49	48	Medical/surgical ward, tertiary referral hospital	75	48	6.7
Poor MQ	Cromarty 1998[68]	BAS	UK	2	B	46	26	Elderly ward, hospital	83	43	6.0
	Patient educational, pharmacotherapy and discharge information transfer related interventions (E,P,D)										
Good MQ	Makowsky 2009[27]	CCT	Canada	6	B	220	231	Internal/family medicine wards, tertiary care hospitals	74	46	NR
	Scullin 2007[32]	RCT	UK	6	B	370	384	Medical wards, general hospital	70	47	NR
	Eggink 2010[59]	RCT	Netherlands	4	B	41	44	Cardiology ward, teaching hospital	73	67	9.5
	Naunton 2003[28]	RCT	Australia	4	A	54	59	Medical wards, teaching hospital	76	37	8.0
	Nickerson 2005[73]	RCT	Canada	4	B	134	119	Family practice units, academically affiliated hospital	65	32	7.5
Poor MQ	Bolas 2004[20]	RCT	UK	2	B	81	81	Medical admissions ward, general hospital	74	49	6.8
	Brookes 2000[22]	h-CCT	UK	2	B	109	734	Medical admission ward, hospital	75	NR	8.0
	Burnett 2009[66]	q-RCT	UK	2	B	59	58	Medical wards, hospital	NR	NR	7.5
	Hugtenburg 2009[38]	CCT	Netherlands	2	A	336	379	Community pharmacies	71	48	7.4
	Pickrell 2001[47]	CCT	UK	2	B	15	17	Medical admission unit, hospital	64	47	6.7
	Vuong 2008[54]	RCT	Australia	2	A	127	132	Acute-care wards, tertiary teaching hospitals	72	53	10.5
	Sands 1994[29]	CCT	US	1	B	1364	801	General medical ward, teaching hospital	NR	NR	NR
	Cannon 1999[57]	RCT	UK	0	B	19	17	Acute care unit, hospital	81	23	NR

Table 2 Continued

MQ of study	Study reference	Study characteristics				Patients		Characteristics study population			
		Design*	Country†	MQ‡ score	M§	Number analysed¶ I	C	Setting	Age (mean/range)	Gender (% men)	No. drugs at discharge (mean/range)
	Pharmacotherapy related interventions (P)										
Good MQ	Schnipper 2009[31]	c-RCT	US	4	B	162	160	General medicine wards, academic hospitals	NR	45	1-33
	Varkey 2007[77]	BAS	US	4	B	51	51	Family medicine care unit, academic hospital	56	36	9.9
Poor MQ	Rose 2005[76]	CCT	UK	3	B	50	50	Hospital	NR	NR	NR
	Birdsey 2005[64]	BAS	Australia	2	B	35	39	Cardiology ward, tertiary referral hospital	NR	NR	7.9
	Setter 2009[33]	CCT	US	2	A	110	110	Visiting nurse association	74	45	9.6
	Chantelois 2003[67]	CCT	US	1	B	22	37	General medicine service, tertiary care hospital	NR	NR	NR
	Rahman 2005[75]	BAS	UK	1	B	128	133	General surgical ward, teaching hospital	NR	NR	4.7
	Whitty 2001[78]	CCT	Australia	1	B	29	26	General medical wards, hospital	NR	NR	5.1
	Lovitt 1992[72]	BAS	Australia	0	B	33	515	Surgical ward, hospital	NR	NR	4.0
	Pharmacotherapy and discharge information transfer related interventions (P,D)										
Good MQ	Stowasser 2002[36]	RCT	Australia	5	B	104	105	Acute wards/orthopaedic ward, hospitals	66	55	7.6
Poor MQ	Paquette-L. 2001[74]	BAS	Canada	3	B	34	55	Internal medicine wards, hospital	61	37	6.8
	deClifford 2009[69]	BAS	Australia	2	B	40	40	Neurology/respiratory wards, tertiary referral hospital	NR	NR	8.0
	Gray 2008[71]	BAS	UK	0	C	41	45	Community hospitals	NR	NR	NR

MQ = methodological quality, NR= not reported

* BAS= before, after study, CBA= controlled before, after study (a control group both in the usual care and in the intervention phase), CCT= controlled clinical trial (no random allocation described), h-CCT= CCT with historical control group, RCT= randomised controlled trial, c-RCT = cluster randomised controlled trial (randomisation based on cluster of patients instead of individuals), q-RCT= quasi randomised controlled trial (e.g. randomisation based on alternate allocation)

† UK= United Kingdom, US= United States

‡ MQ= methodological quality score, see Appendix B for the questionnaire and Appendix E for the score per item

§ M= moment of intervention: A= intervention performed after discharge, B= intervention performed before discharge, C= combined intervention performed both before and after discharge

¶ C= control, I= Intervention. The number of patients analysed differs for several outcomes, so in this table the lowest numbers of analysed patients (for the outcomes relevant for this review) are provided.

randomised studies, the randomisation procedure and the concealment of allocation was frequently not described. Also, the blinding of patients, intervention performers, and outcome assessors was not performed or not described in the studies. Most studies implemented patient educational related intervention (38%) and 79% of studies were conducted before discharge (Appendices C-E gives an alphabetic overview of the studies).

Readmission, health services use and mortality

In 17 studies the outcome readmission was reported (see Table 3).[19-36] Half of studies failed to define the readmissions as planned and/or unplanned. Also, 30% of studies measured the outcome through patient self-report. Most studies implemented the combination of patient educational (Ed), pharmacotherapy (Ph) and discharge information transfer (Dt) related interventions (35%) followed by patient educational interventions (29%). Three (18%) of 17 studies reported a significant decrease of readmissions. Al Rashed et al. implemented a patient educational intervention in patients who were over 65 years and prescribed ≥4 regular medications.[19] They reported that 33% of patients were readmitted in the control group vs 12% in the intervention group ($p<0.05$) two to three weeks post-discharge.[19] Stewart et al. included high risk congestive heart failure patients and implemented an "Ed,Dt" related intervention.[35] This study showed that patients in the intervention group were hospitalised less often after six months (10% control vs 0% intervention with ≥3 unplanned admissions, $p=0.02$).[35] Finally, Scullin et al. implemented an "Ed,Ph,Dt" related intervention for high risk patients (e.g. ≥65 years, ≥4 regular medications, had a hospital admission in the previous six months).[32] They reported an 8% reduction of readmissions after one year (49% control vs 41% intervention, $p=0.027$).[32]

In 10 studies the outcome health services use was reported.[19,23,24,26,27,31,33-37] The studies implemented different interventions ("Ed", "Ph", "Dt"). Four studies (40%) were effective in decreasing the health services use after discharge.[19,24,36,37] Three studies reported a decrease in healthcare practitioner visits and one study showed a decrease in emergency department visits.

Five studies assessed mortality.[28,32,35,36,38] None of these studies showed a significant benefit of the intervention.

Knowledge and adherence

In 20 studies the outcome knowledge was reported (Table 4).[19,20,37,39-56] Seventy percent of the studies implemented patient educational related interventions only, and the other studies implemented educational interventions together with other intervention types. Of the 20 studies 15 reported (75%) significant increases in patient knowledge.[19,20,39-41,43-50,52,53,55] The method for assessing medication knowledge differed from patient interviews at home, at the hospital or by phone to postal patient questionnaires.

Table 3 Outcome: hospital readmission (readm), health services use (HSU) and mortality

MQ*	M†	Reference	Measurement	Duration of follow up‡	NA	Outcome (measurement unit) §	P¶	Results			Conclusion**
								I	C	RR	(p-value)
		Patient educational related interventions (E)									
Poor	B	Al Rashed 2002[19]	Pat self-report (home)	2w-3w	83	Readm: unplanned (% of pat)	Y	12	33	0.36	**p<0.05**
			Pat self-report (home)	(3w to) 3m	83	Readm: unplanned (% of pat)	Y	7	38	0.19	**p<0.05**
			Pat self-report (home)	2w-3w	83	HSU: unplanned GP visits (% of pat)	Y	44	68	0.65	**p<0.05**
			Pat self-report (home)	(3w to) 3m	83	HSU: unplanned GP visits (% of pat)	Y	56	80	0.70	**p<0.05**
		Kellaway 1979[25]	NR	NR	757	Readm: NR (% of pat)	N	15	18	0.86	ns
		Schneider 1993[30]	Hospital's records	1m	54	Readm: admissions within 31 days (% of pat)	Y	8	29	0.27	p=0.05
	A	Braun 2009[21]	Pat self-report (phone)	1m	309	Readm: NR (% of pat)	Y	7	8	0.94	ns
			Pat self-report (phone)	3m	309	Readm: NR (% of pat)	Y	26	35	0.72	p=0.062
		Sherrard 2009[34]	Pat self-report (phone)	6m	280	Readm: NR (% of pat)	N	18	15	1.24	p=0.519
			Pat self-report (phone)	6m	280	HSU: ED visits (% of pat)	N	30	31	0.97	p=0.897
			Pat self-report (phone)	6m	280	Comb: adh↓ and ED/readm↑ (% of pat)	Y	49	62	0.80	**p=0.041**
		Patient educational and pharmacotherapy related interventions (E,P)									
Good	A	Dudas 2001/2002[23,24]	Hospital's records	1m	221	Readm: NR (% of pat)	N	15	25	0.60	p=0.07
			Hospital's records	1m	221	HSU: ED visits (% of pat)	N	10	24	0.42	**p=0.005**
Poor	B	Kramer 2007[26]	NR	1m	283	Readm: NR (% of pat)	N	6	12	0.51	ns
			NR	1m	283	HSU: ED visits (% of pat)	N	9	6	1.44	ns
	A	Begley 1997[37]	Pat self-report (home)	(0w to) 2w	124	HSU: patients consulting GP (% of pat)	N	11	12	0.92	ns
			Pat self-report (home)	(2w to) 1m	124	HSU: patients consulting GP (% of pat)	N	8	15	0.53	ns
			Pat self-report (home)	(1m to) 3m	124	HSU: patients consulting GP (% of pat)	N	29	44	0.66	ns
			Pat self-report (home)	(3m to) 1y	124	HSU: patients consulting GP (% of pat)	N	54	74	0.73	**p<0.01**
		Patient educational and discharge information transfer related interventions (E,D)									
Good	C	Stewart 1998[35]	Hospital's records	6m	97	Readm: unplanned (% of pat)	N	49	65	0.76	p=0.12
			Hospital's records	6m	97	Readm: ≥3 unplanned admissions (% of pat)	N	0	10	-	**p=0.02**
			Hospital's records	6m	97	Readm: rehospitalisations days (tot. days)	N	261	452	-	p=0.05
			Hospital's records	6m	97	HSU: ED visits (tot. number)	N	48	87	-	p=0.05
			Local registry	6m	97	Mortality (% of pat)	N	12	25	0.49	p=0.11
			Hospital/local registry	6m	97	Comb: unplanned readm/death (mean/pat)	Y	0.8	1.4	-	**p=0.03**

Table 3 Continued

MQ*	M†	Reference	Measurement	Duration of follow up‡	NA	Outcome (measurement unit) §	P¶	Results			Conclusion**
								I	C	RR	(p-value)
		Patient educational, pharmacotherapy and discharge information transfer related interventions (E,P,D)									
Good	B	Makowsky 2009[27]	Regional database	3m	452	Comb: any readm or ED (% of pat)	N	36	46	0.63[a]	**p=0.024**
			Regional database	6m	452	Comb: any readm or ED (% of pat)	N	51	56	0.78[a]	p=0.217
		Scullin 2007[32]	Hospital's computer	1y	754	Readm: NR (% of pat)	N	41	49	0.84	**p=0.027**
			Hospital's computer	1y	754	Readm: rehospitalisation days (mean days)	N	9.7	13.1	-	p=0.068
			Hospital's computer	1y	754	Readm: time to readm (mean days)	N	262	242	-	**p=0.036**
			NR	1y	754	Died at admission/readm/home (% of pat)	N	18	20	0.92	p=0.578
	A	Naunton 2003[28]	Hospital/ask pat	3m	121	Readm: unplanned (% of pat)	Y	28	45	0.62	p=0.05
			Hospital's records	3m	121	Out-of-hospital deaths (% of pat)	Y	5	8	0.63	ns
Poor	B	Bolas 2004[20]	Hospital's records	3m	162	Readm: NR (tot. number)	N	NR	NR	-	p>0.05
		Brookes 2000[22]	Hospital's records	4m	843	Readm: unplanned (% of pat)	N	6	9	0.67	NR
		Sands 1994[29]	Hospital's records	1m	nr	Readm: time to emergency readm (NR)	N	NR	NR	-	ns
	A	Hugtenburg 2009[38]	Pharmacy data	9m	715	Mortality (% of pat)	N	22	22	1.00	ns
		Pharmacotherapy related interventions (P)									
Good	B	Schnipper 2009[31]	Hospital's records	1m	322	Comb: readm/ED, NR (% of pat)	N	20	24	0.76[a]	ns
Poor	A	Setter 2009[33]	Pat self-report (phone)	2m	220	Readm: rehospitalisation days (mean days)	N	0.4	1.1	-	ns
			Pat self-report (phone)	2m	220	HSU: planned physician visits (mean/pat)	N	2.9	3.5	-	ns
			Pat self-report (phone)	2m	220	HSU: unplanned physician visits (mean/pat)	N	0.2	0.4	-	ns
		Pharmacotherapy and discharge information transfer related interventions (P,D)									
Good	B	Stowasser 2002[36]	Hospital's records	1m	240	Readm: unplanned (% of pat)	N	8	9	0.89	ns
			Pat questionnaire (post)	1m	209	HSU: (un)planned visits to HP (mean/pat)	N	7.5	9.9	-	**p<0.05**
			Pat questionnaire (post)	1m	209	HSU: planned visits to HP (mean/pat)	N	6.3	8.6	-	**p<0.05**
			Hospital's records	1m	240	Comb: (un)planned readm/ED (% of pat)	N	11	13	0.85	p=0.076
			Hospital's record/carer	1m	209	Mortality (% of pat)	N	2	2	0.75	ns

C= control, I= Intervention, NA= number analysed (patients), NR= not reported, RR= relative risk

* MQ= methodological quality score, see Appendix B for the questionnaire and Appendix E for the score per item.

† M= moment of intervention: A= intervention performed after discharge, B= intervention performed before discharge, C= combined intervention performed both before and after discharge.

‡ d= days, w= weeks, m= months, y= years. Duration of follow up not starting from the moment of discharge is written between brackets, e.g. " (3w) to 3m" means that the duration of follow-up is starting at 3 weeks and ending at 3 months. However, "1m-2m" means that the outcome was assessed from discharge to 1-2 month(s) after discharge. So duration of follow-up could be 1 month after discharge for one patient and 2 months after discharge for another patient.

§ adh= adherence, comb= combined outcome, ED= emergency department visits, HP= healthcare providers, HSU= health services use, GP= general practitioner, readm = readmission.

¶ P = primary outcome, as defined or outcome mentioned in the study objective (Y=yes, N=no).

** ns= non-significant. For studies with statistically significant outcomes p-values are given in bold.

[a]= adjusted OR

Table 4 Outcome: knowledge (knowl) and adherence (adh)

MQ*	M†	Reference	Measurement	Duration of follow up‡	NA	Outcome (measurement unit)§	P¶	Results			Conclusion** (p value)
								I	C	RR	
		Patient educational related interventions (E)									
Good	B	Louis-S. 2004[45]	Interview (phone)	1w-2w	809	Knowl: drug purpose, precautions, side effects (% of drugs)	Y	61	45	1.34	**p<0.001**
		Manning 2007[46]	Interview (phone)	1w-2w	135	Knowl [3] : frequency, purpose, instructions (mean score)	Y	2.0	1.7	-	**p=0.029**
Poor	B	Al Rashed 2002[19]	Interview (home)	2w-3w	83	Knowl: drug purpose , frequency, dose (% of drugs)	N	97	81	1.19	**p<0.05**
			Interview (home)	(3w) to 3m	83	Knowl: drug purpose , frequency, dose (% of drugs)	N	98	82	1.19	**p<0.05**
			Pill count (home)	2w-3w	83	Adh: 85%-115% correct dosage units (% of dosage units)	N	48	16	3.00	**p<0.001**
			Pill count (home)	3m	83	Adh: 85%-115% correct dosage units (% of dosage units)	N	70	16	4.38	**p<0.001**
		Baker 1984[40]	Questionnaire (post)	1w	21	Knowl [3]: name, purpose, dose (% of questions) *Effect written information*	Y	44	41	1.09	p>0.05
			Questionnaire (post)	1w	29	Knowl [3]: name, purpose, dose (% of questions) *Effect verbal counselling*	Y	61	41	1.49	**p<0.05**
			Questionnaire (post)	1w	20	Knowl [3]: name, purpose, dose (% of questions) *Effect written info and verbal counselling*	Y	77	41	1.89	**p<0.05**
		Baker 1991[39]	Questionnaire (post)	2w	101	Knowl: recall receiving info, e.g. purpose (% of questions)	Y	68	35	1.94	**p<0.05**
		Cole 1971[58]	Interview/pill count (phone)	2w	50	Adh: e.g. under-,over dosage, stop (% of pat) *Effect pharmacist discharge counselling*	Y	92	6	15.33	**p<0.05**
			Interview/pill count (phone)	2w	50	Adh: e.g. under-,over dosage, stop (% of pat) *Effect discharge counselling + self-administration teaching*	Y	88	6	14.67	**p<0.05**
		Edwards 1984[41]	Interview (home)	6d	82	Knowl: recall drug regimen (NR)	N	NR	NR	-	**p<0.02**
			Interview/pill count (home)	6d	82	Adh: correct amount of dosage units (% of drugs)	Y	85	76	1.12	**p<0.01**
		Esposito 1995[60]	Interview/pill count (home)	2w/1m/2m	42	Adh: correct amount of dosage units (adh score)	Y	NR	NR	-	NR
		Hawe 1990[42]	Interview (home)	1m	219	Knowl: drug purpose (mean score)	N	85.3	86.6	-	p>0.05
			Interview (home)	3m	148	Knowl: drug purpose (mean score)	N	85.6	87.3	-	p>0.05
			Interview (home)	1m	156	Adh [≥4]: self-report used drugs (% of pat)	Y	78	66	2.1[a]	p>0.05
			Interview (home)	3m	100	Adh [≥4]: self-report used drugs (% of pat)	Y	68	45	2.5[a]	**p<0.05**
		Johnston 1986[43]	Interview (discharge)	discharge	27	Knowl: recall e.g. name, purpose, dose (median score)	Y	93	77	-	**p=0.02**
		Kellaway 1979[25]	Interview (clinic)	NR	757	Adh: self-report correct use (% of pat)	Y	80	68	1.18	**p<0.01**
		MacDonald 1977[61]	Interview (clinic)	1w	67	Adh: e.g. under-, over dosage, old medication (% of pat)	Y	83	46	1.80	**p<0.05**

Table 4 Continued

MQ*	M†	Reference	Measurement	Duration of follow up‡	NA	Outcome (measurement unit)§	P¶	Results			Conclusion**
								I	C	RR	(p value)
			Interview (clinic)	3m	67	Adh: e.g. under-, over dosage, old medication (% of pat)	Y	71	35	2.03	**p<0.05**
		Raynor 1993[49]	Interview (home)	10d	197	Knowl: frequency, dose, administration time (% of pat)	N	83	47	1.74	**p<0.001**
			Pill count (home)	10d	191	Adh: correct dosage units (% of pat with score >85%)	Y	86	63	1.37	**p<0.001**
		Stitt 1979[51]	Interview (home)	7d-10d	89	Knowl [2]: e.g. name, purpose (% better than control)	Y	23	-	-	p>0.05
			Pill count (home)	7d-10d	89	Adh [2]: e.g. medication, dose, frequency (adh %) *Effect of written instructions*	N	83	80	1.04	p>0.05
			Pill count (home)	7d-10d	89	Adh [2]: e.g. medication, dose, frequency (adh %) *Effect of audiovisual instructions*	N	92	80	1.15	**p<0.05**
		Strobach 2000/2001[52,53]	Interview (discharge)	discharge	33	Knowl: indication (% of NR)	Y	82	40	2.05	**p<0.05**
			Interview (phone)	2w	19	Knowl: indication (% of NR)	Y	90	41	2.20	**p<0.05**
			Interview (discharge)	discharge	33	Knowl: frequency of medication (% of NR)	Y	61	22	2.77	**p<0.05**
			Interview	2w	19	Knowl: frequency of medication (% of NR)	Y	100	55	1.82	**p<0.05**
		Sweeney 1989[62]	Pill count (home)	1w	88	Adh: prescribed vs taken (% of pat)	Y	74	35	2.12	**p<0.05**
			Pill count (home)	6w-7w	68	Adh: prescribed vs taken (% of pat)	Y	55	31	1.80	**p<0.05**
		Whyte 1994[55]	Interview (home)	2d-5d	48	Knowl: name, purpose, special instructions (NR)	Y	NR	NR	-	**p<0.05**
			Interview (home)	2d-5d	48	Knowl: description of drug, time, administration amount (NR)	Y	NR	NR	-	p>0.05
		Wolfe 1992[56]	Interview (home)	3w-6w	38	Knowl: e.g. dose, instructions, side effects (mean score)	Y	44.7	45.8	-	p>0.05
			Interview (home)	3w-6w	38	Adh: e.g. right dose, frequency, duration (% of pat)	Y	50	65	0.77	p>0.05
	A	Braun 2009[21]	Interview (phone)	3m	309	Adh: self-report, e.g. obtain all medications (% of pat)	Y	91	82	1.11	**p=0.04**
		Bjork Linne 1999[44]	Questionnaire (clinic)	1m	114	Knowl: e.g. side effects, crush tablets (mean score)	Y	17.6	12.9	-	**p<0.0001**
			Questionnaire (clinic)	6m	108	Knowl: e.g. side effects, crush tablets (mean score)	Y	17.2	14.3	-	**p=0.0051**
		Sherrard 2009[34]	Interview (phone)	6m	280	Adh: patient reported (% of pat)	N	75	50	1.50	**p<0.0001**

Table 4 Continued

MQ*	M†	Reference	Measurement	Duration of follow up‡	NA	Outcome (measurement unit)§	P¶	Results			Conclusion** (p value)
								I	C	RR	
		Patient educational and pharmacotherapy related interventions (E,P)									
Poor	A	Begley 1997[37]	Interview (home)	(0w) to 2w	124	Knowl: e.g. name, purpose, dose (mean score in %)	N	82	76	1.08	p>0.05
			Interview (home)	(2w) to 1m	124	Knowl: e.g. name, purpose, dose (mean score in %)	N	78	71	1.10	p>0.05
			Interview (home)	(3m) to 1y	124	Knowl: e.g. name, purpose, dose (mean score in %)	N	70	68	1.03	p>0.05
			Pill count (home)	(0w) to 2w	124	Adh: ≥ 85% correct drug doses (mean score in %)	Y	94	73	1.29	**p<0.0001**
			Pill count (home)	(2w) to 1m	124	Adh: ≥ 85% correct drug doses (mean score in %)	Y	95	73	1.30	**p<0.0001**
			Pill count (home)	(3m) to 1y	124	Adh: ≥ 85% correct drug doses (mean score in %)	Y	86	75	1.15	**p<0.0001**
		Polack 2008[48]	Interview (phone)	1m-2m	9	Knowl: stop drug if values are normal? (% of pat correct)	Y	100	0	-	**p<0,001**
			Interview (home visit)	1m-2m	9	Adh: self-reported medication taking (% of pat)	Y	75	80	0.94	p>0.05
		Patient educational and discharge information transfer related interventions (E,D)									
Good	B	Sandler 1989[50]	Interview (clinic)	4w	131	Knowl: drug names, frequency, purpose (% of pat)	Y	89	49	1.81	**p<0.001**
		Patient educational, pharmacotherapy related and discharge information transfer related interventions (E,P,D)									
Good	B	Eggink 2010[59]	Interview (clinic)	3w	85	Adh: self-reported e.g. stop , miss dose (% of pat)	N	22	21	1.07	p>0.05
	A	Naunton 2003[28]	Pill count (home)	3m	121	Adh: taking more/less medication (% of pat)	N	94	78	1.21	**p<0.01**
			Interview (home)	3m	121	Adh: self-report; never miss a medication (% of pat)	N	87	44	1.98	**p<0.001**
Poor	B	Bolas 2004[20]	Interview (phone/home)	10d-14d	171	Knowl: drug name, dose, frequency (mean error rate/pat %)	Y	85	60	1.43	**p<0.001**
		Cannon 1999[57]	Interview (phone)	1m	36	Adh: self-report, e.g. frequency, miss dose (mean score)	N	NR	NR	-	p>0.05
		Pickrell 2001[47]	Interview (phone/home)	2w	32	Knowl: self-report, e.g. indications, dose (mean score)	N	84	36	-	**p<0.05**
		Sands 1994[29]	Interview (phone)	NR	NR	Adh: self-report medication taking (% of pat)	N	96	87	1.10	p=0.3
	A	Vuong 2008[54]	Interview (phone)	8w-12w	259	Knowl: e.g. name, dose, purpose, side effects (mean score)	N	0.7	0.8	-	**p=0.001**
			Interview (phone)	2m-3m	259	Adh: self-report, e.g. forget, stop (mean score, low=better)	N	0.2	0.4	-	**p=0.028**

C= control, I= Intervention, NA= number analysed (patients), NR= not reported, RR= relative risk

* MQ= methodological quality score, see Appendix B for the questionnaire and Appendix E for the score per item.

† M= moment of intervention. A= intervention performed after discharge, B= intervention performed before discharge, C= combined intervention performed both before and after discharge.

‡ d= days, w= weeks, m= months, y= years. Duration of follow up not starting from the moment of discharge is written between brackets, e.g. " (3w) to 3m" means that the duration of follow-up is starting at 3 weeks and ending at 3 months. However, "1m-2m" means that the outcome was assessed from discharge to 1-2 month(s) after discharge. So duration of follow-up could be 1 month after discharge for one patient and 2 months after discharge for another patient.

§ adh= adherence, knowl = knowledge. [number]=outcome was assessed per patient for this number of drugs, thus "knowl: [2]" means that for only two drugs the knowledge was asked.

¶ P = primary outcome, as defined or outcome mentioned in the study objective (Y=yes, N=no).

** ns= non-significant. For studies with statistically significant outcomes p-values are given in bold. Only Vuong et all. reported significant better knowledge outcomes in the control group.

[a]= adjusted OR

Table 5 Outcome: Drug-related problems (DRPs)

MQ*	M†	Reference	Measurement	Duration of follow up‡	NA	Outcome§	P¶	Results			Conclusion**
								I	C	RR	(p-value)
		Patient educational related interventions (E)									
Good	B	Manning 2007[46]	Pat interview (phone)	1w-2w	129	Self-reported error: e.g. wrong time, missed pill (mean score/pat)	Y	0.8	0.8	-	p=0.88
		Patient educational and pharmacotherapy related interventions (E,P)									
Poor	B	Barrett 2002[63]	Interventions by dispensary pharmacist	discharge	NR	No intervention required: e.g. interactions, illegibility's (% of DP)	N	99	94	1.06	**p<0.05**
		Boorman 2000[65]	Compare discharge vs in-hospital list	discharge	289	No alterations: e.g. prescribing errors, omission (% of DP)	Y	92	68	1.35	**p<0.0001**
		Eurich 2001[70]	Pat interview (phone)	1w	86	No interchange problems: e.g. use only original drug (% of pat)	Y	97	86	1.13	p>0.05
		Kramer 2007[26]	Compare in-hospital vs home list	discharge	283	Interventions: e.g. dose changes, allergy documentation (number)	N	48	24	-	**p=0.0003**
		Patient educational and discharge information transfer related interventions (E,D)									
Poor	B	Cromarty 1998[68]	Pat interview (home)	10d-14d	72	No management problems: e.g. restart old drugs (% of pat)	N	78	54	1.44	**p<0.05**
		Patient educational, pharmacotherapy and discharge information transfer related interventions (E,P,D)									
Good	B	Eggink 2010[59]	Review + discharge vs post-discharge list	3w	85	No deviations in medication use/no prescription errors (% of pat)	Y	61	32	1.92	**p<0.05**
		Makowsky 2009[27]	Review + compare discharge vs home list	discharge	451	Indicators: e.g. vaccination, prophylactic drugs (% of indicators)	Y	56	45	1.25	**p<0.05**
		Nickerson 2005[73]	Compare discharge vs in-hospital list	discharge	147	No interventions required: e.g. alterations, delete drug (% of pat)	Y	96	44	2.21	**p<0.05**
	A	Naunton 2003[28]	Review DRPs (home)	3m	121	No drug issues: e.g. interaction, duplication, use (% of pat)	N	35	14	2.50	**p<0.01**
			Review NSAID use (home)	3m	113	No re-use of discontinued NSAIDs or use of NSAIDs (% of pat)	N	91	76	1.20	**p<0.05**
Poor	B	Bolas 2004[20]	Compare discharge vs post-discharge list	10d-14d	171	Mismatch: name differs post-discharge (mismatch rate/pat in %)	Y	2	7	0.21	**p<0.005**
			Compare discharge vs post-discharge list	10d-14d	171	Mismatch: dose differs post-discharge (mismatch rate/pat in %)	Y	10	17	0.59	p<0.07
			Compare discharge vs post-discharge list	10d-14d	171	Mismatch: frequency differs post-discharge (mismatch /pat in %)	Y	11	18	0.61	**p<0.004**
		Burnet 2009[66]	MAI instrument for scoring discharge list	discharge	117	MAI: appropriateness of drugs (mean MAI, low score is better)	Y	5.7	10.0	-	**p=0.03**
		Cannon 1999[57]	Pat interview (phone)/GP contact	1m	36	No medication changes: changes post-discharge (% of pat)	N	56	18	3.16	**p<0.05**
		Pickrell 2001[47]	Compare in-hospital list vs pat/GP info	discharge	32	No changes: e.g. omission, dose error (% of drugs)	N	88	40	2.22	**p<0.001**
	A	Hugtenburg 2009[38]	Pharmacy computer system signals/review	discharge	715	Community pharmacy intervention: not dispensed (% of pat)	N	24	14	1.68	**p=0.001**
			Pharmacy computer system signals/review	discharge	715	Intervention: additional dispensed (% of pat)	N	9	3	3.07	**p=0.001**
			Pharmacy computer system signals/review	discharge	715	Intervention: change dose (% of pat)	N	13	8	1.68	**p=0.02**
			Pharmacy computer system signals/review	discharge	715	Intervention: change dosage form (% of pat)	N	5	5	1.00	p=0.968
			Pharmacy computer system signals/review	discharge	715	Intervention: substitution (% of pat)	N	28	26	1.09	p=0.497
			Pharmacy computer system signals/review	discharge	715	Intervention: change due to signal (% of pat)	N	8	8	1.11	p=0.684

Table 5 Continued

MQ*	M†	Reference	Measurement	Duration of follow up‡	NA	Outcome§	P¶	Results			Conclusion**
								I	C	RR	(p-value)
		Pharmacotherapy related interventions (P)									
Good	B	Schnipper 2009[31]	Compare discharge vs home/in-hospital list	discharge	322	Incidents with potential for injury related to a drug (mean/pat)	Y	0.8	1.1	0.67[a]	**p<0.05**
		Varkey 2007[77]	Compare discharge vs home/in-hospital list	discharge	102	Discrepancies: e.g. medication name, dose, schedule (mean/pat)	Y	1.8	3.3	-	**p=0.003**
Poor	B	Birdsey 2005[64]	Review + compare discharge vs in-hospital list	discharge	74	No prescribing errors: e.g. omission, dose error (% of DP)	Y	100	74	1.35	**p<0.05**
		Chantelois 2003[67]	Review + compare discharge vs in-hospital list	discharge	59	Accurate prescription: orders accepted as written (% of DP)	Y	96	56	1.71	**p<0.05**
		Lovitt 1992[72]	Questions from dispensing pharmacist	discharge	nr	No errors: e.g. illegibility, wrong drug , unsigned, (% of DP)	N	68	13	5.24	**p<0.001**
		Rose 2005[76]	Compare discharge vs in-hospital list	discharge	100	Accurate prescription: orders accepted as written (% of DP)	Y	98	91	1.08	**p<0.01**
		Whitty 2001[78]	Compare discharge vs in-hospital list	discharge	55	No queries raised: e.g. omission, incorrect dose (% of DP)	Y	99	92	1.08	**p<0.05**
		Rahman 2005[75]	Compare discharge vs in-hospital list	discharge	261	Errors: wrong drug, dose, omission (number)	Y	1	118	-	**NR**
	A	Setter 2009[33]	Compare discharge vs in-hospital list	2m	220	No discrepancies: e.g. dose, drug (% of discrepancies resoluted)	Y	67	55	1.22	**p<0.05**
		Pharmacotherapy and discharge information transfer related interventions (P,D)									
Good	B	Stowasser 2002[36]	Compare discharge vs home//in-hospital list	discharge	240	Intervention: e.g. discontinue, dose error, add drug (% of pat)	N	68	44	1.55	**p<0.05**
Poor	B	deClifford 2009[69]	Compare discharge vs in-hospital list	discharge	80	Prescribing errors, e.g. drug omission, incorrect drug (mean/pat)	Y	0.1	0.8	-	**p=0.0005**
		Paquette-L. 2001[74]	Compare discharge vs post-discharge list	10d	89	Conformity rate: pharmacy correct documentation (% of pat)	Y	82	40	2.05	**p<0.001**
	C	Gray 2008[71]	Review recommendations follow-up	6w	86	Implementation of treatment plans (% of pat)	Y	83	51	1.62	**p<0.05**

C= control, I= Intervention, NA= number analysed (patients), NR= not reported, RR= relative risk

* MQ= methodological quality score, see Appendix B for the questionnaire and Appendix E for the score per item.

† M= moment of intervention. A= intervention performed after discharge, B= intervention performed before discharge, C= combined intervention performed both before and after discharge.

‡ d= days, w= weeks, m= months, y= years.

§ DP= discharge prescriptions, NSAIDs = non-steroidal anti-inflammatory drugs.

¶ P = primary outcome, as defined or outcome mentioned in the study objective (Y=yes, N=no).

** ns= non-significant. For studies with statistically significant outcomes p-values are given in bold.

[a]= adjusted OR

Knowledge was assessed on aspects such as drug purpose, dose, frequency and side effects.

Twenty studies reported results on adherence.[19,21,25,28,29,34,37,41,42,48,49,51,54,56-62] Of these 65% implemented patient educational interventions, followed by the combination of "Ed, Ph, Dt" related interventions (25%). Of the 20 studies 14 (70%) reported significant increases in adherence.[19,21,25,28,34,37,41,42,49,51,54,58,61,62] Adherence was assessed through patient interviews (at home, at the hospital or by phone) and pill counts. Studies failed to report the definition of acceptable adherence, but in general ≥85% correct use of the amount of dosage units was used.

Drug-related problems

In 28 studies DRPs were analysed (Table 5).[20,26-28,31,33,36,38,46,47,57,59,63-78] Studies mostly implemented pharmacotherapy related interventions (32%) and the combination of "Ed, Ph, Dt" related interventions (32%). Twenty-six studies (93%) reported significant results in decreasing DRPs.[20,26-28,31,33,36,38,47,57,59,63-69,71-78] Studies focused on eliminating discrepancies between the medication list at hospital discharge versus the home or in-hospital medication list. Discharge medication lists could also be reviewed to prevent duplication of medications or incorrect doses. Seven studies showed that pharmacists/pharmacy technicians discharge transcribing/preparing decreased medication errors in the discharge medication list (compared with hospital physician discharge prescribing).[63-65,67,69,75,76]

Costs

Studies generally do not report the cost-effectiveness of the interventions implemented. One study reported that mean costs of hospital-based care tended to be lower in the intervention group ($3200, 95% CI $1800-$4600, Australian dollars) compared with the control group ($5400, 95% CI $3200-$6800). Also, costs associated with community-based healthcare ($620/patient intervention vs $680/patient control) were non-significant between groups.[35]

Comparison of effective and ineffective studies

Two (29%) of 7 studies with good and 1 (10%) of 10 studies with poor methodological quality were effective in decreasing hospital readmissions (Table 6). The methodological quality of the study did not influence the effectiveness of the outcomes health services use and DRPs. For the outcome knowledge all three good quality studies were effective compared to 71% of poor quality studies. For the outcome adherence poor quality studies were more frequently effective (72% poor vs 50% good). However, there were only two good quality studies measuring adherence.

Table 6 Comparison of study characteristics between effective (eff) and ineffective (ineff) studies

Characteristic of DMI	**Readmission (n=17)**		**Health serv. use (n=10)**		**Knowledge (n=20)**		**Adherence (n=20)**		**DRPs (n=28)**	
(number of studies)	Eff (n=3)	Ineff (n=14)	Eff (n=4)	Ineff (n=6)	Eff (n=15)	Ineff (n=5)	Eff (n=14)	Ineff (n=6)	Eff (n=26)	Ineff (n=2)
[% of total number of studies]	[18%]	[82%]	[40%]	[60%]	[75%]	[25%]	[70%]	[30%]	[93%]	[7%]
Methodological quality										
Good	2 (29%)	5 (71%)	2 (40%)	3 (60%)	3 (100%)	-	1 (50%)	1 (50%)	7 (88%)	1 (13%)
Poor	1 (10%)	9 (90%)	2 (40%)	3 (60%)	12 (71%)	5 (29%)	13 (72%)	5 (28%)	19 (95%)	1 (5%)
Outcome defined as primary										
Yes	1 (25%)	3 (75%)	1 (100%)	-	11 (85%)	2 (15%)	9 (75%)	3 (25%)	17 (89%)	2 (11%)
No	2 (15%)	11 (85%)	3 (33%)	6 (67%)	4 (57%)	3 (43%)	5 (63%)	3 (38%)	9 (100%)	-
Number analysed (sample)		a						a	a	
0 - <100	2 (67%)	1 (33%)	1 (50%)	1 (50%)	8 (80%)	2 (20%)	6 (55%)	5 (45%)	10 (91%)	1 (9%)
100 - <200	-	2 (100%)	1 (100%)	-	6 (86%)	1 (14%)	4 (100%)	-	6 (86%)	1 (14%)
200 - <300	-	5 (100%)	2 (40%)	3 (60%)	-	2 (100%)	2 (100%)	-	5 (100%)	-
>300	1 (17%)	5 (83%)	-	2 (100%)	1 (100%)	-	2 (100%)	-	3 (100%)	-
Intervention moment										
Before	2 (18%)	9 (82%)	2 (40%)	3 (60%)	13 (81%)	3 (19%)	9 (64%)	5 (36%)	22 (92%)	2 (8%)
After	-	5 (100%)	2 (50%)	2 (50%)	2 (50%)	2 (50%)	5 (83%)	1 (17%)	3 (100%)	-
Combined	1 (100%)	-	-	1 (100%)	-	-	-	-	1 (100%)	-
Intervention type*										
Educational (Ed)	1 (20%)	4 (80%)	1 (50%)	1 (50%)	11 (79%)	3 (21%)	11 (85%)	2 (15%)	-	1 (100%)
Pharmacotherapy (Ph)	-	2 (100%)	-	2 (100%)	-	-	-	-	9 (100%)	-
Ed,Ph	-	2 (100%)	2 (67%)	1 (33%)	1 (50%)	1 (50%)	1 (50%)	1 (50%)	3 (75%)	1 (25%)
Ed,Dt (Discharge transfer)	1 (100%)	-	-	1 (100%)	1 (100%)	-	-	-	1 (100%)	-
Ph,Dt	-	1 (100%)	1 (100%)	-	-	-	-	-	4 (100%)	-
Ed,Ph,Dt	1 (17%)	5 (83%)	-	1 (100%)	2 (67%)	1 (33%)	2 (40%)	3 (60%)	9 (100%)	-

Table 6 Continued

Characteristic of DMI	Readmission (n=17)		Health serv. use (n=10)		Knowledge (n=20)		Adherence (n=20)		DRPs (n=28)	
(number of studies)	Eff (n=3)	Ineff (n=14)	Eff (n=4)	Ineff (n=6)	Eff (n=15)	Ineff (n=5)	Eff (n=14)	Ineff (n=6)	Eff (n=26)	Ineff (n=2)
[% of total number of studies]	[18%]	[82%]	[40%]	[60%]	[75%]	[25%]	[70%]	[30%]	[93%]	[7%]
Number of intervention types										
One intervention type	1 (14%)	6 (86%)	1 (25%)	3 (75%)	11 (79%)	3 (21%)	11 (85%)	2 (15%)	9 (90%)	1 (10%)
Two intervention types	1 (25%)	3 (75%)	3 (60%)	2 (40%)	2 (67%)	1 (33%)	1 (50%)	1 (50%)	8 (89%)	1 (11%)
Three intervention types	1 (17%)	5 (83%)	-	1 (100%)	2 (67%)	1 (33%)	2 (40%)	3 (60%)	9 (100%)	-
Intervention performer †		b			b		b	b		b
Involves Hospital physician (H)	-	4 (100%)	-	2 (100%)	3 (100%)	-	2 (67%)	1 (33%)	9 (100%)	-
Involves Nurse (N)	1 (14%)	6 (86%)	-	5 (100%)	5 (83%)	1 (17%)	4 (80%)	1 (20%)	3 (100%)	-
Involves Pharmacist (P)	3 (23%)	10 (77%)	4 (44%)	5 (56%)	13 (76%)	4 (24%)	12 (80%)	3 (20%)	26 (96%)	1 (4%)
Number of intervention performers		b			b		b	b		b
1 intervention performer	2 (18%)	9 (82%)	4 (67%)	2 (33%)	9 (64%)	5 (36%)	10 (63%)	6 (38%)	14 (93%)	1 (7%)
2 intervention performers (various)	1 (50%)	1 (50%)	-	2 (100%)	5 (100%)	-	1 (100%)	-	10 (91%)	1 (9%)
3 intervention performers (H,N,P)	-	3 (100%)	-	2 (100%)	1 (100%)	-	2 (100%)	-	2 (100%)	-

* Ed= educational related intervention, Ph= pharmacotherapy related intervention, Dt= discharge information transfer related intervention

† Healthcare providers performing the study intervention as stated by the study. In one study several healthcare providers could be involved.

a= the number analysed was not reported by the study measuring the outcome readmission (one ineffective study), adherence (one ineffective study) and DRPs (two effective studies)

b= the healthcare providers performing the intervention were not specified by the study measuring the outcome readmission (one ineffective study), knowledge (one effective study), adherence (one effective and ineffective study), and DRPs (one ineffective study).

When the outcome studied was stated as primary, studies tended to be effective more frequently (except for the outcome DRPs) compared to studies not stating that an outcome was primary.
Studies having a larger number of patients analysed (i.e. sample size) tended to be more frequently effective for the outcomes knowledge, adherence and DRPs. For the outcomes readmission and health services use comparison is limited due to the small number of studies per category.
The intervention moment (before or after discharge) did not matter for the outcome DRPs and health services use. For the outcome knowledge, studies implementing an intervention before discharge seemed more frequently effective (81% before vs 50% after). The opposite was the case for the outcome adherence (64% before vs 83% after). For the outcome readmission comparison is limited due to the small number of studies per category.
The intervention type ("Ed", "Ph", "Dt" or combined) does not seem to influence the outcome DRPs. For the outcomes knowledge and adherence focusing on one intervention type (i.e. educational) leads more frequently to effective studies. For the outcome health services use, combining interventions seems more effective and for readmissions no difference was seen.
The number or the profession of the intervention performer (i.e. nurse, physician, pharmacist) does not seem to influence the outcome DRPs. For knowledge and adherence, involving different intervention performers, leads more frequently to effective studies. For the outcome health services use, one intervention performer was effective. However, there were limited studies in the different categories, which was also the case for hospital readmission.

DISCUSSION

This review showed that various and multicomponent discharge medication related interventions have been developed and influenced a variety of outcomes. Effective studies were 3 of 17 (18%) for hospital readmissions, 4 of 10 studies (40%) for health services use after discharge, 15 of 20 studies (75%) for medication knowledge, 14 of 20 studies (70%) for medication adherence and 26 of 28 studies (93%) for DRPs. No effect was seen on mortality (5 studies) and on cost-effectiveness (1 study). The methodological quality of studies did not influence the outcomes health services use and DRPs. For the outcomes readmission and knowledge good quality studies tended to be more frequently effective. For adherence poor quality studies tended to be more frequently effective. In general, a primary outcome and large sample sizes led more frequently to effective

studies. The intervention moment, number of intervention types and the intervention performer led to heterogeneous results for the outcomes studied.

The discharge medication related interventions focused on continuity of information and management continuity.[1] The limited effect of DMIs on morbidity (e.g. readmission and health services use) may be a result of focusing on all patients instead of high risk patients, the poor methodological quality of studies or the limited sample sizes. However, it could also be that DMIs only influence process measures as medication knowledge, medication adherence and DRPs. Reports discuss that the ideal transition to decrease hospital readmissions should contain several elements and medication related interventions is just one of them.[79-81]

Our results are consistent with previous reviews, but extend previous work by focusing explicitly on medication related interventions around discharge, reporting outcomes of all studies (e.g. also studies with poor methodological quality) and focusing on specific study characteristics. Two reviews similarly reported that drug- related problems can be reduced and that there is limited evidence on reducing morbidity, mortality, or healthcare costs.[82,83] Kaboli et al. found that interventions on medication improved medication adherence and knowledge as was also the case in this review.[84] Parker et al. showed that discharge arrangements across the hospital–community interface are safe (not associated with increased mortality or other adverse outcomes) and that they reduce hospital readmission rates by about 20%, but this review included studies that implemented multiple interventions.[12,85] Spinewine et al. also stressed that the methodological quality of studies focusing on DMIs is low and that studies are underpowered to detect significant improvements in clinical outcomes.[17]

The strength of our review was that we performed a comprehensive study on DMI and reported several outcomes. We did not exclude studies based on their methodological quality or year of publication and therefore give an overview of all published studies. Limitations of this systematic review and included studies also need to be discussed. First, many intervention studies had small sample sizes, and most were single-institution studies, limiting generalisability. Second, we included only published trials, the reported findings may overestimate the true effect of such interventions due to publication bias. However, this study reported a range of studies with effective and ineffective outcomes. Third, we excluded vulnerable patients groups (including cognitive impaired, psychiatric and paediatric patients) to obtain a relative homogeneous study population. However, these patients are at high risk of suffering from adverse consequences of discontinuity of care. Fourth, we only included medication related discharge interventions to be able to demonstrate the effect of these DMI's. Several studies have shown that additional interventions can decrease hospital readmissions by themselves.[86-88] Therefore, we excluded studies that focused on additional interventions as often performed in heart failure populations (e.g. advice on diet or weight, appointments early after discharge).

Reviews on combined interventions have already been published.[8-10,16,86] Finally, different study designs, study characteristics and outcome definitions were used in the studies. It is difficult to standardise the studies, making it impossible to combine results, as in meta-analysis. Through classifying study characteristics we aimed to show their influence. However, it remains difficult to separate the individual components of medication related interventions and therefore definitive conclusions about which characteristics are important for positive outcomes are impossible to draw. Future studies should describe interventions in sufficient detail (for example in a study protocol) so that intervention components are clear. Outcomes should be based on validated and objective measures. Studies should have appropriate sample sizes and should give more insight in the cost-effectiveness of the interventions.

In conclusion, discharge medication related interventions were reported to be effective for medication knowledge, adherence and DRPs. Limited effect was reported on hospital readmission, health services use and cost-effectiveness. This limited effect may be due to the small sample sizes used in the studies and the low methodological quality. It could also be that DMIs solely are not enough to affect morbidity.

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Appendix A	Search strategy in electronic databases		
Search components	**Type**	**Database: Pubmed/Cochrane***	**Database: Embase***
Intervention around discharge AND	Terms	patient education as topic OR patient discharge OR patient care team OR aftercare OR continuity of patient care OR counselling	patient education OR hospital discharge OR patient care OR follow up OR patient counselling
	Text word	OR discharg* OR postdischarge OR seamless OR aftercare	
Related to medication AND	Terms	pharmaceutical preparations OR drug prescriptions OR Pharmacy service, hospital OR pharmacists OR drug utilization review	pharmaceutical care OR pharmacist OR drug use
	Text word	OR medication OR pharmacist	
With the following outcomes	Terms	patient compliance OR patient readmission OR mortality OR medication errors OR cost-benefit analysis	patient compliance OR hospital readmission OR mortality OR medication error OR health care cost
	Text word	OR complian* OR adheren* OR readmission* OR reconciliation OR medication review OR error OR adverse drug events OR drug related problems OR knowledge	
Limitations	Terms and text words	Language selection: AND (English OR German OR Dutch OR Turkish) Publication type: NOT (editorial OR letter OR news OR case reports OR abstract) Population: NOT (psychiatry OR schizophrenia OR schizo* OR psychia* OR childr* OR pediatr*)	

*The indexed terms used differed between the three databases. The same free text words were used in the databases.

Appendix B The Amsterdam-Maastricht score list for randomised clinical trials and controlled clinical trials

1. Were the patients in the study randomly assigned to the intervention?
   O Yes O No O Unclear

2. Was the concealment of allocation adequate?
   O Yes O No O Unclear

3. Was the study free from substantial loss to follow-up?
   O Yes O No O Unclear

4. Were all included patients analysed in the group they were randomised in (intention to treat analysis)?
   O Yes O No O Unclear

5. Were the patients blind to the intervention?
   O Yes O No O Unclear

6. Were the enrolling investigators blind to the intervention?
   O Yes O No O Unclear

7. Were the outcome assessors blind to the intervention?
   O Yes O No O Unclear

8. Were the groups comparable at the start of the trial on different prognostic characteristics (duration of illness, co-morbidity, severity of illness...)?
   O Yes (no, but corrected in the analysis) O No and not corrected in the analysis O Unclear

9. Were the groups, apart from treatment, equally provided with care (co-interventions, contamination, compliance)?
   O Yes O No O Unclear

10. Was the study apparently free from other problems that could put it at a risk of bias?
    O Yes O No O Unclear

Appendix C Study, patient's characteristics and objective of studies

Study (reference)	Study characteristics		Number of patients‡				Characteristics study population					Study objective
	Design*	Country†	Number randomised		Number analysed		Setting	Study population§	Age (mean)	Gender (% men)	No. discharge drugs (mean)	Effect of: on
			I	C	I	C						
Al Rashed 2002[19]	c-RCT	UK	45	44	43	40	Elderly ward, hospital	NR	81	57	7.1	Pre-discharge counselling: patients therapeutic management
Baker 1984[40]	RCT	US	56	16	37	11	Medical/surgical ward, hospital	NR	64	NR	3.4	Pre-discharge counselling: patients knowledge of their drugs
Baker 1991[39]	RCT	UK	61	64	49	52	Cardiology ward, hospital	Cardio	52	63	3.4	Drug leaflets: medication understanding/recall of information
Barrett 2002[63]	BAS	UK	319	284	NR	NR	Diabetes/endocrine ward, hospital	Int	NR	NR	NR	Pharmacist discharge prescription writing: several outcomes
Begley 1997[37]	q-RCT	UK	74	148	61	129	Medical/surgical wards, hospitals	Cardio	82	39	5.0	Domiciliary pharmacy visit post-discharge: drugs management
Birdsey 2005[64]	BAS	Australia	35	39	35	39	Cardiology ward, tertiary referral hospital	Cardio	NR	NR	7.9	Pharmacist discharge prescription writing: medication errors
Bjork Linne 1999[44]	RCT	Sweden	64	66	50	58	Heart failure ward, university hospital	HF	70	64	NR	Systematic education post-discharge: knowledge of medication
Bolas 2004[20]	RCT	UK	119	124	81	81	Medical admissions ward, general hospital	NR	74	49	6.8	Hospital based liaison pharmacist: medicines management
Boorman 2000[65]	BAS	UK	NR	NR	102	187	Medical unit, general hospital	NR	NR	NR	NR	Team-based pharmacist: improve pharmaceutical care
Braun 2009[21]	q-RCT	Israel	200	200	153	156	Internal medicine ward, hospital	Int, resp, cardio	63	51	NR	Telephone follow-up calls post-discharge: several outcomes
Brookes 2000[22]	h-CCT	UK	109	734	109	734	Medical admission ward, hospital	Resp, HF	75	NR	8.0	Community services liaison pharmacists: drug-related problems
Burnett 2009[66]	q-RCT	UK	59	58	59	58	Medical wards, hospital	NR	NR	NR	7.5	Integrated medicines management: medication appropriateness
Cannon 1999[57]	RCT	UK	20	20	19	17	Acute care unit, hospital	NR	81	23	NR	Pharmaceutical care model: post-discharge medication changes
Chantelois 2003[67]	CCT	US	22	37	22	37	General medicine service, tertiary care hospital	NR	NR	NR	NR	Pharmacist discharge prescription writing: medication errors
Cole 1971[58]	q-RCT	US	50	25	50	25	General hospital	NR	18-80	NR	NR	Education/self-administration: medication understanding
Cromarty 1998[68]	BAS	UK	48	42	46	26	Elderly ward, hospital	NR	83	43	6.0	Pharmacy information letter: post-discharge problems
deClifford 2009[69]	BAS	Australia	40	40	40	40	Neurology/respiratory wards, tertiary referral hospital	NR	NR	NR	8.0	Pharmacist discharge prescription writing: medication errors
Dudas 2001/02[23,24]	RCT	US	110	111	110	111	General medical service, academic teaching hospital	Resp, int	55	47	NR	Follow-up telephone call post-discharge: several outcomes
Edwards 1984[41]	RCT	UK	64	20	62	20	Acute medical wards, hospital	NR	79	34	2.1	Pre-discharge counselling: medication adherence
Eggink 2010[59]	RCT	Netherlands	41	48	41	44	Cardiology ward, teaching hospital	HF	73	67	9.5	Clinical pharmacist discharge service: several outcomes
Esposito 1995[60]	RCT	US	24	19	23	19	Community medical centre, hospital	NR	76	37	NR	Educational protocol/schedules: medication adherence

Appendix C Continued

Study (reference)	Study characteristics		Number of patients‡				Characteristics study population					Study objective
	Design*	Country†	Number randomised		Number analysed		Setting	Study population§	Age (mean)	Gender (% men)	No. discharge drugs (mean)	Effect of: on
			I	C	I	C						
Eurich 2001[70]	BAS	Canada	40	55	36	50	Acute care hospitals	NR	69	56	NR	Therapeutic interchange program: drug-related problems
Gray 2008[71]	BAS	UK	NR	NR	41	45	Community hospitals	NR	NR	NR	NR	Sharing information between secondary/primary care: treatment
Hawe 1990[42]	CCT	Australia	149	119	77	71	Elderly ward, hospital	NR	69	42	3.6	Medication education program: medication adherence
Hugtenburg 2009[38]	CCT	Netherlands	336	379	336	379	Community pharmacies	Cardio, int	71	48	7.4	Pharmaceutical care post-discharge: several outcomes
Johnston 1986[43]	RCT	UK	14	13	14	13	Medical wards, hospital	NR	76	31	NR	Pre-discharge counselling: medication knowledge
Kellaway 1979[25]	BAS	New Zealand	NR	NR	280	477	Acute general medical wards, hospital	NR	NR	49	NR	Pre-discharge counselling/drug card: medication adherence
Kramer 2007[26]	BAS	US	136	147	136	147	Adult general medical unit, medical center	Cardio	65	50	7.1	In-hospital medication reconciliation: several outcomes
Louis-S. 2004[45]	CBA	Switzerland	370	439	370	439	General internal medicine wards, university hospitals	Resp, cardio	63	50	5.2	Education/treatment card: medication knowledge
Lovitt 1992[72]	BAS	Australia	33	515	33	515	Surgical ward, hospital	NR	NR	NR	4.0	Computer generated prescriptions: drug related problems
MacDonald 1977[61]	CCT	UK	105	60	105	60	Geriatric medicine ward, hospital	NR	80	8	2.1	Pre-discharge counselling/memory aids: medication adherence
Makowsky 2009[27]	CCT	Canada	221	231	220	231	Internal/family medicine wards, tertiary care hospitals	Resp, cardio, int	74	46	NR	Core pharmacist services: several outcomes
Manning 2007[46]	RCT	US	151	151	72	57	Medical units, academic medical center	NR	68	50	9.4	3D-tool versus discharge worksheet: several outcomes
Naunton 2003[28]	RCT	Australia	57	64	54	59	Medical wards, teaching hospital	Resp, cardio	76	37	8.0	Home visits post-discharge: several outcomes
Nickerson 2005[73]	RCT	Canada	134	119	134	119	Family practice units, academically affiliated hospital	NR	65	32	7.5	Seamless care service: drug-related problems
Paquette-L. 2001[74]	BAS	Canada	34	55	34	55	Internal medicine wards, hospital	NR	61	37	6.8	New discharge form: accuracy of community pharmacy info
Pickrell 2001[47]	CCT	UK	15	17	15	17	Medical admission unit, hospital	Cardio, resp, int	64	47	6.7	In-hospital pharmaceutical care: several outcomes
Polack 2008[48]	RCT	Canada	4	10	4	10	University hospital	NR	64	79	7.4	Post-discharge vs pre-discharge counselling: several outcomes
Rahman 2005[75]	BAS	UK	NR	NR	128	133	General surgical ward, teaching hospital	NR	NR	NR	4.7	Pharmacist discharge prescription writing: medication errors
Raynor 1993[49]	RCT	UK	NR	NR	98	99	General medicine wards, general hospital	NR	69	56	3.6	Reminder chart: medication adherence
Rose 2005[76]	CCT	UK	50	50	50	50	Hospital	NR	NR	NR	NR	Pharmacy technician discharge writing: medication errors
Sandler 1989[50]	q-RCT	UK	65	66	65	66	General medical ward, university hospital	Cardio, resp	62	62	3.9	Discharge booklet: medication knowledge
Sands 1994[29]	CCT	US	1364	801	1364	801	General medical ward, teaching hospital	NR	NR	NR	NR	Computerized medication/leaflets: medication adherence

Appendix C Continued

Study (reference)	Study characteristics		Number of patients‡				Characteristics study population					Study objective
	Design*	Country†	Number randomised		Number analysed		Setting	Study population§	Age (mean)	Gender (% men)	No. discharge drugs (mean)	Effect of: on
			I	C	I	C						
Schneider 1993[30]	q-RCT	US	26	28	26	28	Cardiac nursing unit, medical center	HF	72	50	6.0	Discharge planning: hospital readmissions
Schnipper 2009[31]	c-RCT	US	162	160	162	160	General medicine wards, academic hospitals	NR	NR	45	1-33	Redesigned medication reconciliation: adverse drug events
Scullin 2007[32]	RCT	UK	371	391	370	384	Medical wards, general hospital	NR	70	47	NR	In-hospital pharmaceutical care: several outcomes
Setter 2009[33]	CCT	US	110	110	110	110	Visiting nurse association	NR	74	45	9.6	Pharmacist–nurse collaboration: medication discrepancies
Sherrard 2009[34]	RCT	Canada	164	167	137	143	Cardiac surgical wards, hospital	Cardio	63	NR	NR	Interactive voice response/telephone calls: several outcomes
Stewart 1998[35]	RCT	Australia	49	48	49	48	Medical/surgical ward, tertiary referral hospital	HF	75	48	6.7	Home based intervention: unplanned readmission/deaths
Stitt 1979[51]	CCT	US	75	25	68	21	Medical/surgical/maternity ward, university hospital	NR	47	31	NR	Audio-visual presentation/instruction cards: knowledge
Stowasser 2002[36]	RCT	Australia	113	127	104	105	Acute wards/orthopaedic ward, hospitals	NR	66	55	7.6	Medication liaison services: several outcomes
Strobach 2000/01[52,53]	RCT	Germany	16	21	7	12	Internal medicine wards, university hospital	NR	61	54	6.4	Pre-discharge counselling: medication knowledge
Sweeney 1989[62]	BAS	UK	51	52	29	39	Acute medical wards, general hospital	NR	72	46	4.1	Education/leaflets/adherence aids: medication adherence
Varkey 2007[77]	BAS	US	51	51	51	51	Family medicine care unit, academic hospital	NR	56	36	9.9	Multidisc. medication reconciliation: drug-related problems
Vuong 2008[54]	RCT	Australia	152	164	127	132	Acute-care wards, tertiary teaching hospitals	NR	72	53	10.5	Post-discharge home visit: several outcomes
Whitty 2001[78]	CCT	Australia	29	26	29	26	General medical wards, hospital	NR	NR	NR	5.1	Pharmacist reviewing prescriptions: medication errors
Whyte 1994[55]	CCT	UK	24	24	24	24	Medical wards, hospital	Resp, cardio	61-95	NR	3.5	Medication record card: medication knowledge
Wolfe 1992[56]	CCT	US	25	25	18	20	Teaching and community hospital	Cardio	74	42	4.6	Pre-discharge counselling: medication knowledge/adherence

NR= not reported

* BAS= before, after study, CBA= controlled before, after study (a control group both in the usual care and in the intervention phase), CCT= controlled clinical trial (no random allocation described), h-CCT= CCT with historical control group, RCT= randomised controlled trial, c-RCT = cluster randomised controlled trial (randomisation based on cluster of patients instead of individuals), q-RCT= quasi randomised controlled trial (e.g. randomisation based on alternate allocation)

† UK= United Kingdom, US= United States

‡ C= control, I= Intervention. The number of patients analysed differs for several outcomes, so in this table the lowest numbers of analysed patients (for the outcomes relevant for this review) are provided.

§ Cardio = cardiovascular diseases, HF = heart failure patients, Int= internal medicine diseases, Resp= respiratory diseases

Appendix D Characteristics of usual care and interventions

Study reference	Usual Care	Description of intervention (performed by, moment, main intervention type and characteristics of interventions)																		
		IVP*	M†	Main IV‡	Interventions before discharge§								Interventions after discharge§							
					Educational				Pharmacoth.		DIT related		Educational				Pharmacoth.		DIT related	
					Verb	Writ	Aud	Adh	Disc	Rev	Verb	Writ	Verb	Writ	Aud	Adh	Disc	Rev	Verb	Writ
Al Rashed 2002[19]	Counselling by nurse/written information	P	B	Ed	✓															
Baker 1984[40]	No pre-discharge counselling	P	B	Ed	✓	✓														
Baker 1991[39]	Informal verbal pre-discharge counselling	P	B	Ed		✓														
Barrett 2002[63]	Doctor writes discharge prescription	H,P	B	Ed,Ph	✓				✓c											
Begley 1997[37]	No domiciliary home visit after discharge	P	A	Ed,Ph									✓	✓a				✓a		
Birdsey 2005[64]	Doctor writes discharge prescriptions	H,P	B	Ph					✓c	✓										
Bjork Linne 1999[44]	Counselling by a doctor using a medication list	N,P	A	Ed									✓	✓	✓					
Bolas 2004[20]	No discharge counselling	P	B	Ed,Ph,Dt	✓	✓			✓b			✓								
Boorman 2000[65]	Doctor writes discharge prescriptions	H,P	B	Ed,Ph	✓a				✓c											
Braun 2009[21]	No telephone call post-discharge	NR	A	Ed									✓							
Brookes 2000[22]	NR	P	B	Ed,Ph,Dt	✓	✓			✓b		✓	✓								
Burnett 2009[66]	No medication reconciliation	P,PT	B	Ed,Ph,Dt	✓	✓			✓b	✓		✓								
Cannon 1999[57]	No pharmaceutical care assessment	P	B	Ed,Ph,Dt	✓				✓b	✓	✓									
Chantelois 2003[67]	Doctor writes discharge prescriptions	H,P	B	Ph					✓c											
Cole 1971[58]	No pharmacist consultation,/self-administration	P	B	Ed	✓			✓												
Cromarty 1998[68]	Discharge counselling, but no information letter	P	B	Ed,Dt		✓						✓								
deClifford 2009[69]	Junior doctor prepares discharge prescription	P	B	Ph,Dt					✓c			✓								
Dudas 2001/02[23,24]	No phone call post-discharge	P	A	Ed,Ph									✓					✓		
Edwards 1984[41]	No education	H,N,P	B	Ed	✓															
Eggink 2010[59]	No clinical pharmacist intervention	P	B	Ed,Ph,Dt	✓	✓			✓b	✓		✓								
Esposito 1995[60]	Counselling by floor nurse/written information	O	B	Ed	✓	✓														
Eurich 2001[70]	No/minimal therapeutic interchange program	P	B	Ed,Ph	✓				✓d											
Gray 2008[71]	Discharge letters not sent to community pharmacist	P	C	Ph,Dt								✓						✓		
Hawe 1990[42]	Dummy intervention: no information on medication	P	B	Ed	✓	✓														

Appendix D Continued

Study reference	Usual Care	Description of intervention (performed by, moment, main intervention type and characteristics of interventions)																		
		IVP*	M†	Main IV‡	Interventions before discharge§								Interventions after discharge§							
					Educational				Pharmacoth.		DIT related		Educational				Pharmacoth.		DIT related	
					Verb	Writ	Aud	Adh	Disc	Rev	Verb	Writ	Verb	Writ	Aud	Adh	Disc	Rev	Verb	Writ
Hugtenburg 2009[38]	Usual prescriptions check by community pharmacist	P	A	Ed,Ph,Dt									✓	✓			✓b	✓		✓
Johnston 1986[43]	Patient education by ward staff	P	B	Ed	✓															
Kellaway 1979[25]	No education provided	H,N,P	B	Ed	✓	✓														
Kramer 2007[26]	Medication reconciliation by ward staff	H,N,P	B	Ed,Ph		✓			✓b											
Louis-S. 2004[45]	Patient counselling by residents if needed	H	B	Ed	✓	✓														
Lovitt 1992[72]	Doctor writes discharge prescriptions	H,P	B	Ph					✓c											
MacDonald 1977[61]	No intensive patient counselling	P	B	Ed	✓	✓		✓												
Makowsky 2009[27]	No pharmacist participation during admission	P	B	Ed,Ph,Dt	✓	✓a			✓b	✓	✓a									
Manning 2007[46]	Patient counselling/usual medication worksheet	P,O	B	Ed		✓														
Naunton 2003[28]	No home visit	P	A	Ed,Ph,Dt									✓			✓a		✓	✓	
Nickerson 2005[73]	Counselling by a nurse/transcribes discharge notes	P	B	Ed,Ph,Dt	✓	✓			✓c	✓		✓								
Paquette-L. 2001[74]	Usual discharge prescription used	P	B	Ph,Dt					✓b			✓								
Pickrell 2001[47]	No routine counselling by nurse/no extra info for GP	P	B	Ed,Ph,Dt	✓				✓b			✓								
Polack 2008[48]	Pre-discharge nurse or pharmacist education	P	A	Ed,Ph									✓					✓		
Rahman 2005[75]	Doctor writes discharge prescription	H,P	B	Ph					✓c											
Raynor 1993[49]	Routine brief patient counselling by a nurse	N,P	B	Ed		✓														
Rose 2005[76]	Doctor writes discharge prescriptions	P,PT	B	Ph					✓c											
Sandler 1989[50]	Normal discharge summary	H,N	B	Ed,Dt		✓						✓								
Sands 1994[29]	No use of the computerized program by physicians	H	B	Ed,Ph,Dt		✓			✓b	✓		✓								
Schneider 1993[30]	Usual patient counselling by staff nurses	N	B	Ed	✓	✓														
Schnipper 2009[31]	No comprehensive medication reconciliation	H,N,P	B	Ph					✓b											
Scullin 2007[32]	Traditional clinical pharmacy services	P,PT	B	Ed,Ph,Dt	✓	✓			✓b	✓		✓								
Setter 2009[33]	Sporadic pharmacy consultation	N,P	A	Ph													✓c			
Sherrard 2009[34]	Telephone call, no questions on medications	N	A	Ed									✓							
Stewart 1998[35]	No domiciliary home visit	N,P	C	Ed,Dt	✓								✓	✓a		✓a			✓	

Appendix D Continued

Study reference	Usual Care	Description of intervention (performed by, moment, main intervention type and characteristics of interventions)																		
		IVP*	M†	Main IV‡	Interventions before discharge§								Interventions after discharge§							
					Educational				Pharmacoth.		DIT related		Educational				Pharmacoth.		DIT related	
					Verb	Writ	Aud	Adh	Disc	Rev	Verb	Writ	Verb	Writ	Aud	Adh	Disc	Rev	Verb	Writ
Stitt 1979[51]	No audio-visual or written instruction	P	B	Ed		✓	✓													
Stowasser 2002[36]	No medication liaison services	P	B	Ph,Dt					✓b	✓		✓								
Strobach 2000/01[52,53]	No patient counselling by clinical pharmacist	P	B	Ed	✓	✓														
Sweeney 1989[62]	No patient counselling by a pharmacist	P	B	Ed	✓	✓a		✓a												
Varkey 2007[77]	No multidisciplinary medication reconciliation	H,P	B	Ph					✓b											
Vuong 2008[54]	Counselling/adherence aids when necessary	P	A	Ed,Ph,Dt									✓				✓c	✓	✓a	✓
Whitty 2001[78]	No checking of prescriptions by ward pharmacist	P	B	Ph					✓c											
Whyte 1994[55]	No medication record card provided to patients	N,P	B	Ed		✓														
Wolfe 1992[56]	No patient counselling, no written information	N	B	Ed	✓	✓														

GP, general practitioner, NR= not reported

* IVP= intervention performer. H= hospital physician(s), N= nurse(s), P= Pharmacist(s), PT= Pharmacy Technician(s), O= Other

† M= moment of intervention: A= intervention performed after discharge, B= intervention performed before discharge, C= combined intervention performed both before and after discharge

‡ Main IV= main intervention category. Ed= educational related intervention, Ph= pharmacotherapy related intervention, Dt= discharge information transfer related intervention

§ verb= verbal, writ= written, aud= audiovisual, adh= adherence aids, disc= discrepancies, rev= review

a = intervention performed if necessary.

b= main focus: discrepancies between pre-admission prescribed medication and discharge medication using for example community pharmacy records, general practitioner medication records or information from patients/caregivers.

c= main focus: discrepancies between in-hospital prescribed medication and discharge medication using for example admission medication lists or in-hospital computerised patient records.

d= main focus: discrepancies between the pre-admission prescribed medication and post-discharge medication due to the hospital formulary

Appendix E Study outcomes and methodological quality of studies

Study reference	SS*	Measured study outcomes †							Methodological quality study ‡										
		Readm	Mort	Knowl	Adh	DRPs	HSU	Costs	1	2	3	4	5	6	7	8	9	10	Score
Al Rashed 2002[19]	N	**X**		X	X		**X**		N	N	Y	U	U	N	U	Y	U	N	2
Baker 1984[40]	N			**X**					U	U	N	N	U	Y	Y	N	U	N	2
Baker 1991[39]	N			**X**					U	U	Y	N	U	U	U	Y	Y	N	3
Barrett 2002[63]	N					X			N	N	U	U	U	N	U	U	U	N	0
Begley 1997[37]	N			X	**X**		X		N	Y	N	N	N	N	U	N	U	N	1
Birdsey 2005[64]	N					**X**			N	N	Y	Y	U	N	N	U	U	N	2
Bjork Linne 1999[44]	Y			**X**					Y	U	N	N	N	N	U	N	U	N	1
Bolas 2004[20]	N	X		**X**		**X**			Y	U	N	N	U	U	U	Y	U	N	2
Boorman 2000[65]	N					**X**			N	N	U	U	U	N	U	U	U	N	0
Braun 2009[21]	N	**X**			**X**				N	N	N	N	U	N	U	Y	N	N	1
Brookes 2000[22]	N	X							N	N	Y	Y	U	N	N	U	U	N	2
Burnett 2009[66]	N					**X**			N	N	Y	Y	U	N	N	U	U	N	2
Cannon 1999[57]	N				X	X			U	U	N	N	U	U	U	U	U	N	0
Chantelois 2003[67]	N					**X**			N	N	U	Y	U	N	U	N	U	N	1
Cole 1971[58]	N				**X**				N	N	Y	Y	U	U	U	U	U	N	2
Cromarty 1998[68]	N					X			N	N	N	N	U	N	U	Y	Y	N	2
deClifford 2009[69]	Y					**X**			N	N	Y	Y	N	N	N	U	U	N	2
Dudas 2001/02[23,24]	N	X					X		U	U	Y	Y	U	U	U	Y	Y	N	4
Edwards 1984[41]	N			X	**X**				U	U	Y	Y	U	U	Y	N	U	N	3
Eggink 2010[59]	Y				X	**X**			Y	N	Y	Y	N	N	U	Y	U	N	4
Esposito 1995[60]	N				**X**				Y	U	N	N	N	N	N	N	N	N	1
Eurich 2001[70]	N					**X**			N	N	Y	N	U	N	N	Y	N	N	2
Gray 2008[71]	N					**X**			N	N	N	N	U	N	U	U	U	N	0
Hawe 1990[42]	N			X	**X**				N	N	Y	N	U	N	Y	Y	U	N	3
Hugtenburg 2009[38]	N		X			X			N	N	Y	Y	U	N	N	N	N	N	2
Johnston 1986[43]	N			**X**					U	U	Y	U	U	U	Y	Y	U	N	3
Kellaway 1979[25]	N	X			**X**				N	N	U	U	U	N	U	U	U	N	0

Appendix E Continued

Study reference	SS*	Measured study outcomes †							Methodological quality study ‡										
		Readm	Mort	Knowl	Adh	DRPs	HSU	Costs	1	2	3	4	5	6	7	8	9	10	Score
Kramer 2007[26]	Y	X				X	X		N	N	Y	Y	N	N	N	N	U	N	2
Louis-S. 2004[45]	N			**X**					N	N	Y	Y	U	N	N	N	Y	Y	4
Lovitt 1992[72]	N					X			N	N	U	U	U	N	N	U	U	N	0
MacDonald 1977[61]	N				**X**				N	N	Y	Y	N	N	U	Y	U	N	3
Makowsky 2009[27]	Y	X				**X**	X		N	U	Y	Y	N	N	Y	Y	Y	Y	6
Manning 2007[46]	N			**X**		**X**			Y	U	N	N	N	N	Y	Y	Y	N	4
Naunton 2003[28]	N	**X**	**X**		X	X			Y	N	Y	Y	U	N	N	Y	U	N	4
Nickerson 2005[73]	N					**X**			Y	Y	Y	N	N	N	U	N	Y	N	4
Paquette-L. 2001[74]	N					**X**			N	N	Y	Y	U	N	U	Y	U	N	3
Pickrell 2001[47]	N			X		X			N	N	Y	Y	N	N	U	U	U	N	2
Polack 2008[48]	N			**X**	**X**				U	Y	Y	N	N	N	Y	U	U	N	3
Rahman 2005[75]	N					**X**			N	N	U	Y	U	N	U	U	U	N	1
Raynor 1993[49]	N			X	**X**				U	U	N	N	N	N	N	Y	Y	N	2
Rose 2005[76]	N					**X**			N	N	Y	Y	U	Y	U	U	U	N	3
Sandler 1989[50]	N			**X**					N	N	Y	Y	N	N	N	Y	U	Y	4
Sands 1994[29]	N	X			X				N	N	U	U	U	N	U	Y	U	N	1
Schneider 1993[30]	N	**X**							N	N	Y	Y	N	N	U	Y	U	N	3
Schnipper 2009[31]	Y	X				**X**	X		N	N	Y	Y	N	N	N	Y	U	Y	4
Scullin 2007[32]	N	X	X						Y	Y	Y	N	N	N	Y	Y	U	Y	6
Setter 2009[33]	N	X				**X**	X		N	N	U	Y	N	N	U	Y	U	N	2
Sherrard 2009[34]	Y	**Xa**			**Xa**		X		U	Y	N	N	U	N	N	U	Y	N	2
Stewart 1998[35]	N	**Xa**	**Xa**				X	X	U	Y	N	Y	N	N	U	Y	Y	N	4
Stitt 1979[51]	N			**X**	X				N	N	Y	N	N	N	N	Y	U	N	2
Stowasser 2002[36]	N	X	X			X	X		Y	U	Y	Y	N	N	U	Y	Y	N	5
Strobach 2000/01[52,53]	N			**X**					Y	U	N	N	N	N	U	U	U	N	1
Sweeney 1989[62]	N				**X**				N	N	N	N	N	N	N	U	U	N	0
Varkey 2007[77]	N					**X**			N	N	Y	Y	N	N	U	Y	Y	N	4

Appendix E Continued

Study reference	SS*	Measured study outcomes †							Methodological quality study ‡										
		Readm	Mort	Knowl	Adh	DRPs	HSU	Costs	1	2	3	4	5	6	7	8	9	10	Score
Vuong 2008[54]	Y			X	X				Y	U	N	N	N	N	U	N	Y	N	2
Whitty 2001[78]	N					**X**			N	N	U	Y	U	N	U	U	N	N	1
Whyte 1994[55]	N			**X**					N	N	Y	Y	N	N	U	U	U	N	2
Wolfe 1992[56]	N			**X**	**X**				N	N	N	N	N	N	N	Y	U	N	1

* SS = sample size, Y= sample size calculation is provided, N= sample size calculation is absent

† Readm= hospital readmission, Mort= mortality, Knowl= medication knowledge, Adh= medication adherence, DRPs= drug- related problems, HSU= health services use, Costs= costs of health services
X = primary outcome as stated by the authors or the outcome mentioned in the objective (a = combined primary outcome)

‡ Y=Yes, N=No, U= Unclear; see Appendix B for the explanation of the questions 1-10

Science never solves a problem without creating ten more.

(George Bernard Shaw: Irish playwright, 1856-1950)

Designed by Denis Tenev

PART

3

Development of a transitional care program for hospitalised patients

CHAPTER

3.1

Informational needs of general practitioners regarding discharge medication: content, timing and pharmacotherapeutic advices

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ABSTRACT

Objective: To investigate the needs of Dutch general practitioners on discharge medication, both regarding content, timing and the appreciation of pharmacotherapeutic advices from clinical pharmacists.

Setting: A general teaching hospital in Amsterdam, the Netherlands.

Method: A prospective observational study was performed. A questionnaire with regard to the content, optimal timing (including way of information transfer) and appreciation of pharmacotherapeutic advices was posted to 464 general practitioners. One reminder was sent.

Main outcome measure: Description of the needs of general practitioners was assessed. For each question and categories of comments frequency tables were made. The Fisher-exact test was used to study associations between the answers to the questions.

Results: In total, 149 general practitioners (32%) responded. Most general practitioners (75%) experienced a delay in receiving discharge medication information and preferred to receive this on the day of discharge. GPs wished to receive this information mainly through e-mail (44%). There was a significant correlation (p= 0.002) between general practitioners who wanted to know whether and why medication had been stopped (87%) and changed (88%) during hospital admission. The general practitioners (88%) appreciated pharmacotherapeutic advices from clinical pharmacists.

Conclusion: This study indicates how information transfer on discharge medication to GPs can be optimised in the Netherlands. The information arrives late and GPs want to be informed on the day of discharge mainly by e-mail. GPs wish to know why medication is changed or discontinued and appreciate pharmacotherapeutic advices from clinical pharmacists.

INTRODUCTION

Patients are often discharged from the hospital on drug therapy regimens different from those used before hospitalisation.[1-3] A recent study showed that in 98% of patients the pharmacotherapy was changed in hospital and in 60% of patients at least five changes were recorded.[4] These changes can be caused by for example alterations in disease state or the need for increased drug efficacy.[1] Medical care in chronic illness is moving increasingly from secondary to primary care.[5] The general practitioner (GP), who is responsible for the patient after discharge, must decide whether or not to maintain these changes, often without valid information with respect to the reasons for these changes.[6]

At present information on medication is mainly transferred through discharge letters, which arrive relatively late and do not necessarily contain the information the GP needs. Studies have shown the possible consequences of inaccurate medication communication, for example the inappropriate restart of medication, that has been stopped during hospital admission due to adverse drug reactions.[7,8] In order to improve the information transfer, policy documents outlining strategies to promote medication safety for patients moving from one care environment to another have been produced in the United Kingdom, the United States and recently in the Netherlands.[9-11] Implementing recommended strategies for safe medication transfer is likely to be more successful when these strategies match with the information needs of GPs. Limited (older) studies have focused on the information needs of GPs regarding discharge medication.[1,12-14] However, the above mentioned policy documents[9-11] may have changed the need of GPs in recent years.

Additionally, in the policy documents the need for more cooperation between healthcare providers is discussed. In recent years clinical pharmacist have supported information transfer through checking for medication errors, counselling of the patient at hospital admission or discharge and provision of discharge medication lists to GPs.[12,15] Clinical pharmacists seek for more collaboration with GPs as hospital physicians do not always feel responsible for the complete pharmacotherapy. However, it is unknown whether GPs appreciate pharmacotherapeutic advices from clinical pharmacists. Therefore, the aim of our study is to investigate the needs of GPs on discharge medication, both regarding content, timing (including way of information transfer) and appreciation of pharmacotherapeutic advices.

METHOD

Setting and study population

A prospective observational study was performed at the St. Lucas Andreas Hospital in Amsterdam, the Netherlands, a 550-bed general teaching hospital. An anonymous questionnaire was posted to all GPs within the catchment area of the hospital according to the hospital's information system (n= 464) in July 2007. GPs could reply by mail or fax. In July and August questionnaires were received whereupon a reminder was sent in September 2007, allowing a response period of two months. The month of September was also chosen for sending the reminder, to enable general practitioners to respond who were on holiday during the summertime. This study was exempt from review by the institutional review board, since the study concerned healthcare professionals and did not involve any intervention. The data were collected anonymously and stored in accordance with privacy regulations.

Questionnaire and outcome

In our hospital, in general, a provisional discharge letter is sent soon after hospitalisation to inform the GP with a brief summary. In this provisional discharge letter the discharge medication should be mentioned. However, the discharge letter contains the ward-specific medication and not the complete list of medication the patient should be using. Information on which medication is changed or discontinued and reasons for this are generally not provided.

Therefore, a questionnaire was designed to measure the needs of GPs concerning discharge medication with regard to the optimal timing, the optimal way of information transfer, content of information and appreciation of pharmacotherapeutic advices from clinical pharmacists. Examples of pharmacotherapeutic advices are: adding medication according to evidence-based guidelines (e.g. statin for secondary prevention in a patient with type 2 diabetes), discontinuation of not indicated pre-admission used medication (e.g. iron tablets), monitoring compliance of a patient, therapeutic drug monitoring, or monitoring of electrolytes (e.g. potassium in patients using RAS-inhibitors) and kidney (mal)function (e.g. digoxin).

The questionnaire contained seven closed and one open question and was based on previous studies in primary care.[1,13,16] Topics were: delay in receiving information, the preferred time and way to receive this, requirement of information about changes or discontinuations in the pharmacotherapy, appreciation of pharmacotherapeutic advices and suggestions to improve the communication transfer. The GP was invited to comment on each question. The questionnaire was piloted on two persons. The revised questionnaire was posted to the GPs.

Data analysis

Analysis was performed with SPSS 14.0. For each question, frequency tables were made. The content of the open questions was qualitatively analysed, and three to six exclusive categories for each question were defined by FK and SDB. Each answer was classified in one of these categories and presented in frequency tables; differences in classification were solved by discussion. To study potential associations between the answers the Fisher-exact test was used.

RESULTS

In total, 149 GPs (32%) responded to the questionnaire, of whom 59 (12%) responded after the reminder. The results of the questionnaire can be found in Table 1. Almost all GPs (n= 143) added one or more additional remarks/suggestions to the questions, which are described in detail in Table 2.

Timing of information

Most GPs (75%) experienced a delay in receiving information about discharge medication and preferred to receive this on the day of discharge (see Table 1). Of the GPs that commented 55% stated that they were confronted with questions of patients or family immediately after patient discharge and 26% wanted to arrange care activities after discharge. Twelve percent of GPs considered medication information essential to be responsible for the patient's medication (see Table 2). Some GPs (7%) remarked that information was not needed instantly but could wait a few days as long as the patient was well informed and it was easy to contact the hospital.

Content of information

The GPs wanted to know whether and why medication had been stopped (87%) and changed (88%) during hospital admission. In their comments they explained that this information was important for educational purposes for themselves (38%), to counsel the patient (29%) and to prevent medication errors (14%). Furthermore, one GP used this information to document any drug-related problems in his computer system to prevent re-prescription of an inappropriate drug.

Pharmacotherapeutic advices

Most GPs (88%) appreciated pharmacotherapeutic advices by clinical pharmacists concerning possible improvements on discharge medication. They remarked (38%) that they could learn from these advices. GPs (38%) further noticed that the implementation of a pharmacotherapeutic advice in individual patients should be a choice of the GP:

Table 1 GPs needs about the moment and content of information about medication prescribed at discharge (n=149)

Subject	Yes (%)	No (%)
Moment of discharge medication information		
Is there a delay in receiving information?	*75*	*25*
What is the preferred time to receive information?		
· day of discharge	86	
· within some days of discharge	7	
· other	7	
Content of information		
Is information about changes in medication during hospital admission necessary?		
· yes, only what changes	9	
· yes, both what changes and reasons for this	88	
· not necessary	3	
Is information about stopped medication during hospital admission necessary?		
· yes, only what stops	11	
· yes, both what stops and reasons for this	87	
· not necessary	2	
Pharmacotherapeutic advices		
Are pharmacotherapeutic advices from hospital pharmacists about possible improvements appreciated?	88	12
Method of information transfer		
Is it a problem to receive discharge prescriptions separate from the discharge letter?	25	75
What is the preferred way of information transfer?		
· (discharge) letter	13	
· fax	22	
· e-mail	44	
· other	21	

there may be good reasons for not following the advice. Twelve percent of GPs did not want pharmacotherapeutic advices at all. Two GPs commented that improvements in the pharmacotherapy are the exclusive responsibility of the GP.

Method of information transfer and additional suggestions

GPs (75%) didn't mind to receive the medication information separate from the discharge letter as long as the information was clear. The GPs (25%) that did mind receiving a separate medication list commented that the GP should not have to search for the information. GPs wished to receive information regarding medication mainly through e-mail (44%).

In their open suggestions, 55 GPs noted some suggestions for further improvements such as clear and complete discharge medication communication, informing the patient about discharge medication, providing the right medication supply to the patient, and substitution of medication in the hospital to the medication used outside the hospital.

Table 2 Comments of GPs on the questions (n=143)

Questions	Nr of comments (%)
What is the preferred time to receive information?	
Day of discharge	42 (100%)
Patient or family have questions	23 (55%)
To arrange care activities	11 (26%)
GP is responsible for medication after discharge	5 (12%)
Other reasons	3 (7%)
Within some days after discharge	4 (100%)
Patient or family have questions	1 (25%)
To arrange care activities	1 (25%)
If GP has questions he can contact the hospital	1 (25%)
As long as patient has been well informed	1 (25%)
Other	3 (100%)
Both options are possible as long as patient has been well informed	2 (67%)
Depends on the patient (co-morbidities)	1 (23%)
Is information about changes and discontinued medication during hospital admission necessary?	
yes, both what changes or stops and reasons for this	7 (100%)
GP could possibly learn from it	3 (43%)
To answer questions of patients	2 (29%)
To check whether the adjustment are intentional to prevent re-prescription	2 (28%)
Are pharmacotherapeutic advices from hospital pharmacists about possible improvements appreciated?	
Yes	8 (100%)
GP could possibly learn from it	3 (38%)
However implementation is a choice of GP	3 (38%)
However sometimes there are reasons for not prescribing a certain drug	2 (24%)
No	2 (100%)
Task and responsibility of GP	
Is it a problem to receive discharge prescriptions separate from the discharge letter?	
Yes	8 (100%)
Not advisable as GPs have to search for the information	
No	14 (100%)
As long as the information is clear	5 (36%)
As long as GP receives information	5 (36%)
Other reasons	4 (28%)
Do you have further suggestions to improve the communication of medication information?	
Yes	55 (100%)
Clear and complete information regarding discharge medication is important (no handwritten forms, reason for changes provided etc.)	17 (31%)
Good initiative, further improvement is necessary	12 (22%)
Patient should also be informed with a medication list	7 (13%)
The right medication supply should be provided	5 (9%)
Substitution of medication in hospital should be prevented	5 (9%)
Consider cooperation with community pharmacy	2 (4%)
Other recommendations	7 (12%)

Association between answers

There were no associations between the information transfer being delayed and the preferred time to receive the information, the information need about medication changes and discontinuations and the appreciation of pharmacotherapeutic advices (see Table 3). The wish to know which medication was changed was significantly correlated with the wish to know which medication was discontinued (p= 0.002). This was not correlated with the appreciation of pharmacotherapeutic advices.

Table 3 Association between provided answers

Questions	Association with		P value
	Delay in information transfer		
	Yes	**No**	
Preferred time to receive information			0.774
Day of discharge	92 (75.4%)	30 (24.6%)	
Days later	13 (72.2%)	5 (27.8%)	
Information need about medication changes			1.000
Changes (plus reasons)	102 (73.9%)	36 (26.1%)	
Not important	5 (83.3%)	1 (16.7%)	
Information need about medication discontinuations			1.000
Discontinuations (plus reasons)	103 (75.2%)	34 (24.8%)	
Not important	2 (66.7%)	1 (33.3%)	
Appreciation of pharmacotherapeutic advices			1.000
Yes	87 (74.4%)	30 (25.6%)	
No	13 (76.5%)	4 (23.5%)	
Discharge prescriptions separate from the discharge letter			0.504
Yes	27 (79.4%)	7 (20.6%)	
No	75 (72.8%)	28 (27.2%)	
	Information need about medication changes		
	Yes	**No**	
Information need about medication discontinuations			0.002
Discontinuations (plus reasons)	142 (98.6%)	2 (1.4%)	
Not important	1 (33.3%)	2 (66.7%)	
Appreciation of pharmacotherapeutic advices			0.512
Yes	121 (96.8%)	4 (3.2%)	
No	18 (94.7%)	1 (5.3%)	

DISCUSSION

In our study 75% of GPs experienced a delay in receiving information about discharge medication and 86% preferred to receive this information on the day of discharge mainly because they were confronted with questions of patients and family immediately after patient discharge or wanted to arrange care activities after discharge. GPs wished to know why medication was changed (88%) or discontinued (87%) for educational pur-

poses for themselves, to counsel the patient and to prevent medication errors. Most GPs (88%) appreciated pharmacotherapeutic advices.

Changes in the pharmacotherapy during hospitalisation may cause adverse drug reactions and/or drug interactions at home.[6] Furthermore, reports have shown that many changes in drug therapy on transfer of care are due to medication errors.[12,13] After being discharged from the hospital, patients often contact their GP.[16] The late or non-arrival of information and the failure to inform GPs about changes in the pharmacotherapy could lead to the continuation of medication errors in primary care.[1,2,5,6,13,17] Studies reported that 77%–96% of GPs want to know why medication is changed or discontinued, which is consistent with the results in our study.[1,13] Only Munday et al. investigated in 1997 the reasons for these findings and they documented the same reasons as in our study, namely primarily to facilitate continuity of care, to inform the patient, to avoid the risks of adverse drug reactions, to eliminate prescribing errors and for educational purposes.[1] Himmel et al. showed that GPs received detailed information about drug changes in only five of the 130 hospital discharge letters showing the necessity for improvement.[6] These problems may have substantial implications for continuity of care and patient safety.[16,18] A recent study showed a trend toward a decreased risk of readmission within 3 months if patients were seen by a GP who had received a discharge letter (relative risk, 0.74; 95% CI 0.05–1.10).[19]

Our study adds that the majority of GPs (88%) appreciated pharmacotherapeutic advices by clinical pharmacists concerning possible improvements in the discharge medication. This provides collaboration possibilities between clinical pharmacist and general practitioners for example in situations where the hospital physician does not feel responsible for certain medication regimens (e.g. undertreatment), extra monitoring of medication is needed (e.g. kidney malfunction) or drug-related problems (e.g. compliance, side effects) are identified. A recent study showed that GPs accepted advices and that these were well received because the advices provided new information, helped to better understand hospital recommendations and influenced prescribing.[20] It is important to recognise both the possible contribution of the clinical pharmacist to give a clinically relevant advice to optimise pharmacotherapy, as the responsibility of the GP to fit this advice in the individual drug therapy of the patient. Furthermore, the role of the community pharmacist within this process needs to be explored further.

There are several ways to inform GPs. In 1997 postal communication was preferred.[1] As nowadays more GPs have access to fax machines and electronic mail, these communication methods are preferred in our population.

In this study it seems that not only GPs who experience a delay in the information transfer wish to receive information on the day of discharge, as no significant association was identified between the answers to these questions. Furthermore, the delay in information transfer was not associated with the information need on medication

changes, medication discontinuation and appreciation of pharmacotherapeutic advices implicating that this information was considered relevant anyway. The information need on medication changes and medication discontinuation was significantly correlated (p= 0.002) which is logical due to the relation of the two information types. However the information need on medication changes or discontinuations was not correlated with the appreciation of pharmacotherapeutic advices which implicates that different interventions can be developed to meet with the information needs of GPs.

Although this is one of the few studies clearly showing the informational needs of GPs, some limitations need to be discussed. First, the results reflect the findings in one geographical area, therefore limiting the generalisability of the results, although the results are comparable to the few other studies that have been conducted.[1,13,16] Second, the response rate was relatively low, even though we sent a reminder. This may have led to selection bias, because only the GPs with a more positive attitude may have responded. Unfortunately, we were unable to investigate this bias because of the anonymity of the survey.

Notwithstanding these limitations, we believe that this questionnaire provides important insight in the needs of GPs concerning discharge medication.

Future studies should focus on implementing medication transfer systems tailored to GPs information needs and on the effect of implementing such systems on patient safety. Medicine management teams who reconcile medication, document changes and communicate this information to GPs have been described in literature.[2] Furthermore, future studies should also focus on how information regarding discharge medication can be transferred using standardised discharge letters. In the study of Van der Linden et al. it did not matter whether an adverse drug reaction was mentioned in the discharge letter or not for prevention of re-prescription of inappropriate drugs.[7] This implies that GPs probably did not notice the information on the adverse drug reaction. By designing future studies using a before–after design and studying clinically relevant endpoints (such as hospital readmissions), these studies will be able to contribute to our knowledge on the impact of implementing measures to improve the transfer of discharge medication to GPs. The results of the survey we have carried out, can aid in designing these measures for improvement of discharge medication transfer. Future interventions will reveal how sharing knowledge about optimal pharmacotherapy by an advice of the clinical pharmacist contributes to quality of pharmacotherapy.

CONCLUSION

This study indicates how information transfer on discharge medication can be optimised in the Netherlands. It shows that the information transfer to the GPs arrives late and that they want to be informed on the day of discharge mainly by e-mail. GPs wish to know why medication was changed or discontinued and appreciate pharmacotherapeutic advices from clinical pharmacists. For the further development of discharge interventions, these findings can be useful to design accurate discharge medication information sheets, organise timely transfer of information, and give pharmacotherapeutic advices to streamline the communication process between hospital and general practitioner.

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CHAPTER

3.2

Information needs about medication according to patients discharged from a general hospital

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ABSTRACT

Objective: Medication regimens change during hospital admission, and these discrepancies can lead to an increased risk of patient harm after hospital discharge. Information about medication according to the patient's needs may contribute to patient safety by improvement of knowledge and adherence. The goal of this study is to explore the patient's needs on information about medication at hospital discharge.

Research design and methods: Qualitative, semi-structured interviews were performed with 31 patients from the pulmonology, internal medicine and cardiology departments who were discharged with at least one prescribed drug from the hospital to primary care in the Netherlands. Interviews were analysed with content analysis.

Results: Patients had variable needs concerning information about discharge medication. Most patients wanted to receive basic information about their medication, alternatives for the prescribed medication and side effects. Some patients did not need basic information or explicitly mentioned that information about side effects would negatively influence their attitude towards medication. Patients preferred a combination of oral instructions and written information.

Conclusions: Information at discharge should be tailored to the individual needs of the patient. In the process of providing patient information at hospital discharge, the preference of some patients for non-disclosure of information should be recognised.

INTRODUCTION

Treatment regimens before and after hospital discharge are often different and these discrepancies may lead to an increased risk of patient harm after hospital discharge.[1] Medication reconciliation is an important tool to reduce medication errors and is defined as 'the process of obtaining and maintaining a complete and accurate list of the current medication use of a patient across healthcare settings'.[2] This process includes verification of medication lists, pharmacotherapeutic evaluation of the quality of pharmacotherapy and communication to the next healthcare provider(s). These activities lead to interventions that can prevent patient harm by changes in prescriptions or support of optimal medication use by the patient. Examples of such interventions are stopping incorrectly prescribed drugs (digoxin prescribed for another patient) or adding drugs based on best practice standards (a laxative added to opioid treatment).[3] However, the patient is not necessarily included in this process.[4]

The patient has been recognised as a valuable source of information: he provides the additional information on drug use or needs in drug therapy compared to sources that do not include the patient.[3,5] Moreover, inclusion of the patient in information transfer offers the opportunity to counsel the patient on optimal drug use and improves knowledge about medication. In general, knowledge about medication and information on drug use improve medication adherence, thus enabling treatment targets to be reached in patients with varying diseases.[6,7]

Patients express that they need information about medication as they are discharged from the hospital, and rate this highly compared to other informational needs around discharge.[8] In practice, only a small proportion of patients (49%) was educated about medication at discharge, and an even smaller proportion (30%) reported to have received written information.[9] Complicating in information transferral at discharge is that many patients are relatively vulnerable[10] and limited in their time and capacity to comprehend information.[11] In this context the question is what information about medication should be provided to patients at hospital discharge.

In several studies patient's informational needs were topic of research. Most studies found that basic information about medication is wanted, such as the names of the different drugs, dosing schedule and indication.[12] Important side effects of medication were often not told in a way patients could understand them, but patients wanted to be informed about possible side effects.[12,13] Also, patients would like to receive information about the treatment options that were available.[12] Currently, most (educational) discharge activities are based on opinions of healthcare professionals.[14] To our knowledge, no study has explored the needs of information about medication at hospital discharge according to the patient.

As the patient perspective is important in the further development of patient counselling about discharge medication, we performed a qualitative study in which the viewpoints of patients were investigated. The goal of the study was to explore the needs of patients on information about medication at hospital discharge.

RESEARCH DESIGN AND METHODS

Patient information in the hospital

During the study period, an intervention in patient counselling was implemented in the St. Lucas Andreas Hospital, a 550 bed general teaching hospital.[3] This intervention facilitated the inclusion of both patients who received usual care (no patient counselling) and patients who received the intervention (counselling at discharge). Patients from three wards received usual care: patients at the pulmonology ward before implementation of the intervention, and patients from the internal medicine and cardiology ward where the intervention was not implemented during the study period. Usual care consisted of doctors and/or nurses informing a patient when they thought the patient needed information or when the patient explicitly requested information.

In the intervention group, medication reconciliation was performed and improvements in the medication regimen were proposed to the treating physician.[3] Hereafter, patient counselling was performed at hospital discharge. Counselling was aimed at gathering extra information about drug use, educating the patient and answering questions about medication. The patient was counselled at his/her bedside by a pharmaceutical consultant – a pharmacy technician who followed an additional 3-year bachelor program which is focussed on pharmaceutical patient care.

Patients received a printed medication sheet (Figure 1) that was the basis for oral consultation, in which indication, use and potential side effects (of newly prescribed drugs) were subjects of counselling. For medication newly prescribed in the hospital – and for all other medication on request – the patient also received a patient friendly, one-page summary of the official package leaflet. During the consultation, patients or informal caregivers could ask questions about the medication and were invited to talk about their opinions about medication.

Patient selection

All adult patients being discharged from the wards of internal medicine, pulmonology and cardiology were eligible to be interviewed when they met the following inclusion criteria: (1) being discharged with at least one chronically prescribed drug, (2) being discharged to their home, (3) physically and mentally able to be interviewed, and (4) adequate command of Dutch or English language.

Figure 1 Example of a patient information leaflet

Sint Lucas Andreas Ziekenhuis

Medication summary per: 12 May 2010

Page 1

Patient: Mr. Example, O. 16-10-1923
Patient-id: 04585632

Specialist: Dr. Internal
Ward: A6, Internal medicine

ALLERGY: PENICILLIN
CONTRA-INDICATION: DECREASED KIDNEY FUNCTION

Start until	Stop	Medication name (brand name)	Medication used for or to prevent	Dose	Administration scheme Morning	Noon	Evening	Night
04-05-10		Omeprazole 20 mg capsule (Losec)	Stomach pain	One table daily Do not chew or crush the capsules				
04-05-10		Glimepiride 2 mg tablet (Amaryl)	Type 2 diabetes mellitus	Two tablets daily Take just before the meal				
04-05-10		Acenocoumarol 1 mg tablet (Sintrom)	Blood thinning	Use according to blood tests Swallow your tablets whole with a drink of water	Use according to dosage scheme of anticoagulation clinic			
04-05-10		Furosemide 40 mg tablet (Lasix)	Water retention (oedema)	One tablet daily				
04-05-10		Metoprolol 50 mg SR tablet (Lopresor SR)	Cardiac illness	One tablet daily Swallow your tablets whole, do not chew				
04-05-10		Perindopril 4 mg tablet (Coversyl)	Cardiac illness	One tablet daily **Dose decreased due to decreased kidney function (date 12/5: 39 ml/min)**				
04-05-10		Atorvastatin 40 mg tablet (Lipitor)	Lower lipids	One tablet daily Swallow your tablets whole with a drink of water				
04-05-10	06-05-10	Spironolactone 25 mg tablet (Aldactone)	Water retention (oedema)	One tablet daily **Discontinued due to increased potassium (date 12/5: 4.7 mmol/l)**				
04-05-10	11-05-10	Lactulose 3.35 g/5 ml (Duphalac)	Obstipation	15 ml twice daily as required **Discontinued, no indication**				

For each drug that was used before hospital admission or that was continued/started after hospital discharge the next information was given: start date, stop date, medication name (generic and brand name), what the medication is used for/ intends to prevent (underlying disease or symptoms), dose including instructions for intake, and an administration scheme. For discontinued medication the reason for discontinuation was given. This form was the basis for oral consultation: the information leaflet was explained, questions were answered and moments of intake were agreed and filled out.

Each patient who met the inclusion criteria was approached by the pharmaceutical consultants or the investigators of the wards. If the patient was interested in participation, one of the investigators (Fatma Karapinar-Çarkit – FK or Emmy Hoffmann – EH) described the aim of the interview briefly and gave a detailed information sheet to the potential participant. After the patient gave informed consent, the investigators made an appointment to arrange an interview. This study was exempt from review by the institutional review board, as it did not affect the patient's integrity. Patient's data were sampled and stored in accordance with Dutch privacy regulations.

To include opinions of a wide range of patients, a theoretical sampling strategy was used.[15] As being counselled about medication stimulates thinking about medication, we expected that patients who received usual care and patients who participated in the intervention might have different views. Also, informational needs might depend on gender and age.[16,17] Hence, we aimed to include a range of patients with different combinations of these criteria.

Interviews

Semi-structured, in-depth interviews were carried out at bedside or in a separate room if the patient preferred so. Patients were interviewed for 25–40 min guided by a topic list about their opinions concerning information about medication in the hospital at discharge (see Table 1). No information from the patient interview was made known to the treating physician or nurses. All interviews were audio-taped, transcribed verbatim and rendered anonymous. The investigators read the transcript while listening to an interview to ensure textual accuracy. The transcripts of the interviews then served as data.

All interviews were performed by a health sciences student (EH) from March to June 2007. Prior to this study an interview training was followed. During the entire interview period she was supervised by the coordinating pharmacist (FK) and an experienced qualitative researcher (Sander Borgsteede – SB).

Table 1 Topics of the interview

- What was the content of information about your discharge medication?
- How was information about discharge medication transferred (verbal/written)?
- Who provided information about discharge medication to you?
- What information about discharge medication did you need?
- What is your preferred way of information transfer?
- How did you experience the quality and quantity of information about discharge medication?

Analysis

A content analysis was used for data analysis, supported by Kwalitan 5.0, an established software package for ordering qualitative data. After ten interviews, certain themes began to be repeated (data saturation). The investigators (EH and SB) coded the first ten transcripts independently to identify key themes, using the themes from the topic list and themes that the patients considered to be important as codes. In the subsequent interviews these themes were further developed until additional interviews provided no new information with respect to the research question. During the analysis, the authors ensured the validity of the results by critical discussion and searching for cases which seemed to verify or to conflict with the insights derived from the interim analysis.

RESULTS

Patient characteristics

Between March and June 2007, 34 patients were approached for an interview. A total of 31 patients was included in the study: three patients could not be interviewed because the actual moment of discharge was before the moment the interview was scheduled. Table 2 summarises the characteristics of the patients.

Aspects emerging from the analysis

From the interviews, four aspects emerged as important issues in information about medication at discharge: (1) basic information (i.e. name of drug, indication and use), (2) information about side effects, (3) information about alternatives, and (4) what to do when medication problems are encountered. Moreover, patients stated that they preferred a combination of oral instructions and written information and both patients with or without the intervention were generally satisfied with counselling at discharge. For some aspects, we found different opinions in patients who had received usual care and patients who received counselling from the pharmaceutical consultant: we report for which aspects the opinions differ. We found no indication for differences between male and female patients neither for different aspects raised by younger and elderly patients or patients from the different wards. The citations shown are exemplary for the opinions of the patients.

Table 2 Characteristics of the interviewees (n=31)

	Patient received usual care	Patient received consultation about medication at discharge	Total
Gender			
Male	10	6	16
Female	11	4	15
Age			
< 50 years	4	3	7
50-70 years	6	4	10
> 70 years	11	3	14
Ward			
Pulmonology	3	10	13
Internal Medicine	15	-	15
Cardiology	3	-	3
Total	**21**	**10**	**31**

Basic information

Most patients were given sufficient basic information about their medication according to their needs. This information included the names of the drugs, for what they were prescribed and how they should be used:

> *The doctor told me that these were the tablets I had to use, and that this tablet is for that disease. He also told me when to take them, before the meals, after the meals and how long thereafter… I think that such information should be enough.*
> (male, 55 years old, internal medicine, without intervention)

Some patients without counselling were not informed in detail, and their knowledge about medication was somewhat superficial:

> *Interviewer: "The doctor has told you what your medication is prescribed for?"*
> *Respondent: "Yes, for my heart and sugar, to lower, or such…"*
> (female, 65 years old, internal medicine, without intervention)

Some patients expressed they had no need for detailed information. A typical example is an 83-year old lady who was not convinced about the usefulness of information:

> *I have to use them anyhow, so why do I need information? They tell you what it [the medication] is for… well, in the end you have to swallow everything anyhow. So I don't need information. I am 83 years old, and there are millions who don't reach my age, so I don't care.*
> (female, 83 years old, internal medicine, without intervention)

Other reasons why patients did not express a need for further information were because they trusted their doctor's knowledge:

> *Well, I don't have any real questions about the medication. They give me something, and I have to trust the one who gives it. I did not study for it.*
> (male, 21 years old, pulmonology, with intervention)

Patients who were counselled about discharge medication, expressed more – and also more specific – knowledge about medication.

Information about side effects

The informational needs about side effects of medications differed widely. Two contrasting responses could be distinguished. First, there were patients who wanted to be fully informed about all possible side effects. Patients who were counselled expressed more specific needs concerning information about side effects, such as what side effects could be expected for different drugs, and how they could be recognised. Other patients did not want to be informed about side effects at all. This group also contained patients who received counselling.
By knowing about side effects, some patients wanted to be assured that their medicine is the right choice and is safe:

> *I search for information about side effects and if it [drug use] has consequences for my disease. I want to be sure it is not hazardous for me, and that it is the right drug.*
> (male, 46 years old, internal medicine, without intervention)

Another reason that patients expressed, was to be prepared in case they experienced side effects. Knowledge about 'what can be expected' assured them they would recognise the unwanted effects in the future:

> *I want to know the side effects, because then I can say 'since I started that drug I have these symptoms'. Then I hope I will recognise them, and I know why I have these symptoms.*
> (male, 56 years old, pulmonology, with intervention)

Information about possible side effects is for some patients fearsome, and for that reason they preferred not to be informed:

> *I don't like to read [information about] medicines, because one reads so many things that are not good that it's better not to take the medicines. The doctor also said 'better don't read that'.*
> (female, 86 years old, internal medicine, without intervention)

Also patients indicated that knowledge about possible side effects would lead to actual experience of these side effects. For this reason, it was thought better not to know the side effects before:

> *I never read information leaflets before. A close family member does, and he gets all possible complaints. He experiences every symptom that is named in the information leaflet. So, you have to learn not to read the leaflet before.*
> (female, 67 years old, internal medicine, without intervention)

Alternatives

A topic that emerged from the interviews was that some patients wanted to be informed about alternatives for their current medication. This included alternative drugs, (lower) dosages of the same drug or other ways of administration:

> *Is there no alternative drug? I am still using the same dosage. I have been admitted two weeks ago and now I am in the hospital again. There must have been developed another product the last years.*
> (female, 75 years old, pulmonology, without intervention)

Other patients wanted to quit their prescribed medication, or wanted to be informed about replacement of their current medicines by alternatives such as homeopathic treatment:

> *I would like to know whether there are homeopathic alternatives for what I am using now. Some physicians are enthusiastic about alternatives, others don't trust that. [...] I don't know if it is possible to replace my medicines by homeopathic alternatives.*
> (female, 82 years old, internal medicine, without intervention)

Problems with medication

Many patients had no need for additional information as long as they had no medication related problems and did not suffer side effects. Patients did not need information, because as long as things were going well, there was no need for:

> *Look, my medicines work quite well, so as long as I don't experience disadvantages, I will not ask questions. [...] As long as I feel well and you think 'this works', there is no need for further knowledge*
> (male, 42 years old, internal medicine, without intervention)

In contrast with these patients, there were patients who wanted to be informed what to do in case they encountered problems. What signals could be expected that the medicines were not working as they should do and how should they react if this occurred to them.

Combining written and oral information

Generally, patients who were counselled appreciated the combination of written and oral information:

> *I appreciate the counselling, it [the information] is simply much clearer. Not all information was present on the previous medication information sheet. With an old sheet in my pocket, the information was incomplete. I am satisfied they added the new information, so I feel safe now when I walk on the street.*
> (male, 50 year, pulmonology, with intervention)

Patients who were not counselled did not receive any written information. They expressed a need for written information:

> *I would like to receive a booklet about my medicine, I will ask for that. It is useful for me that I have more information, so that I can read it at home.*
> (male, 55 year, internal medicine, without intervention)

Written information could mean the official package leaflet, or a one-page summary of the official leaflet with less information without complicated medical terminology. Many patients expressed that the language of the package leaflet was complicated. When compared to the one-page summary, patients preferred simplified information:

> *From your colleague I received a sheet with information about side effects. Simple, no medical terminology that you don't understand. If it's too complicated, I close the chapter and think: it's alright.*
> (male, 56 years old, pulmonology, with intervention)

Patient satisfaction

Generally, all patients were satisfied with the information provided about medication at discharge, although some patients mentioned that they would have preferred to have had (more) information about medication during admission. Some patients experienced they were not given enough information, but were not dissatisfied as long as the professionals took them seriously and were understanding:

I wanted to see the doctor and he visited me and said: 'you don't need oxygen'. A moment later his colleague came by, and he said 'you need that oxygen continuously'. I wanted that he would have explained why properly. But he's a fine doctor, he's understanding. He is as patient as a rock.
(female, 89 years old, pulmonology, with intervention)

Patients who were counselled were more satisfied, and felt reassured that their medication was checked, was complete and that they had an overview with the printed medication sheet. They were also satisfied because they had the opportunity to ask questions, and were informed about medication that would be discontinued after discharge. The next patient used hypnotics during admission, and during counselling at discharge information was given about discontinuation:

Nowadays it's good that when you are discharged, you speak with someone before you leave. If I would have left [without being counselled], I would have thought: 'what about my sleeping pills?'
(female, 74 years old, pulmonology, with intervention)

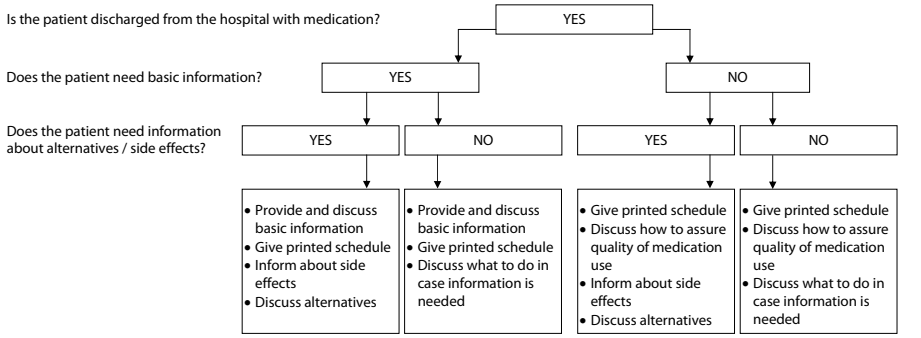
DISCUSSION

Patients had variable needs concerning information about discharge medication. Most patients wanted to receive basic information about their medication concerning the goal of pharmacotherapy, dosing and usage. Reasons for not wanting information were that patients trusted their healthcare professionals and did not consider information useful. However, patients that received patient counselling appreciated the information. Other important informational aspects were side effects, alternatives for medication and what to do when problems were encountered. Some patients explicitly mentioned they did not want to be informed about possible side effects. Patients preferred a combination of oral instructions and written information, and those who were counselled by a pharmaceutical consultant were satisfied with counselling.

The information needs of patients concerning discharge medication are comparable with information needs about medicines found in other settings. As in earlier studies, our patients were generally satisfied with counselling activities.[18] Basic information about discharge medication was considered important: names of drugs, dosing schedules, how long medication should be taken and underlying conditions.[12,19] Results from studies on information about side effects are conflicting. Many patients prefer to receive as much information as possible about side effects of their medication[20,21], which our study confirmed. A novel finding in our study was that we also found patients who explicitly

mentioned they preferred not to be informed about side effects, because they expected that being informed would negatively influence their attitude towards medication.
Another new finding was that concerning general information, some patients did not want detailed information because 'they had to use the medicine anyway' and trusted the competence of their healthcare professional. However, without wanting to be informed about details of the drug or therapeutic goal, they were open for practical advice. The patients in our study and in hypothetical situations[22] expressed a need for information about alternatives for their current medication. Alternatives could mean pharmaceutical alternatives (lower dosages, new drugs), or other alternatives such as quitting or homeopathy. Talking about possible alternatives for prescribed medication is uncommon in current pharmaceutical practice. Discussion about alternatives between healthcare professionals and patients might stimulate responsibility and self management of medication by the patient.
The current view to achieve optimal outcomes of pharmacotherapy, is to achieve concordance between patients and professionals according to therapy and therapeutic goals.[23] For concordance to occur, patients and professionals should first exchange information and views about medication.[24,25] Next they should agree on the goals and make a plan how to achieve these. The healthcare provider's role is one of supporting patients in decision making.[26] Within this process, essential information should be provided by the professional and essential questions should be asked by the patient. Next, additional knowledge can be added by the professional or requested by the patient.
Within this process attention should be paid to information that might hamper the patient in desired drug behaviour. In hypothetical situations, people preferred explanations about medication that did not convey negative information.[22] Our results also show that some people do not want to be informed about side effects and that more information would possibly lead to decreased adherence. Non-exchange of information does not mean that patient and health professional are not working effectively together to reach shared decisions.[27] To achieve concordance, health professionals should respect the patient's opinion not to receive information and provide essential information in a way that fits the patient's attitude towards medicine. Concordance does not automatically mean 'maximal information transfer'.
In Figure 2 we suggest a potential scheme for providing information about discharge medication, in which basic information, information on side effects and alternatives for medication are provided according to the needs of the patient. This scheme is not meant to be a standard operating procedure that is identical for each patient, as the individual needs will vary among patients.
When patients need basic information, this should be provided with verbal instructions supported by a medication card. If the patients desire an information leaflet, this information can also be given. In case patients do not want information this should be

Figure 2 Schedule for tailored counselling on discharge medication



explored with respect to the main risk, namely that the patient does not effectively use the prescribed medication. On the other hand, the patient might already have sufficient knowledge, so more information is a waste of time. In this case a printed schedule is sufficient to support the patient. Second, the patient might not want information, because the prescribed medication is not needed/wanted. In this case, patient and healthcare provider need to discuss this openly, possibly resulting in changes or discontinuation of medication. Third, the patient might not be motivated to be responsible for his own medication. Here, the patient and healthcare provider need to discuss how quality of medication usage can be optimised. Next, issues such as support in medication-handling can be discussed.

With respect to information about side effects and alternatives for prescribed medication, patients should be given the most important information if this is wanted. Patients who prefer not to be informed should know how to obtain information when needed. The primary task is to identify the individual needs and effectively communicate the most essential information during patient counselling.

Strengths and the limitations of this study

Strengths were that we included patients from different departments with a wide range with respect to age, as well as patients who were not counselled about discharge medication. Obviously, our study has certain limitations. First, patients were discharged after a period of hospital care, which might lead to social desirable answers in which patients express their gratitude for having received hospital care, for some patients including counselling at discharge. Second, the interviews were performed in the hospital setting and the ambulatory care after discharge was planned to be performed by the treating specialists. This might have limited free expression of thought, although we assured that patient information would remain confidential and that confidentiality was assured. Yet,

given the limitations, we are of the opinion that they do not change the meaning of our findings.

Implications for future research or clinical practice

Currently, in hospitals, pharmaceutical care activities such as counselling at discharge are being developed.[3,6,28] Our results confirm that counselling should combine verbal and written instructions. This information about medication should be tailored to the patient's needs according to both the professional and the patient. In the process of concordance, purposely *not informing patients* should have attention. Future research should study programs that inform patients tailored to individual needs and how this influences attitude towards medication, knowledge about medication and medication adherence.

A next issue is who should provide information about medication. It has been shown that doctors, pharmacists, (trained) pharmacy technicians and nurses could perform this task[19,29], although pharmacists and physicians think their own profession should perform this.[30] For the patient this issue is of less importance, as long as someone capable is responsible and performs this task. In all cases, the next healthcare providers should be informed about the activities that were performed or not performed, and motivations for these activities.

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CHAPTER

3.3

Effect of medication reconciliation with and without patient counselling on the number of pharmaceutical interventions among patients discharged from the hospital

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ABSTRACT

Background: Hospital admissions are a risk factor for the occurrence of unintended medication discrepancies between medication used before admission and after discharge. To diminish such discrepancies and improve quality of care, medication reconciliation has been developed. The exact contribution of patient counselling to the medication reconciliation process is unknown, especially not when compared to community pharmacy medication records which are considered reliable in The Netherlands.

Objective: To examine the effect of medication reconciliation, with and without patient counselling among patients at the time of hospital discharge, on the number and type of interventions aimed at preventing drug-related problems.

Methods: A prospective observational study in a general teaching hospital was performed. Patients discharged from the pulmonology department were included. A pharmacy team assessed the interventions on discharge medications for each patient with and without patient counselling.

Results: Two hundred and sixty-two patients were included. Medication reconciliation without patient counselling was responsible for minimally one intervention in 87% of patients (mean 2.7 interventions/patient). After patient counselling in 97% of patients minimally one intervention was performed (mean 5.3 interventions/patient). After patient counselling discharge prescriptions were frequently adjusted due to discrepancies in use or need of medication. Most interventions led to the start of medication due to omission and dose changes due to incorrect dosages being prescribed. Patients also addressed their problems/concerns with the medication use, which were discussed before discharge.

Conclusion: Significantly more interventions were identified after patient counselling. Therefore the information of the patient is essential in medication reconciliation.

INTRODUCTION

Hospital admissions are a risk factor for the occurrence of unintended medication discrepancies between medication used before admission and after discharge.[1-5] These discrepancies can lead to patient harm after discharge.[5-8]

Medication reconciliation has been identified as an important tool to diminish medication errors related to transitions in healthcare (Table 1).[9,10] Studies have shown that a lack of medication reconciliation accounts for 46% of all medication errors and up to 20% of adverse drug events (ADEs) in the hospital setting.[11,12]

Several sources of information can be used for medication reconciliation with each source having certain limitations. The drug records of the community pharmacy may be incomplete (e.g. due to visits to other pharmacies or to use of over-the-counter products) or incorrect (e.g. due to pre-admission changes not communicated to the community pharmacy).[13-15] General practitioner medical records can lack prescriptions issued by other medical specialties.[16] Medication vials are frequently incomplete as patients forget some vials or they store drugs that have already been discontinued.[17] Finally, depending solely on the information provided by the patient may be inaccurate due to recall bias, problems with adherence, and patients not regarding some preparations as medication.[14,18,19]

The sources used for medication reconciliation can vary between settings and countries, depending on the available time and on the availability or accessibility of different sources of information. For example, in the US the patient is considered the most important source.[10] In the Netherlands and UK, community pharmacy records are used most often, as these have been proven to be reliable.[13,20,21] In the literature, medication reconciliation is mostly performed with the use of drug records without patient counselling.[6,7,22-25] However, some studies have shown that patient counselling could significantly reduce ADEs after hospitalisation and more drug-related problems (DRPs) could be identified.[15,18,19] Therefore, the combination of recorded (assessed through the use of medication records) and reported (assessed through patient counselling) medication

Table 1 Medication reconciliation: definition and steps[9,10]

Medication reconciliation: the process of obtaining and maintaining a complete and accurate list of the current medication use of a patient across healthcare settings. It consists of four steps:
1 Verification: the current (in-hospital) medication list is assembled by using one or more sources of information (e.g. pharmacy records, general practitioner medical records, medication vials brought by the patient, information provided by the patient and his/her family in patient counselling)
2 Clarification: the medication and dosages are checked for appropriateness.
3 Reconciliation: newly prescribed medications are compared against the old ones and changes to pharmacotherapy are documented.
4 Transmission: the updated and verified list is communicated to the next provider of care.

use may increase the accuracy of the medication reconciliation process.[18] This may be especially important at the moment of discharge, because after discharge the patient will have to use his the drugs independently again. Wong et al. discussed that studies are needed to assess the exact contribution of patient counselling to the medication reconciliation process at discharge.[26] It is important to gain this insight, because medication reconciliation is time-consuming, and adding even more time-consuming patient counselling should be done only when it has clearly added value. Thus, the objective of this study was to examine the effect of medication reconciliation, with and without patient counselling among patients at the time of hospital discharge, on the number and type of interventions aimed at preventing DRPs.

METHODS

Setting and population

A prospective observational study was performed from March through November 2007 at the St. Lucas Andreas Hospital in the Netherlands, a 550-bed general teaching hospital. All adults discharged with at least one prescribed drug from the department of pulmonology were included. Exclusion criteria were death, transfer to another ward or hospital, discharge within 24 hours or out-of-office hours, discharge to a nursing home (as patients do not administer their own medication in that setting), and patients who could not be counselled (as stated by hospital physician due to physical/mental constraints, language restrictions, or terminal illness). Only the patient's first hospital admission was included. This study was exempt from review by the institutional review board, as Dutch legislation does not request this for studies that do not affect the patient's integrity. Patient data were sampled and stored in accordance with privacy regulations. Information was collected on participant characteristics, including patient age, sex, and duration of hospital stay.

The medication reconciliation process (without and with patient counselling) was carried out by a team of two pharmaceutical consultants who also assessed the patients for eligibility, and by pharmacists as supervisors. Pharmaceutical consultants are pharmacy technicians who have completed an additional three-year bachelor program that is focused on pharmaceutical patient care. They are specifically trained in pharmacotherapy and communication with patients. Because of their lower level of education compared with pharmacists, salary expenditures for pharmaceutical consultants are lower, which is why they are used rather than one supervising pharmacist.

Medication reconciliation without patient counselling

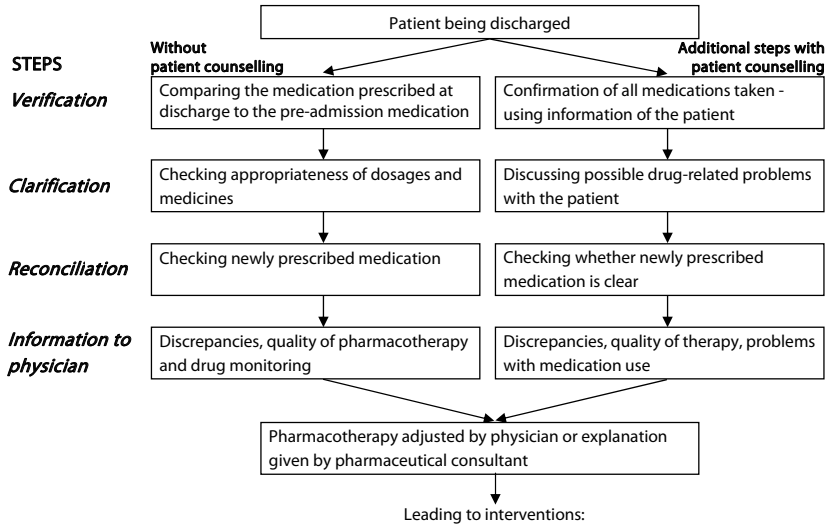
At hospital admission, the physician counselled the patient following routine practice. Hereafter the physician registered the admission prescriptions in the electronic medical record. The pharmaceutical consultant verified these prescriptions using community pharmacy records. This resulted in a small number of interventions (mostly omissions and dose errors) that were communicated to the physician. These interventions were not included in the present study which focused solely on the discharge process.

At discharge, medication reconciliation was repeated using a protocol that contained the steps for medication reconciliation without patient counselling (Figure 1). First, the verification step was performed by using the medication history of the community pharmacy, drug vials if brought into the hospital, and general practitioner records if necessary. The medication identified using these sources was matched and compared regarding dosage, route, and frequency of administration with the drug prescribed at discharge.

Second, in the clarification step, the appropriateness of the pharmacotherapy was checked by considering the continuing need for each medication, identifying suboptimal treatment, considering therapeutic drug monitoring, and identifying clinically relevant drug–drug interactions, contraindications, and costs.[14]

In the third step, the newly initiated drug was evaluated to ensure that all changes were intentional and that unnecessary medication use was prevented.[27-29]

Figure 1 The medication reconciliation process with and without patient counselling



Finally, the results of all steps were discussed with the hospital physician and the prescriptions were adjusted if necessary. Certain recommendations to the physician were made conditionally, for example, "Is it OK to withdraw analgesic, when patient indicates he/she no longer needs it?"

Medication reconciliation with patient counselling

After performing medication reconciliation without patient counselling, the pharmaceutical consultant counselled the patient and/or the family. The counselling was aimed at gathering information about actual medication use and educating the patient. This was carried out by following the steps for medication reconciliation. First, details of all drugs were confirmed in the verification step. By using a printed schedule of the discharge pharmacotherapy (medication sheet), the patient was asked how the medication was used, whether it was not in use anymore, or whether additional medication was used.
Second, the clarification step was performed through checking whether improvements could be made on the safety and quality of pharmacotherapy and explaining or answering questions. The pharmaceutical consultant was supported by a list to check the following items in the given sequence:

1. considering continuing need, to check whether all drugs prescribed still had an indication and to determine whether the patient agreed with discontinuation of a medication (e.g., still had pain when the analgesic had been discontinued);
2. other medication usage, including over-the-counter products, to determine whether there were contraindications or interactions with the medication prescribed at discharge;
3. practical problems with medication use, to check whether the patient was capable of using the drug;
4. adverse drug reactions, to determine whether these could be prevented or minimised; and
5. forgetting of medication, to check whether advices could be given to enhance adherence.

Third, in the reconciliation step, any new drugs prescribed were discussed to evaluate whether patients understood why this drug was prescribed.
The results of all steps were discussed with the hospital physician and the prescriptions were adjusted if necessary. Finally, in the transmission step, the updated medication list was communicated to the next provider of care (e.g. general practitioner, community pharmacist).

Classification of interventions

All questions asked of the physician at discharge were registered. Every change made to the pharmacotherapy due to recommendations of the pharmaceutical consultant and all accepted advices on monitoring of drug therapy were registered as interventions (medication reconciliation without patient counselling). If, after patient counselling, medication was adjusted or explanations on its use were provided to the patient, this was also registered as an intervention (medication reconciliation with patient counselling).

These interventions were classified by FK using an a priori made classification system (Appendix I) that was based on several reports.[14,30] The interventions were classified as prescription-related (leading to adjustments in the discharge prescriptions) and patient medication handling–related (leading to support of optimal medication use by the patient). Adjustment of the discharge prescriptions could be due to the elimination of medication discrepancies or due to the optimisation of pharmacotherapy. The patient medication handling interventions were aimed at improving drug use by the patient.

Outcome

The primary outcome parameter was the number and type of interventions for each patient in the medication reconciliation process at discharge. Each patient served as his/her own control when medication reconciliation without patient counselling was performed and then when patient counselling was performed, resulting in a number of additional interventions. Thus, the number of interventions resulting from medication reconciliation without patient counselling could be compared with the number of interventions from medication reconciliation using all sources (including patient counselling), comparing each patient with himself/herself. The acceptance rate of interventions was calculated by dividing all questions asked of the hospital physician by the number of accepted interventions.

Data analysis

All quantitative data were collected in Microsoft Excel 2003 (Microsoft, Redmond, WA) and were analysed using SPSS version 15.0.1 (SPSS Inc., Cary, NC). The mean number of interventions per patient and the percentage of patients with at least one intervention were calculated. The additional contribution of patient counselling to the number of interventions resulting from medication reconciliation with and without patient counselling was compared using the paired t-test for continuous variables.

RESULTS

A total of 437 patients were screened for eligibility; 175 (40%) patients were excluded (Figure 2), leaving 262 patients who were included in the study. Table 2 describes the characteristics of the included patients.

For the medication reconciliation process, community pharmacy records and patient counselling were always used as a source. The drug vials could be inspected for only 27% of patients, as these were not always brought to the hospital. The general practitioner was contacted in a minority of cases when the community pharmacy records were not totally clear.

At discharge, 940 questions had been asked of the hospital physician, of which 698 (74%) led to an intervention. The physician could not always immediately comment on the questions of the pharmaceutical consultant (e.g. whether a patient still had pain). After this was checked with the patient, an additional 56 questions out of the 940 were acted upon after patient counselling, leading to a total acceptance rate of 80%. Possible interventions that were not accepted were mostly intentional changes made to the pharmacotherapy. Furthermore, the hospital physician did not always want to change the pharmacotherapy, as he believed that some medications were not his responsibility. These possible interventions were then communicated to the patient's general practitioner. In 97% of the patients, at least 1 intervention per patient was recorded (Table 3). At discharge, a mean of 2.7 interventions per patient from medication reconciliation without patient counselling and 5.3 interventions per patient from medication reconciliation with patient counselling were identified. Patient counselling led to a mean of 1 additional prescription-related intervention and a mean of 1.6 patient medication handling related intervention per patient.

Figure 2 Flow of participants

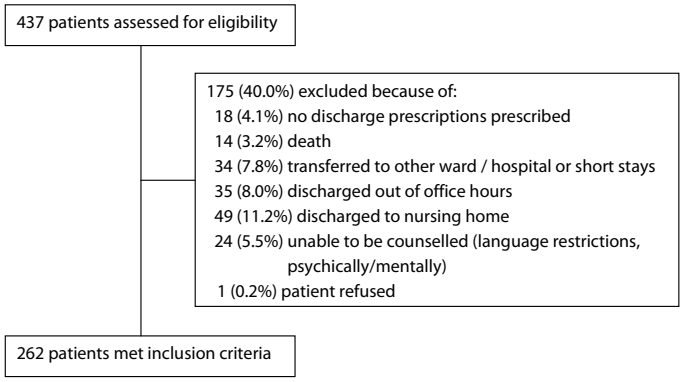


Table 2 Demographics and hospital characteristics of n=262 patients

Characteristics of patients	
Female, n (%)	131 (50.0)
Age, mean y (SD)	65 (17.3)
Planned admission, n (%)	35 (13.4)
Days of stay, range, median SD)	1-81, 9.0 (9.1)
Drugs on admission, n, mean (SD)	6.6 (3.8)
Drugs on discharge, n, mean (SD)*	9.1 (4.7)
Reason for admission, n (%)	
COPD exacerbation	88 (33.6)
Dyspnoea	33 (12.6)
Asthma exacerbation	26 (9.9)
Pneumonia	25 (9.5)
COPD exacerbation/Pneumonia	21 (8.0)
Pulmonary embolism	11 (4.2)
Other (e.g. pneumothorax, lobectomie)	58 (22.2)

COPD = Chronic Obstructive Pulmonary Disease.
* including over-the-counter medications and herbals

Prescription-related interventions

In 72.5% of patients, discrepancies were identified and corrected. In the other 27.5% of patients, no discrepancies were identified or the hospital physician stated that changes to the pharmacotherapy were intentional. As shown in Table 3, interventions were mainly classified as Start (25.2% without vs 42.0% of patients with patient counselling) and Dosage/Schemes (43.1% vs 51.1%, respectively) interventions, with start of medication because of omission and dose adjustments being the most frequent, for example, because the patient added extra information on use of over-the-counter medication. Furthermore, patients stated that some doses were incorrect, as they, for example, used the drug as needed (e.g. self-dosing of laxatives). Some patients used drugs other than those prescribed during hospitalisation, leading to a Switch. In 1.5% of the patients, a commission error was identified. As these incorrect drugs, probably prescribed for the wrong patient during hospitalisation, were discussed with the hospital physician before the patient was counselled, no effect of patient counselling could be seen.

In 76.3% of patients, pharmacotherapy was optimised. Patient counselling led to more interventions, especially in the Switch (11.5% vs 18.3% of patients) and Stop (41.6% vs 55.0% of patients) groups. Some patients did not always agree with the changes made in their pharmacotherapy during hospitalisation (e.g. they were satisfied with their current inhalation therapy) or some patients requested other medication, as their current therapy was not effective (e.g. stronger analgesic needed). Also, patient counselling was necessary to identify continuing need of all temporarily prescribed drugs. Counselling of some patients led to the start of new drug therapy. For example, the hospital physician did not always find it necessary to add inhalation medication as required, but if patients complained of dyspnoea, this drug was added after patient counselling. The

Table 3 Medication reconciliation interventions per patient[a]

Type of intervention	Without patient counselling/pat (% of patients)	With patient counselling/pat (% of patients)	Difference between groups (95% CI)	p-value[b]
Prescription-related: correction discrepancy	1.34 (63.7)	1.88 (72.5)	0.54 (0.43-0.65)	0.000
Start	0.36 (25.2)	0.68 (42.0)	0.32 (0.24-0.40)	0.000
Dosage and schemes	0.60 (43.1)	0.81 (51.1)	0.21 (0.14-0.26)	0.000
Switch	0.37 (27.9)	0.38 (29.0)	0.01 (0.00-0.03)	0.045
Stop	0.02 (1.5)	0.02 (1.5)	-	-
Prescription-related: optimisation therapy	1.31 (67.2)	1.78 (76.3)	0.47 (0.37-0.58)	0.000
Start	0.04 (4.2)	0.08 (8.0)	0.04 (0.01-0.06)	0.001
Dosage and schemes	0.54 (40.1)	0.55 (40.1)	0.01 (-0.003-0.18)	0.158
Switch	0.13 (11.5)	0.21 (18.3)	0.08 (0.04-0.12)	0.000
Stop	0.60 (41.6)	0.95 (55.0)	0.35 (0.26-0.43)	0.000
Patient medication handling-related: improve medication use by the patient	0.02 (1.5)	1.62 (69.8)	1.60 (1.40-1.81)	0.000
Recommendation	0.02 (1.5)	0.57 (40.5)	0.55 (0.46-0.65)	0.000
Explanation	-	0.60 (38.2)	-	-
Medication supply	-	0.45 (22.9)	-	-
TOTAL	2.66 (87.0)	5.28 (97.3)	2.62 (2.33-2.91)	0.000

[a] N = 262 patients
[b] Calculated by using the paired T-test

patient also provided information on inappropriate doses being used, for example, too much analgesic. After discussion between the patient and hospital physician, doses were decreased.

Patient medication-handling interventions

In 69.8% of patients, interventions on medication handling were identified. In the other 30.2%, no problems were identified and therefore no interventions were registered. In 1.5% of the patients, recommendations were made to the hospital physician to monitor the pharmacotherapy at discharge. However, patient medication handling–related interventions were especially recorded after patient counselling. Recommendations on, for example, adverse effects, tapering of drugs to discontinuation, and adherence were made in 40.5% of patients. In 38.2% of patients, it was necessary to explain why a certain medication was prescribed, how it was used, or how it worked.

Medication involved

Thirty-one percent of the interventions in the Start group were recorded for inhalation therapy, mainly due to omission, as hospital physicians forgot to start or restart inhaled corticoids when oral corticosteroids were discontinued at discharge. In the Dosage/Schemes group, 15.9% of the interventions were recorded for inhalation drugs, mainly due to incorrect dosages being prescribed, as hospital physicians did not always con-

sult the medication records of the community pharmacy. Drugs that were frequently switched were gastric acid suppressants (31.6%) and laxatives (12.5%), due to correction of formulary-driven substitution or cost aspects. Interventions in the Stop group were mostly recorded for laxatives (13.5%), gastric acid suppressants (13.1%), and sedatives (7.6%), as no indication remained at discharge. Hospital physicians forgot to discontinue these medications. In the patient medication handling–related group, 30.3% of the interventions were recorded for inhalation medication because patients did not always understand the working mechanism of their drug, leading to incorrect use, for example, the difference between a short-acting bronchodilator (incorrectly used standard instead of as-needed therapy) and a corticosteroid (incorrectly used as needed instead of standard therapy) was frequently not clear.

DISCUSSION

Medication reconciliation without patient counselling was not sufficient for a complete overview of a patient's pharmacotherapy. With patient counselling, an additional 8.8% of patients benefited in terms of correction of discrepancies (interventions in 72.5% of patients with counselling vs 63.7% of patients without counselling) and 9.1% of the patients benefited in terms of optimising the pharmacotherapy (interventions in 76.3% of patients with counselling vs 67.2% of patients without counselling). Also, patient counselling frequently identified incorrect medication handling or problems with its use, such as ADEs.

Medication reconciliation has been studied extensively. Many studies focus on medication reconciliation at admission.[2,17,24,31] Two studies showed that medication errors occur more frequently at discharge.[25,32] Omissions due to hospital physicians forgetting to prescribe drugs used at home that were temporarily discontinued during hospital admission were most frequently identified. This is consistent with the findings in our study. Several other studies showed that medication errors at discharge are common.[4,15,22,26] The percentage of patients having discrepancies at discharge varied widely, from 41% to 71%.[4,15,26] This range is probably due to the different populations being studied and the use of different sources or different classification systems. In our study, discrepancies were identified and corrected in 72.5% of patients.

Interestingly, studies focus on the elimination of discrepancies without checking whether the pharmacotherapy is appropriate. For example, 'no indication' accounted for 1-3% of the interventions in two studies.[4,26] In other studies this intervention was not mentioned.[24,25,32] Recently, Zeigler et al. discussed that medication reconciliation was not able to reduce the possible inappropriate use of gastric acid suppressants.[33] However, in

our study, drugs could be stopped in 55% of the patients, primarily laxatives and gastric acid suppressants, as no indication remained at discharge.

Drug-related problems after hospital discharge do not arise only from an insufficient medication reconciliation process at discharge.[34] They can also arise from inadequate information to the patient regarding his pharmacotherapy.[34-37] A study of discharged patients reported that 32% of patients had initiated or deleted a drug from their discharge prescription and that a further 18% had altered the dose.[38] Several studies have shown that drug use by the patient differs from what is listed in medication records.[5,16,18] Furthermore, the patient is the only constant participant across the healthcare system. Therefore, patient involvement in the medication reconciliation process is necessary.[27] Interestingly, in general, the patient is not structurally involved in medication reconciliation.[6,7,22-25] Therefore, the exact contribution of patient counselling to the entire medication reconciliation process is unclear. The part that patients can play in improving the safety of their care has been recognised only recently, and research into this matter is still in its early stages.[39] This also limits direct comparison of our findings with the findings of other studies, which is hampered even more because of the wide variety in populations studied and methods used for the medication reconciliation.

Several studies did include patient counselling in the medication reconciliation process.[4,15,19,26,32,38,40,41] In most studies however, it is not stated what the contribution of the patient counselling was to the described results.[4,15,26,32,38] For example, in one study, discharge counselling performed by a nurse in the usual care group was compared with the verification of medication records and intensive counselling by a pharmacist with a follow-up telephone call. Thirty days after discharge, preventable ADEs were detected in 11% of patients in the control group and 1% in the intervention group.[15] It is not clear whether the lower number of prevented ADEs in the study group was due to predischarge patient counselling, telephone follow-up, or the use of medication records.

Two other studies, in the outpatient and ambulatory settings, discussed the role of patient counselling in medication reconciliation. Varkey et al. found that the average number of discrepancies decreased from 5.24 to 2.46 per patient after educating the physician on medication reconciliation with patient counselling.[40] In another study, patients were engaged as partners with oncologists in identifying medication discrepancies, and patients identified 1197 (56%) discrepancies in a total of 2146 medications.[41] Although these studies are not fully comparable to our study population, they do show the potential contribution of patient counselling in the medication reconciliation process.

Viktil et al. showed that, in hospitalised patients, a mean of 4.4 DRPs per patient were recorded due to patient counselling versus a mean of 2.4 DRPs due to using medication records and participating in multidisciplinary team discussions.[19] In our study, we recorded interventions to prevent DRPs and found a comparable mean of 2.6 ad-

ditional interventions due to patient counselling. Viktil et al. recorded significantly more interventions after patient counselling in the 'need for additional drug' and 'therapy discussion' categories, which is consistent with our study. In most other categories, more interventions were identified as well after patient counselling, but this did not reach significance. As we had a larger study population, the additional contribution of patient counselling was frequently significant. Furthermore, Viktil et al. discussed the importance of making efforts to elucidate how patients actually take their medication, because inhalation medication frequently was used incorrectly. Our study confirmed that drugs for treatment of obstructive airway diseases were often used incorrectly.

In our study, the hospital physician accepted 80% of the recommendations made after patient counselling. In other studies, an acceptance rate of 96-98% was achieved.[42,43] It is not clear how this acceptance rate was calculated. Probably, intentional changes made to the pharmacotherapy were not rated as an intervention not being followed-up. Another Dutch study found an acceptance rate comparable to the rate in our study (82%).[44] It could also be that hospital physicians in the Netherlands are not used to intensive pharmacist recommendations, leading to a lower acceptance rate.

Although ours is one of the first studies clearly showing the added value of patient counselling to the medication reconciliation process, it has some limitations. First, we did not counsel the patient on admission due to time constraints. Counselling the patient on admission by the pharmaceutical consultant would probably have reduced the number of interventions at discharge. However, we decided to focus on discharge, as counselling on admission by the physician or nurse was covered by routine practice. In addition, after discharge, the patient has to start using his or her medication independently again. Second, patient medication handling interventions often required patient counselling and therefore are biased toward patient counselling. However, these kinds of interventions make it clear that patient-specific information is lost if only medication records are used.

Third, as in most other studies, our study did not assess the impact of the interventions on patients' outcomes.[15,19,41] We identified errors that could have been harmful, such as a digoxin overdose and commission errors (e.g. digoxin, amlodipine, metoprolol incorrectly started during hospitalisation). As 80% of the recommendations that we made were acted upon by the physician, we assume that the interventions were indeed clinically relevant. Furthermore, the aim of our study was to show the additional contribution of patient counselling to the medication reconciliation process.

Finally, there was a high exclusion rate of 40% in our study. Discharge to a nursing home was a major reason for exclusion. Generally, we tried to counsel these patients or their families, but due to the specific patient population, we did not include them in this study. Despite the high exclusion rate, we studied an extensive medication recon-

ciliation process in 262 patients and were able to implement this process in the daily activities of the pulmonary ward.

Notwithstanding these limitations, this study shows that patient counselling is an essential part of the medication reconciliation process, even in countries where community pharmacy medication records are considered reliable, such as the Netherlands.

Some recommendations can be made for further study. First, it is unclear which patients benefit most from the medication reconciliation process.[45] In our study, we were not able to predict this, as we also recorded interventions in patients with relatively simple drug therapy. The medication reconciliation process is time-consuming, so selection of high-risk patients is advisable. More research is necessary in this area. Second, the clinical relevance of the interventions with and without counselling should be explored. Third, additional follow-up interventions may be necessary to eliminate problems after hospital discharge.[38] Finally, the effect of automated medication records available for all healthcare workers (both inside and outside the hospital) on medication discrepancies should be studied.

In summary, in the Netherlands, community pharmacy medication records are used most often to perform medication reconciliation. However, our study showed that these records are not enough to create a complete overview of the drugs and their actual use by the patient. The patient has important additional information on drug use and problems with this use. Furthermore, medication reconciliation should be more than resolving discrepancies and checking appropriateness of therapy. Discussing the ability of the patient to adhere to the prescribed therapy should also be a focus of medication reconciliation. As the patient is the only constant participant across the healthcare system, patient involvement in medication reconciliation is essential.

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Appendix I Classification of interventions

Classification	Reasons	Example
Prescription-related interventions: correction of unintended discrepancies		
Start[a]	- omission; incorrect deletion of a medication	- omission of bisphosphonate or patient still needs painkiller
Dosage / Schemes[b]	- discrepancy with dosage, strength, or formulation used before admission	- furosemide prescribed twice a day instead of once a day
Switch[c]	- discrepancy with medication used before admission	- salbutamol prescribed instead of ipratropium during hospitalisation
Stop[d]	- commission; incorrect addition of a drug not used before admission	- digoxin prescribed for the wrong patient during hospitalisation
Prescription-related interventions: optimisation of pharmacotherapy		
Start[a]	- undertreatment; drug added based on protocols and best practice standards	- adding a laxative to opioid use
Dosage / Schemes[b]	- dosage, administering time, drug regimen, or duration of therapy inappropriate - prescription incomplete or unclear	- too high dosages prescribed for geriatric patient - strength or route unclear
Switch[c]	- drug prescribed not appropriately (contraindication , drug-drug interaction)	- selecting tramadol instead of NSAID in case of kidney malfunction
Stop[d]	- indication no longer present at discharge	- discontinuing analgesics, sedatives
Patient medication-handling interventions: improvement of medication use by the patient		
Recommendation[e]	- advising the physician about the monitoring of drug therapy - advising the patient about, e.g. side effects, adherence, tapering off drugs, self-care	- take blood sample for check on electrolytes - regular use of inhaler steroid/rinse mouth after use
Explanation[f]	- inappropriate medication use by the patient (not used according to protocols) - answering questions of the patient on medication	- short acting inhalation medication not used if required - questions on alcohol use in combination with medication
Medication supply[g]	- adjust medication in the medication supply of the patient	- removing expired antibiotics or discontinued medication

NSAID = Non-Steroidal Anti-Inflammatory Drugs
[a] Initiation of drug
[b] Adjustment in dose regimen, frequency, timepoint, and duration
[c] Change to another medication
[d] Discontinuation of medication
[e] Recommendations to ease drug use or diminish possible problems
[f] Explanation of the pharmacotherapy to increase the knowledge of the patient
[g] Evaluation whether medication supply is correct and complete

CHAPTER

3.4

Effect of medication reconciliation on medication costs after hospital discharge in relation to hospital pharmacy labour costs

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ABSTRACT

Background: Medication reconciliation aims to correct discrepancies in medication use between healthcare settings and aims to check the quality of pharmacotherapy to improve effectiveness and safety. In addition, medication reconciliation might also reduce costs.

Objective: To evaluate the effect of performing medication reconciliation on medication costs after hospital discharge in relation to hospital pharmacy labour costs.

Methods: A prospective observational study was performed. Patients discharged from the pulmonology department were included. A pharmacy team assessed medication errors prevented by medication reconciliation. Interventions were classified into three categories as correcting hospital formulary induced medication changes (e.g. re-substitute brand drug to generic drug used pre-admission), optimising pharmacotherapy (e.g. discontinue unnecessary laxative) and eliminating discrepancies (e.g. restart of omitted pre-admission medication). Because eliminating discrepancies does not represent real costs to society (before hospitalisation the patient was consuming the medication also), these medication costs were not included in the cost calculation. Medication costs at one and six month(s) after hospital discharge and the associated labour costs were assessed using descriptive statistics and scenario analyses. For the six months extrapolation only medication intended for chronic use was included.

Results: 262 patients were included. Correcting hospital formulary changes saved medication costs of €1.63/patient at one month after discharge and €9.79 at six months. Optimising pharmacotherapy saved medication costs of €20.13/patient at one month and €86.86 at six months. The associated labour costs for performing medication reconciliation were €41.04/patient.
Medication cost savings from correcting hospital formulary induced changes and optimising of pharmacotherapy together outweighed the labour costs at six months extrapolation with €55.62/patient (sensitivity analysis €37.25 - €71.10).

Conclusions: The medication savings after hospital discharge outweighed the labour costs of performing in-hospital medication reconciliation with €56/patient. Preventing medication errors through medication reconciliation results in higher benefits than the costs related to the net time investment.

INTRODUCTION

Medication errors are common at interfaces of care such as hospital admission and discharge.[1-3] These medication errors can cause adverse drug events that can result in increased morbidity and mortality, as well as unnecessary costs for society.[4] Medication reconciliation has been developed to reduce harm due to adverse drug events and is defined as the process of creating the most accurate list possible of all medication a patient is taking, with the goal of providing correct medication to the patient at all transition points.[5,6] The Institute for Healthcare Improvement states that the term "medication reconciliation" has been misinterpreted as healthcare providers do not implement all four steps of medication reconciliation.[6] These four steps start with the *verification step*, in which discrepancies between pre-admission and in-hospital prescribed medication are eliminated. Second, in the *clarification step* the pharmacotherapy is evaluated and optimised (e.g. reduction of dosages that are too high for an elderly patient). Third, in the *reconciliation step* changes in the pharmacotherapy are documented. Finally, in the *transmission step* the discharge information is communicated to the patient and the next healthcare provider.[5,6]

Studies often emphasize the time-consuming aspect of medication reconciliation, but few cost evaluation studies have been performed regarding implementing medication reconciliation itself.[2,7,8] Only, Karnon et al. describe a model-based cost-effectiveness analysis at hospital admission and estimated that pharmacist-led medication reconciliation had a probability exceeding 60% of being cost-effective.[9]

Most reports provide limited insight on how time-consuming the complete medication reconciliation process is and what the associated labour costs are.[2,3,8] Furthermore, no studies have evaluated the effect of medication reconciliation on medication costs after hospital discharge.

In the Netherlands, community and hospital pharmacies have different budgets leading to different drug formularies between the settings.[10] In the community setting, prescribing and dispensing of generic drugs are encouraged by government policy. However, inside the hospital original brands are used more frequently because of the fixed budget system and price discounts set by the pharmaceutical industry.[10,11] At admission a patient's drug is replaced by the cheapest brand inside the hospital. When the same brand is continued after hospital discharge, costs will increase as no discount is given outside the hospital. Due to the correction of hospital formulary induced medication changes, the costs may decrease (e.g. re-substitution of expensive medication into the pre-admission used medication). On the other hand, due to eliminating discrepancies, medication costs may increase (e.g. restart of omitted medication). However, these medication-related costs do not represent real costs as the patient was consuming this medication before hospitalisation. The optimisation of pharmacotherapy could increase

(e.g. start of medication due to undertreatment) or decrease medication-related costs (e.g. discontinuation of unnecessary medication). It is unknown how savings and expenditures balance, warranting an economic evaluation.[7,12]
The aim of this study is to evaluate the prevention of medication errors identified during medication reconciliation with respect to the influence on medication costs after hospital discharge in relation to hospital pharmacy labour costs.

METHODS

Setting and study population

A prospective observational study was performed from March to November 2007 at the St. Lucas Andreas Hospital in The Netherlands, a 550-bed general teaching hospital. The data for this analysis were derived from a previous study that has been described elsewhere.[1] In brief, all adult patients discharged with at least one prescribed drug from the department of pulmonology were included. Exclusion criteria were: patients transferred to another ward or hospital, patients discharged within 24 hours or out-of-office hours, patients discharged to a nursing home (as most patients could not be counselled) and patients who could not be counselled for other reasons (due to physical/mental constraints, language restrictions or being terminally ill). Only the patient's first hospital admission during the study period was included. This study was exempt from review by the institutional review board as Dutch legislation does not request this for studies that do not affect the patient's integrity. Patient data were obtained and handled in accordance with privacy regulations.

Medication reconciliation process

Medication reconciliation can be performed by several healthcare providers within the hospital pharmacy. In the Netherlands clinical pharmacists (who have successfully completed a six-year university training) are more expensive to employ than other pharmacy staff. Therefore it is common for pharmacists to delegate tasks to pharmacy technicians or pharmaceutical consultants. Pharmacy technicians have followed a two-year degree program to gain basic knowledge in compounding, dispensing and guiding the patient in the medication use. Pharmaceutical consultants are pharmacy technicians who have followed an additional three-year bachelor degree program. They are specifically trained in pharmacotherapy and communication with patients. Generally, pharmaceutical consultants perform delegated pharmacist tasks that are more complex than the tasks delegated to pharmacy technicians.
In this study the medication reconciliation process was carried out by a team of pharmaceutical consultants, who were trained in medication reconciliation before this study

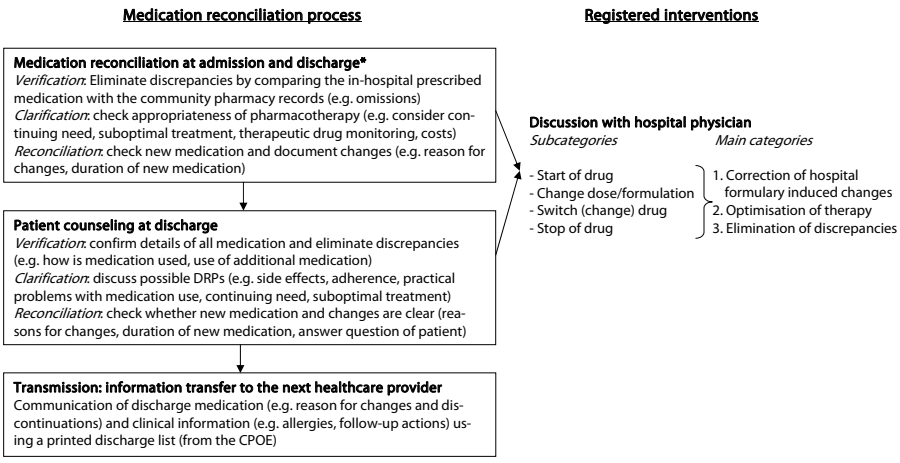
was conducted. The medication reconciliation process has been previously described in detail.[1] The process consisted of medication reconciliation at hospital admission and discharge, patient counselling at hospital discharge and transmission of medication information to the next provider in care (e.g. community pharmacy, general practitioner). The main aspects of the process are illustrated in Figure 1.

Classification of interventions

The pharmaceutical consultant registered every change made by the hospital physician to the pharmacotherapy after medication reconciliation at hospital admission and discharge and after patient counselling. The classification of interventions was based on the first two steps in medication reconciliation that could influence medication costs (i.e. *eliminating discrepancies* and including *hospital formulary induced medication changes* in the verification step and *optimisation of pharmacotherapy* in the clarification step).[1] Although hospital formulary induced medication changes can be regarded as discrepancies also, we classified them separately for this study because of their effect on medication costs (brand products that are cheap in the hospital setting due to price discounts; no discount is given outside the hospital setting).

The medication changes were classified in three mutually exclusive categories as category 1, category 2 or category 3 errors. Category 1 errors relate to the correction of hospital formulary induced medication changes before the patient is discharged. Cat-

Figure 1 Implementation of the medication reconciliation process



DRPs= drug-related problems

CPOE= computerised physician order entry

* For medication reconciliation at admission and discharge we did not counsel the patient, but solely used community pharmacy medication records. Possible interventions were communicated to the hospital physician who could adjust the medication.

egory 2 errors relate to the optimisation of the pharmacotherapy due to evaluating the appropriateness of the pharmacotherapy. Category 3 errors relate to the prevention of medication discrepancies between the pre-admission and in-hospital prescribed medication (excluding the correction of hospital formulary induced medication changes, i.e. category 1). These three categories were defined to make a distinction between real medication costs (i.e. category 1 and 2) and unreal medication costs (i.e. category 3, see also paragraph Outcomes).
The interventions regarding optimisation of pharmacotherapy were further classified into four sub-categories, namely "start" of medication, "stop" of medication, "switch" (change) of medication and change in "dose/formulation". Hospital formulary induced medication changes were further classified in two sub-categories, namely "switch" and "dose/formulation"

Outcomes

Eliminating discrepancies is an important aspect of medication reconciliation but does not represent real costs for society as the patient was consuming these medicines before hospitalisation. Therefore these interventions will not be included in the cost calculation. Thus, the difference between labour costs, and the costs of category 1 (hospital formulary induced changes) and category 2 (optimisation of pharmacotherapy) interventions due to medication reconciliation, was compared.

Cost analysis

All quantitative data were collected using the data of the previous study and entered into MS Excel 2003 and analysed using SPSS® version 15.0.1. Descriptive statistics were used to summarise the frequency of interventions and the time spent on these activities.

Medication-related costs

We analysed the medication costs/savings that arose due to the interventions performed during medication reconciliation. The medication-related costs were analysed from a health insurer's perspective. In The Netherlands the health insurer pays for most medication except over-the-counter drugs and herbal medicines. The payments made to dispensing community pharmacies by health insurers are based on the cost of the medication dispensed plus a fixed dispensing fee of €6.10 (Euros) to cover the routine pharmaceutical services. Medication is dispensed for two weeks the first time it is prescribed. Medication intended for chronic use can be dispensed for a maximum of three months, with the exception of benzodiazepines that are dispensed for a maximum of one month.
At our department of pulmonology, discharge prescriptions were prescribed for one month. This one month period was used to estimate the medication costs after hospital

discharge for chronic medication. For medication not intended for chronic use (e.g. antibiotics, tapering off schemes) medication costs were based on one week as these medicines generally were discontinued within one week. Interventions regarding over-the-counter drugs and herbal medicines were not included in the calculations because these were paid by the patient himself and not by the health insurer. The medication prices as listed in the Dutch pharmaceutical guidelines ('Farmacotherapeutisch Kompas') were used in June 2008.[13] This national manual is written by the Dutch Healthcare Insurance Board to help doctors to prescribe drugs more efficiently. This manual also contains mean medication prices that are based on the Defined Daily Dose (DDD) as defined by the WHO Collaborating Centre for Drug Statistics Methodology. To these drug prices 6% tax was added.

For the "start" and "stop" sub-category of interventions the medication-related costs/savings were estimated for one month including 6% tax and the fixed dispensing fee of €6.10. For the "dose/formulation" sub-category of interventions dose increases and dose decreases were not included in the analysis as these were equally registered and we assumed that the costs and benefits would compensate for each other. To validate this assumption we checked the costs for the most commonly registered interventions (mainly inhalation therapy) and concluded that the medication costs were minimal. Therefore, we only focused on formulation changes in this sub-category. The medication costs/savings for the interventions in the "dose/formulation" and "switch" sub-category were calculated by using the difference in medication/formulation costs between the previously and eventually prescribed medication/formulation at discharge.

Assumptions regarding the medication costs

The calculation of medication costs, due to medication reconciliation interventions performed by the pharmaceutical consultants, could be overestimated as other healthcare providers could also perform the interventions. In these cases medication costs or savings could not be attributed to the in-hospital medication reconciliation process performed by the pharmaceutical consultants. We made the following assumptions based on literature reports.

Hospital formulary adjusted medication can be corrected after discharge.[10,11,14,15] However, a healthcare provider will hesitate to adjust a therapeutic switch (i.e. another therapeutic substance in the same group, e.g. perindopril instead of lisinopril) as they will assume that the patient is given the last in-hospital prescribed medication intentionally by the hospital physician. Product substitution (i.e. same active substance, e.g. brand vs generic or different formulation) will be applied.[16] Studies report that 8.0% to 28.5% of medications are substituted back after hospital discharge (mean 19%).[10,11,14,15] Therefore, the medication costs for the prevention of category 1 errors were reduced by 20%.

With the optimisation of pharmacotherapy it is expected that healthcare providers would notice these medication errors earlier if the computer system generated a warning signal, for example, with duplicated or contra-indicated therapy, or if the medication was actively reviewed. This assumption is strengthened by studies that show that in-hospital prescribed medication is frequently used for a longer time period.[17-20] This implies that errors such as overtreatment are noticed less often since computer systems do not recognise these.[21] Studies report rates of discontinuation between 2.2% to 26.3% (mean 10.4%).[11,15,21,22] Therefore, the medication costs for the prevention of category 2 errors were reduced by 10%.

To give an overview of the medication costs over a longer time period, we made a 6 month extrapolation for medication intended for chronic use (assuming one prescription fee for the first month and two prescription fees for the remaining five months). We chose for a 6 months period extrapolation as studies showed that in-hospital prescribed medication can be continued this long.[17,19,20] For benzodiazepines a prescription fee for each month was included in the extrapolation (see Table 1 for examples and cost calculations).

Table 1 Examples of interventions and calculations on medication costs at one month and six months per patient

Example of interventions	NR	1 month drug costs[a] (euro)	PF (euro)	Medication costs t=1 and t=6[b] (euro)	Medication costs after reduction[c] (euro/patient)
Category 1: Acetylcysteine sachets vs tablets	2	Tablets: 20.88 Sachets: 10.07	n.a.	t=1: 2 x (20.88-10.07) = 21.62 t=6: 2 x (6 x 20.88 – 6 x 10.07) = 129.72	- 20% of 21.62 = 17.30 (0.07/patient) - 20% of 129.72 = 103.78 (0.40/patient)
Category 1: Omeprazole generic vs Pantozol brand	20	Brand: 34.16 Generic: 1.26	n.a.	t=1: 20 x (34.16-1.26) = 658.00 t=6: 20 x (6 x 34.16 – 6 x 1.26) = 3948.00	- 20% of 658.00 = 526.40 (2.01/patient) - 20% of 3948.00 = 3158.40 (12.05/patient)
Category 2: Stop of Temazepam capsules	15	Capsules: 3.71	6.10	t=1: 15 x (3.71 + 6.10) = 147.15 t=6: 15 x (6 x 3.71 + 6 x 6.10) = 882.90	- 10% of 147.15 = 132.44 (0.51/patient) - 10% of 882.90 = 794.61 (3.03/patient)

n.a. = not applicable. NR= number of interventions performed in 262 patients. PF= prescription fee. t=1 and t=6 calculation of medication costs at one and six months.

[a] Based on the Dutch pharmaceutical guidelines. To the drug costs 6% tax was added.

[b] at t=1 one prescription fee was included and at t=6 three prescription fees were included for the start and stop sub-category of interventions. For benzodiazepines a prescription fee for each month was included as these drugs are dispensed for a maximum of one month.

[c] As it is expected that some interventions will be performed in usual care, the estimates of medications costs due to medication reconciliation are reduced with respectively 20% and 10% for interventions in category 1 and 2. The medication costs per patient were calculated by dividing the medication costs with 262 patients.

Labour related costs

The time spent on the medication reconciliation process by the pharmaceutical consultant was converted into labour costs. The pharmaceutical consultants recorded the time they needed in 59 patients by using a stopwatch. To estimate the costs, the mean year salary of a pharmaceutical consultant (€50.000) was used. When assuming 46 annual working weeks and an efficiency rate of 70%, the one hour salary was €39.25. The efficiency rate of 70% was based on time not directly related to specific medication reconciliation activities, such as courses, meetings and instructions to new hospital physicians.[23,24] We did not focus on time spent by other healthcare providers, such as the clinical pharmacist or the hospital physician. Most tasks were performed by the pharmaceutical consultants who generally worked independently.

Sensitivity analyses

We performed a sensitivity analysis to examine best- and worst-case scenarios. To investigate the robustness of the assumptions regarding the medication costs, we varied the variables on reducing the medication costs with 50%. Thus for the sensitivity analysis 10% and 30% reduction on medication costs was applied for hospital formulary induced interventions (initial reduction was 20% based on previous studies, see paragraph "assumptions regarding the medication costs"). For optimising pharmacotherapy we initially reduced medication costs with 10%. Thus, for the sensitivity analysis 5% and 15% reduction was applied.

For the labour costs we varied the following variables: the mean annual salary of the pharmaceutical consultant (normal 100%, sensitivity analysis 80% and 120%), working weeks per year (normal 46, sensitivity analysis 44 and 50), and efficiency rate (normal 70%, sensitivity analysis 50% and 90%).[23,24] We also estimated what the labour costs would be if a pharmacy technician (mean year salary €40.000) or a clinical pharmacist (mean year salary €60.000) performed the process.

RESULTS

In total 262 patients were included. Table 2 describes the characteristics of the included patients.

Table 3 shows the amount of interventions performed and the associated medication costs at one and six months after discharge. Correcting hospital formulary induced changes (i.e. category 1 errors) and optimising the pharmacotherapy (i.e. category 2 errors) saved €1.63/patient and €20.13/patient at one month after discharge, respectively (€9.79/patient and €86.86/patient respectively at six months).

With the correction of hospital formulary induced changes, medication reconciliation led to medication costs when more expensive formulations were used in the community setting (e.g. sachet instead of solution). Medication cost savings were established due to re-substitution of more expensive in-hospital prescribed medication (e.g. brand Pantozol® instead of generic omeprazole).

With the optimisation of pharmacotherapy, medication reconciliation led to costs when medication was added for suboptimal treatment (e.g. addition of short acting bronchodilator for dyspnoea instead of therapy with solely an inhalation corticosteroid). Savings were generally recorded due to the discontinuation of medication no longer indicated at hospital discharge (e.g. gastric acid suppressants, laxatives, sedatives and analgesics) and due to the selection of cheaper alternatives.

Table 2 Demographics and hospital characteristics of n=262 patients

Characteristics of patients	
Female, n (%)	131 (50.0)
Age, mean years (SD)	65 (17)
Admission type	
Planned (%)	35 (13)
Length of stay, range, median days (SD)	1-81, 9.0 (9.1)
N. of drugs on admission, mean (SD)	6.6 (3.8)
N. of drugs on discharge, mean (SD)	9.1 (4.7)
Reason for admission	
COPD exacerbation, n (%)	88 (33.6)
Dyspnoea	33 (12.6)
Asthma exacerbation, n (%)	26 (9.9)
Pneumonia, n (%)	25 (9.5)
COPD exacerbation/Pneumonia, n (%)	21 (8.0)
Pulmonary embolism, n (%)	11 (4.2)
Other (e.g. pneumothorax, lobectomie)	58 (22.2)

COPD = Chronic Obstructive Pulmonary Disease
SD = Standard deviation

Table 3 Interventions performed and medication costs and savings at one and six month(s) after discharge (n=262)

Type of intervention	Nr[b]	Main drugs Involved	One month			Six months[d]		
			Savings (euro/pat)	Costs (euro/pat)	Difference[c] (euro/pat)	Savings (euro/pat)	Costs (euro/pat)	Difference[c] (euro/pat)
Category 1: Correction of formulary changes	70	-	2.14	0.51	1.63	12.84	3.06	9.79
Dose/formulation[a]	18	Laxatives	0.13	0.16	-0.04	0.76	0.98	-0.22
Switch	52	Inhalation therapy	2.01	0.35	1.67	12.09	2.08	10.01
Category 2: Optimisation of pharmacotherapy	303	-	21.13	1.00	20.13	91.11	4.24	86.86
Start	20	Inhalation therapy	-	0.74	-0.74	-	2.67	-2.67
Dose/formulation[a]	21	Laxatives	0.09	0.08	0.01	0.53	0.46	0.08
Switch	35	Protonpumpinhibitors	2.48	0.19	2.29	14.87	1.12	13.75
Stop	227	Protonpumpinhibitors	18.57	-	18.57	75.71	-	75.71
Total	373	-	23.27	1.51	21.77	103.95	7.30	96.65

[a] Dosage adjustments are not included as dose decreasing and increasing was equally registered.

[b] Number of interventions. Interventions for over-the-counter drugs and herbals are not included as these are paid by the patient himself.

[c] Negative values indicate costs for the healthcare insurance; positive values indicate cost savings.

[d] The extrapolation to six months only includes medication intended for chronic use. Category 1 interventions were related to medication intended for chronic use. Category 2 interventions could also be related to temporarily prescribed medication (e.g. discontinue antibiotics, correct tapering off schemes). These interventions were not included in the six months extrapolation.

In Table 4 the time spent on the medication reconciliation process and the associated labour costs of €41.04 per patient (sensitivity analysis €25.56 – €59.40) are described. Most time was spent on admission and discharge medication reconciliation (32.9 min) followed by patient counselling (26.6 min).

In Table 5 several scenario analyses are presented. Correcting hospital formulary induced changes and optimising of pharmacotherapy led to medication savings of €21.77/patient at one month and €96.65/ patient at six months. The labour costs (of the pharmaceutical consultants) were €41.04/patient (sensitivity analysis €25.56 - €59.40, see Table 4). This implies that after one month the medication savings due to the prevention of category 1 and category 2 errors (€21.77/patient) do not outweigh the labour costs of the medication reconciliation process (€41.04/patient). However, in-hospital prescribed medication is frequently continued after hospital discharge. After six months extrapolation the labour costs (€41.04/patient) are outweighed by medication cost savings (€96.65/ patient) with €55.62/patient (sensitivity analysis €37.25 - €71.10) due to correcting hospital formulary induced medication changes and optimising of pharmacotherapy. Savings were consistently calculated in the sensitivity analysis when the pharmacy technician (€63.82/patient) or pharmacist (€47.41/patient) performed the medication reconciliation.

Table 4 Mean time per patient spent and associated labour costs including a sensitivity analysis (n=59)

Steps of medication reconciliation process	Mean time in min (SD)	Labour costs Normal[a] (euro)	Labour costs Best scenario[b] (euro)	Labour costs Worst scenario[c] (euro)
Medication reconciliation at admission and discharge (incl. discussion with hospital physician)	32.9 (6.6)	21.52	13.40	31.15
Patient counselling (incl. discussion results with hospital physician)	26.6 (9.8)	17.38	10.82	25.16
Transfer of medication information (incl. adjustments in final discharge prescriptions)	3.3 (2.8)	2.14	1.33	3.09
Total	62.7 (14.6)	41.04	25.56	59.40

[a] Based on a mean year salary of a pharmaceutical consultant of €50.000, 46 working weeks and a productivity of 70%.
[b] Based on a mean year salary of a pharmaceutical consultant of €40.000, 50 working weeks and a productivity of 90%.
[c] Based on a mean year salary of a pharmaceutical consultant of €60.000, 44 working weeks and a productivity of 50%.

Table 5 Sensitivity analyses (n=262)

Type of intervention	One month			Six months		
	Normal[a] (euro/pat)	Sensitivity analysis[b] Best case (euro/pat)	Sensitivity analysis[c] Worst case (euro/pat)	Normal[a] (euro/pat)	Sensitivity analysis[b] Best case (euro/pat)	Sensitivity analysis[c] Worst case (euro/pat)
Category 1: correct formulary changes	1.63	1.84	1.43	9.79	11.01	8.56
Category 2: optimise pharmacotherapy	20.13	21.25	19.02	86.86	91.69	82.04
Total: sum category 1 and 2	21.77	23.09	20.44	96.65	102.70	90.60
Medication costs vs labour costs PC[d]	-19.27 (-3.79 – -37.64)	-17.95 (-2.47 – -36.32)	-20.59 (-5.11 – -38.96)	55.62 (37.25 – 71.10)	61.66 (43.30 – 77.14)	49.57 (31.20 – 65.05)
Medication costs vs labour costs PT[d]	-11.06 (-25.76 – 1.32)	-9.74 (-24.44 – 2.64)	-12.39 (0.00 – -27.08)	63.82 (49.13 – 76.21)	69.87 (55.18 – 82.26)	57.77 (43.08 – 70.16)
Medication costs vs labour costs CP[d]	-27.48 (-8.90 – -49.52)	-26.16 (-7.58 – -48.20)	-28.80 (-10.23 – -50.84)	47.41 (25.37 – 65.98)	53.46 (31.42 – 72.03)	41.36 (19.32 – 59.94)

PC = Pharmaceutical consultant. Labour costs: €41.04 (sensitivity analysis 25.56 - 59.40)

PT = Pharmacy technician. Labour cost: €32.83 (sensitivity analysis 20.45 - 47.52)

CP = Clinical pharmacist. Labour cost: €49.24 (sensitivity analysis 30.67 - 71.28)

[a] Normal; Reduction category 1: 20%, category 2: 10%.

[b] Best case; Reduction category 1: 10%, category 2: 5%.

[c] Worst case; Reduction category 1: 30%, category 2: 15%.

[d] Positive values indicate that the medication cost savings outweighed labour costs.

DISCUSSION

This study shows that correcting hospital formulary induced changes and optimising the pharmacotherapy leads to medication cost savings as frequently more expensive medication is prescribed in hospital and not indicated (temporarily prescribed) medication can be discontinued at hospital discharge. The medication reconciliation process takes approximately one hour per patient. The medication cost savings outweighed the labour costs at six months extrapolation with €55.62/patient.

Karnon et al. reported that pharmacist-led medication reconciliation had a probability exceeding 60% of being cost-effective.[9] Their model-based cost-effectiveness analysis was based only on hospital admission. We showed that pharmaceutical consultant-led medication reconciliation from hospital admission to discharge resulted in higher benefits than the costs related to the net time investment. No previous published study has evaluated the effect of medication reconciliation on medication costs after hospital discharge. Although medication costs comprise a relatively small portion of the healthcare costs, for insurance companies this expense can be quite significant as many high cost drugs are initiated in hospital.[19,25] Furthermore, temporarily indicated or inappropriate medicines initiated in the hospital are continued in primary care.[17,19,20,26] Recent trends suggest that health insurance companies may be willing to pay for patient safety projects if they improve drug therapy outcomes and reduce healthcare costs.[27]

With medication reconciliation several medication errors can be prevented. We excluded category 3 errors from the medication cost calculation as the patient was using these medicines before hospitalisation also. Unnoticed discrepancies could lead to healthcare problems that increase healthcare costs. Studies have shown that medication reconciliation can diminish adverse drug events after discharge and reduce rehospitalisation rates.[9,28-31] Boockvar et al. showed that 4.8% of discrepancies caused adverse drug events.[32] Estimates of costs per adverse drug event range from €900 - €1800.[9,33] For our study this would mean an additional cost saving of €18.000 - €36.000 (€69 - €137 per patient) as we eliminated 409 discrepancies of which theoretically 20 would cause an adverse drug event.

Indirect costs can also occur when formulary induced medication changes are not corrected or the medication is not optimised. Patients may become confused when products appear completely different leading to non-adherence or patients may use both products if they do not realise that medication has been interchanged.[34] Non-optimisation of pharmacotherapy could lead to under- or overtreatment which both could lead to additional costs due to deterioration of a condition or adverse effects resulting from an unnecessary medication.[27]

The need for medication reconciliation is clear.[35] Still, healthcare providers are hesitant to initiate medication reconciliation projects because of concerns about the resources.[7,28,35]

Studies discuss that medication reconciliation is time-consuming, but they do not explain how much time medication reconciliation takes using objective measurements.[9,29,36,37] Only Bayley et al. reported the time they spent on medication reconciliation per process (in patients using the same amount of medication as in our study population).[37] To collect the medication history at hospital admission they needed 45 min/patient and 22.5 min/patient to type a medication list at hospital discharge. At admission and discharge we needed less time, namely 32.9 min (see Table 4). These differences may be explained due to the design of the program (e.g. we printed a discharge medication list instead of typing one) and the nature of the intervention. We spent 26.6 minutes on patient counselling at discharge which is comparable with the 30 minutes in the study of Bayley et al.[37]

The strength of this study is that we performed all steps of medication reconciliation. Although it is one of the first studies clearly showing the medication-related costs after hospital discharge and the time spent during a medication reconciliation process, our study has some limitations. First, through extrapolating the medication costs we assumed that patients actually filled their prescriptions, were adherent and that patients continued to use the medication on a chronic basis. Several studies have shown that in-hospital started medication is frequently continued after discharge.[17,19,20] Second, the applicability of our findings to other populations may be limited because we excluded patients who were discharged to nursing homes and the medication reconciliation was performed in one department. Results may be different for other departments or regions. Still, we believe that it is important to have more insight on the effects of medication reconciliation and the associated labour costs. In this way, it will be clear what the benefits are and how much time is acceptable or normal to spend. Third, we only included the first hospitalisation for each patient in this study. We lack data regarding readmitted patients. It is expected that less but similar interventions (e.g. correct formulary adjusted medication, discontinuation of temporarily intended medication) would be performed. This would decrease medication cost savings but also the time needed for medication reconciliation. Finally, our assessment only focused on the program costs and was not designed as a comprehensive cost-effectiveness analysis. The actual benefit of the medication reconciliation process in terms of patient and medication safety requires additional studies. Such studies should also determine if similar cost savings can be seen in other settings when the medication is optimised and the costs the hospital would save by preventing medication errors (e.g. the time/costs needed to rectify a medication error). More research is necessary to make the medication reconciliation process more efficient. For example, automating the information transfer between community pharmacies and hospital pharmacies (and vice versa) is expected to save time.

In summary, this study suggests that a medication reconciliation process can be implemented for reasonable labour costs. The medication savings 6 months after hospital

discharge, due to correcting hospital formulary induced changes and optimising of pharmacotherapy, outweighed the labour costs of performing in-hospital medication reconciliation with €56/patient.

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CHAPTER

3.5

Effect of instruction manuals on completeness of electronic patient files in community pharmacies after discharge from hospital

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(submitted)

ABSTRACT

Objective: To investigate the effect of instruction manuals on completeness of electronic patient files in community pharmacies for patients discharged from hospital.

Methods: A before-after study was performed in patients with a discharge medication overview. The intervention consisted of faxing an instruction manual to community pharmacies specifying how to document medication changes and clinical information in the community pharmacy information system.
Community pharmacy's files were compared with the initial discharge overviews regarding completeness of medication changes (i.e. explicit explanation that medication had been changed) and clinical information documentation. Logistic regression was used for analysis.

Results: Two hundred and eighteen patients (112 before-106 after) were included. Completeness of medication changes documentation increased marginally after the intervention (46.6% vs 56.3%, adjusted OR 1.4 [95% CI 1.07-1.83]). No differences were seen for allergy/contraindication documentation**.**

Conclusion: Instruction manuals marginally increased completeness of documentation. Manuals alone are insufficient to achieve complete electronic patient files at discharge.

INTRODUCTION

Patients with complex medical care needs frequently require care in different settings.[1,2] As information systems are usually not linked between settings (due to government regulations, e.g. security issues, or technical barriers), communication gaps can occur. In recent years guidelines have stressed the importance of communicating information between healthcare providers regarding the patient's pharmacotherapy, such as, (the reason for) medication changes and clinical information to prevent medication errors.[3-6] These guidelines state that pharmacists have a key role in coordinating this information transfer.[3-6] At hospital discharge, coordination can be achieved by implementing an information-exchange system between the hospital and the community pharmacy.[7-11] This has the potential to improve care as it enables community pharmacies to perform complete medication surveillance and provide patient education.[10] Furthermore, community pharmacies can help ensure that therapy changes, made in hospital, are continued after discharge.[7-9,11,12] Vice versa, at hospital admission community pharmacies can produce a complete and correct overview of pre-admission medication.[10]

In every day practice paper forms are used to exchange information to the community pharmacy at hospital discharge. Consequently, the community pharmacy must enter the information manually in its pharmacy information system. Dvorak et al. reported that only 62% of community pharmacists found discharge information of value to their patient files for future care indicating that pharmacists do not document all received information.[13] One study showed that communication at hospital discharge improved patient profiles, while another demonstrated no effect.[14,15] It is suggested that more instruction is needed on how to deal with accurate documenting, especially because community pharmacy information systems are mainly used as dispensing-software.[15,16]

Previous studies did not focus on whether medication changes are actually documented by community pharmacies and whether instruction can improve documentation to enhance optimal information transfer.

Therefore, the aim of this study is to investigate the effect of instruction manuals on completeness of electronic patient files (regarding medication changes and clinical information) in community pharmacies for patients discharged from hospital.

METHODS

Setting and study population

A before-after study was performed (July 2009-August 2010) at the St. Lucas Andreas Hospital in The Netherlands, a 550-bed general teaching hospital. Patients discharged from the cardiology and/or pulmonology ward with a discharge medication overview,

containing a change in pre-admission medication and/or clinical information, were included. Exclusion criteria were patients not discharged home and patients not giving informed consent.
In The Netherlands pharmacy technicians enter prescriptions and clinical information in a computer.[17] If a prescription is not dispensed by the community pharmacy, this medication can be documented through an "observation prescription" for medication surveillance purposes and maintaining an up-to-date electronic patient file.
This study was exempt from review by the institutional review board as the Dutch legislation does not request this for studies that do not affect the patient's integrity. Community pharmacies were unaware that a before-after study was being performed.

Intervention

In our hospital a discharge medication overview is produced after medication reconciliation and patient counselling.[18] The discharge medication overview (see Figure 1) contains all information regarding the medication a patient uses, (reasons for) medication changes, allergies, contraindications (e.g. kidney malfunction) and a specification of whether medication needs to be dispensed by the community pharmacy.
Single-page instruction manuals, specific for the community pharmacy´s information systems, were developed for the intervention. The content of the instruction manuals was based on interviews with community pharmacies and their software providers about problems and possibilities with documentation using the pharmacy information system. Also, specific problems experienced with a test discharge medication overview (see Figure 1) were taken into account. The instruction manuals described the method for complete documentation of medication changes, non-dispensed medication and clinical information.
The instruction manuals were presented to community pharmacies (50% attended) and their software providers. Finally, the instruction manuals were e-mailed to all community pharmacies, including those that did not attend the meetings, notifying them that the manual would be sent together with every discharge medication overview.
From July to August 2009 usual care was provided in the before-period, i.e. faxing only the discharge medication overview without any additional documenting instructions. From January 2010 to June 2010 the instruction manuals were developed. From July 2010 to August 2010 the intervention was implemented in the after-period, i.e. faxing the discharge medication overview together with the specific instruction manual.

Figure 1 Example of discharge medication overview

Sint Lucas Andreas Ziekenhuis — Medication overview and discharge prescriptions per: 05-01-10 — Page 1

Hospital Pharmacy
Jan Tooropstreet 164
1061 AE Amsterdam
Tel. 020-5108589
Fax. 020-5108458
ZIC: 4KW9

Patient: Mr. Example, T. 03-05-42
Patient number: TEST
Admission date: 02-03-09

CONTRA-INDICATION: DECREASED KIDNEY FUNCTION
ALLERGY: PENICILLIN

Specialist: Dr. Test, Cardiology ward
AGB Code: 10054321
Ward: B3 Cardiology

Start until	Stop	Medication name	Dose	Remarks	Number to deliver*	Administer route
05-01-10		Acenocoumarol 1 mg tablet	Use according to blood tests			Oral
05-01-10		Bumetanide 1 mg tablet	Two tablets daily	In stead of furosemide 40 mg, dose bumetanide increased due to water retention		Oral
05-01-10	05-01-10	Diclofenac 50 mg enteric coated tablet	Three tablets daily	Discontinued due to kidney malfunction		Oral
05-01-10		Lactulose 3.35 g/5 ml oral solution 300 ml	15 ml twice daily plus 15 ml once as required	Patient states to use this medication this way		Oral
05-01-10		Pantoprazole 40 mg gastro-resistant tablet	One tablet daily	Dose increased due to stomach complaints		Oral
05-01-10		Perindopril 2 mg tablet	One tablet daily	Dose decreased due to kidney malfunction (date 5-1-10: GFR 24 ml/min)		Oral
05-01-10	05-01-10	Spironolactone 50 mg tablet	One tablet daily	Discontinued due to increased potassium (date 5-1-10: 4.6 mmol/l)		Oral
05-01-10		Supradyn multivitamin forte tablet	One tablet daily			Oral
05-01-10		Insulin NovoMix 30 FlexPen 100 U/ml pen 3 ml	Two times daily 22 units			Subcutaneous

Name hospital physician : .....
Signature : .....

Community pharmacy : Pharmacy Medicine man
Fax :
Please deliver medication: Yes / No , date .....

Deliver pill box : Yes / No
The patient has received an administration scheme
This information is also sent to the general practitioner
Please inform anticoagulation clinic

Resubstitutions have been performed in hospital (unless intentional medication change)
Community pharmacy please consider above active medication as discharge prescriptions

* If number = 0, do not deliver medication, patient has a stock

This overview was used as a test overview. Several problems were incorporated in this discharge medication overview; kidney malfunction as a contraindication, penicillin allergy, medication that had been changed/discontinued, medication that did not have to be dispensed and an over-the-counter vitamin product containing vitamin K which interacts with the vitamin-K-antagonist acenocoumarol that this test patient used. During the meetings the documentation problems of this test overview were presented to the community pharmacies.

Outcomes

Two weeks after discharge, six-month medication files including all clinical information, were gathered by fax from community pharmacies and compared with the information on the initially sent discharge medication overviews.

Changed pre-admission medications on the discharge medication overview were classified regarding the type of change and the logistic activities. The type of changes were new (newly started in hospital), dose change (dose increased/decreased), switch (replacement) or stop (discontinuation). Logistic activities specified on the discharge medication overview were dispensing of changed medication (i.e. the community pharmacy should provide the patient with a supply) or non-dispensing of medication. No medication supply was needed when the patient still had a supply at home (e.g. use half of tablet), medication was already provided in the hospital, or medication was discontinued. Finally, clinical information was classified as allergy or contraindication.

Documentation of dispensed medication changes was considered complete if the community pharmacy's patient files explicitly explained that medication had been changed (see Figure 2 for examples). Documentation of non-dispensed medication was considered complete, if an "observation prescription" was present for the new, dose and switch

Figure 2 Examples of how medication changes could be documented completely in community pharmacy's patient files

Processing text	Perindopril now 2 mg and pantoprazol 40 mg/ furosemide discontinued

Perindopril 2 mg tablet	15 tablets	One tablet daily PERINDOPRIL 4 MG DISCONTINUED
Pantoprazole 40 mg gr tablet	15 tablets	One tablet daily PANTOZOL 20 MG DISCONTINUED

Pantoprazole 40 mg gr tablet	90 tablets	One tablet daily, dose increased due to stomach complaints

Diclofenac 50 mg tablet Diclofenac	3 times daily	05012010	stop
Spironolactone 50 mg tablet Spironolactone	1 times daily	05012010	stop
Perindopril 2 mg tablet Perindopril	1 times daily	05012010	

See also figure 1 for the discharge medication overview; perindopril dose was decreased, pantoprazole dose increased, furosemide was replaced by bumetanide, diclofenac and spironolactone were discontinued.

sub-category or medication was discontinued for the stop sub-category. Finally, documentation of clinical information was considered complete when they corresponded.
One assessor (student, BB) judged the documentation of the information. A second assessor (pharmacist, FK) checked 50% of patients. Differences were discussed and resolved. As there were no major differences in judgments between the assessors, the other half of patients was assessed by the first assessor only.
The number and percentage of completely documented information was assessed for the type of medication change (start, dose, switch, stop), logistics of medication change (dispensing or non-dispensing) and clinical information (allergy/contraindication).

Data analysis

Data were analysed using SPSS® version 18.0.0. The independent T-test was used for continuous variables and the chi-square test for frequencies. Frequencies were calculated for the proportion of correct documentation. Multivariable logistic regression analysis was used to compare the before- and after-period, adjusting for differences in baseline characteristics. A manual stepwise forward logistic regression model was used. Possible confounders ($p<0.1$) were entered consecutively into the model. When the β coefficient changed with at least 10%, the contribution of the confounder was considered relevant

and the confounder remained in the model. Crude and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) and p-values were calculated.

RESULTS

A total of 357 patients were screened for eligibility; 139 (39%) patients were excluded (Figure 3), leaving 218 patients (112 before, 106 after) who were included in the study. There were no differences in the number of medications, medication changes and clinical information (Table 1). In the after-period significantly fewer patients were discharged from the pulmonology department and significantly more prescriptions were dispensed.

Medication changes documentation

New medication was documented in over 90% of discharge prescriptions in both periods (Table 2). Non-documentation included over the-counter-medication, medication for which the patient needed to pay (and probably was unwilling) and medication already provided in the hospital.

Complete documentation of dose changes increased significantly in the after-period from 1.4% to 8.6% (adjusted OR 6.6, 95% CI 1.41-30.56). Non-documentation was seen as most community pharmacies added the last prescribed dose to their files without documenting that a dose had changed. This could lead to confusion about whether doses should be combined or not.

Figure 3 Flow of participants

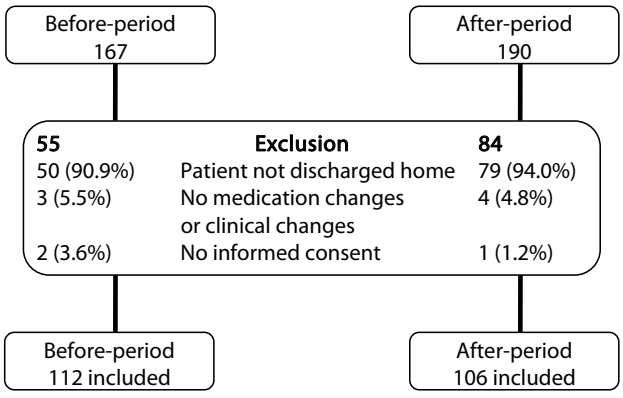

Table 1 Patient demographics and discharge medication characteristics

Patient characteristics (number of patients)	Before (n=112)	After (n=106)	p-value
Female, n (%)	46 (41.1)	54 (50.9)	0.14
Age, y, mean ± SD	68.1 ± 14.1	69.6 ± 14.9	0.44
Length of stay, days, mean ± SD	9.3 ± 5.7	8.1 ± 4.4	0.09
Drugs on discharge, n, mean ± SD	10.6 ± 4.3	10.1 ± 4.9	0.44
Lung department, n (%)	50 (44.6)	29 (27.4)	<0.01
Cardiology department, n (%)	62 (55.4)	77 (72.6)	<0.01
Community pharmacies, n, (%)	50 (44.6)	44 (41.5)	0.64
Discharge medication characteristics	**Before**	**After**	**p-value**
All medication changes, n (% of all items*)	455 (36.3)	444 (39.0)	0.17
Type of medication change			
New, n (% of medication changes)	214 (47.0)	226 (50.9)	0.25
Dose change, n (% of medication changes)	141 (31.0)	116 (26.1)	0.11
Switch, n (% of medication changes)	31 (6.8)	35 (7.9)	0.54
Stop, n (% of medication changes)	69 (15.2)	67 (15.1)	0.98
Logistics of medication change			
Dispensed, n (% of medication changes)	275 (60.4)	304 (68.5)	0.01
Non-dispensed, n (% of medication changes)	180 (39.6)	140 (31.5)	0.01
Clinical information	-	-	-
Allergies, n (% of patients)	13 (8.9%)	28 (12.3%)	0.42
Contraindications, n (% of patients)	17 (15.2%)	24 (22.6%)	0.16

* All items present on the discharge medication overview, i.e. prescribed medication plus discontinued medication

Table 2 Complete documentation of medication changes (dispensed and non-dispensed), and clinical information

Prescription type	Before-period Complete, n (%)	After-period Complete, n (%)	Unadjusted analysis OR (95% CI)	p-value	Adjusted analysis OR (95% CI)	p-value
Type of medication change						
New (B: n= 214, A: n=226)	200 (93.5)	213 (94.2)	1.2 (0.53-2.50)	0.73	0.9 (0.40-2.03)[a]	0.80
Dose change (B: n=141, A: n=116)	2 (1.4)	10 (8.6)	6.6 (1.41-30.56)	0.02	6.6 (1.41-30.56)	0.02
Switch (B: n=31, A: n=35)	6 (19.4)	8 (22.9)	1.2 (0.38-4.06)	0.73	1.4 (0.41-4.67)[a]	0.60
Stop (B: n=69, A: n=67)	4 (5.8)	19 (28.4)	6.4 (2.06-20.13)	<0.01	6.4 (2.06-20.13)	<0.01
All changes (B: n=455; A: n=444)	212 (46.6)	250 (56.3)	1.5 (1.14-1.92)	<0.01	1.4 (1.07-1.83)[a]	0.01
Logistics of medication change						
Dispensed (B: n= 275 , A: n= 304)	208 (75.6)	227 (74.7)	1.0 (0.65-1.39)	0.79	0.9 (0.63-1.35)[a]	0.67
Non-dispensed (B: n= 180, A: n=140)	4 (2.2)	23 (16.4)	8.7 (2.92-25.66)	<0.01	8.7 (2.92-25.66)	<0.01
Clinical information						
Allergy (B: n= 13, A: n= 28)	7 (53.8)	23 (82.1)	3.9 (0.92-16.94)	0.07	5.7 (0.93-34.50)[a]	0.06
Contraindication (B: n= 17, A: n=24)	6 (35.3)	7 (29.2)	0.8 (0.20-2.85)	0.68	0.8 (0.20-3.22)[a]	0.75

* B = before-period, A = after-period, n= number of medications, OR = Odds Ratio, CI= confidence interval
a= adjusted for department type (lung/cardiology department)

For switched medication no difference was found after the intervention (19.4% before vs 22.9% after). Again, the last prescribed medication was added to the patient file.
Complete documentation of stopped medication increased significantly from 5.8% to 28.4% (adjusted OR 6.4, 95% CI 2.06-20.13) after the intervention. Non-documentation occurred when community pharmacies failed to actively discontinue medication.
The completeness of documentation for all medication changes (start, dose change, switch and stop) together increased marginally from 46.6% to 56.3% (adjusted OR 1.4, 95% BI 1.07-1.83).
The need for dispensing of medication determined whether medication changes were documented completely (75.1% of dispensed medication changes was documented completely versus 8.4% of non-dispensed medication changes, Table 2). Documentation of non-dispensed medication improved in the after-period due to the presence of "observation prescriptions" for 4 new medications and due to discontinuing 19 medications (adjusted OR 8.7, 95% CI 2.92-25.66).

Clinical information documentation

Allergy documentation improved non-significantly in the after-period (53.8% vs 82.1%, adjusted OR 5.7, 95% CI 0.93-34.50, Table 2). No improvements were seen in the documentation of contraindications (35.3% vs 29.2%, adjusted OR 0.8, 95% CI 0.20-3.22).

DISCUSSION

The instruction manuals improved completeness of medication changes documentation marginally from 47% to 57%. For medication changes not necessitating a pharmacy dispensing activity the number of complete documentation was low and hardly improved after the intervention. Also, documentation of clinical information was dissatisfactory.
To ensure optimal medication safety and information transfer, pharmacies are responsible for a system of medication surveillance and, hence, for high quality and complete electronic patient files.[19-22] This means that community pharmacies need to fully use the opportunities of their dispensing-software system. However, in this study we recorded only marginal effects of the instruction manuals on completeness of electronic patient files. These results may be explained by the fact that pharmacy information systems between settings are not linked and therefore information is transcribed manually. Dispensing software cannot always easily document all information and drug-dispensing functions occupy too much time.[13] Therefore, documentation of (non-dispensed) medication changes and clinical information were marginally performed as these required additional actions. Studies have shown the possible consequences of inaccurate docu-

mentation, for example the inappropriate restart of medication, that has been stopped during hospital admission due to adverse drug reactions.[23-25]

A novel aspect of this study was the focus on completeness of documenting medication changes with the help of instruction manuals. Previous studies focused on the effect of additional communication to community pharmacies.[9,10,12,14] Lamontagne et al. reported that dispensing of medications at discharge was a determining factor in documentation.[14] This was also observed in our study. Similarly, a Dutch study reported that information regarding non-dispensed medication, over-the-counter medication and allergies was lacking in electronic patient files for patients visiting the community pharmacy for the first time.[26] Lalonde et al. found no effect of sending a medication discharge plan to a community pharmacy and the treating physician (discrepancy in 66% intervention vs 68% control patients).[15] In our study we noted only some marginal improvements.

Strengths of this study were that we approached a large number of community pharmacies. We made a first base set for standardised documentation of discharge medication related information within electronic patient files with manuals.

Yet, some limitations need to be discussed. First, our baseline characteristics were not similar. More patients were discharged from the cardiology unit and more medication was dispensed in the after-period. However, we adjusted for the first one and stratified for the influence of dispensing in the analysis. Second, this research is performed in just one region. Finally, we only evaluated the information presented on the fax and did not check which information was documented in the information systems. However, in daily practice this is not feasible. Pharmacists need to be able to exchange data easily and the fax still is the way to do this.

Notwithstanding these limitations, our study shows that several improvements can be made in documentation. In order to further improve this, the documentation process should be facilitated by information technology, e.g. by linkage of hospital pharmacy and community pharmacy information systems and teaching the appropriate use of these systems.[26] Future studies should look into the effect of such measures.

In conclusion, instruction manuals marginally increased completeness of documentation by community pharmacies. Manuals alone are insufficient to achieve complete electronic patient files at discharge. As non-dispensed medication and clinical information frequently was lacking medication surveillance at and after hospital discharge were jeopardised.

Acknowledgement

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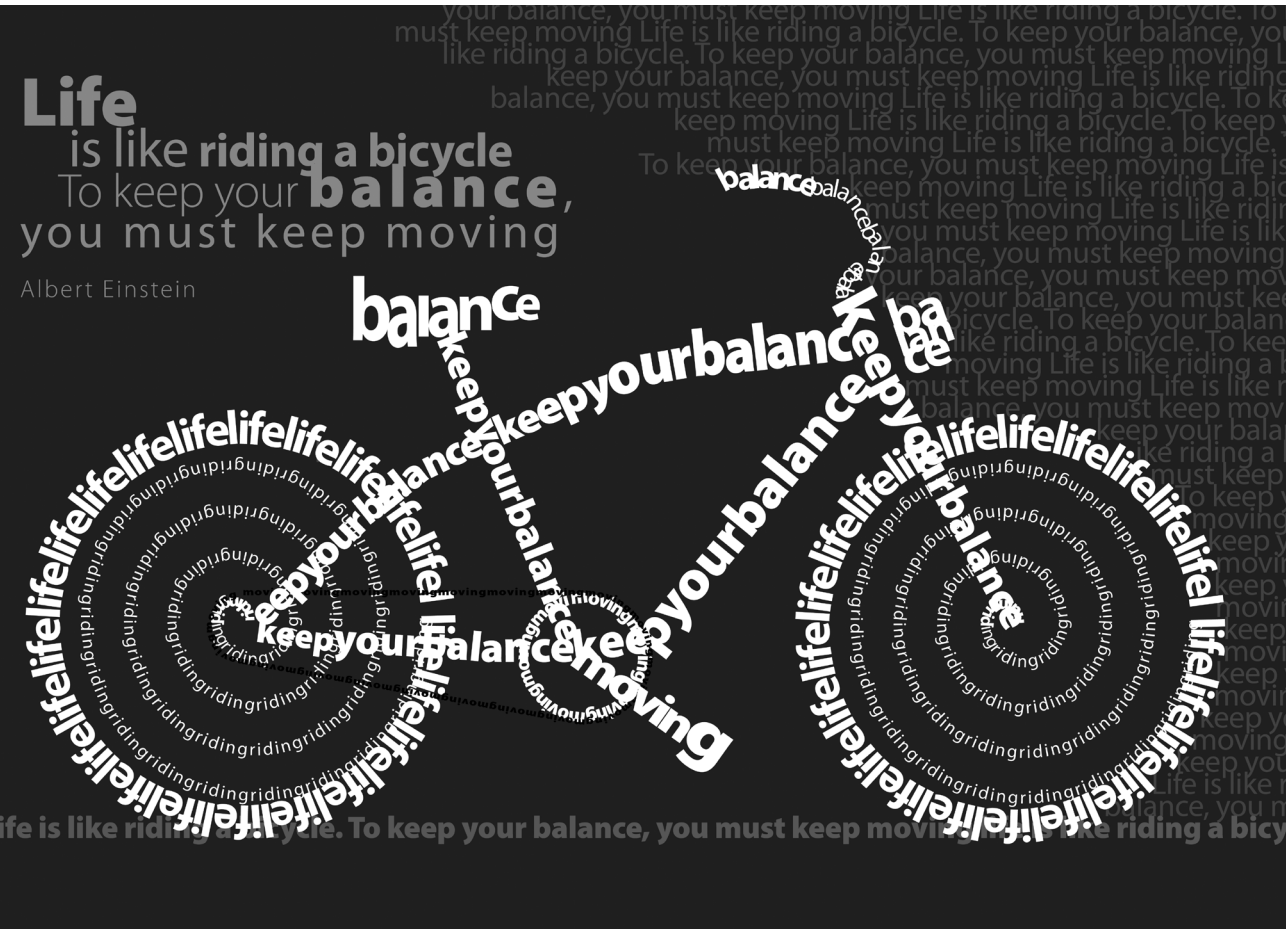


Life is like riding a bicycle.
To keep your balance, you must keep moving.

(Albert Einstein: scientist, 1879 -1955)

Designed by Denis Tenev

PART

4

Evaluation of a transitional care program for hospitalised patients

CHAPTER

4.1

Study protocol: The effect of the COACH program (Continuity Of Appropriate pharmacotherapy, patient Counselling and information transfer in Healthcare) on readmission rates in a multicultural population of internal medicine patients

F Karapinar-Çarkıt, SD Borgsteede, J Zoer, C Siegert, M van Tulder, ACG Egberts, PMLA van den Bemt.

BMC Health Serv Res. 2010;10:39.

ABSTRACT

Background: Medication errors occur frequently at points of transition in care. The key problems causing these medication errors are: incomplete and inappropriate medication reconciliation at hospital discharge (partly arising from inadequate medication reconciliation at admission), insufficient patient information (especially within a multicultural patient population) and insufficient communication to the next healthcare provider. Whether interventions aimed at the combination of these aspects indeed result in less discontinuity and associated harm is uncertain. Therefore the main objective of this study is to determine the effect of the COACH program (Continuity Of Appropriate pharmacotherapy, patient Counselling and information transfer in Healthcare) on readmission rates in patients discharged from the internal medicine department.

Methods/Design: An experimental study is performed at the internal medicine ward of a general teaching hospital in Amsterdam, which serves a multicultural population. In this study the effects of the COACH program are compared with usual care using a pre-post study design. All patients being admitted with at least one prescribed drug intended for chronic use are included in the study unless they meet one of the following exclusion criteria: no informed consent, no medication intended for chronic use prescribed at discharge, death, transfer to another ward or hospital, discharge within 24 hours or out-of-office hours, discharge to a nursing home and no possibility to counsel the patient. The intervention consists of medication reconciliation, patient counselling and communication between the hospital and primary care healthcare providers. The following outcomes are measured: the primary outcome readmissions within six months after discharge and the secondary outcomes number of interventions, adherence, patient's attitude towards medicines, patient's satisfaction with medication information, costs, quality of life and finally satisfaction of general practitioners and community pharmacists.
Interrupted time series analysis is used for data-analysis of the primary outcome. Descriptive statistics are performed for the secondary outcomes. An economic evaluation is performed according to the intention-to-treat principle.

Discussion: This study will be able to evaluate the clinical and cost impact of a comprehensive program on continuity of care and associated patient safety.

Trial registration: Dutch trial register: NTR1519

BACKGROUND

Medication errors are the most common type of errors affecting patient safety, occurring most frequently at points of transition in care.[1-3] There are three key problems causing these medication errors at hospital admission and discharge. The first problem is incomplete and inappropriate medication lists. This problem starts at hospital admission for example due to recall bias of the patient, incomplete medication records (e.g. absence of over-the-counter drugs) and inappropriately prescribed drugs (e.g. indication of prehospital prescribed drugs not evaluated).[4] These admission medication errors can carry over to the discharge medication and new medication errors can occur for example when hospital physicians forget to restart temporarily discontinued medication or do not evaluate the appropriateness of discharge medication.[5,6] The second problem is insufficient patient information. While receiving care in hospital, patients often get help with the preparing and administering of their medication by hospital staff. However, following hospital discharge, patients are abruptly expected to manage their medication themselves, with little support or preparation.[3] The last problem regards insufficient communication to the next healthcare provider. Discharge letters and discharge prescriptions generally do not contain the entire pharmacotherapy.[7,8] This incompleteness could lead to confusion about whether the medication which is not listed is discontinued or just not mentioned. Both the general practitioner and community pharmacy are not informed on reasons for changes in the pharmacotherapy leading to confusion whether these changes should be maintained or were temporal.[9,10] Evidence exists on the effect of discharge medication related interventions on reducing adverse events, reducing the readmission rate and improving adherence.[5,11-15] However, some studies showed no effect and Holland et al. reported contradictory results on readmission rates.[16-18] Most studies have not combined intervention types to solve the problems as described above. For example, medication reconciliation is often performed with the use of medication records without active involvement of patients, or in case patients are involved, patients who are unable to speak the native language of the study location are excluded.[12,16,19-21] In contrary, some studies are so comprehensive that it is expected that most hospitals cannot implement such time-consuming interventions (e.g. one study reports two hours per patient).[21-23] Furthermore, in general the intervention is performed (partly) by pharmacists making the intervention expensive.[5,11-19,21-23] It is unknown what the effect is of discharge medication related interventions when they are performed by healthcare providers with a lower level of education. Therefore, the COACH (Continuity Of Appropriate pharmacotherapy, patient Counselling and information transfer in Healthcare) program is designed to improve continuity of care by combining interventions, including non-native patients and using pharmaceutical consultants (i.e. pharmacy technicians who have followed additional training) to perform the intervention. The intervention consists

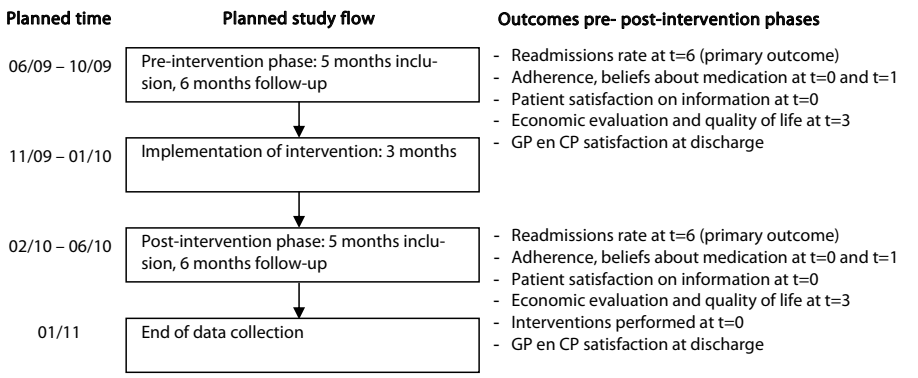
of medication reconciliation at discharge (in addition to medication reconciliation at admission to prevent medication errors from carrying over to the discharge medication), patient counselling at discharge and communication of medication information to the next healthcare providers. At present it is unknown whether such an intervention program indeed can lead to less discontinuity and associated patient harm. Therefore, the main objective of this study is to determine the effect of the COACH program on readmissions after six months in a multicultural population from the internal medicine department.

METHODS/DESIGN

Design

A prospective experimental study with a before-after design is performed at the St. Lucas Andreas Hospital in the Netherlands, a 550-bed general teaching hospital serving a multicultural population. The study is carried out from June 2009 through January 2011. The effects between a usual care group and an intervention group (pre- and post-intervention measurement design) are compared. First, patients are included during five months in the usual care group (pre-intervention phase with six months follow-up). Second, the intervention is implemented in the study ward (implementation phase of 3 months). Finally, patients are included during five months in the intervention group (post-intervention phase with six month follow-up, see Figure 1 for flowchart and measurements).

Figure 1 Study flow of the COACH program



t=0,1,3,6; at hospital discharge, one month, three months, six months after hospital discharge.
GP= general practitioner, CP= community pharmacist

Study population

The study is performed at the internal medicine ward. All patients admitted with at least one prescribed drug intended for chronic use are invited to participate. Exclusion criteria are: no informed consent, no medication intended for chronic use prescribed at discharge, death, transfer to another ward or hospital, discharge within 24 hours or out-of-office hours, discharge to a nursing home (as patients do not administer their own medication) and patients who cannot be counselled (as stated by the resident due to physical/mental constraints, being critically ill or due to language restrictions without relatives or healthcare personnel to translate, i.e. languages other than Dutch, Turkish, English and Arabic/Berber). Only the patient's first hospital admission is included in the study period (readmissions are the main outcome measure). The St. Lucas Andreas Hospital institutional review board has stated that this study is exempt from review by the institutional review board as the Dutch legislation does not request this for studies that do not affect the patient's integrity. In this study the burden was considered minimal for the patient and therefore the medical ethics committee waived the review. The burden is minimal as the patient will receive counselling about his discharge medication in the intervention group. This should be usual practice as the hospital has a legal obligation to inform patients. The patients are also asked to fill in questionnaires and cost diaries. This is expected to take 60 minutes of the patient's time. To respect the wish of a patient to participate in a study, we decided to ask the patients for an informed consent to obtain information from their general practitioner on readmission rates and for filling in the questionnaires/cost diaries. Patient data are sampled and stored in accordance with privacy regulations.

Study procedures

Usual care

Medication reconciliation on admission

At hospital admission residents mostly use the information provided by patients (or relatives) or previous hospital records (e.g. discharge letters, patient charts) to examine the pre-admission medication. However, medication reconciliation is not structurally performed by the resident. Residents can consult the medication records of the community pharmacy through a link in the hospital's Computerized Physician Order Entry (CPOE) system for patients that are within the catchment area of the hospital. If a community pharmacy is not connected to the hospital's CPOE, the resident can request the hospital pharmacy to obtain a faxed medication list from the community pharmacist. The resident registers the admission prescriptions in the hospital's CPOE where after the prescriptions are checked during hospital admission by the clinical pharmacist on

dosages, double medication, drug-drug interactions and contraindications. At present information on allergies is not structurally provided to the clinical pharmacist making medication surveillance on allergies impossible.

Medication reconciliation at discharge

The resident prints a medication list from the hospital's CPOE. On this medication list the resident can adjust the medication and he then indicates which medication should be dispensed by the community pharmacy. The medication list is sent to the hospital pharmacy. The pharmacy technician screens the list for obvious errors (e.g. dose not provided) but no structured medication reconciliation is performed.

Patient counselling at discharge

To support the patient counselling a medication list is written down by the resident using the information in the hospital's CPOE. At present, residents and nurses are involved in patient instructions on pharmacotherapy. For both professionals this aspect is only a relatively small part of a large amount of tasks, making the time to be spent on medication related patient instructions rather limited or the patient counselling is not performed at all. Also, the knowledge necessary for providing adequate instructions is often insufficient in residents (inexperienced) and nurses (training provides little knowledge on drugs).

Communication of discharge medication

After screening of the medication list by the pharmacy technician at discharge, the discharge prescriptions are sent to the community pharmacy. The community pharmacist is mostly informed on medication which should be dispensed. The reasons for changes in therapy or clinical information such as allergies are not provided. The communication to the general practitioner takes place through the discharge letter in which the medication is typed by the resident. The medication list in the discharge letter is generally incomplete and provides little or no information on changes in the pharmacotherapy and the reasons for these changes.

COACH intervention program

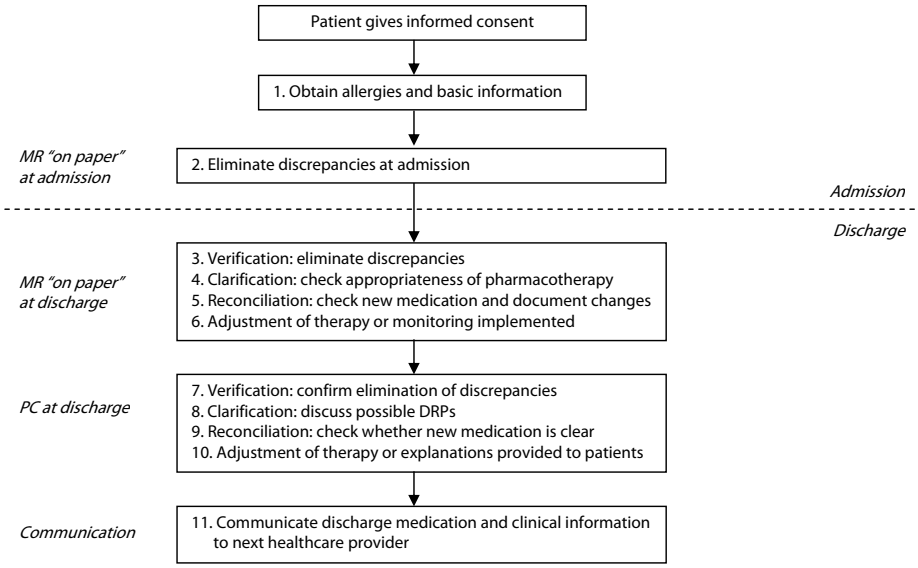
The COACH intervention program is carried out by a team of pharmaceutical consultants with clinical pharmacists as supervisors. Pharmaceutical consultants are pharmacy technicians who have followed an additional three-year bachelor program which is focused on pharmaceutical patient care. They are specifically trained in pharmacotherapy and communication with patients. In contrast to nurses and residents, they can dedicate more time to the patient, as this job is their main task. Because of their lower level of

education, when compared to pharmacists who have had a six-year university training, salary expenditures for pharmaceutical consultants are lower, which is why they are used besides a supervising pharmacist.
As 30-40% of the patient population in the St. Lucas Andreas hospital is originating from foreign countries (migrants, mostly Turkish and Moroccan) information leaflets and questionnaires are available in Dutch, Turkish, Arabic and English. Arabic is the written language of Morocco, but Moroccan immigrants in the Netherlands often use the Berber language (a non-written language) and are unable to read Arabic. In those cases relatives or healthcare personnel are asked to translate the information leaflets.
The COACH program consists of four main processes that are subdivided in subprocesses (see Figure 2). Although the program focuses on discharge, a small part of the intervention is carried out on admission to prevent admission medication errors to carry over to the discharge medication.

Obtaining basic information and medication reconciliation on admission

After the pharmaceutical consultant gets informed consent from the patient at admission the consultant asks the patient about possible allergies. If any are mentioned the pharmaceutical consultant registers the allergy in the CPOE for medication surveillance purposes. Furthermore, the language spoken by the patient is checked. If a patient cannot speak or understand Dutch a family member or friend is asked to be present and translate or a specific healthcare worker speaking the native language of the patient is added to the team. Finally, the pharmaceutical consultant asks some additional basic information (see Figure 2 and Table 1, step 1). Hereafter an information leaflet is given to the patient. This leaflet informs the patient further about the project and motivates the patients to ask questions about medication during patient counselling at discharge.
After the resident registers the admission prescription in the hospital's CPOE the pharmaceutical consultant verifies these prescriptions using community pharmacy records without counselling the patient (due to time constraints and because the resident already counsels the patient following routine care). All discrepancies ("on paper") with the pre-admission medication, known allergies and possible drug-related problems are communicated to the resident with a standardised form (see Figure 2 and Table 1, step 2). The resident can adjust the prescriptions if necessary.

Figure 2 Implementation of the COACH program



MR= medication reconciliation
PC= patient counselling following the steps for medication reconciliation
DRPs= drug-related problems

Medication reconciliation at discharge

At discharge medication reconciliation is performed again using a protocol which contains the steps for medication reconciliation (see Figure 2 and Table 1, step 3-5).[24] First, in the verification step the presence of discrepancies with the pre-admission medication is examined again by using the medication history of the community pharmacy. Second, in the clarification step the appropriateness of the pharmacotherapy is checked and the pharmacotherapy is evaluated. Also the international normalized ratio, glomerular filtration rate, glucose, sodium and potassium blood levels are checked to adjust medication if necessary. In the third step the newly initiated medication is evaluated to ensure all changes are intentional and changes in the pharmacotherapy are documented. Finally, the results of all steps are discussed with the resident and the prescriptions are adjusted if necessary.

Table 1 Protocols used for the steps shown in Figure 2

Steps	Protocols used consists of
1	Questions asked: allergies, presence of relative during patient counselling at discharge, marital status, birth country patient and parents, education, readmission rate previous six months
2	Check: - Matching of medication at admission with pre-admission medication regarding drug, dose, route and frequency
3	Check: - Matching of medication at discharge with pre-admission medication regarding drug, dose, route and frequency - Whether temporally discontinued medication and substituted medication (due to hospital formulary policy) should be resumed
4	Check: - Continuing need: discontinue not indicated (temporally prescribed) medication - Consider right dose (e.g. for geriatric patient), simplify drug regimen (e.g. modified release product in stead of plain drug), duration of therapy (e.g. antibiotic prescribed too long, gradually reduce prednisolone) - Laboratory values: international normalized ratio, glomerular filtration rate, glucose, sodium and potassium blood levels to adjust medication if necessary. - Identify suboptimal treatment (e.g. laxative with opioid, gastroprotection with NSAID and risk factors, rescue medication with inhaled corticosteroid, bisfosfonate with long-term prednisolone, isordil with ACS, statin with diabetes mellitus type II) - Drug-drug interactions (pharmacokinetic and pharmacodynamic) and contraindications (e.g. NSAID with heart failure, COX-2 inhibitor with ischemic heart disease) - Consider cost (e.g. brand to generic drug) - Consider monitoring (e.g. therapeutic drug monitoring, electrolytes, creatin)
5	Check: - Appropriateness of new medication - Documentation of (reasons for) changes between discharge prescriptions and pre-admission medications
7	Check: - How medication is used by the patient and at what time point. - Continuing need: discontinue not indicated (temporally prescribed) medication or restart medication if patient does not agree with discontinuation (e.g. patient still has pain) - Other medication usage (e.g. over-the-counter medication or herbals) to evaluate whether there are contraindications or interactions with the medication prescribed at discharge
8	Check: - Practical problems with medication use: check whether patient is capable of using his medication (e.g. big tablets, type of inhalator) - Occurrence of adverse drug reactions: check whether these could be prevented or minimised - Forgetting of medication: check whether patient is compliant and what the possible reasons are for non-adherence. Problems with adherence are further explored and possible tools, such as pill boxes, are discussed.
9	Check: - Understanding of new prescribed medication - Knowledge of side effects (e.g. bloody or black tarry stools with anticoagulants to recognise bleeding, risk of fracture and prednisolone, increase of blood sugar and prednisolone, rapid heart beats and bronchodilators, sore throat and inhalation corticosteriods to rinse mouth, stomach pain and NSAID, headache and nitrates/ beta-blockers, muscle pain and lipid-lowering medicines, orthostatic hypotension and antihypertensives, diarrhoea and antibiotics, risk of falls / drowsiness and hypnotics, muscle weakness and paraesthesia to recognise low/high potassium) - Written information need: give patient information leaflet for new prescribed medication - Whether there are questions - Which medication the patient still has in stock at home and which medication should be dispensed.
11	Register on the medication discharge overview: changes in medication and reasons, possible drug-related problems and follow-up procedures (e.g. therapeutic drug monitoring). This information is automatically registered on the medication summary for the patient also.

ACS= Acute coronary syndrome

Patient counselling at discharge

To support patient counselling a comprehensive medication summary for the patient is developed (see Figure 3 and 4). This double sided medication summary is printed from the hospital's CPOE. One side contains contact information of the hospital, advices on side effects and advices on patient involvement in healthcare (see Figure 3). This information is based on several literature reports.[25-27] The other side contains patient data, clinical information (e.g. allergies, contraindications), hospital physician information, start and stop date for medication, medication name (brand and generic for the patient to recognise his medication), dose information and advices, reason for changes in pharmacotherapy (bold text) and a daily time table (see Figure 4).

After the medication reconciliation has been performed and discussed with the resident, the pharmaceutical consultant counsels the patient and/or his family. The patient counselling is also carried out by following the steps for medication reconciliation (see Figure 2 and Table 1, step 7-9). First, details of all medications are confirmed in the verification step by using the medication summary. The pharmaceutical consultant asks the patient how medication is used (to see whether the use is correct), whether medication is not in use anymore or whether additional medication is used. Second, the clarification step is performed through checking whether improvements can be made on safety and quality of pharmacotherapy and explaining or answering questions. Third, in the reconciliation step new medication is discussed to evaluate whether the patient understands why this medication is prescribed.

The counselling is not only aimed at gathering information about the actual medication usage but also at educating the patient about changes in the pharmacotherapy and involving the patient in the optimisation of the medication usage. If relevant, special attention is paid to subjects relevant for specific patient populations, such as use of medication during fasting. The counselling is inside the hospital, at bedside or in a separate room if preferred by the patient.

The results of patient counselling are discussed with the resident and the prescriptions can be adjusted if necessary. This results in the final discharge medication.

Communication of discharge medication

To support the communication of discharge medication a discharge medication overview is developed (see Figure 5). This discharge medication overview is printed from the hospital's CPOE and contains contact information of the hospital, patient data, clinical information (e.g. allergies, contraindications), hospital physician information, start and stop date of medication, generic medication name, dose information, reasons for changes in pharmacotherapy, drug-related problems, follow-up actions, the amount of medication that has to be dispensed by the community pharmacy, information on tools

Figure 3 Medication summary for the patient (reverse side)

The medication summary is folded to an A6-format.

Figure 4 Medication summary for the patient (front side)

Sint Lucas Andreas Ziekenhuis

Medication summary per: 13 march 2009

Page 1

Patient: Mr. Example, O. 16-10-1923
Patient-id: 04585632
Admission date: 02-03-09

Specialist: Dr. Internal
Ward: A6, Internal medicine

ALLERGY: PENICILLIN
CONTRA-INDICATION: DECREASED KIDNEY FUNCTION

Start until	Stop	Medication name (brand name)	Medication used for or to prevent	Dose	Administration scheme Morning	Noon	Evening	Night
02-03-09		Omeprazole 20 mg capsule (Losec)	Stomach pain	One table daily Do not chew or crush the capsules				
02-03-09		Glimepiride 2 mg tablet (Amaryl)	Type 2 diabetes mellitus	Two tablets daily Take just before the meal				
02-03-09		Acenocoumarol 1 mg tablet (Sintrom)	Blood thinning	Use according to blood tests Swallow your tablets whole with a drink of water	Use according to dosage scheme of anticoagulation clinic			
02-03-09		Furosemide 40 mg tablet (Lasix)	Water retention (oedema)	One tablet daily				
02-03-09		Metoprolol 50 mg SR tablet (Lopresor SR)	Cardiac illness	One tablet daily Swallow your tablets whole, do not chew				
02-03-09		Perindopril 4 mg tablet (Coversyl)	Cardiac illness	One tablet daily **Dose decreased due to decreased kidney function (date 13/3: 39 ml/min)**				
02-03-09		Atorvastatin 40 mg tablet (Lipitor)	Lower lipids	One tablet daily Swallow your tablets whole with a drink of water				
02-03-09	05-03-09	Spironolactone 25 mg tablet (Aldactone)	Water retention (oedema)	One tablet daily **Discontinued due to increased potassium (date 13/3: 4.7 mmol/l)**				
02-03-09	13-03-09	Lactulose 3.35 g/5 ml (Duphalac)	Obstipation	15 ml twice daily as required **Discontinued, no indication**				

The administration scheme is filled in with the help of the patient. In bold text the reasons for changes in the pharmacotherapy, drug-related problems and follow-up actions can be specified.

Figure 5 Discharge medication overview for community pharmacist and general practitioner

Sint Lucas Andreas Ziekenhuis

Medication overview and discharge prescriptions per: 13 march 2009

Page 1

Hospital Pharmacy
Jan Tooropstreet 164
1061 AE Amsterdam
Tel. 020-5108589
Fax. 020-5108458
ZIC: 4KW9

Patient: Mr. Example, O. 16-10-1923
Patient-number: 12345678
Admission date: 02-03-09

ALLERGY: PENICILLIN
CONTRA-INDICATION: DECREASED KIDNEY FUNCTION

Specialist: Dr. Internal
AGB Code: 10013321
Ward: A6, Internal medicine

Start until	Stop	Medication name	Dose	Remarks	Number to deliver*	Administer route
02-03-09		Omeprazole 20 mg capsule	One table daily			Oral
02-03-09		Glimepiride 2 mg tablet	Two tablets daily			Oral
02-03-09		Acenocoumarol 1 mg tablet	Use according to blood tests			Oral
02-03-09		Furosemide 40 mg tablet	One tablet daily			Oral
02-03-09		Metoprolol 50 mg SR tablet	One tablet daily			Oral
02-03-09		Perindopril 4 mg tablet	One tablet daily	Dose decreased due to decreased kidney function (date 13/3: 39 ml/min)		Oral
02-03-09		Atorvastatin 40 mg tablet	One tablet daily			Oral
02-03-09	05-03-09	Spironolactone 25 mg tablet	One tablet daily	Discontinued due to increased potassium (date 13/3: 4.7 mmol/l)		Oral
02-03-09	13-03-09	Lactulose 3.35 g/5 ml	15 ml twice daily as required	Discontinued, no indication		Oral

Name hospital physician : ……..
Signature : ……..

Community pharmacy : Pharmacy medicine man
Fax : 020-5013204
Please deliver medication: Yes / No , date ……..

Deliver pill box : Yes / No
The patient has received an administration scheme
This information is also sent to the general practitioner
Please inform anticoagulation clinic

Resubstitutions have been performed in hospital (unless intentional medication change)
Community pharmacy please consider above active medication as discharge prescriptions

* If number = 0, do not deliver medication, patient has a stock

In the remarks section reasons for changes in the pharmacotherapy, drug-related problems and follow-up actions can be specified. This overview is faxed to the community pharmacist. If Vitamin K antagonists are prescribed the text "Please inform anticoagulation clinic" is printed to request the community pharmacy to inform the anticoagulation clinic about the final discharge prescriptions. The information in the blocked areas is mailed to the general practitioner.

for adherence and preference of patient to have his medication delivered at home by the pharmacy.
The discharge medication overview is faxed to the community pharmacy before discharge. The overview is also send to the general practitioner by e-mail.

Study endpoints and data collection

The primary outcome of this study is the readmission rate within six months after discharge. In addition, several secondary outcome measures with respect to medication safety are measured and analysed: number of interventions, adherence, patient's attitude towards medicines and satisfaction with medication information, costs-effectiveness of the intervention, quality of life and satisfaction of general practitioners and community pharmacists.
For collection of outcome parameters, hospital patient records, primary care patient records and validated questionnaires/forms are used. Data are collected prospectively during the pre-intervention and post-intervention period, and in the period up to six months after discharge. The following parameters are registered:

- readmission within six months after discharge (primary outcome): the hospital information system is used to register readmissions of the patients in the same hospital. The patient's general practitioner is asked for readmissions in other hospitals.
- patient characteristics: these are extracted from the medical records of the hospital information system including gender, age, morbidities, length of stay.
- interventions performed in the discharge intervention process: prescribed medication at discharge is extracted from the initial medication order forms in the hospital's CPOE. All changes (due to correction of medication errors or optimisation of pharmacotherapy) in these initial medication orders are registered by the research pharmacist. Also all explanations provided to the patient during patient counselling are registered as an intervention. Interventions performed in the admission process are not documented for this study. The interventions at discharge are classified according to our previously described classification system.[28]
- patients are asked to fill out a questionnaire about their adherence to drug treatment (MARS; Medication Adherence Rating Scale)[29] satisfaction with information about medicines (SIMS)[30] and their attitude towards drugs (BMQ; Beliefs about Medicines Questionnaire).[31] After the discharge counselling the patient is given a questionnaire (MARS, BMQ, SIMS) which is filled out before discharge. After one month a second short questionnaire (MARS, BMQ) is sent to evaluate whether adherence and the beliefs about medication have changed after one month.

- satisfaction of GPs and community pharmacies: a questionnaire is sent to the patient's general practitioner and community pharmacist within two days of discharge to evaluate their satisfaction with the information on the patient's discharge medication.
- cost-effectiveness estimate and quality of life: the aim of the economic evaluation is to determine and compare the total costs of the COACH program compared with usual care in patients and to relate these costs to the effects of these two approaches. The pharmacist and counsellors register the time and material spent on the intervention.
- All patients are asked to collect data about healthcare utilisation and quality of life (EuroQol) through monthly sent cost diaries (up to three months).[32] These cost diaries have been proven to be valid and reliable and have previously been used in economic evaluations in primary care that included patients of Moroccan and Turkish origin.[33-38] The cost diaries are translated and supplied in the patient's preferred language. Healthcare costs, patient and family costs, and production losses are included. All costs of healthcare are assessed as it is hard to distinguish which costs are related to medication use. Healthcare costs include the costs of visits to the general practitioner, medical specialist, hospitalisations and medication costs. Patient and family costs include costs of over-the-counter medication, informal care and alternative treatments. Costs of productivity losses due to the absence from paid and unpaid work are also estimated.

Sample size

The primary outcome measure is the readmission rate within six months after discharge. The effects of previous studies into pharmacist pre-discharge medication reconciliation combined with patient counselling on the reduction of the frequency of readmission vary widely.[12,13,15,21-23] Four studies report an absolute decreased readmission rate of 13-30% and two studies report 5-9% (median 15%). Based on a conservative interpretation of these studies, it is estimated that the intervention reduces the proportion of readmitted patients in a comparable population with 10% from 25% in the usual care group to 15% in the intervention group. However, the populations in these studies are not fully comparable to our population: previous studies were limited to elderly patients and our study also includes younger patients. We expect a lower proportion of readmitted patients in both the usual care as the intervention group, because hospital admissions related to medication are less frequent in younger patients compared to elderly, and this probably also applies to hospital readmissions after discharge. As there are no exact numbers for the proportion of readmissions in younger patients, we use the most conservative approach that no patients younger than 65 will be readmitted. At the internal ward in our hospital, the proportion of patients younger than 65 years being discharged is about 20%. Given the assumption that no younger patients are readmitted, the proportion of readmitted patients is 20% lower in both groups. The estimated proportions of readmitted patients are 20% in the usual care and 12% in the intervention group. With

these proportions, the expected reduction of readmitted patients is 8%. With a type 1 error of 0.05, a power of 80%, and equal sample sizes, a total of 360 patients per group is needed.

At the Department of Internal Medicine 150-180 patients are being discharged each month. With an estimated proportion of 40% of the patients being excluded due to the exclusion criteria and considering loss to follow-up, it is expected that the period to evaluate usual care and the intervention will take about five months for each group.

Subjects can leave the study at any time for any reason if they wish to do so without any consequences. The number of excluded patients and reasons for exclusion are registered. The same applies to patients who drop out of the study after inclusion. If the agreement with informed consent is not withdrawn, data that have been collected until drop out are included in the analysis.

Data analysis

Patients from the intervention and control group are compared for all baseline characteristics using relative risks with 95% confidence intervals. For the primary endpoint (readmissions) interrupted time series analysis is used for data-analysis. Baseline data are collected over 5 months (with 3 separate measurements), as will be the post-intervention data. The study design thus meets the criteria for a robust interrupted time series analysis, that is 3 data-points pre- and post-intervention, each consisting of at least 30 patients.[39] Subgroup analysis is performed for ethnicity and the results are corrected for potential confounders such as gender, age and underlying disease. Descriptive statistics is performed for the secondary outcomes (interventions registered, adherence, patient's attitude towards medicines, satisfaction with medication information and satisfaction of the general practitioner and community pharmacist). Continuous measures are summarised using means and standard deviations and categorical measures are summarised using percentages.

The economic evaluation is performed according to the intention-to-treat principle and from a societal perspective. Bootstrapping is used for pair-wise comparison of the mean differences in total costs between treatment groups. Confidence intervals are obtained by bias corrected and accelerated bootstrapping, using 5000 replications. Both a cost-effectiveness and cost-utility analysis is performed. Cost-effectiveness ratio's are calculated by dividing the difference between the mean costs of the two treatment groups by the difference in the mean effects of the two treatment groups. Cost-utility is based on the EuroQol and expressed in costs per quality adjusted life year. Cost-effectiveness and cost-utility ratios are estimated using bootstrapping techniques and graphically presented on cost-effectiveness and cost utility planes. Acceptability curves are also presented. Sensitivity analyses on the most important cost drivers are performed in order to assess the robustness of the results.

DISCUSSION

Several randomised controlled trials have been performed which dealt with continuity of care and described one or more interventions which are also conducted in our study (medication reconciliation, patient counselling and transfer of information on medication to primary care).[5,12-15] Contrary to these studies we regarded a randomised design as not feasible, because previous experiences with pilot projects have shown that the COACH program contaminates usual care as residents and other healthcare providers learn from the COACH program. The program therefore influences prescribing behaviour and the organisation of care. Therefore, we have chosen for an observational before-after design including interrupted time series as the preferred alternative.[39]

We expect this study to have several strengths. First, we have gained experience due to previous pilot projects and have been able to optimise the process such as accurate medication reconciliation and more structured patient counselling. We have also optimised documents such as the medication summary for the patient and the medication overview for the general practitioner and community pharmacist. Second, due to previous experiences pharmaceutical consultants are trained in recognising drug-related problems. Third, in contrast to other studies we are also conducting a cost-effectiveness assessment. Finally, in this study we will estimate the effect of the COACH program in a multicultural population which will provide more insight in the effect of discharge counselling in ethnic minority patients.

This study also has some limitations. First, selection bias is possible as especially ethnic minority groups might not want to cooperate. This could also lead to failure to reach the recruitment target and hence could reduce the study's statistical power to detect differences in the primary outcome. Second, previous studies have shown mixed results. It is unknown which interventions are effective and how long the follow-up period should be. Nevertheless, we believe the comprehensive COACH program will be able to show effect on patient safety related outcomes. Finally, as it concerns a monocenter study this may limit generalisability.

Studies generally have shown the effect of discharge medication related interventions on reducing adverse events, medication errors and drug-related problems.[5,12-15] This study however, will be able to evaluate the clinical and cost impact of a comprehensive program on continuity of care. The possible impact of the COACH program on hospital readmissions will provide insight in the quality of care. The findings from this study will provide information of interest to many stakeholders, including patients, healthcare managers, policy makers and healthcare professionals.

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CHAPTER

4.2

The effect of a pharmaceutical transitional care program on unplanned rehospitalisations in internal medicine patients

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ABSTRACT

Background: Medication errors occur frequently at points of transition of care and have a negative effect on patient safety. The main objective of this study was to determine the effect of a transitional pharmaceutical care program on unplanned rehospitalisations within six months after discharge.

Methods: A before-after study was performed at the internal medicine ward of a general teaching hospital. All patients admitted with at least one prescribed drug intended for chronic use were included. The transitional pharmaceutical care program COACH consisted of medication reconciliation, patient counselling at discharge and communication to primary care healthcare providers. The primary outcome was the frequency of patients with an unplanned rehospitalisation within six months after discharge. Secondary outcomes included number of interventions to prevent drug-related problems (DRPs), adherence, believes about medication and patient satisfaction. Interrupted time series analysis was used for the primary outcome. Descriptive statistics were performed for the secondary outcomes.

Results: In the before-period 341 patients were included and in the after-period 365 patients. In the before-period 27.3% of patients had an unplanned rehospitalisation, whereas this became 33.2% in the after-period. The introduction of the COACH program led to a non-significant increase of 12.7% (95% CI: -7.3 – 32.7) of unplanned rehospitalisations. The change in trend between the before- and after-period was non-significant (-0.2%, 95% CI: -4.9 – 4.6). For all patients included in the COACH program interventions were performed to prevent DRPs (mean interventions: 10 per patient). No effect was seen on adherence and believes about medication. Patients were significantly more satisfied with counselling provided by a pharmacy member compared to the resident (68.9% resident vs 87.1% pharmacy).

Conclusion: The COACH program showed no effect on unplanned rehospitalisations. For all patients interventions were performed to prevent DRPs. The program increased patient satisfaction with counselling. No effect was seen on other secondary outcomes.

Trial registration: Dutch trial register: NTR1519

BACKGROUND

Medication errors occur frequently at points of transition of care and have a negative effect on patient safety.[1-3] Four key factors contribute to these medication errors. The first factor is that incomplete and inappropriate medication is prescribed at hospital admission. This can be the result of using incomplete community pharmacy files or recall bias of the patient.[4] These admission medication errors can carry over to the discharge medication. The second factor is that new errors can occur during hospitalisation. For example when hospital physicians forget to restart temporarily discontinued medication or do not optimise the medication (e.g. no evaluation of medication intended for temporal use such as hypnotics).[5,6] The third factor is insufficient patient involvement. Hospitalised patients often get help with the preparing and administering of their medication by hospital staff. However, after hospital discharge patients are abruptly expected to manage their medication themselves, with little support or preparation.[3] The last factor regards insufficient communication from the hospital physician to the primary healthcare provider. Discharge letters and discharge prescriptions generally do not present an overview of the entire pharmacotherapy and changes therein.[7,8] This incompleteness could lead to confusion about whether the unlisted medication is discontinued or just not mentioned. Both the general practitioner and community pharmacy are not informed on reasons for changes in the pharmacotherapy, making it unclear whether changes should be maintained or were only temporal.[9,10]

Transitional care programs, focusing on the transition from hospital discharge to the community setting, have been developed during recent years. Evidence exists on the effect of discharge medication related interventions on reducing adverse events, reducing readmissions and improving adherence.[5,11-15] However, some studies showed no effect and Holland *et al.* reported contradictory results on readmissions.[16-18] Most studies have implemented single interventions using educational strategies or medication reconciliation.[5,12,19-24] Multiple interventions are needed to address the four key factors described above.

Therefore, the COACH (Continuity Of Appropriate pharmacotherapy, patient Counselling and information transfer in Healthcare) program is designed to improve continuity of pharmaceutical care by combining interventions.[25] The main objective of this study was to determine the effect of the COACH program on unplanned rehospitalisations within six months after discharge from the internal medicine department.

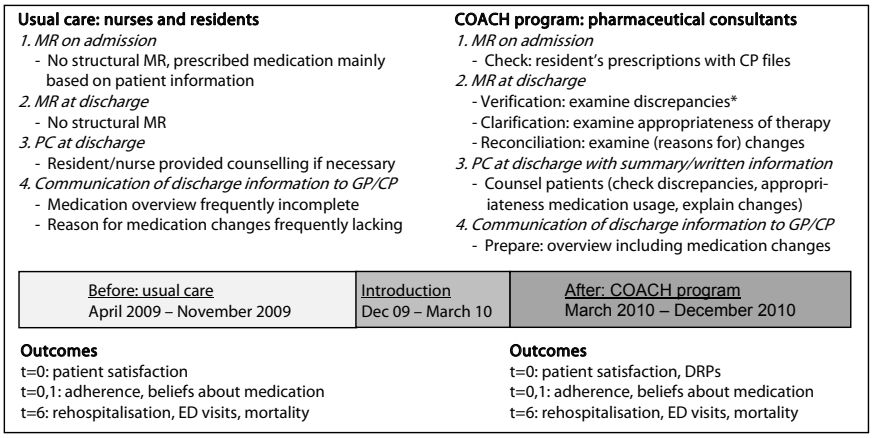
METHODS

Design

A prospective experimental study with a before-after design was performed at a 550-bed general teaching hospital; St. Lucas Andreas Hospital, Amsterdam, The Netherlands. The study analysis was set up as an interrupted time series that is characterised by a series of measurements over time interrupted by an intervention.[26]

Usual care patients were included during eight months (April 2009-November 2009), see Figure 1. During the next 3.5 months the COACH program was introduced (December 2009-March 2010). Intervention patients were included during nine months from March 2010 to December 2010. The study protocol has been described elsewhere.[25] The study is described briefly in the following sections.

Figure 1 Timeline of the COACH program and of the introduction and implementation of the program



*discrepancies between medication prescribed pre-admission and medication prescribed in the hospital.
CP= community pharmacy, DRPs= drug-related problems, ED= emergency department, GP= general practitioner, PC= patient counselling, MR= medication reconciliation, t=0, 1, 6: respectively, at discharge, 1 month after discharge and 6 months after discharge

Study population

The study was performed on the internal medicine ward. All patients admitted (planned or unplanned) with at least one prescribed drug intended for chronic use were invited to participate. Exclusion criteria were: no informed consent, no medication intended for chronic use prescribed at discharge, died during index admission, transfer to another ward or hospital, discharge within 24 hours or out-of-office hours, discharge to a nursing home (because patients do not administer their own medication there) and counsel-

ling not possible (as stated by the resident due to physical/mental constraints, being critically ill or due to language restrictions without relatives or healthcare personnel to translate). Patients could be included in the study only once. As we were unable to obtain rehospitalisation data for patients outside the catchment area of our hospital, these patients were excluded.
The St. Lucas Andreas Hospital institutional review board has stated that this study was exempt from review by the institutional review board as the Dutch legislation does not request this for studies that do not affect the patient's integrity. Patients were asked informed consent for gathering data and for filling in questionnaires. Patients could refuse to fill in questionnaires, but still have given informed consent for collecting clinical data.

Usual care in the before-period

At hospital admission and discharge no structural medication reconciliation was performed (see Figure 1). Residents mostly used the information provided by patients, carers or previous hospital records to prescribe the admission medication. Residents could consult the community pharmacy medication records through a link in the hospital's Computerized Physician Order Entry (CPOE) system or through requesting a faxed medication history from the community pharmacy. Resident's prescriptions were checked during hospital admission by the clinical pharmacist on dosages, double medication, drug-drug interactions and contraindications.
Residents and nurses were involved in patient instructions on pharmacotherapy. However, no structural patient counselling was provided at hospital discharge to explain medication changes. Discharge medication information was communicated to the general practitioner and community pharmacy. Completeness of medication, including pre-admission prescribed medication, was not checked and little or no information on (reasons for) changes in the pharmacotherapy was communicated.

COACH intervention program in the after-period

The COACH intervention program was carried out by a team of pharmaceutical consultants with clinical pharmacists as supervisors. Pharmaceutical consultants are pharmacy technicians who have followed an additional three-year bachelor program focusing on pharmaceutical patient care.
At hospital admission medication reconciliation was performed by verifying the admission prescriptions in the hospital's CPOE with community pharmacy records. Discrepancies with the pre-admission medication and possible drug-related problems were communicated to the resident.
At hospital discharge a second medication reconciliation was performed using a protocol.[25] The results were discussed with the resident and prescriptions were adjusted if necessary.

To support patient counselling and communication of discharge information to primary care healthcare providers a patient medication summary and discharge overview were prepared. Both forms contained the same information regarding all known pharmacotherapy and (reasons for) medication changes. The pharmaceutical consultant counselled the patient and/or his carer using the medication summary and faxed the discharge medication overview to the community pharmacy before discharge. The resident needed to upload the discharge medication overview into the discharge letter for the general practitioner.

Study endpoints and data collection

The primary outcome of this study was the frequency of patients with at least one unplanned rehospitalisation within six months after discharge. An unplanned rehospitalisation was defined as an unscheduled hospitalisation after discharge to the St. Lucas Andreas Hospital or any other hospital within the catchment area. Other hospital contacts, i.e. planned rehospitalisations and emergency department (ED) visits not resulting in a hospitalisation, and mortality were regarded as secondary outcomes. Data regarding hospital contacts and mortality within six months after discharge were collected using the hospital information systems of the St. Lucas Andreas Hospital and five other hospitals in the catchment area.

Other secondary outcomes included interventions performed to prevent drug-related problems (DRPs), adherence to drug treatment, patient´s attitude towards drugs, patient satisfaction with information about medicines and patient's general satisfaction with counselling.

Interventions performed to prevent drug-related problems were extracted from the checklists used by pharmaceutical consultants. All medication changes (due to correction of medication errors or optimisation of pharmacotherapy) due to the pharmaceutical consultant advices were registered. Also, all explanations provided by the pharmaceutical consultant to the patient during patient counselling were recorded as an intervention. The interventions were classified according to our previously described classification system.[27]

Patients were asked to fill out validated questionnaires with a 5-point Likert scale about their adherence to drug treatment (MARS; Medication Adherence Rating Scale), their attitude towards drugs (BMQ; Beliefs about Medicines Questionnaire), satisfaction with information about medicines (SIMS) and their general satisfaction (questionnaire developed in the St. Lucas Andreas Hospital).[28-32] After discharge counselling the patient was given a questionnaire (MARS, BMQ, SIMS, general satisfaction) and was requested to fill it in before discharge. After one month a second short questionnaire (MARS, BMQ) was sent. Patients were contacted by telephone at least three times if they had given informed consent to fill in questionnaires but failed to respond.

Patient characteristics were extracted from the medical records of the hospital information system including gender, age, co-morbidities, length of hospital stay, and previous hospitalisations (i.e. planned/unplanned admissions) and hospital contacts (i.e. hospitalisations, one day-care and emergency department visits) in the six months before inclusion. The Charlson co-morbidity score was used to evaluate the severity of co-morbidities.[33] This score has been shown to associate with hospitalisations.[33,34] Validated forms were used to assess other characteristics, e.g. ethnicity, help with medication use, and marital status. Fidelity of the intervention (i.e. whether the intervention was implemented as planned) was also assessed.

Sample size

The calculated sample size was based on the rehospitalisation frequency within six months after discharge. Results of previous studies into pharmacist pre-discharge medication reconciliation combined with patient counselling vary widely.[12,13,15,35-37] Four studies report an absolute decreased of readmission frequency of 13-30% and two studies report 5-9% (median 15%). However, the populations in these studies are not fully comparable to our population: previous studies were limited to elderly patients and our study also included younger patients. Therefore, a conservative approach was used estimating the following proportions: 20% of rehospitalised patients in the usual care and 12% in the intervention group. The expected absolute reduction is 8%. With a type 1 error of 0.05, a power of 80%, and equal sample sizes, a total of 360 patients per group was needed.

Data analysis

Patients from the before and after group were compared for all baseline characteristics using the independent T-test for continuous variables and the chi-square test for frequencies. For the before- and after-period the frequencies for unplanned and planned rehospitalisations, ED visits and mortality were calculated. Interrupted time series analysis was used. Data were collected over an 8-month before-period during usual care and over a 9 month after-period during the COACH program. The data points for the time-series were aggregated per four weeks. For example, for unplanned rehospitalisations the number of patients with an unplanned rehospitalisation was divided by the total number of patients included in that data point. As there was only a small number of patients included in the last month in both periods (5 patients before-period and 28 patients in the after-period), these patients were added to the previous month. Thus, there were 7 data points for the before-period and 8 data points (8 and 9 months minus one, respectively) for the after-period. The study design meets the EPOC criteria for a robust interrupted time series analysis, that is at least three data-points before and after the intervention, each consisting of at least 30 patients.[38] Segmented linear regression

analysis was used to assess a trend for the percentage of patients with above mentioned outcomes. Durbin-Watson statistics and visual inspection of the residuals versus time were used to check for possible autocorrelation (serial correlation between an outcome and consecutive observations, non-significant Durbin-Watson means no autocorrelation).

To estimate the level and trend of the outcomes in the before-period and to estimate the changes in level and trend after the implementation of the COACH program, the following linear regression model was used.[26]

$Y_t = \beta_0 + \beta_1 * time_t + \beta_2 * intervention_t + \beta_3 * time\ after\ intervention_t + e_t$

β_0 = baseline level of the outcome = value at time zero

β_1 = slope prior to the intervention = baseline trend

β_2 = change in outcome immediately after the intervention

β_3 = change in the slope from before to after intervention

Potential confounders were added to this model to evaluate the impact of imbalances in the case-mix in the before- and after-period.

Descriptive statistics were performed for the secondary outcomes (interventions registered, adherence, patient's attitude towards medicines and satisfaction) as described in previous studies.[27-32]

RESULTS

A total of 2274 patients were screened for eligibility; 1568 (69%) patients were excluded (Figure 2), leaving 706 patients (341 before-period, 365 after-period) who were included in the study. Main exclusion criteria were discharge within 24 hours or out-of-office hours (19.4%), transfer to another ward, hospital or nursing home (16.8%) and no chronic medication use (15.6%). Reason for exclusion differed between the before- and after-period regarding no chronic medication use (22.3% before vs 11.9% after), discharge not communicated (6.9% vs 23.3%) and no informed consent (19.4% vs 8.6%). Patients who did not give informed consent were significantly older (68.7 years vs 65.5 years, p=0.02) and stayed, non-significantly, longer in hospital (11.2 days vs 9.3 days, p=0.20). No difference was found for type of admission (planned/unplanned) and gender.

The patients in the before- and after-period differed in baseline characteristics (Table 1). Patients in the after-period received more frequently help with their medication use (18.8% before vs 30.8% after, p<0.01), had more hospital contacts in the six months before inclusion (1.3/patient vs 1.7/patient, p=0.03) and had a higher number of co-morbidities (3.4/patient vs 3.9/patient, p<0.01) which were also more severe (higher Charlson co-morbidity score, p<0.01).

Figure 2 Flowchart of inclusion of patients participating in the before- and after-period

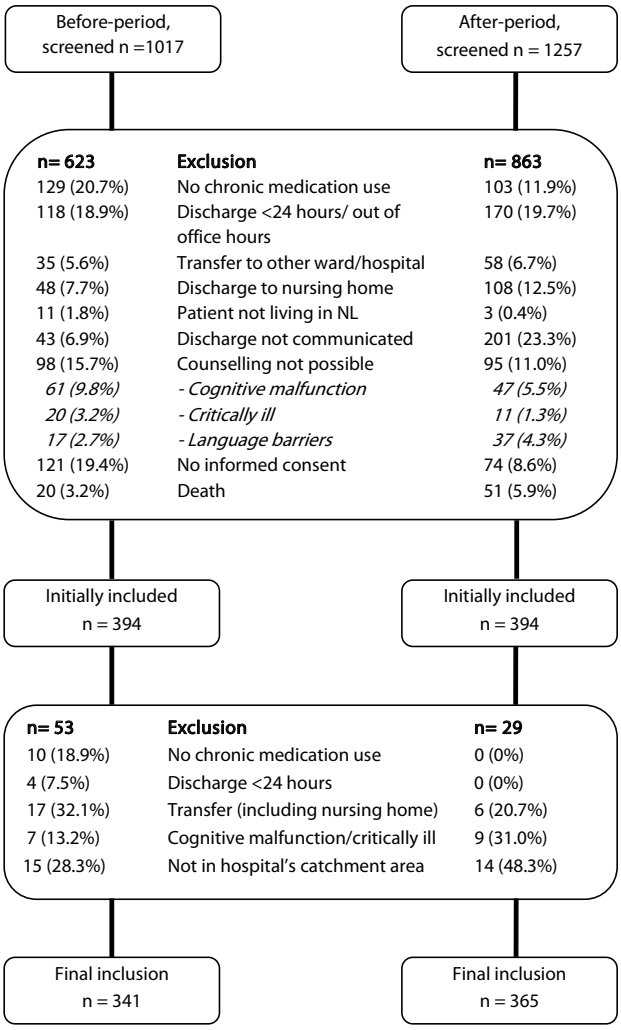


Table 1 Characteristics of patients participating in the before- and after-period

Characteristic	Before-period (n=341)	After-period (n=365)	p-value
Female, n (%)	165 (48.4)	191 (52.3)	0.30
Age, mean years (SD)	64.3 (16.7)	66.7 (16.0)	0.06
Native Dutch (%)	231 (67.9)	239 (65.5)	0.48
No or low education level (%)	267 (78.5)	298 (82.1)	0.23
Married or having a partner (%)	152 (44.6)	154 (42.3)	0.54
Help with medication use, yes (%)	64 (18.8)	112 (30.8)	<0.01
All hospital contacts* in the last 6 m, mean (SD)	0.83 (1.3)	1.08 (1.7)	0.03
Previous hospitalisations† in the last 6 m, mean (SD)	0.52 (0.93)	0.62 (1.1)	0.20
Admission type, planned (%)	98 (28.7)	99 (27.1)	0.63
Length of stay, range, median days (SD)	8.8 (7.8)	9.7 (10.4)	0.16
N. of drugs on admission, mean (SD)	6.5 (3.5)	6.9 (4.0)	0.13
Reason for admission (%)			
Renal/urological	54 (15.8)	61 (16.7)	0.56
Liver/bile/pancreas	41 (12.0)	48 (13.2)	
Infection	63 (18.5)	50 (13.7)	
Gastrointestinal	62 (18.2)	64 (17.5)	
Diabetes	33 (9.7)	42 (11.5)	
Cancer	29 (8.5)	34 (9.3)	
Aspecific symptoms	33 (9.7)	28 (7.7)	
Other	26 (7.6)	38 (10.4)	
Kidney function (%)			
Dialysis	23 (6.7)	24 (6.6)	0.46
Decreased kidney function‡	68 (19.9)	91 (24.9)	
Unknown	16 (4.7)	15 (4.1)	
Total co-morbidities, mean (SD)	3.4 (2.1)	3.9 (2.4)	<0.01
Charlson co-morbidity score (%)			
0-1	177 (51.9)	161 (44.1)	0.01
2-3	101 (29.6)	102 (27.9)	
4-5	41 (12.0)	54 (14.8)	
>6 (severe)	22 (6.5)	48 (13.2)	

* includes one-day care, ED visits, planned and unplanned admissions in the last 6 months before inclusion
† includes planned and unplanned admissions in the last 6 months before inclusion
‡ kidney function less than 60 ml/min during at least 3 months

Unplanned rehospitalisations

The proportion of patients with an unplanned rehospitalisation did not differ (27.3% before vs 33.2% after, Table 2). In the unadjusted analysis the baseline trend showed a non-significant decrease in unplanned rehospitalisations (i.e. β_1, -1.7%, 95% CI: -4.8 – 1.4) in the before-period. The introduction of the COACH program led to a non-significant increase of unplanned rehospitalisations (i.e. β_2, 8.5%, 95% CI: -8.4 – 25.5). The change of trend of 2.3% (i.e. β_3, 95% CI: -1.7 – 6.3) per 4 weeks was also non-significant.

After adjustment for confounders again non-significant results were found. β_1 became -2.1% (95% CI: -5.2 – 1.1), β_2 increased to 12.7% (95% CI: -7.3 – 32.7) and β_3 decreased

to -0.2% (95% CI: -4.9 – 4.6). In Figure 3 the proportion of patients with an unplanned rehospitalisation versus the study month is graphically presented.

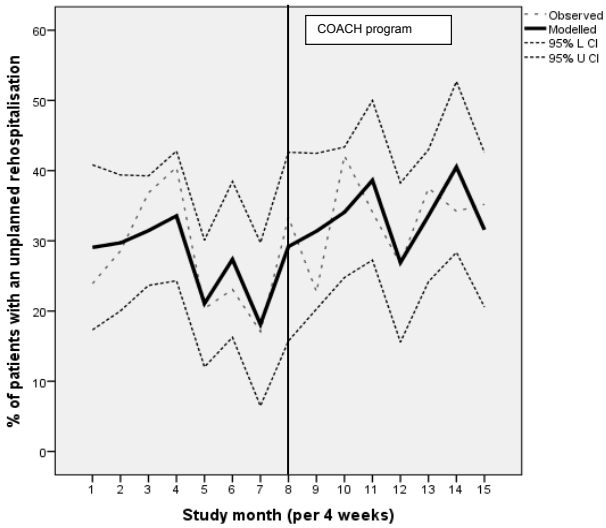
Table 2 Effect of COACH program on hospitalisations, emergency department visits and mortality (n=341 before and n=365 after)

Original data	**Before (% of pat)**	**After (% of pat)**
Unplanned rehospitalisation	93 (27.3)	121 (33.2)
Planned rehospitalisation	79 (23.2)	79 (21.6)
Any rehospitalisation	142 (41.6)	166 (45.5)
Emergency department visit	62 (18.2)	54 (14.8)
Mortality	26 (7.6)	24 (6.6)
ITS unplanned rehospitalisation	**Unadjusted**	**Adjusted***
β_0 (95% CI)	34.0 (20.2; 47.9)	11.3 (-28.7; 51.2)
β_1 (95% CI)	-1.7 (-4.8; 1.4)	-2.1 (-5.2; 1.1)
β_2 (95% CI)	8.5 (-8.4; 25.5)	12.7 (-7.3; 32.7)
β_3 (95% CI)	2.3 (-1.7; 6.3)	-0.2 (-4.9; 4.6)

β_0 = baseline level of the outcome, β_1 = baseline trend, β_2 = change in outcome immediately after the intervention, β_3 = change in the slope from before to after the intervention. β values were calculated using segmented regression analysis. ITS=interrupted time series analysis

* Adjusted for baseline differences: help with medication use, all hospital contacts in the last 6 months, mean Charlson score

Figure 3 Impact of the COACH program on unplanned rehospitalisations per study month (adjusted for confounders)



Secondary outcomes

The proportion of patients with any rehospitalisation, planned rehospitalisation and ED visit did not differ (Table 2, results of interrupted time series analysis are not shown). Also, mortality did not differ (7.6% before vs 6.6% after).

In 100% of patients at least one intervention was recorded aimed at preventing DRPs (with a mean of 10 per patient, Table 3). At hospital admission discrepancies with pre-admission used medication was eliminated in 62.4% of patients. At hospital discharge discrepancies were still corrected in 68.2% of patients (e.g. restart temporarily discontinued medication). Furthermore, at discharge the medication was optimised in 75.1% of patients (e.g. discontinue hypnotics). During patient counselling in 97.8% of patients interventions were aimed to optimise the patient's medication handling (e.g. answer questions regarding side effects, discuss adherence).

Patients who filled in questionnaires (at discharge and at one month after discharge) in the before-period did not differ regarding baseline characteristics with patients in the after-period. Patients reported high medication adherence with mean values of 23 (maximum score: 25, Table 4). No significant difference was seen at discharge and at one month after discharge regarding adherence and the four domains of the beliefs about medication questionnaire.

Patient satisfaction with the extent of information regarding medicines as measured with the SIMS questionnaire did not differ after implementing the COACH program (mean score 9.98 before vs 9.99 after, p=0.99).

The general satisfaction questionnaire showed that in the after-period 46.9% of patients received information regarding medication from the resident without asking. In the after-period this increased to 73.7% (p<0.01). Although all patients were counselled in the after-period by the pharmaceutical consultants, 26.3% of patients reported they were not counselled. There was no significant difference in satisfaction regarding the amount of information received (83.6% resident vs 88.6% pharmaceutical consultant, p=0.41)

Table 3 Effect of the COACH program on medication reconciliation interventions per patient (n=365)

Outcome: drug-related problems	Hospital admission mean/pat (%§)	Hospital discharge mean/pat (%§)	Patient counselling mean/pat (%§)	Total mean/pat (%§)
Elimination of discrepancies*	1.65 (62.4)	1.43 (68.2)	0.82 (49.7)	3.90 (89.2)
Optimisation of pharmacotherapy†	0.10 (9.7)	1.76 (75.1)	0.15 (13.0)	2.02 (80.4)
Optimisation medication handling‡	-	-	4.15 (97.8)	4.15 (97.8)
Total	1.75 (64.1)	3.19 (93.4)	5.12 (98.9)	10.07 (100.0)

* Examples: omission of pre-admission used diabetes drug started at hospital admission, temporarily discontinued anticoagulant restarted at hospital discharge, patient used a different dose of inhalation medication pre-admission

† Examples: a laxative added to opioid use at admission, analgesics or protonpumpinhibitor discontinued at discharge, patient states that sedative is no longer needed

‡ Examples: questions of patient regarding side effect answered, adherence to medication and helping tools discussed, medication changes explained

§ Percent of patients for whom at least one intervention was registered

and regarding the understandability of information (77.0% vs 88.4%, p=0.09). Patients were significantly more satisfied with the information provided by the pharmaceutical consultant (68.9% resident vs 87.1% pharmaceutical consultant, p=0.01).

Table 4 Results of patient questionnaires: SIMS, MARS, BMQ and general satisfaction

Outcome: SIMS, MARS and BMQ	**Before-period**	**After-period**	**p-value**
Patient questionnaire at t=0 (B: 106, A: 104)			
Satisfaction SIMS*, mean score (SD) (B: 88, A:77)	9.98 (5.6)	9.99 (5.4)	0.99
Adherence MARS†, mean score (SD) (B: 99, A: 97)	23.40 (2.4)	23.38 (2.8)	0.95
BMQ‡, mean score (SD)			
Necessity (B: 99, A: 99)	18.23 (3.9)	18.68 (4.1)	0.43
Concerns (B: 98, A: 97)	16.47 (4.0)	16.29 (4.6)	0.77
General-overuse (B: 93, A: 98)	10.91 (2.8)	10.99 (2.7)	0.85
General-harm (B: 93, A: 98)	9.88 (3.0)	9.81 (2.8)	0.86
Patient questionnaire at t=1 (B: 66, A: 62)			
Adherence MARS†, mean score (SD) (B: 65, A: 58)	23.57 (2.1)	23.88 (2.2)	0.42
BMQ‡, mean score (SD)			
Necessity (B: 61, A: 57)	17.87 (4.0)	19.11 (4.2)	0.11
Concerns (B: 60, A: 60)	16.77 (4.1)	16.78 (5.1)	0.98
General-overuse (B: 62, A: 56)	11.24 (3.0)	11.48 (3.1)	0.67
General-harm (B: 60, A: 59)	10.07 (2.6)	10.02 (2.8)	0.92
Outcome: general satisfaction in the after-period§	**Resident**	**Consultant**	**p-value**
Received information regarding medication (R: 98, C: 99)			
Yes, without asking for it	46 (46.9)	73 (73.7)	
Yes, but after asking	15 (15.3)	0 (0)	<0.01
No	37 (37.8)	26 (26.3)	
Amount of information received (R: 61, C: 70)			
Enough	51 (83.6)	62 (88.6)	0.41
Satisfaction with information (R: 61, C: 70)			
(Very) satisfied	42 (68.9)	61 (87.1)	0.01
Information was clear (R: 61, C: 69)			
(Very) clear	47 (77.0)	61 (88.4)	0.09

A= After-period: number of patients, B= Before-period: number of patients, t=0: at discharge, t=1: 1 month after discharge, R=resident, C=pharmaceutical consultant

* Satisfaction with Information about Medicines Scale (SIMS). Higher scores indicate a higher degree of overall satisfaction (17 items: score range 0-17).[30]

† Self-report Medication Adherence Rating Scale (MARS). Higher scores indicate higher adherence (5-items: score range 5-25).[31,32]

‡ Beliefs about medication (BMQ). BMQ-necessity: higher scores indicate beliefs about the necessity and efficacy of medicines (5 items, score range 5-25). BMQ concerns: higher scores indicate concerns about the harmful effects of medicines (6 items, score range 6-30). BMQ General-overuse and BMQ General-harm: higher score indicate beliefs that medicines are over-used by doctors and are harmful addictive poisons (both 4 items, score range 4-20).[28,29]

§ Patient's general satisfaction with counselling by the resident did not significantly differ between the before- and after-period.

Fidelity COACH program

All steps of the COACH program were implemented in 48 patients (12.6%), see Table 5. At hospital admission for 8.2% of patients medication reconciliation could not be performed due to a short hospitalisation. Medication reconciliation at discharge, patient counselling at discharge and information transfer to community pharmacies were performed in all patients. In 72.1% of patients residents failed to upload the discharge medication overview into the discharge letter. For 102 patients (27.9%) information was uploaded, but in 48 (13.2%) the information of the discharge medication overview was adjusted.

Table 5 Fidelity of the COACH program (n=365)

Implementation of	After-period (% of pat)
Medication reconciliation at hospital admission	335 (91.8)
Medication reconciliation at hospital discharge	365 (100.0)
Patient counselling at hospital discharge	365 (100.0)
Information exchange to community pharmacist	365 (100.0)
Information exchange to general practitioner	102 (27.9)
Including complete overview*	48 (13.2)
All steps of the COACH program	46 (12.6)

* resident adjusted the discharge medication overview prepared by the pharmaceutical consultant, e.g. deleted information regarding discontinued (in-hospital/pre-hospital) medication, allergies or contraindications

DISCUSSION

This study showed that the transitional care COACH program did not decrease unplanned rehospitalisation frequency. For all patients interventions were performed to prevent DRPs. The program increased patient satisfaction with counselling. No effect was seen on other secondary outcomes.

Fidelity with the implementation of the COACH program was good for all interventions that the pharmaceutical consultants performed themselves. Fidelity with informing the general practitioner was poor (27.9% of patients) as residents failed to upload the discharge medication overview prepared by the pharmaceutical consultant into the discharge letter. This could have been caused by the high turn-over of residents or the many tasks of the resident. When residents did upload the discharge medication overview they adjusted the information in half of patients. For example, residents often regarded discontinued (in-hospital or pre-admission) medication as irrelevant. However, previous studies have shown that general practitioners and community pharmacies want to be informed regarding discontinued medication.[9,39]

Previous studies regarding transitional pharmaceutical care programs showed high variability in results regarding rehospitalisations.[12,37,40-45] This variability may be due to the

context of the study, the patient population, the implementation fidelity, the intervention complexity, the sample size, the quality of community care, definitions, the measurement method and period etc. For example, Scullin et al. reported an 8% reduction in the readmission frequency after one year (49% control vs 41% intervention, p=0.027).[37] Their intervention was more comprehensive than ours and they included a pre-defined high risk patient group. A second study showed decreased 30-day readmission rates (odds ratio 0.61, 95% CI: 0.42-0.88) for patients where the intervention was implemented completely.[46] No decrease was seen for patients who received parts of the intervention. In our study only 46 patients received the complete COACH program, so the sample size was limited to perform subgroup analysis.

Comparable to other studies, we found no decrease in rehospitalisations.[40,41,43,45,47] Several explanations may be considered. We focused mainly on the discharge process, on the pharmacotherapy (and not on other medical aspects) and we used pharmaceutical consultants to perform the intervention. Further, we included all patients instead of high risk patients and intervention fidelity regarding the communication to the general practitioner was low. Finally, it may be that a program such as COACH only influences drug-related rehospitalisations or less severe outcomes such as primary care healthcare use or adverse drug events. Previous studies with benefits had a broader intervention (including admission interventions and/or post-discharge interventions), did not focus solely on the pharmacotherapy (e.g. appointment schedules, diet, exercise), tended to focus on high risk patients and used a combination of healthcare providers (pharmacists, nurses, physicians).[35,37,46,48-50] Evidence on components effective for patient safety interventions is limited.[51,52] It is also unknown to what degree the quality of care after hospital discharge influences the effect of transitional care programs. For example, studies have shown that discharge medication related information is not completely documented by community pharmacies and general practitioners. This leads to renewed prescribing of previously discontinued medication.[8,53,54]

Previous studies also showed mixed results for adherence.[12,47,55-58] In this study the one-time patient counselling at discharge was not enough to increase adherence, beliefs about medication, and satisfaction regarding medication information. Although there were significant differences in some questions, these differences were lost after aggregating the BMQ and SIMS questionnaire results. Patients were more satisfied with counselling by the pharmaceutical consultant than the counselling by the resident. In a previous qualitative study we showed that patients felt satisfied with patient counselling and written material that they received.[59] However, in this previous study patients were generally satisfied. This could lead to a ceiling effect and any additional satisfaction may be difficult to distinguish with questionnaires such as SIMS. Patients also reported very high medication adherence which again could lead to a ceiling effect.

The strength of this study was that we assessed rehospitalisations to multiple hospitals instead of only readmissions to the study hospital. We performed an interrupted time series analysis and we assessed numerous outcomes. Limitations of this study also need to be discussed. First, there was selection bias as patients in the before- and after-period differed in baseline characteristics. Patients in the after-period had more co-morbidities (in number and severity), reported to receive more frequently help with medication use and had more hospital contacts in the six months before inclusion. We adjusted for these baseline characteristics. Second, only 31% of screened patients were eventually included. In the after-period, we did perform (parts of) the COACH program also for excluded patients. However, we did not include them in the study to keep the study population homogenous. In the before-period 19.4% of patients did not give informed consent to obtain data for this study (compared to 8.6% in the after-period). This difference may be caused by the fact that patients were told that they would receive discharge counselling during which their medication and changes would be explained. Patients who did not give informed consent were significantly older and tended to stay longer in hospital, suggesting that patients who were more severely ill refused to participate. It is expected that these patient are rehospitalised more often, so the rehospitalisation frequency may be underestimated. Third, as this study concerns a monocenter study at one department the generalisability is limited. Finally, patients did not want to fill in questionnaires as they considered this as a burden or they were not interested in research. To increase response patients who had not send their questionnaires back were contacted by telephone. Still, the sample size with respect to the questionnaires was limited and the results may be biased as patients who were more interested in the study might have participated. Future studies need to assess what effective components are for transitional care programs. Also, studies need to improve fidelity with their intervention and stimulate continuity of care after discharge by primary healthcare providers.

In conclusion, the transitional care COACH program did not decrease unplanned rehospitalisations. Interventions to prevent DRPs were recorded in all patients and the program increased patient satisfaction with counselling. No effect was seen on other secondary outcomes.

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CHAPTER

4.3

Cost-effectiveness of a transitional pharmaceutical care program for patients discharged from the hospital

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ABSTRACT

Background: Transitional care programs are being developed to decrease medication errors and improve continuity of care. However, the cost-effectiveness of these programs is unknown. This study aims to determine the cost-effectiveness of the COACH program (Continuity Of Appropriate pharmacotherapy, patient Counselling and information transfer in Healthcare) in comparison with usual care in patients discharged from an internal medicine department.

Methods: A before-after study was performed at the internal medicine ward of a general teaching hospital. All admitted patients using at least one prescribed drug for chronic use were included. The transitional pharmaceutical care program COACH consisted of medication reconciliation, patient counselling at discharge and communication to primary care healthcare providers. The primary clinical outcome was the proportion of patients with an unplanned rehospitalisation within three months after discharge. Secondary outcome was the number of quality-adjusted life-years (QALYs) based on the EQ-5D. The economic evaluation was conducted from a societal perspective. Data regarding healthcare use and productivity losses were collected through three monthly sent cost diaries. Cost differences and incremental cost-effectiveness ratios were adjusted for confounders using regression techniques. Uncertainty surrounding cost differences and incremental cost-effectiveness ratios between the groups was estimated by bootstrapping the regression models.

Results: In the COACH program 168 patients were included and in usual care 151 patients. There was no significant difference in the proportion of patients with unplanned rehospitalisations in the three months after discharge (21.4% COACH vs 20.5% usual care, 95% CI for adjusted difference: -8.88 – 8.55) and in QALYs (0.15 vs 0.17, 95% CI for adjusted difference -0.0170 – 0.0001). Total costs for the COACH program (€6845 per patient) did not statistically significantly differ with usual care (€7952). The adjusted difference in costs between groups was -€1160 per patient (95% CI: -3168 – 847), which was not statistically significant. Cost-effectiveness planes showed that the COACH program was not cost-effective compared with usual care for unplanned rehospitalisations and QALYs gained.

Conclusion: Based on this study, the COACH program was not considered cost-effective. Future studies should focus on high risk patients and a more comprehensive intervention as this may increase the chances of a cost-effective intervention.

Trial registration: Dutch trial register: NTR1519

BACKGROUND

Due to the decentralized and fragmented nature of the healthcare delivery system, discontinuity of care is likely when patients see multiple healthcare providers of whom none have access to complete information regarding the patient's healthcare status.[1] It is therefore not surprising that medication errors occur most frequently at transitions of care such as hospital admission and discharge.[2-4] Studies show that up to 95% of patients experience medication errors at hospital admission and 41%-73% of patients experience medication errors at hospital discharge.[4-8] The causes of these medication errors are multi-factorial, such as the patient's inability to recall medication, incomplete information transfer between healthcare settings and incorrect transcription of information. Because medication transfer errors are an important groups of errors affecting patient safety, numerous guidelines on medication transfer have been published.[9-13] These guidelines advocate the implementation of transitional care programs that include medication reconciliation, patient counselling and communication of medication related information between settings. Although studies have shown that these transitional care programs are effective in decreasing medication errors,[4-8] their effects on reducing rehospitalisations are not consistent.[14-21]

In a context of increasing healthcare costs and limited resources, hospitals and professionals are concerned about the cost-effectiveness of approaches to improve continuity of pharmaceutical care.[22] However, only few cost-effectiveness studies have been performed until now.[17,23] Moreover, published economic evaluations for transitional care programs generally only consider healthcare costs, exclude the costs of the intervention, use intermediate outcome measures, lack sensitivity analyses to account for uncertainty around key estimates or assumptions and lack an incremental analysis.[24]

We developed a transitional pharmaceutical care program (COACH, Continuity Of Appropriate pharmacotherapy, patient Counselling and information transfer in Healthcare) to improve the transition of patients from hospital discharge to the community setting.[25] The main objective of this study was to evaluate the cost-effectiveness of the COACH program in patients discharged from the internal medicine department in comparison with usual care.

METHODS

Design

An economic evaluation alongside a before-after study with three months follow-up was performed at a 550-bed general teaching hospital; St. Lucas Andreas Hospital, Amsterdam, The Netherlands. This economic evaluation was part of a larger study focusing on

rehospitalisations six months after discharge. As we expected that patient compliance with filling in cost diaries would decrease over time, patient follow-up for the economic evaluation was limited to three months (instead of the six months in the main study).
Usual care patients were included during an eight months before-period (April 2009-November 2009), see Figure 1. During the next 3.5 months the intervention was rolled out (December 2009-March 2010). Intervention patients were included during a nine months after-period from March 2010 to December 2010. The study protocol has been described in detail elsewhere.[25] Here we focus on the economic evaluation.

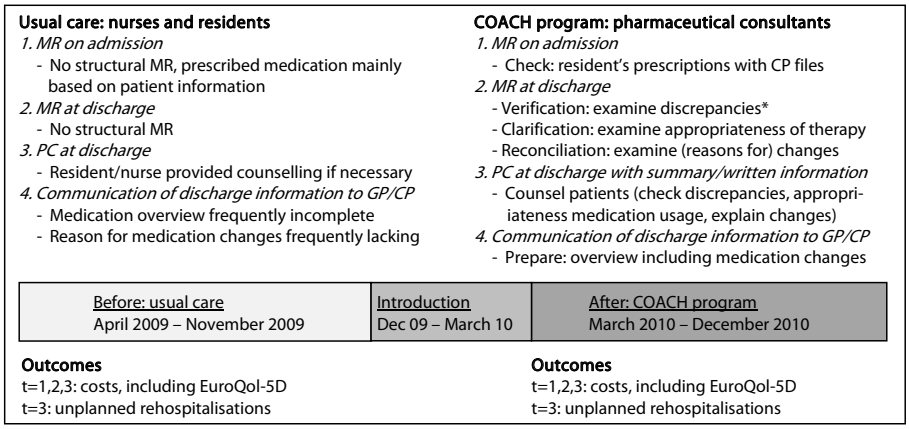
Study population

The study was performed at the internal medicine ward. All admitted patients using at least one prescribed drug for chronic use at hospital admission were invited to participate. Exclusion criteria were: no informed consent, no medication for chronic use prescribed at discharge, died during index admission, transfer to another ward or hospital, discharge within 24 hours or during out-of-office hours, discharge to a nursing home (because patients do not administer their own medication there) and counselling not possible (as stated by the resident due to physical/mental constraints, being critically ill or due to language restrictions without relatives or healthcare personnel to translate). Patients could be included in the study only once. As we were unable to obtain rehospitalisation data for patients outside the catchment area of the hospital, these patients were excluded as well.
This study was exempt from review by the hospital institutional review board as this is not required for studies that do not affect the patient's integrity (according to Dutch legislation). Patients were asked informed consent for gathering data regarding healthcare use and for filling in cost diaries. Patients could participate in the main study, but refuse to fill in cost diaries.

Usual care: before period

In the usual care condition, no structural medication reconciliation was performed at hospital admission and discharge, see Figure 1. Residents used the information provided by patients/carer or previous hospital records to obtain pre-admission medication.
Residents and nurses were both involved in instructing patients on how to use their medication. However, no structured patient counselling was provided at hospital discharge to explain medication changes. Discharge medication information was communicated to the general practitioner and community pharmacy. Completeness of medication, including pre-admission prescribed medication, was not checked and little or no information on (reasons for) changes in the pharmacotherapy was communicated to primary care providers.

Figure 1 Timeline of the COACH program and of the introduction and implementation of the program



*discrepancies between medication prescribed pre-admission and medication prescribed in the hospital.
CP= community pharmacy, GP= general practitioner, PC= patient counselling, MR= medication reconciliation, t=1, 2, 3: 1 month after discharge, 2 and 3 months after discharge respectively

Intervention: after period

The intervention consisted of the COACH program. At hospital admission and discharge, medication reconciliation was performed by pharmaceutical consultants using a protocol as described previously (Figure 1).[25] The results were discussed with the resident and prescriptions were adjusted if necessary.

To support patient counselling and communication of discharge information to the next healthcare provider, a patient medication summary and discharge overview were prepared (with complete pharmacotherapy and medication changes). The pharmaceutical consultant counselled the patient and/or his family on the complete pharmacotherapy including the medication changes. The general practitioner and community pharmacist were informed regarding the discharge medication and (reason for) changes.

Study measures

Outcome measures

The primary clinical outcome of this study was the proportion of patients with at least one unplanned rehospitalisation within three months after discharge. An unplanned rehospitalisation was defined as an unscheduled hospitalisation to the St. Lucas Andreas hospital or any other hospital within the catchment area of the study hospital. Data on rehospitalisations, one-day care and emergency department (ED) visits within three months after discharge were gathered using the hospital information systems of the St. Lucas Andreas Hospital and the five other hospitals in the catchment area.

To assess quality of life the EuroQol-5D (EQ-5D) was used.[26] The EQ-5D was included in the cost diary that was sent to the patient each month. Thus, the EQ-5D was assessed at one, two and three months after discharge. The EQ-5D result at one month was used as baseline estimate. Utility values for each health state were estimated using the Dutch tariff.[27] Quality-adjusted life-years (QALYs) were calculated by multiplying the utilities with the amount of time a participant spent in a particular health state. Transitions between health states were linearly interpolated.[28]

Cost measures

Cost data were collected from a societal perspective and categorised into primary care costs, secondary care costs, medication costs, supportive care costs and lost productivity costs (Table 1). Patients received monthly cost-diaries during three months.[29-33] If cost diaries were not returned (after two postal reminders), information was collected by telephone. Three attempts were made to reach patients by telephone.

Primary care costs consisted of costs for contacts with the general practitioner and other primary healthcare providers such as social work, paramedical and complementary care givers. Secondary care costs consisted of hospital admission costs (i.e. hospitalisations, one-day care and ED-visits), costs for outpatient visits and laboratory tests. Medication costs consisted of costs for prescription and non-prescription (i.e. over-the-counter) medication. Supportive care costs consisted of costs for home care, help from family/friends and help for housekeeping. Costs due to productivity losses consisted of absenteeism from paid and unpaid work.

Data regarding admissions and prescription medication were not collected through cost diaries. Data on admissions were collected using the hospital information systems of the St. Lucas Andreas hospital and the five other hospitals. Information on prescription medication was extracted from the hospital's CPOE (Computerized Physician Order Entry) at discharge. Medication costs were calculated using Dutch prices from September 2011.[34] The medication costs at hospital discharge were extrapolated to three months.

Dutch guideline prices were used to value resource use (Table 1).[35] When the number of hours of home care received was unknown, the mean number of hours reported by a leading Dutch home care organisation was used.[36] Paid work absenteeism was valued with Dutch standard costs using the mean income of the Dutch population according to age and gender. It was assumed that one working day matched eight productive hours. Unpaid work absenteeism was valued with Dutch standard costs.[35] If a patient did not report the amount of unpaid work hours lost, the mean society's number of hours according to gender was used.[37]

Table 1 Prices used in the economic evaluation, corrected for the year 2010

Type of utilization	Price weight (euro)
Intervention costs (per patient)	
COACH program	41.04
Primary care: GP (per consult)	
GP consultation at practice	28.35
GP home visit	43.53
GP contact by phone / repeat recipe	14.17
GP contact unknown	28.68
Primary care: other (per consult)	
Mental healthcare	
Social worker	65.80
Psychologist	80.99
Psychiatrist	104.27
Regional institute for mental welfare	173.11
Paramedical care	
Physiotherapist	36.44
Manual therapist	54.67
Clinical nurse specialist	14.44
Dietician	13.67
Complementary care	
Complementary therapists	Patient[a]
Secondary care: admission	
Hospital admission/day (general hospital)	440.37
Hospital admission/day (academic hospital)	582.09
Intensive care unit/day	2209.93
Emergency department/visit	152.86
One-day hospital care/visit	254.10
Secondary care: other (per consult)	
Specialist	
Specialist visit at outpatient department	72.89
Specialist contact by phone	36.44
Laboratory test	13.06
Medication (per prescription)	
Prescription drugs	Dutch prices[b]
Non-prescription drugs	Patient[a]
Help received (per hour)	
Help for family welfare	24.30
Help from family/friends	12.65
Home care[c]	35.43
Productivity losses (per hour)	
Absenteeism from paid work	23.91 - 39.61[d]
Absenteeism from unpaid work[e]	12.65

[a] Costs were based on the information provided by the patient
[b] Medication costs for medication prescribed at discharge were extrapolated for three months using Dutch prices[34,41]
[c] If number of hours was not specified, 22 hours per month was assumed (based on mean use per month as reported by a leading Dutch homecare organisation)
[d] Range of costs depending on age and sex
[e] Absenteeism from household, voluntary work or study/course
GP= General Practitioner

Intervention costs

A bottom-up calculation was done to determine the costs of the COACH intervention.[38] For this calculation, the time spent by the pharmaceutical consultant on the intervention was converted into labour costs. The pharmaceutical consultants needed on average 62.7 minutes (standard deviation: 14.6) per patient. Based on a mean year salary of €50.000, assuming 46 annual working weeks and an efficiency rate of 70%, the labour costs for the intervention were €41.04/patient. We did not include costs of time spent by other healthcare providers, such as the clinical pharmacist or the hospital physician, because the extra tasks were performed by the pharmaceutical consultants.

Baseline characteristics

Patient characteristics were extracted from the medical records of the hospital information system including gender, age, length of stay, and previous hospitalisations (i.e. planned/unplanned admissions) and hospital contacts (i.e. planned/unplanned admissions, one-day care and ED visits) in the six months before inclusion. The Charlson co-morbidity score was used to evaluate the severity of co-morbidities.[39] Data regarding co-morbidities were obtained from the discharge letter and hospital information system. Increased Charlson co-morbidity scores have been shown to be associated with an increased number of hospitalisations.[39,40] Validated forms were used to obtain information on other characteristics from patients themselves, including information on ethnicity, help with medication use, and marital status.

Data analysis

Patients included in the COACH program and usual care group were compared on all baseline characteristics using independent T-tests for continuous variables and chi-square tests for categorical variables.

Analyses were based on group allocation, regardless of whether patients received the complete COACH program, i.e. intention-to-treat analysis. Missing cost and effect data were imputed separately for the usual care and COACH group using multiple imputation with Fully Conditional Specification and Predictive Mean Matching in SPSS 19.[41] A multiple imputation model was built that included patient's baseline characteristics that differed between patients with complete and incomplete follow-up, were associated with an unplanned rehospitalisation ($p<0.20$) or with total costs after three months ($p<0.20$). Included characteristics were sex, age, race, marital status, education level, receiving help with medication use, admission type (planned/unplanned), Charlson co-morbidity score, kidney function, number of medications at hospital admission and previous hospitalisations in the six months before inclusion. Five complete data sets were created.[41]

To estimate adjusted cost differences and associated standard errors regression models were bootstrapped with 5000 replications in StataSE 10 to allow correction for confounding variables ($p<0.10$). Next, the estimates per data set were pooled using Rubin's rules.[42] Both a cost-effectiveness and cost-utility analysis were performed while correcting costs and effects for confounders. Incremental cost-effectiveness ratios (ICER) were calculated by dividing the adjusted difference between the mean costs of the two groups by the adjusted difference in the mean outcomes at three months. To avoid double counting, we excluded the costs of unplanned rehospitalisations in the ICER calculation with unplanned rehospitalisation as effect measure. The uncertainty surrounding the ICERs was estimated by bootstrapping bivariate regression models in StataSE 10 including a separate set of confounders for costs and effects (5000 replications).

The bootstrapped cost effect pairs were represented visually using the cost-effectiveness plane.[43] The horizontal axis divides the plane according to incremental cost (more expensive above, less expensive below) and the vertical axis divides the plane according to incremental effect (more effective on the right, less effective on the left). This divides the incremental cost-effectiveness plane into four quadrants.[44] The distribution of the cost-effectiveness pairs over the four quadrants is an indication of the uncertainty around the ICER. Cost-effectiveness acceptability (CEA) curves were also estimated. In a CEA curve the horizontal axis shows the threshold (ceiling ratio), which represents the maximum amount of money that a decision maker is willing to invest to gain 1 unit of effect extra. The vertical axis shows the probability that the intervention is considered cost-effective in comparison with usual care for a specific ceiling ratio.[45]

Sensitivity analyses

Sensitivity analyses were performed to assess the robustness of the results. In the first analysis only complete cases (i.e. patients for which cost diaries for all three months were present) were included. In the second sensitivity analysis, costs of productivity losses were excluded from the total costs.

As a sensitivity analysis for the cost-utility analysis, we used a baseline quality of life value at the moment of discharge (0.39) as reported in a previous study that also included a similar internal medicine patient population.[46]

RESULTS

A total of 2274 patients were screened for eligibility for the main study; in total 1486 (65%) patients were excluded (Figure 2), leaving 788 patients (394 patients COACH program, 394 patients usual care) who were included in the main study. Of these 788 patients, 469 (60%) were excluded and 319 patients consented to collect data through monthly sent cost diaries (168 patients COACH, 151 patients usual care). Sixty-five patients (39% of 168) in the COACH program group and 41 patients (27% of 151) in the usual care group were lost to follow up. Reasons for dropout were: patient was unreachable, loss of interest, and feeling too ill to participate in the study.

Patients who participated in the main study, but did not give informed consent for collecting data through cost-diaries received more often help with their medication use (31% no consent vs 18% with consent, $p<0.01$) and were more often non-native Dutch (38% vs 27%, $p<0.01$) than patients who did give informed consent. No differences were found for other baseline characteristics.

Patients included in the COACH group had a higher Charlson co-morbidity score (more severe co-morbidities) compared to patients in the usual care group (Table 2). Other baseline patient characteristics did not differ between the two groups.

Outcomes and costs

In Table 3 the unadjusted and adjusted pooled outcomes and costs are summarised. The proportion of patients with an unplanned rehospitalisation did not significantly differ between groups (21.4% COACH vs 20.5% usual care, adjusted 95% CI: -8.88 – 8.55). There was also no significant difference in QALY's (0.15 COACH vs 0.17 usual care, adjusted 95% CI: -0.0170 – 0.0001). Secondary care costs and lost productivity costs were the greatest contributors to total costs in both groups (68% for COACH vs 75% for usual care, Table 3). Primary care costs and lost productivity costs were higher for usual care patients than for patients included in the COACH program. Secondary care costs and costs for supportive care were higher for the patients included in the COACH program. However, only the costs for lost productivity were statistically significantly lower for the COACH program group in comparison with usual care (€2249 COACH vs €3879 usual care, adjusted 95% CI: -2773 – -342).

Total societal costs at three months after discharge did not statistically differ between groups (€6845 COACH vs €7952 usual care, adjusted difference -€1160, 95% CI: -3168 – 847).

Figure 2 Flowchart of inclusion of patients

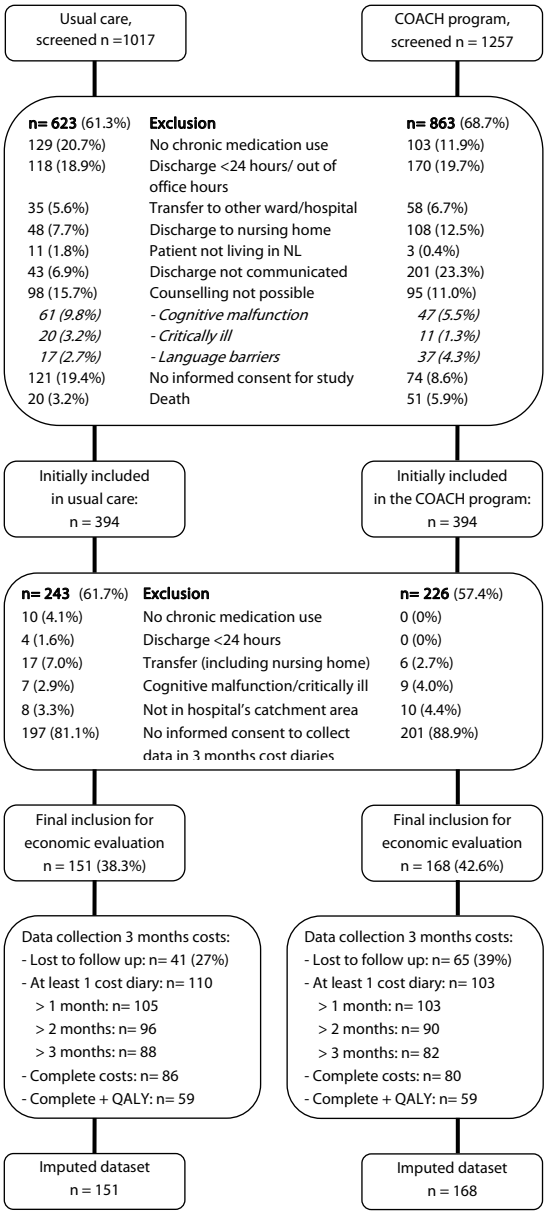


Table 2 Patient characteristics for usual care (before) and the COACH program (after)

Characteristic	Usual care (n=151)	COACH (n=168)	p-value
Female, n (%)	71 (47.0)	82 (48.8)	0.75
Age, mean years (SD)	64.5 (15.5)	64.5 (16.5)	0.99
Native Dutch (%)	114 (76.0)	118 (70.2)	0.25
No or low education level (%)	118 (78.1)	129 (77.2)	0.85
Married or having a partner (%)	73 (48.3)	74 (44.0)	0.44
Help with medication use, yes (%)	24 (15.9)	32 (19.0)	0.46
All hospital contacts in the last 6 m*, mean (SD)	0.98 (1.4)	0.95 (1.5)	0.87
Previous hospitalisations in the last 6 m†, mean (SD)	0.60 (1.0)	0.51 (0.9)	0.40
Admission type, planned (%)	40 (26.5)	41 (24.4)	0.67
Length of stay, range, mean days (SD)	8.4 (6.9)	8.8 (7.2)	0.64
N. of drugs on admission, mean (SD)	6.5 (3.4)	6.7 (3.9)	0.67
Reason for admission (%)			
Renal/urological	23 (15.2)	27 (16.1)	0.87
Liver/bile/pancreas	23 (15.2)	22 (13.1)	
Infection	30 (19.9)	25 (14.9)	
Gastrointestinal	24 (15.9)	27 (16.1)	
Diabetes	11 (7.3)	18 (10.7)	
Cancer	12 (7.9)	18 (10.7)	
Aspecific symptoms	13 (8.6)	14 (8.3)	
Other	15 (9.9)	17(10.1)	
Kidney function‡ (%)			
Dialysis	9 (6.0)	9 (5.4)	0.80
Decreased kidney function	32 (21.2)	43 (25.6)	
Unknown	8 (5.3)	7 (4.2)	
Total co-morbidities, mean (SD)	3.6 (2.0)	3.7 (2.3)	0.51
Charlson co-morbidity score (%)			
0-1	85 (56.3)	72 (42.9)	0.02
2-3	43 (28.5)	49 (29.2)	
4-5	16 (10.6)	27(16.1)	
>6	7 (4.6)	20 (11.9)	

* includes one-day care, ED visits, planned and unplanned admissions in the last 6 months before inclusion
† includes planned and unplanned admissions in the last 6 months before inclusion
‡ kidney function less than 60 ml/min during at least 3 months

Table 3 Pooled total effects and costs and differences in total effects and costs during follow-up

Pooled variables	COACH (n=168)	Usual care (n=151)	Difference unadjusted‡ (95% CI)	Difference adjusted‡ (95% CI)
Effects				
Unplanned rehospitalisation, n (% of pat)	36 (21.4)	31 (20.5)	0.90 (-9.09; 10.89)	-0.17 (-8.88; 8.55)
QALY*, mean	0.15	0.17	-0.0249 (-0.0407; -0.0091)	-0.0085 (-0.0170; 0.0001)
Costs, mean				
Intervention†	41†	0	41†	41†
Primary care	284	430	-146 (-338; 46)	-137 (-325; 51)
GP	101	101	0 (-31; 31)	1 (-29; 31)
Other	183	329	-146 (-338; 46)	-138 (-326; 50)
Secondary care	2409	2121	287 (-688; 1262)	251 (-679; 1182)
Admission	2095	1724	371 (-583; 1324)	352 (-563; 1267)
Other	314	397	-83 (-203; 36)	-101 (-221; 19)
Medication	448	430	18 (-145; 181)	-67 (-219; 86)
Prescription drugs	441	415	26 (-136; 188)	-59 (-212; 93)
Non-prescription drugs	7	15	-8 (-17; 1)	-7 (-17; 2)
Supportive care	1413	1091	322 (-194; 838)	308 (-230; 846)
Lost productivity	2249	3879	-1630 (-2827; -433)	-1558 (-2773; -342)
Total costs	**6845**	**7952**	**-1107 (-3108; 893)**	**-1160 (-3168; 847)**

* The maximum amount of QALY that can be achieved in three months is 0.25 units

† Based on our previous study. The time spent on the medication reconciliation process by the pharmaceutical consultant was converted into labour costs.

‡ The difference between the COACH program costs vs usual care costs. The effect difference for unplanned rehospitalisations was corrected for the following confounders: Charlson co-morbidity score, help with medication use, number of previous hospitalisations in the last 6 months before inclusion and number of drugs on admission. The effect difference for QALY was corrected for: Charlson co-morbidity score, number of drugs on admission, help with medication use and EuroQol value at baseline. The costs difference was corrected for the following confounders: age, number of previous hospitalisations in the last 6 months before inclusion, help with medication use, length of hospital stay and Charlson co-morbidity score.

Cost-effectiveness analyses

The main analyses (Table 4) showed that the incremental cost-effectiveness ratio (ICER) for decreasing rehospitalisations was -627251 (mean difference in societal costs, -€1038, divided by the mean difference in rehospitalisation, 0.0017). As the effect difference is very small, the ICER becomes very large and is, therefore, not easily interpretable. However, the bootstrapped cost-effectiveness pairs were mostly distributed among the Southeast and Southwest of the CE plane (Figure 3a), confirming the statistically non-significant differences found in the separate cost and effect analyses. The acceptability curve (Figure 3b) shows that the COACH program had a probability of being cost-effective in comparison with usual care ranging from 89% at a ceiling ratio of €0 to 68% at a ceiling ratio of €50.000. The probability that the COACH program was cost-effective, at a ceiling ratio of €5000, was 87%.

Table 4 Results of cost-effectiveness and cost-utility analyses

Outcome effect	Sample size					Distribution (%) cost-effectiveness plane			
	COACH	Usual care	Cost difference‡ (95% CI)	Effect difference§ (95% CI)	ICER¶	North east[a]	South east[b]	South west[c]	North west[d]
Main analyses									
Unplanned rehospitalisation*	168	151	-1038 (-2892; 815)	0.0017 (-0.0855; 0.0888)	-627251	5	47	41	7
QALY	168	151	-1158 (-3158; 842)	-0.0085 (-0.0170; 0.0001)	137059	0	1	88	11
Sensitivity analyses									
QALYest† in main analysis	168	151	-1158 (-3161; 845)	-0.0085 (-0.0170; 0.0001)	137059	0	1	88	11
Complete cases									
Unplanned rehospitalisation*	80	86	-834 (-2637; 969)	-0.0326 (-0.1355; 0.0703)	25592	4	23	59	13
QALY	80	86	-603 (-2618; 1413)	-0.0057 (-0.0128; 0.0015)	105951	1	4	70	24
Exclude productivity losses costs									
Unplanned rehospitalisation*	168	151	516 (-520; 1552)	0.0021 (-0.0854; 0.0895)	251750	43	10	6	41
QALY	168	151	398 (-817; 1614)	-0.0085 (-0.0170; 0.0001)	-47053	0	1	25	73

ICER=incremental cost-effectiveness ratio, calculated by difference in costs divided by difference in % of patients with an unplanned rehospitalisation or difference in quality adjusted life years (QALYs).

* To avoid double counting we excluded the costs of unplanned rehospitalisations in the cost calculation.

† Baseline quality of life used of a previous study

‡ The difference between the COACH program vs usual care. A positive cost difference means that the COACH program is more costly than usual care.

§ The difference between the COACH program vs usual care. A positive value for effect difference means that the COACH program is more effective than usual care. For the rehospitalisation outcome the effect difference value was multiplied with -1 to keep the cost-effectiveness plane understandable.

¶ Measures the additional cost per unit of health gain. A negative value indicates that the COACH program is in the northwest or southeast quadrant. A positive value indicates that the COACH program is in the northeast or southwest quadrant.

[a] COACH program more effective and more costly than usual care.

[b] COACH program more effective and less costly than usual care.

[c] COACH program less effective and less costly than usual care.

[d] COACH program less effective and more costly than usual care.

Cost-utility analyses

Both the cost and effect differences between the COACH and usual care group were not statistically significant. The adjusted difference in QALYs gained over three months was -0.0085 (adjusted 95% CI: -0.0170 – 0.0001) and the cost difference was -€1158 (adjusted 95% CI: -3158 – 842), resulting in an incremental ICER of 137059 (Table 4). This large ICER is again caused by the small effect difference and is not easily interpreted.

The cost-effectiveness plane (Figure 4a) shows that 88% of the bootstrapped cost-effect pairs are situated in the Southwest quadrant, indicating that the intervention is less effective and less costly than usual care albeit not statistically significantly. The acceptability curve (Figure 4b) showed a maximum probability of 89% that the COACH program was cost-effective compared with usual care at a ceiling ratio of €0 and decreased with increasing values for willingness to pay per QALY.

Figure 3a Cost-effectiveness plane for the risk of unplanned rehospitalisations

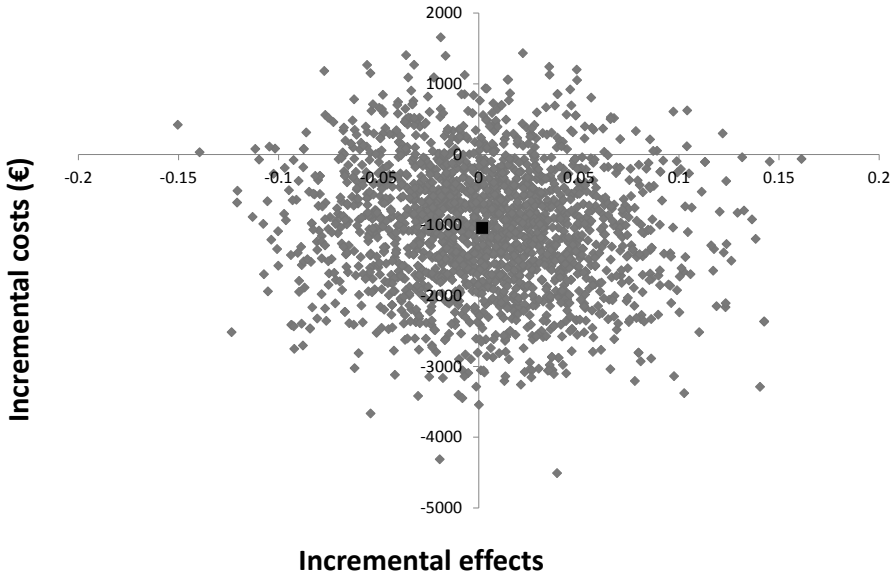


Figure 3b Acceptability curve for the cost-effectiveness analyses

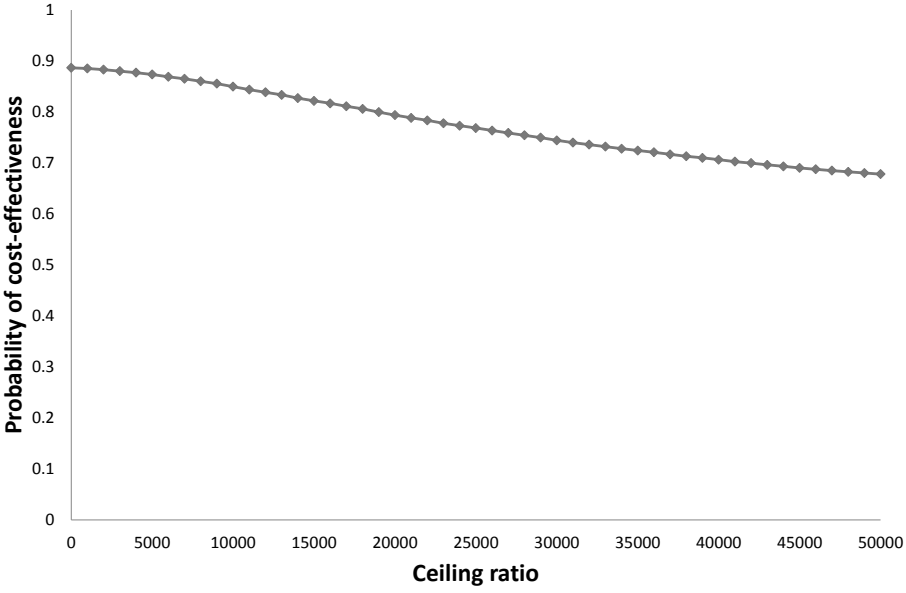


Figure 4a Cost-effectiveness plane for quality adjusted life years

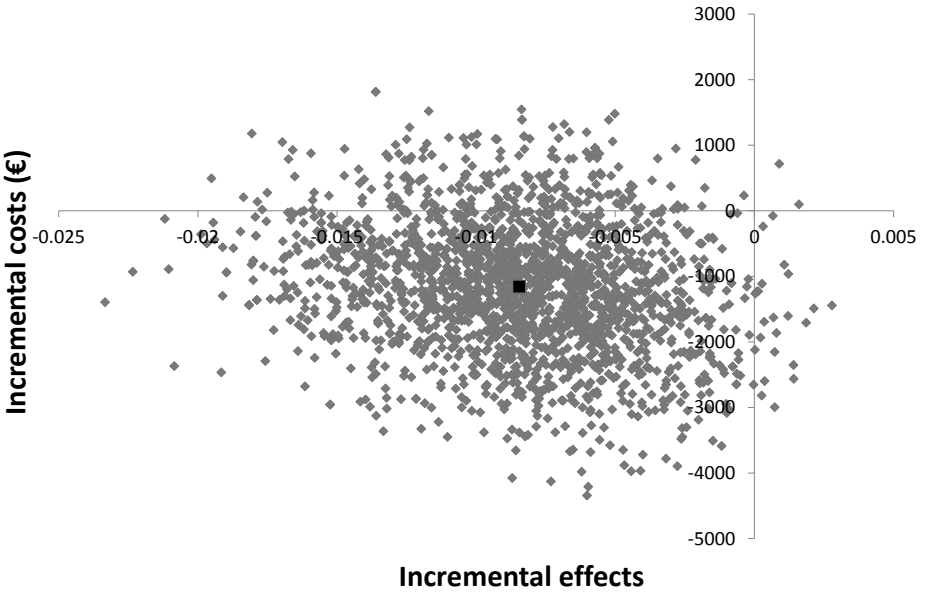
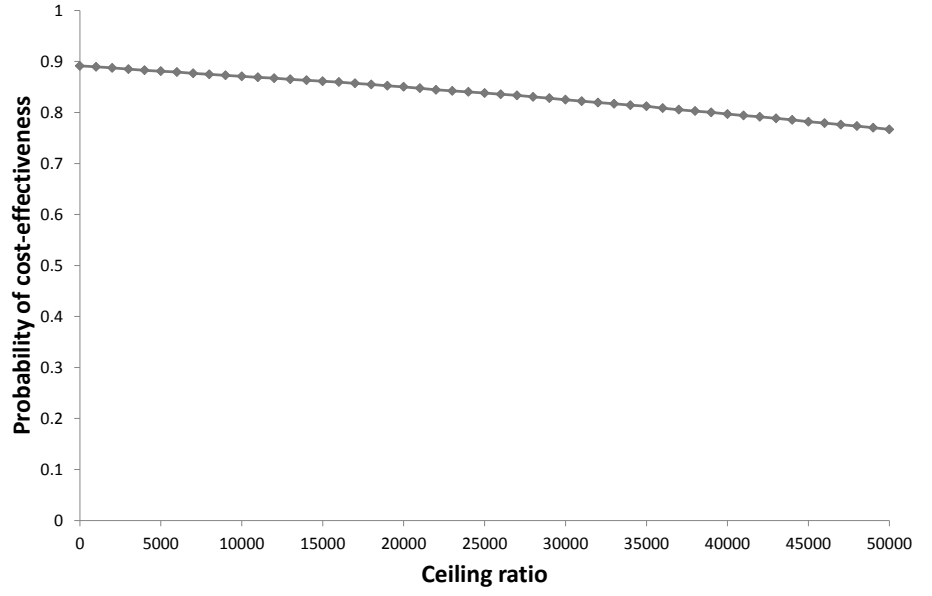


Figure 4b Acceptability curve for the cost-utility analyses



Sensitivity analysis

Results of the complete cases analyses also showed no statistically significant differences between groups (Table 4). A cost-difference of -€834 (adjusted 95% CI: -2637 – 969) in favour of the COACH group and effect difference of -3.26% (adjusted 95% CI: -13.55 – 7.03) in favour of the control group was seen. In this analysis, the COACH program was also not considered cost-effective in comparison with usual care.

Exclusion of lost productivity costs also showed no statistically significant differences (Table 4). However, the cost-difference in this sensitivity analysis favoured the control group (€516, 95% CI -520 – 1552). The acceptability curve showed a probability of 16% that the COACH program was cost-effective at a willingness to pay no additional money to 44% at a willingness to pay €50.000 compared with usual care. The acceptability curve for QALY showed similar reductions in the probability to be cost-effective compared to the main analysis (figures not shown).

The results of the sensitivity analysis for the quality-adjusted life-years showed no difference with the main analysis (Table 4).

DISCUSSION

This study showed that the COACH program with three months follow-up was neither statistically significantly effective in reducing the risk for unplanned rehospitalisations (21.4% COACH program vs 20.5% usual care) nor that it had a favourable effect on quality-adjusted life-years gained (0.15 vs 0.17) or total costs (€6845 vs €7952). Based on the cost-effectiveness and cost-utility analyses it was concluded that the COACH program is not cost-effective in comparison with usual care.

Previous economic evaluations showed variable results.[17,23,24] Karnon et al. described a model-based cost-utility analysis of a pharmacist-led medication reconciliation intervention at hospital admission in comparison to usual care (no structural medication reconciliation).[23] The pharmacist-led medication reconciliation intervention had the highest expected net benefits on decreasing adverse drug events, and a probability of being cost-effective of over 60% for willingness to pay values of £10.000 per QALY or more. In another study, total costs per patient in the intervention group were $230 lower than costs in the control group, but this difference was not statistically significant.[17] In our economic evaluation we found no difference in total costs. Although the cost-difference was in favour of the COACH program for the main analysis, confidence intervals were very wide due to the small sample. The main cost driver was the lost productivity costs. After exclusion of these costs the cost-effectiveness planes and acceptability curves showed that the COACH program cannot be considered to be cost-effective.

Limited healthcare budgets increase awareness regarding the benefits and cost-effectiveness of new interventions. Similar to other studies, we found no effect on rehospitalisations and quality of life.[15,16,18,21,47-50] Previous studies have shown that more intensive interventions for high risk patients and a longer follow-up had positive effects on rehospitalisations and quality of life.[17,20,46] Therefore, we expect that transitional care programs could be cost-effective, but research should indicate what the effective components are. Furthermore, some costs are difficult to measure. With medication reconciliation medication errors may be prevented. The hospital could save time and thus money as less medication errors need to be rectified. The same may apply for primary healthcare providers who may need less time to clarify whether medication changes are intentional. Furthermore, uncorrected medication errors could lead to adverse drug events.[51-53] Estimates of costs per adverse drug event range from €900 - €1800.[23,54] In this study, adverse drug evens were not measured.

Strengths of this study are that we collected multiple cost data from a societal perspective and we obtained admission data in other hospitals also. Limitations of this study also need to be discussed. First, a selection bias is likely. Only 21% of patients included in the main study also participated in the economic evaluation. Patients regarded the data collection as a burden or were not interested in the study. Patients not participating in the economic evaluation received significantly more frequent help with using medication and were significantly more frequent non-native Dutch. This limits generalisability of the results. Also, patients included in the COACH program had more severe co-morbidities than usual care patients. We adjusted for this, but unknown confounders may be present. Second, complete cost data were available for 54% of the patients. Although patients were contacted by telephone to increase response, this had only a limited effect. Multiple imputation was used to impute missing data. However, it would have been better to obtain more data from registries and to telephone patients instead of sending a cost diary by post. Baseline data for quality of life at the moment of discharge was not assessed. Therefore, the results of the cost-utility analysis should be interpreted with caution. Finally, the follow-up of three months may have been too short to show an effect on quality of life.

Recommendations for future research include the following. It needs to be assessed which components of transitional care programs are effective. New studies should evaluate more intensive interventions, focus on higher risk groups and assess multiple outcomes. Finally, follow-up should be extended to a period of at least one year.

In conclusion, the total costs and outcomes for the COACH program did not significantly differ from the total costs and outcomes for usual care. From a societal perspective, after three months the COACH program was not considered cost-effective compared to usual care. Future studies are needed to assess whether and which components are effective for patients transitioning from the hospital setting to the community setting.

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We shall not cease from exploration,
and the end of all our exploring
will be to arrive where we started
and know the place for the first time.

(T. S. Eliot: poet, 1888-1965)

Arabic translation of quote and design by Everitte Barbee

PART

5

General discussion

The consequence of current fragmented healthcare is that patients see multiple healthcare providers who are not always aware of medication prescribed by others. National and international guidelines stress the importance of transitional care programs for enhancing continuity of pharmaceutical care to decrease patient harm or discomfort.[1-5] The objective of this thesis was to summarise existing evidence on transitional pharmaceutical care interventions and to develop and evaluate a transitional care program with respect to effects and costs.

In Part 2 of this thesis a systematic review showed that various discharge medication related interventions were mainly reported to be effective for process measures (knowledge, adherence and drug-related problems). In Part 3 it was shown in Chapter 3.1 that general practitioners desired information regarding the reasons for changes in the pharmacotherapy. Patients had variable needs concerning information about discharge medication, e.g. regarding side effects, so information at discharge should be tailored to individual needs (Chapter 3.2). Patient participation in medication reconciliation was shown to be essential in Chapter 3.3. Discharge prescriptions were frequently adjusted after patient counselling due to discrepancies in use or need of drug therapy. With medication reconciliation interventions were performed aimed at preventing drug-related problems. These interventions resulted in higher medication cost savings after hospital discharge than the costs related to the net time investment (Chapter 3.4). In Chapter 3.5 it was shown that continuity of pharmaceutical care after hospital discharge failed in the majority of community pharmacies as relevant discharge medication information (e.g. allergies/medication changes) was not documented. In Part 4 the development of the transitional care program, COACH (Continuity Of Appropriate pharmacotherapy, patient Counselling and information transfer in Healthcare), was described (Chapter 4.1). The COACH program prevented DRPs in all patients and increased patient satisfaction with counselling, but showed no decrease of all-cause unplanned rehospitalisations (Chapter 4.2). A cost-effectiveness study (Chapter 4.3) showed that the COACH program was not considered cost-effective.

In this final Part 5 the presented studies will be put into broader perspective. First, the importance of a pre-implementation evaluation and a conceptual model of the healthcare system (a causal chain) will be discussed. The pre-implementation evaluation and causal chain will aid in our understanding of linking complex interventions to outcomes and in interpreting patient safety research. Thereafter, the pre-implementation evaluation and the causal chain will be applied to the COACH program to show the specific context and show where the program intervened in the causal chain. Second, the causal chain will be used to discuss the methodological issues of patient safety research and the COACH program. We will focus on the COACH program as this was our final transi-

tional care program and main intervention. Finally, the implications of this thesis and further research questions will be discussed.

PRE-IMPLEMENTATION EVALUATION AND CAUSAL CHAIN

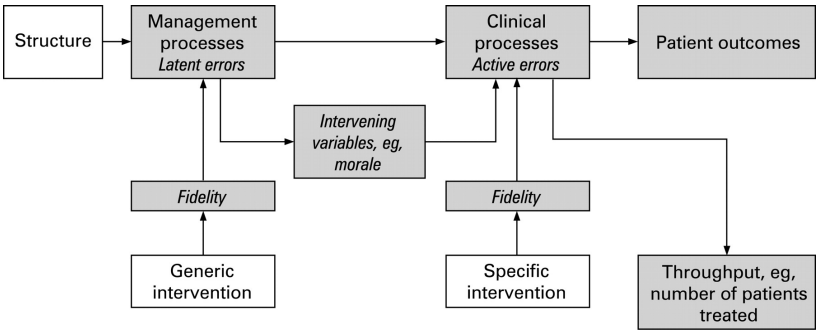
As patient safety interventions are often complex and are applied in a complex healthcare system, they need to be evaluated before implementation. This pre-implementation evaluation is conceptualised in four stages, see Table 1.[6]

The quantity of patient safety research has risen substantially over the past decade since the Institute of medicine published *To Err Is Human: Building a Safer Health System*.[7,8] Nevertheless, concerns remained over the quality of much of this research. As a result, the American Medical Research Council published a report with a conceptual model of the system within which a healthcare organisation operates. This causal chain links interventions to outcomes, see Figure 1.[7] The chain starts with the "structure" (i.e. exogenous factors, e.g. national directives, licensing procedures, budgets). Next come the endogenous processes that are under local control. With "management processes", such as a human resource policy or structural training of new staff, latent errors at an organisational level can be prevented. Interventions focused on management processes can affect patient safety outcomes through their effect on intervening variables such as the culture of an organisation, knowledge, beliefs and staff behaviours.[6] The following step is formed by "clinical processes" (e.g. adoption of safety practices, quality of patient education) that are important to prevent active errors which involve direct interaction with the patient.[6] Interventions on clinical processes are expected to have a large effect on a small number of errors whereas management interventions will have a smaller effect across many clinical processes and outcomes.[7]

Table 1 Four stages of the pre-implementation evaluation

Stage	Explanation
1	Recognising the need for an intervention to improve patient safety
2	Identifying the main problems in existing practice
3	Design and describe the intervention in detail
4	Re-design intervention after proactive risk assessment

Figure 1 Causal chain linking interventions to outcomes; conceptual model of the system within which a healthcare organisation operates[6]



The shaded boxes represent the end points that could be measured in an evaluation of a patient safety intervention. Surrogate end points are shown in italics.
Latent errors = A defect in the design, organisation, training or maintenance in a system that leads to operator errors and whose effects are typically delayed or lay dormant in the system for lengthy periods of time.[9] Active errors = An error that occurs at the level of the frontline operator and whose effects are felt almost immediately.[9] Fidelity = Measures whether an intervention was implemented as planned.[7]

A mixed methods research (i.e. qualitative and quantitative) is advocated to make observations at different levels across the causal chain, to help explain findings, generate theory and help contextualise and generalise results.[10] It is also recommended to use patient outcomes and surrogate end points. If results point out in the same direction causality between intervention and effect will be more plausible. Fidelity measures whether an intervention was implemented as planned. Therefore, a positive result for fidelity shows that positive results further down the causal chain are plausible, while a negative result can help to explain a null result.[7,11]

For patient safety research in general, understanding of the pre-implementation evaluation and the causal chain are important. Safety interventions are notoriously prone to back fire (e.g. residents forgetting to write discharge prescriptions and counsel patients when the hospital pharmacy did/could not perform the COACH program). For this reason proposed interventions to improve safety should all be screened though a systematic process of pre-implementation.[6] The idea is to reduce the risks that an intervention will not work well or will introduce new hazards. The causal chain highlights the opportunities for making multiple observations to obtain a rich picture of the effect of implementing a safety intervention and understand why an intervention works in one setting and does not in the other (e.g. differences in fidelity, context and culture). If an intervention was implemented with high fidelity, resulted in positive changes in intervening variables, reduced errors and improved outcomes, this tells a story even if the effect on outcomes itself was not statistically significant.[7]

Development and implementation of the COACH program

The studies presented in Chapter 2 and 3 of this thesis describe the pre-implementation evaluation of the COACH program (Table 2).

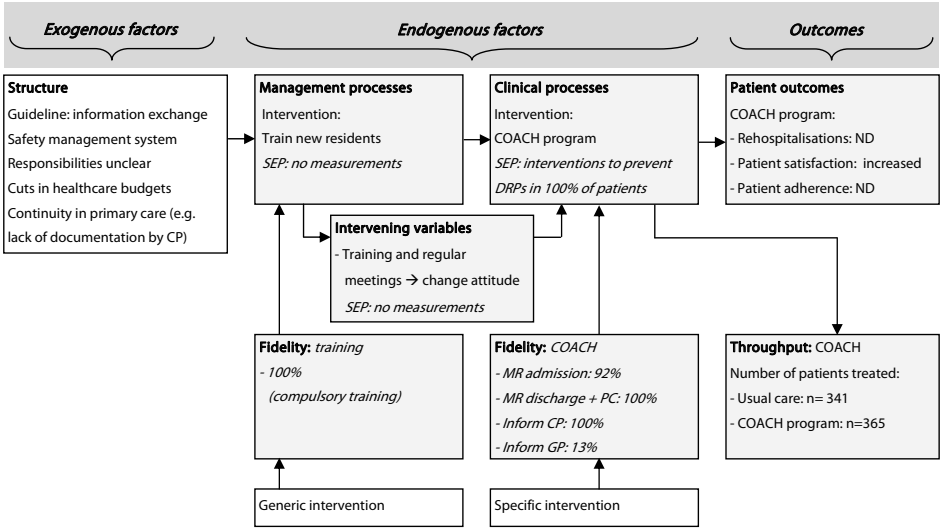
Table 2 Pre-implementation evaluation and the development of the COACH program

Stage	COACH program development
1 assess intervention need	• Current evidence base: systematic review (Chapter 2) • Experiences of clinical staff/patient questionnaires
2 identify main problems	• Information from literature and meetings with department staffs • Patient and general practitioner preferences (Chapter 3.1 and 3.2) • Type of medication errors that can be prevented (Chapter 3.3) • Documentation of discharge medication related information by community pharmacies (Chapter 3.5)
3 design and describe	• Develop COACH program in hospital (using Chapters 3.1-3.4) • Study protocol for COACH program (Chapter 4.1) • Develop instruction manuals for community pharmacies (Chapter 3.5)
4 Re-design	• Interview staff/patients: adjust COACH program (e.g. phone staff at standard times, train staff, adjust contents for patient counselling) • Interview community pharmacies: adjust instruction manuals (e.g. stepwise explanation of method for documentation)

The COACH program is a specific intervention mainly focusing on clinical processes; see Figure 2 for the causal chain of the COACH program.

The pre-implementation evaluation (Table 2) and the causal chain (Figure 2) put the COACH program into perspective. The COACH program addressed parts of the causal chain, measured some surrogate end points and patient outcomes. The causal chain also shows the exogenous context in which the COACH program had to operate. Although there were factors supporting the implementation of the COACH program (i.e. guideline regarding medication information transfer and the hospital safety management system regarding medication reconciliation), responsibilities of different healthcare providers were not clearly defined in these reports. Also, cuts in healthcare budgets made implementation of COACH more difficult. Furthermore, continuity of care in the primary care setting was hampered as community pharmacies failed to document discharge medication related information. Regarding endogenous context, compulsory training was implemented for (new) residents to influence management processes and the COACH program itself was implemented to influence clinical processes. The fidelity with the implementation of the COACH program was good, except for the part of informing general practitioners regarding the discharge medication. The program had a significant impact on the surrogate end point drug-related problems (DRPs). At least one intervention to prevent DRPs was recorded in all patients. Regarding patient outcomes the

Figure 2 Causal chain linking interventions to outcomes: implementing the COACH program



COACH= Continuity Of Appropriate pharmacotherapy, patient Counselling and information transfer in Healthcare, CP= community pharmacy, GP= general practitioner, MR= medication reconciliation, ND= no significant difference, PC= patient counselling, SEP= Surrogate End Points

COACH program did not reduce unplanned rehospitalisations and did not increase patient adherence. Patients were more frequently satisfied with counselling provided by pharmaceutical consultants compared to residents.

Now that patient safety research and the implementing of the COACH program has been put into perspective, the methodological issues concerning this kind of research can be made clear in the following paragraph.

METHODOLOGICAL ISSUES REGARDING DISCHARGE MEDICATION RELATED INTERVENTIONS

Study designs

Experts debate what constitutes rigor in the design of studies evaluating interventions on patient safety.[8] Table 3 shows the potential study designs.

For the COACH program a parallel randomised controlled trial was considered not feasible for the following reasons. First, the program changed the way care was organised at the department. It would be far more difficult to turn the intervention on and off than it would be in a single drug trial. During pre-implementation we observed that some

Table 3 Quantitative study designs for patient safety research (in order of methodological strength)[7,12,14]

Quantitative study design	Advantages	Disadvantages
Randomised designs	• Best method for evaluating efficacy and explaining cause-effect • High internal validity	• Time consuming and expensive • May have ethical restrictions* • Low external validity
1 Randomised controlled trials (randomisation on patient level)	• Randomisation minimises confounding • Allocation concealment minimises bias	• Contamination of control group (dilution of intervention effect)
2 Cluster randomised trials (randomisation on group level)	• Less contamination of control group • Quicker and more straightforward for health interventions	• Reduced variability of responses (larger sample size needed) • Comparability clusters?
Nonrandomised designs	• May be more ethical*; all patients receive the intervention • In general more practical	• Unknown confounders • Increased possibility of bias
3 Stepped wedge design (controlled before-after study with sequential rollout of interventions over clusters, the order of rollout may be randomised)	• Clusters are their own controls minimising bias • Effect of time can be included • Series of observations possible: interruptions evidences cause-effect better	• Large amount of data collection • Large amount of resources needed (increasing costs)
4 Before-after studies with time series (including the effect of trends)	• Practical and less costs than 3 and 5 • Effect of time can be included • Series of observations possible	• Effects could be attributed to developments other than the intervention
5 Controlled before-after studies (data collected in both control and study patients before and after the intervention)	• Less confounding and bias than 4 if groups are comparable • Effect of time can be included	• Difficulty in suitable control group • More data collection than design 4
6 Uncontrolled before-after studies (data collected in single before and after observations)	• Practical and low cost	• Effect of time/trends is missing • Effects could be attributed to other developments

*patient safety interventions are often anticipated to do more good than harm. The emphasis is generally on how treatments can be delivered effectively, rather than on the measuring the difference an idealised treatment makes.[12,15]

residents learned from the intervention. This contamination of the control group due to receiving parts of the intervention would dilute the effect of the COACH program.[12] As our primary outcome, rehospitalisations, is influenced by many aspects of care and the COACH program addressed parts of these, we did not expect a high magnitude of change. Second, during pre-implementation we observed that medication reconciliation decreased medication errors, that patients notified the patient counselling activities and asked the pharmaceutical consultants when they would counsel them. We did not feel comfortable in providing the intervention to a selected group of patients. Instead, all patients received the COACH program as far as possible.

The problems addressed above could be solved by using a cluster randomised controlled trial. However, larger sample sizes would be needed due to loss in power as patients in a cluster show less variability in outcomes than individual patients. Increasing the sample size would be costly. Second, we would have needed to define a comparable cluster. This was not possible since we have only one internal medicine department in our hospital. A multicenter trial was not possible at that time due to financial constraints and lack of

man power. We could have clustered residents within the department, but this would again increase the risk of contamination.

To reduce the risk of bias when randomised trials are considered unsuitable, a stepped wedge design is advocated. An intervention is rolled-out sequentially to the trial participants (e.g. multiple clusters) over a number of time periods.[12,14] Clusters in the trial act as their own controls. In the statistical model the effects of time can be included, hence controlling for temporal changes in the effectiveness of the intervention.[12] The stepped wedge design needs multiple clusters and therefore is more suitable for multicenter trials. The COACH program was studied at one department only.

Much safety improvement research involves before and after studies in single institutions as this is a practical method of evaluation.[12] Controlled before-after studies are costly. Uncontrolled before-after studies are a relatively weak method to distinguish cause and effect. The change measured could plausibly be attributed to developments in the service other than the intervention of interest or care.[12] Therefore, we have chosen for an observational before-after design including interrupted time series as the preferred alternative. A series of observations (time series) provides better evidence of cause and effect than differences in single before and after observations as regression to the mean is less likely if serial observations show improvements. But, it should be kept in mind that unknown confounders and bias remain a concern.

Patient outcomes and surrogate end points

A focus on clinical outcomes (morbidity) may seem ideal, but as the signal to noise ratio tends to be low there is a high risk of false negative results.[7] Regarding readmissions, Krska et al. reported that only 22% of all (un)planned admissions were related to pharmaceutical care issues and 13% were possibly preventable by pharmacist intervention. They discuss that it is better to focus on medication-related admissions instead of all-cause readmissions, but this would inevitably increase the sample size as the mean number of all admissions was 0.13/patient versus medication-related admissions at 0.04/patient.[16] The sample size for the COACH program was based on a median reduction of readmitted patients with 8%, extrapolated from literature (20% usual care vs 12% intervention). However, these studies included nursing home patients and interventions were not solely based on medication.[17-20] When taking the results of the systematic review into account (Chapter 2), larger sample sizes would be calculated. One could argue that if an intervention requires a high number needed to treat, then the individual patient will not benefit and therefore the intervention is ineffective. However, decreasing rehospitalisations at a population level could have substantial effects on healthcare.

Hospital readmission as an outcome has been widely used in evaluating the quality of healthcare provided because it is prevalent, costly and possibly preventable.[21-23] In contrast, several problems have been identified with this outcome. First, several definitions

are listed in literature, some focus on the first readmission, while others focus on the proportion of patients readmitted or the mean number of readmissions per patient.[22-24] The difference between readmission (hospitalisations to study hospital only) versus rehospitalisation (all hospitalisations, including other hospitals) is frequently not stated. Second, the exact time frame for measuring readmissions is unclear. In recent studies, 30 day readmission rate is frequently measured because there is an early peak of readmissions within a few weeks of discharge. A longer time frame is believed to be associated with the inclusion of higher number of false positives or unrelated readmissions (e.g. readmissions due to natural disease progression).[23] For a transitional pharmaceutical care program as COACH, this argument may not apply. For example, side effects of medication can occur later, preventive medication (e.g. adding a bisphosphonate for a patient using chronic prednisolone aiming to prevent osteoporosis) may need more time to sort effect (i.e. prevent a rehospitalisation due to a fall). We lack knowledge regarding when medication related rehospitalisations occur, and therefore do not know what the exact time frame should be. Third, the quality of community care can act as a confounder. Rehospitalisation may be prevented by exceptional community care and vice versa.[23] Finally, risk factors for (preventable) rehospitalisations remain unknown.[25] A recent systematic review showed that 26 risk prediction models had poor predictive ability.[26] Lack of knowledge regarding risk factors equals lack of knowledge regarding possible confounders that need to be measured in studies. A second review discussed that of 43 articles no single intervention implemented was regularly associated with reduced risk of 30-day rehospitalisation.[27]

The problems described above raise the question whether rehospitalisations are a good outcome to evaluate interventions such as COACH. Measuring rehospitalisations is still important because we need to understand this outcome better. Furthermore, it is important to check whether a certain intervention does not lead to patient harm. But, the focus should not be solely on rehospitalisations. For transitional pharmaceutical care programs we need measures that are more related to medication and more prevalent. Adverse drug events (ADEs) are the most common post-discharge complications, are correlated to hospital readmissions and are also costly.[28-30] The disadvantage of this outcome is that it is harder to assess than rehospitalisations. Schnipper et al. contacted patients after discharge and used screening questions to assess ADEs.[31]

As patient outcomes are insensitive to most safety interventions, Brown et al. discuss that surrogate outcomes and fidelity should also be measured within the causal chain.[11] In 100% of patients interventions to prevent drug-related problems were performed, showing that the COACH program had a significant impact on this outcome. The COACH program was implemented with good fidelity except for the part of informing the general practitioner regarding the discharge medication. Residents did not always want to wait until the discharge overview was delivered by pharmaceutical consultants after

patient counselling. They copy pasted an incorrect or incomplete medication list from the computerized physician order entry system into the discharge letter. Furthermore, in Chapter 3.5 it was shown that community pharmacies fail to document discharge medication related information and therefore fail to proceed continuity of care after hospital discharge.

Discharge medication related interventions: why don't they all work?

Numerous guidelines and reports have been published discussing the need for continuity of pharmaceutical care. Yet, as shown in the systematic review (Chapter 2), there is a high variability in the results. This variability may be due to the context of the study, the patient population, the fidelity and complexity of implementing the intervention, the methodological quality of the study, the sample size, the measurement method etc. Even when taking these factors into account, the amount of studies that decreased readmissions is disappointing (18%, 3 of 17 studies, Chapter 2). The COACH program also did not decrease rehospitalisations. Several explanations may be considered. First, the question arises whether the focus on medication related interventions is enough. Systematic reviews for improving the discharge of heart failure patients showed significant decreases in hospital readmissions.[32,33] This could be due to the specific patient population, additional post-discharge support by healthcare providers, more collaboration between settings or because the intervention focus was not restricted to medication only. Evidence on components effective for patient safety interventions is limited.[34] Second, in many studies a pharmacy healthcare provider was added to the care team. This could lead to more complexity and fragmentation of care. In the studies on heart failure, mainly nurses and physicians performed the intervention and the pharmacist could support some parts of the intervention.[32,33] Pharmacy members may lack knowledge about all relevant aspects regarding the patient's care (e.g. disease factors, lifestyle factors). Third, reducing rehospitalisations or increasing continuity of care is not only a hospital based issue.[35] All healthcare providers within the continuum have a role in providing continuity. With the COACH program we were able to change the processes that were performed by the pharmaceutical consultants themselves (i.e. medication reconciliation at admission and discharge, patient counselling and communication to community pharmacy). We had far more difficulties in improving the communication to general practitioners as residents had to upload the prepared medication overview into the discharge letter. And even if communication was performed, we showed that the majority of community pharmacies failed to document relevant discharge medication related information and therefore failed to provide continuity (Chapter 3.5). As long as healthcare providers do not work as a continuum, a decrease in (drug-related) rehospitalisations is a distant goal. Finally, studies that did decrease readmissions were more

comprehensive. The COACH program focussed mainly on the discharge process, while effective studies intervened also on admission and during hospital admission.[36,37]
The COACH program did not differ in satisfaction with information about medicines (SIMS questionnaire), beliefs about medication and adherence. Also, a general satisfaction question was asked. Patients were significantly more satisfied with the counselling provided by the pharmaceutical consultant (87.1%) compared to the resident (68.9%). The qualitative study in chapter 3.2 also showed that patients appreciated the discharge counselling and especially found the written material useful. Patients who were counselled were more satisfied, and felt reassured that their medication was checked and was complete. They were also satisfied because they had the opportunity to ask questions. These aspects were not covered by the SIMS questionnaire. So, this might explain the difference between the results of the SIMS questionnaire versus the results of the general questionnaire and the qualitative study. Furthermore, the qualitative study showed that patients generally were not dissatisfied with usual care. This aspect was also seen in the results of the questionnaires as high scores were reported.
The lack of improvements regarding beliefs about medication and adherence was not surprising. Although, the systematic review (Chapter 2) showed that 70% of studies increased adherence, our study including only one counselling session at discharge did not change patient's beliefs and attitude to adhere. Interestingly, patient's reported adherence was high for usual care and COACH program patients (mean 23, while maximum score is 25). So, a ceiling effect may be possible. It could also be that previous studies dedicated more time to the counselling or were better able to influence patients. Further, the discharge moment may not be the appropriate time to counsel patients. Counselling at home may be a less stressful moment and patients may be more concentrated on the counselling provided.[38]

Generalisability of this thesis

Patient safety research faces substantial challenges. As was shown in the systematic review (Chapter 2), interventions on discharge medication related interventions are usually multifactorial and complex, targeting multiple persons (including patients, clinicians and care teams across settings). Therefore patient safety research includes more variation than intervening for example with one drug and patient safety interventions are more difficult to define, develop, document and reproduce. So any intervention needs to be accurately described in order for others to replicate the intervention. Also, characteristics of the organisation and its environment (i.e. the context) can influence the implementation and effectiveness of patient safety interventions.[8,12]
We defined our COACH program after reading literature, after observing a similar study in Northern Ireland and after a pre-implementation evaluation. In a study protocol we specified the intervention and procedures. Pharmaceutical consultants were trained to

perform the intervention according to a protocol, but they may vary in terms of pharmacotherapeutic knowledge, organisation and management of the COACH program. Other, endogenous factors (see the causal chain, Figure 1) such as the high turnover of residents in a teaching hospital and the patient safety culture could also influence results. Residents may have varied in terms of cooperation, organisation and management. With feedback and meetings problems were discussed, the why and how were repeated and the intrinsic motivation to improve patient safety was addressed.
The exogenous factors (the "structure" in the causal chain, Figure 1) may have influenced results. The Dutch guideline "information transfer regarding medication in the care continuum" could have changed the information needs of patients and healthcare providers. They could have been more aware of the need for extra information at hospital discharge. However, the results correspond with findings in literature. Also, as discussed previously the quality of primary healthcare may influence results.
Multiple studies have shown that drug-related problems can be prevented with medication reconciliation.[39-46] This was also the case in our studies (Chapter 3.3 and 4.2). Other aspects of the COACH program probably are far less generalisable. Pharmaceutical consultants performed the COACH program and this profession is relatively new. Discharge medication related interventions are generally performed by pharmacists (Chapter 2). In the Netherlands, pharmacists are too expensive to perform all elements of medication reconciliation. In contrast to many studies, we followed all steps in medication reconciliation including optimising the pharmacotherapy, counselling the patient and informing the next healthcare provider. To provide continuity of pharmaceutical care we acknowledged the role of the patient and the next healthcare provider.

IMPLICATIONS FOR PRACTICE AND FOR RESEARCH

In this thesis the method for implementing medication reconciliation and involving the patient and healthcare providers within the continuum of care has been emphasized. Further implications for practice and for research will be discussed.

Study design and the pre-implementation phases

Future studies regarding transitional care programs should use the stepped wedge design and various outcomes such as (drug-related) hospitalisations and adverse drug events. Low fidelity may be a sign that the intervention is too complex or the urgency for the intervention is not felt by all healthcare providers. Qualitative research involving healthcare professionals and patients can provide more information on which success factors and barriers for change may exist.

Future studies also need to assess what effective components are for improving continuity of pharmaceutical care. For example, US researchers study the effect of a minimal intervention versus an enhanced intervention on adverse drug events and readmissions.[47]
In the pre-implementation phase the selection of interventions was discussed and chosen at preliminary meetings. However, at the departments the transitional pharmaceutical care program was regarded as a pharmacy project rather than a multidisciplinary effort to improve patient safety. Staff hospital physicians were involved, but eventually only staff nurses attended all meetings in the pre-implementation phase. This may reflect lack of time in the busy hospital environment or lack of interest.
We did define responsibilities, but it remained a challenge to involve (especially new) residents. Due to the many responsibilities that residents had, medication reconciliation was not a priority in the first weeks of a new resident.
The following recommendations can be made. First, time and effort are needed in developing and testing the intervention in the pre-implementation phases. For example, we thought residents would upload the complete discharge medication overview as this would save time. Also, even if the pharmaceutical consultant's overview was uploaded, some residents deleted the information regarding discontinued medication as they considered this specific information as irrelevant. Second, it is necessary to train residents before they start working on the department. Third, it is crucial to have a staff leader that acknowledges the importance of medication reconciliation and that can motivate residents. Medication reconciliation is best implemented in wards that have an interest in medication reconciliation.[48,49] Interest of other wards can be gained by continuously showing the results of medication reconciliation.

Collaboration between settings: from discharging to transitioning patients

Collaboration between settings means that hospitals do not discharge but transition patients to the next healthcare provider.[50] Collaboration also means that healthcare providers should act on the information they receive. Continuity cannot be provided within one setting. Hospital care represents only a fraction of a patient's use of healthcare services.[51] We therefore recommend eliminating the division between hospital and out of hospital safety strategies. Improving the transition of responsibilities from one organisation and set of providers to another requires coordination among providers. A broader view of medication reconciliation (or patient safety) will mean that adverse events no longer relate only to episodic errors and failures in procedures at specific times, but also to cumulative failures throughout a patient's journey within the healthcare continuum.[51]
Professionals need to think of the needs of the patient and organise care around the patient. One cannot provide continuity of pharmaceutical care without involving the patient. The patient is namely the only constant participant across the healthcare system.[4]
We showed that the information of the patient is crucial in medication reconciliation

(obtaining a medication history, evaluating need and use of drugs at discharge and providing education, Chapter 3.3). Also, by empowering the patient or his carer an extra barrier can be introduced to prevent serious medication errors. Teach Back methods (i.e. asking patients to restate in their own words what they heard during education) should be applied to address any gaps in understanding.[52]

More research is needed into the aspect how patients can be involved best in the continuum of care and whether patients see a role for themselves in decreasing communication gaps between settings. Although there is some evidence of recognising the role of patients as active participants in the process of securing appropriate, effective, safe and responsive healthcare, the data are preliminary.[53] For example, it is frequently suggested that patient-held medication overviews could help to determine all the medicines a patient is taking. Favourable results have been shown, as the medication overview increased patient's sense of responsibility.[54] Others, however, showed that patients lost the medication overview and that compliance with the use decreased significantly over a longer time period.[55-57]

Design and redesign: fit into the working process

There are no plug-and-play models for medication reconciliation. Therefore, medication reconciliation should be designed, implemented and redesigned and its effectiveness should be measured.[58] For example, in the beginning we performed the verification step of medication reconciliation by providing residents with a medication history from the community pharmacy. This failed, as residents stated that the medication histories contained too much information, were too long and took too much time to evaluate. This meant that discrepancies were not corrected until discharge, when the pharmaceutical consultant explicitly addressed the discrepancies. Thereafter, we attached a sheet specifically mentioning the discrepancies between medication prescribed in-hospital and the pre-admission medication. Again, this failed, as residents stated that they should pay attention to the sheet, but they lacked time. Subsequently, the pharmaceutical consultants telephoned the resident and discussed discrepancies for all patients at once. Again, this failed, as residents forgot or lacked time to adjust the medication in the computerized physician order entry system (CPOE). As a final change in the process pharmaceutical consultants added the medication to the CPOE and the resident only needed to authorise the medication. Even then, residents forgot to authorise the medication, making a second phone call necessary.

Several aspects of the process need to be made clear, e.g. responsibilities, sources used for the verification step in medication reconciliation, documentation of information in the computer system and communication of relevant information (e.g. reasons for changes in the pharmacotherapy, laboratory values, follow-up actions). Developing standard operating procedures, checklists and predefined forms will support healthcare

professionals delivering these services.[59] Our study protocol (Chapter 4.1) provides the checklists and the forms that were used in the COACH program.

Role of information technology and the policymaker/payer

The lack of a single patient record that is accessible to all healthcare providers compounds the issue of discontinuity of care and makes coordination of care during transitions more complex.[60] Plans for a national Electronic Health Record in the Netherlands are still in a developing phase after being put on hold after the Dutch Senate voted against further implementation mainly because of confidentially and security issues. Lack of good information technology makes medication reconciliation processes inefficient. However, even where national electronic patient records are available users must be adequately trained to consistently document accurate and relevant information. Since medication reconciliation is time-consuming, a valid computer software program that could compare medication records from two or more sources would be helpful. The output, highlighting medication discrepancies, could then be critically assessed by the healthcare provider.[59]
Future studies should focus on the role of information technology and on mechanism to decrease administrative task (e.g. linkage of hospital pharmacy and community pharmacy information systems and teaching the appropriate use of these systems).

Policy makers and payers should take their responsibility. Although, the guideline "information transfer regarding medication in the care continuum", that was signed by all relevant parties (e.g. pharmacists, doctors, dentists, anticoagulation clinics etc.), responsibilities still are unclear. Generally, pharmacists are aware of the guideline while general practitioners and hospital physicians are not. This means that insufficient effort has been taken to inform doctors. In recent years numerous guidelines have been published, which all need to be implemented. On the other hand, budgets are cut. As for every new intervention, development and implementation takes additional time, so start-up budgets are needed. The new guideline also increases administrative workload, so regular support is needed for healthcare providers to document all information. As Pronovost et al. discussed, improved quality and safety will save money in the long run, but this will not be possible without significant investing in patient safety infrastructure.[61] To improve safety, it is essential to ensure that sufficient numbers of qualified healthcare providers are staffed to provide care, to create mechanisms to train leaders, to support in organisational management and to support change.[61-63] Ultimately, society must decide how much it is willing to pay to improve patient safety.[61]

CONCLUSION

The research presented in this thesis has enriched the understanding of discharge medication related interventions, the information needs of patients and general practitioners and the implementation and effect of a transitional pharmaceutical care program for patients discharged from the hospital. Much effort is needed to provide continuity of pharmaceutical care. With medication reconciliation many interventions were performed to prevent drug-related problems. Further improvements on implementing the process with good fidelity, making the process logistically more easy (and thus less time-consuming) and evaluating the effects are needed. This provides opportunities for further research into the effectiveness and cost-effectiveness of transitional pharmaceutical care programs in enhancing continuity of pharmaceutical care. Continuity of care goes beyond the walls of the hospital setting. Collaboration between settings and adequate follow-up of a patient after hospital discharge is needed. Research into this matter should be performed multicenter, including high-risk patients and a stepped wedge design is advocated using multiple outcomes such as rehospitalisations and adverse drug events.

Transitional pharmaceutical care programs are not projects that can only be performed when time allows, it should be usual care to provide continuity of care. For this continuity everyone in the healthcare continuum has to take his/her responsibility, from patients to hospitals to primary care providers to policy makers.

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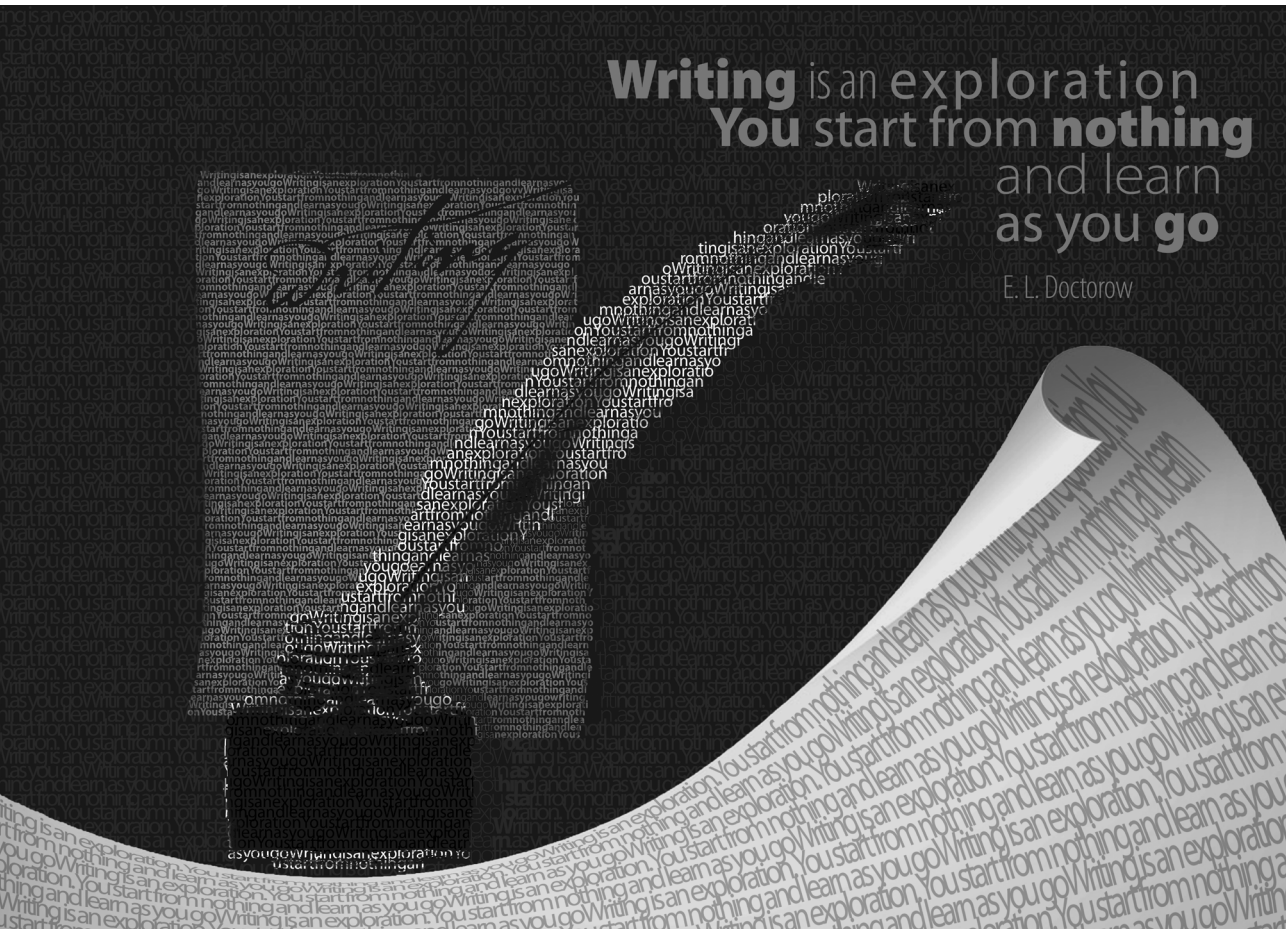

Writing is an exploration.
You start from nothing and learn as you go.

(E.L. Doctorow: author and editor, 1931)

Designed by Denis Tenev

PART

6

Summary in English and Dutch

SUMMARY

Part 1: introduction

In Part 1 the scope, objective and outline of this thesis are described. This introductory chapter provides an overview of the complexity of today's decentralised and fragmented healthcare system. Patients visit multiple healthcare providers, neither of whom have access to complete information regarding the patient's healthcare status. This lack of information can result in discontinuity of care and is especially profound when patients are transferred from one healthcare setting to another, e.g. at hospital admission and at hospital discharge. Studies have shown that medication errors are frequent at transitions between healthcare settings. The causes of these medication errors are multi-factorial: the patient's inability to recall medication use, incomplete information transfer between healthcare settings and incorrect transcription of information. Medication reconciliation has been developed to prevent medication errors due to transitions in care. Medication reconciliation includes creating the most accurate overview of all medication a patient is taking, patient counselling to educate the patient regarding changes in the pharmacotherapy and the transfer of information to the next healthcare provider.

This thesis focuses on the transition of patients from hospital discharge to home. This is the moment that the patient needs to resume responsibility for his medication. Thus, the patient needs to be counselled regarding his discharge medication and changes in the pharmacotherapy. Also, healthcare providers such as the general practitioner and the community pharmacist, need to be informed regarding the medication at hospital discharge. With this information they can provide adequate patient support after hospital discharge. The objective of this thesis is to summarise existing evidence on interventions regarding discharge medication and to develop and evaluate a transitional pharmaceutical care program with respect to effects and costs.

Part 2: systematic review

Chapter 2.1 reviews existing evidence regarding discharge medication related interventions. After a systematic literature search in several scientific databases 58 original studies were reviewed. These studies described multi-component interventions that included various types of discharge medication related interventions. Examples of discharge medication related interventions included medication reconciliation at discharge, patient counselling (verbal, written or audiovisual) and information transfer to the next healthcare provider (verbal or written). Of the 58 studies 17 studies measured the outcome hospital readmission; of these 17 studies three (18%) significantly reduced hospital readmissions. In four of ten studies (40%) health services use was decreased, e.g. general practitioner or emergency department visits. The discharge medication related interventions were mainly reported to be effective for process measures: 75% of

studies improved knowledge about medication, 70% improved adherence and 93% of studies prevented drug-related problems. Study characteristics influenced outcomes: in general, studies with larger sample sizes led more frequently to effective studies. Studies with good methodological quality tended to be more frequently effective for the outcomes readmission and knowledge.

Part 3: development of a transitional pharmaceutical care program

To improve medication information transfer from hospital discharge to the outpatient setting, the informational needs of general practitioners regarding discharge medication were investigated in a prospective observational study (Chapter 3.1). A questionnaire was posted to general practitioners. Most general practitioners (75%) experienced a delay in receiving discharge medication information and preferred to receive this on the day of discharge. General practitioners desired information regarding the reasons for changes in the pharmacotherapy (88%) and discontinuations of medication (87%). Finally, general practitioners (88%) appreciated pharmacotherapeutic advices from clinical pharmacists. This provided collaboration possibilities between clinical pharmacists and general practitioners for example in situations where the hospital physician did not feel responsible for certain medication regimens (e.g. undertreatment), extra monitoring of medication was needed (e.g. kidney malfunction) or drug-related problems (e.g. compliance, side effects) were identified.

To involve the patient in medication reconciliation and support the development of patient counselling, the informational needs of patients regarding discharge medication were explored (Chapter 3.2). Qualitative, semi-structured interviews were performed with 31 patients from several departments who were discharged with at least one prescribed drug. It was shown that patients mainly wanted to receive basic information concerning the goal of the pharmacotherapy, dosing regimens and medication usage. However, patients had variable needs. Some patients did not need basic information or explicitly mentioned that information about side effects would negatively influence their attitude towards medication. Patients preferred a combination of oral instructions and written information. Thus, patient counselling at discharge should be tailored to the individual needs of the patient.

In the Netherlands, the medication history of the community pharmacy is used as an information source to continue pre-admission medication in the hospital. However, community pharmacy data can be incomplete or incorrect as the patient may use over-the-counter drugs or may visit several community pharmacies. To get insight in the additional contribution of patient counselling to medication reconciliation an observational study was conducted at the department of pulmonary medicine (Chapter 3.3).

In 262 patients, a pharmacy team assessed the interventions on discharge medication for each patient before patient counselling (using community pharmacy data) and after patient counselling (using additional patient information). Medication reconciliation without patient counselling was responsible for minimally one intervention in 87% of patients (mean 2.7 interventions per patient). After patient counselling in 97% of patients minimally one intervention was performed (mean 5.3). Patient counselling led to adjustments in discharge prescriptions due to differences in use or need of medication. Most interventions led to the start of medication due to omission of pre-admission medication and dose changes due to incorrect dosages being prescribed. Patients also addressed their problems or concerns with their medication use, which were discussed before discharge. This study showed that patient participation contributed significantly to medication reconciliation.

Medication reconciliation is time-consuming and will therefore increase labour costs. On the other hand, evaluation of discharge medication could reduce medication costs after hospital discharge by decreasing the use of redundant medication. For the 262 patients described in Chapter 3.3, the effect of performing medication reconciliation was evaluated regarding pharmacy labour costs in relation to medication costs (Chapter 3.4). The labour costs for performing medication reconciliation were €41 per patient. With medication reconciliation hospital formulary induced medication changes were corrected (e.g. re-substitute brand drug to generic drug used pre-admission) and the pharmacotherapy was optimised (e.g. discontinue redundant drug). These interventions together saved €97 per patient at six months extrapolation after hospital discharge. Thus, at six months after hospital discharge, medication cost savings outweighed the labour costs with €56 per patient (sensitivity analysis €37 - €71). This study showed that medication reconciliation resulted in higher benefits than the costs related to the net time investment.

To provide continuity of care after hospital discharge, community pharmacies need to update the information in their information system when they receive new information. In this way, community pharmacies could help to ensure that therapy changes, initiated by the hospital, are continued after discharge. In a before-after study (Chapter 3.5) the effect of instruction manuals on completeness of patient files in community pharmacies was explored. In the before-group only hospital discharge medication overviews were communicated to community pharmacies. In the after-group, an instruction manual was sent additionally with every discharge medication overview. The instruction manual specified how community pharmacies could document medication changes and clinical information (e.g. allergies) in their information system. After two weeks, the patient files of the community pharmacy were compared with the initial discharge medication

overviews regarding completeness of medication changes (i.e. explicit explanation that medication had been changed) and clinical information documentation. Completeness of medication changes documentation increased marginally (47% of medication changes before-group versus 56% after-group, adjusted OR 1.4 [95% CI 1.1-1.8]). Allergies and contraindications were documented with similar frequencies in both groups. This study showed that community pharmacies failed to document relevant discharge medication related information. Also, instruction manuals alone were insufficient to achieve complete patient files in community pharmacies.

Part 4: evaluation of the transitional pharmaceutical care program COACH

To improve the transition from hospital discharge to home a transitional pharmaceutical care program was designed. In Chapter 4.1 the protocol for the study into the effects and costs of the COACH (Continuity Of Appropriate pharmacotherapy, patient Counselling and information transfer in Healthcare) program is described. All patients admitted to the internal medicine ward, who were using at least one prescribed drug that was intended for chronic use, were included in the study. Patients were excluded if they met one of the following exclusion criteria: no informed consent, no medication intended for chronic use prescribed at discharge, transfer to another ward or hospital, discharge within 24 hours or out-of-office hours, discharge to a nursing home, no possibility to counsel the patient, and death. The COACH program was designed using the information from the studies in the systematic review (Chapter 2.1), the general practitioner's and patient's informational needs regarding discharge medication (Chapter 3.1 and 3.2) and acknowledging the patient's contribution in medication reconciliation (Chapter 3.3). The COACH program was performed by a pharmacy team and consisted of medication reconciliation at hospital admission and discharge, patient counselling at discharge and communication between the hospital and primary care healthcare providers at discharge. The primary outcome was the frequency of patients with an unplanned rehospitalisation within six months after discharge. Secondary outcomes included the number of interventions to prevent drug-related problems, patient's adherence, patient's believes about medication and patient's satisfaction.

In Chapter 4.2 the evaluation of the COACH program is presented. In the before-group (usual care) 341 patients were included and in the after-group (COACH-program) 365 patients. The groups were not comparable at baseline as the patients in the COACH-program had more co-morbidities that were also more severe. Of the usual care patients 27% had an unplanned rehospitalisation within six months after discharge compared to 33% of patients included in the COACH program. The introduction of the COACH program led to a non-significant increase of 13% (95% CI: -7 – 33) of unplanned rehospitalisations.

For all patients interventions were performed to prevent drug-related problems (mean number of interventions: 10 per patient). Examples of interventions included re-starting of pre-admission prescribed medication, adjusting dosing schemes due to kidney malfunction, discontinuing redundant medication etc. No effect was seen on patient's adherence and patient's believes about medication. Patients were significantly more satisfied with counselling provided by a pharmacy member compared to the resident (69% resident versus 87% pharmacy). Comparable to the results of the systematic review (Chapter 2.1), the COACH program was mainly effective for process measures (i.e. drug-related problems and patient satisfaction), but it showed no decrease of unplanned rehospitalisations.

Transitional pharmaceutical care programs are developed more and more internationally. In a context of increasing healthcare costs and limited resources, the cost-effectiveness of approaches to improve continuity of pharmaceutical care has become increasingly important. In Chapter 4.3 we studied the cost-effectiveness of the COACH program in comparison with usual care using the clinical outcome unplanned rehospitalisations and quality-adjusted life-years (QALY). Patients in the before- and after-group were asked to fill in cost diaries regarding use of healthcare after hospital discharge, use of supportive healthcare and productivity losses. As it was expected that patient compliance with filling in cost diaries would decrease over time, patient follow-up for the economic evaluation was limited to three months (instead of the six months in the main study, Chapter 4.2). In the economic evaluation 168 patients were included in the COACH program and 151 patients in the usual care group. The proportion of patients with unplanned rehospitalisations in the three months after discharge did not differ statistically significantly (21% COACH versus 21% usual care, 95% CI for adjusted difference: -9 – 9) nor did the QALYs (0.15 versus 0.17, 95% CI for adjusted difference -0.0170 – 0.0001). At three months after discharge, costs for the COACH program (€6845/patient) did not statistically significantly differ in comparison to usual care (€7952/patient). The adjusted difference in costs between groups was -€1160/patient (95% CI: -3168 – 847), which was not statistically significant. Based on these results, the COACH program was not considered cost-effective.

Part 5: discussion

In part 5, the discussion, the studies presented in this thesis are discussed in a broader perspective. Topics included the explanation of the methodology of patient safety research, the methodological aspects of the several studies, the implications of the COACH program and further research questions.

CONCLUSION

In conclusion, transitions in care can be considered as vulnerable periods for patients with respect to medication errors. This thesis showed that medication reconciliation resulted in many interventions aimed at preventing drug-related problems, but that these interventions did not influence unplanned rehospitalisations. This may have been caused by insufficient collaboration between the hospital and primary care healthcare providers. Transitional pharmaceutical care needs to extend beyond the hospital walls. Collaboration between healthcare settings and adequate follow-up of a patient after hospital discharge is needed. Only then will transitional pharmaceutical care programs be able to provide continuity of patient care.

SAMENVATTING

Transities in de zorg

De organisatie van de Nederlandse gezondheidszorg is complex. Dit geldt met name voor de zorg rondom het gebruik van medicijnen omdat hier vaak verschillende zorgverleners bij betrokken zijn. Er zijn verschillende complexe problemen te benoemen. Ten eerste hebben zorgaanbieders geen van allen toegang tot het gehele medicatiedossier. Hierdoor is niet altijd duidelijk of nieuwe medicatie wel past bij de medicatie die eerder voorgeschreven is door andere zorgverleners. Ten tweede informeren zorgverleners elkaar niet altijd goed over aanpassingen in de medicatie. Of zorgverleners weten niet wie er allemaal betrokken zijn bij de behandeling van een patiënt. Ten derde wordt het medicatiedossier van een patiënt niet beheerd door één zorgverlener. Hierdoor kan het medicatiedossier in elk computersysteem (van de huisarts, apotheek, specialist, etc.) incompleet zijn. Tot slot weten niet alle patiënten welke medicatie zij voor welke aandoening gebruiken en de daarbij horende dosering.
Doordat informatie over medicatiegegevens versnipperd is, kunnen er medicatiefouten ontstaan. Deze medicatiefouten komen vooral voor wanneer de patiënt van de ene zorginstelling naar een andere gaat, ook wel transitie genoemd. In dit proefschrift komen diverse aspecten aan de orde om medicatiefouten ten gevolge van een transitie te voorkómen.

Deel 1: inleiding

Deel 1 van dit proefschrift is een inleiding waarin wordt ingegaan op de complexiteit van de gezondheidszorg. De nadruk wordt gelegd op de transitie (oftewel overgang) van het ziekenhuis naar thuis. Immers na ziekenhuisontslag moet de patiënt veelal weer zelfstandig zijn medicatie gebruiken. Het is hierbij belangrijk dat de patiënt voorlichting krijgt over zijn ontslagmedicatie, waarom medicatie gewijzigd is en hoe deze te gebruiken. Daarnaast dient bij ontslag ook de volgende zorgverlener, zoals de huisarts en de openbare apotheker, geïnformeerd te worden over de ontslagmedicatie. Met deze informatie kunnen zij de patiënt begeleiden na ontslag uit het ziekenhuis.
Om medicatiefouten ten gevolge van transities in de zorg te voorkomen is *medication reconciliation* ontwikkeld. Het doel van *medication reconciliation* is het waarborgen van de continuïteit van de behandeling. *Medication reconciliation* omvat allereerst het opstellen van het meest accurate medicatieoverzicht van alle medicijnen die een patiënt gebruikt, bijvoorbeeld bij opname in het ziekenhuis. Wijzigingen in de therapie worden vastgelegd en aan de patiënt uitgelegd. Tot slot worden, bijvoorbeeld bij ontslag, de medicatiegegevens overgedragen naar elke volgende zorgverlener van de patiënt (huisarts, openbare apotheek, verpleeghuis etc.).

Het doel van dit proefschrift is:

- het samenvatten van de resultaten van eerdere onderzoeken om problemen met ontslagmedicatie te voorkomen en zo de transitie van ziekenhuisontslag naar thuis te verbeteren (deel 2 van dit proefschrift),
- het ontwikkelen van een nieuw programma voor farmaceutische transitiezorg bij ziekenhuisontslag (deel 3),
- en tot slot het evalueren van een dergelijk programma met betrekking tot gezondheidseffecten en kosten (deel 4).

Deel 2: literatuuronderzoek

In hoofdstuk 2.1 worden de resultaten van eerdere onderzoeken naar programma's om problemen met ontslagmedicatie te voorkomen, samengevat. Na een systematisch literatuuronderzoek met verschillende wetenschappelijke zoekmachines werden 58 originele onderzoeken beoordeeld. Deze onderzoeken beschreven verschillende manieren om problemen met ontslagmedicatie te voorkomen, zoals het uitvoeren van *medication reconciliation*, het begeleiden van de patiënt (mondeling, schriftelijk of audiovisueel) en het informeren van de volgende zorgverlener (mondeling of schriftelijk). De onderzoeken hebben verschillende uitkomsten gemeten om het effect te bepalen. Van de 58 onderzoeken keken 17 onderzoeken naar het effect op ziekenhuisheropnames; hiervan bleken drie onderzoeken (18%) ziekenhuisheropnames significant te verminderen. Daarnaast keken 10 onderzoeken naar vermindering van het zorggebruik, zoals het bezoeken van een huisarts. Vier (40%) daarvan verminderden het zorggebruik. De onderzoeken bleken vooral effectief in het verbeteren van minder harde uitkomsten: 75% van de onderzoeken verhoogden de kennis van patiënten over medicijnen, 70% verbeterden de therapietrouw van de patiënt en 93% verminderden medicatiegerelateerde problemen. Kenmerken van de onderzoeken waren van invloed op de uitkomsten. Onderzoeken met meer patiënten leidden vaker tot een positieve uitkomst. Onderzoeken met een goede methodologische kwaliteit waren vaker effectief voor de uitkomstmaten ziekenhuisheropname en kennis over medicijnen.

Deel 3: ontwikkelen van een transitiezorg programma

In hoofdstuk 3.1 wordt onderzocht hoe informatieoverdracht aan huisartsen verbeterd kan worden. Huisartsen kregen een vragenlijst toegestuurd. Zij werden gevraagd wanneer zij informatie over ontslagmedicatie wilden ontvangen en welke informatie dan belangrijk was. De meeste huisartsen (75%) ervoeren een vertraging in het ontvangen van ontslagmedicatie gerelateerde informatie. Zij hadden de voorkeur om de informatie op de dag van ontslag te ontvangen. Huisartsen wilden weten of medicatie gewijzigd (88%) en/of gestaakt was (87%). Tot slot gaven huisartsen (88%) aan dat zij adviezen van een apotheker, om de behandeling met geneesmiddelen te verbeteren, op prijs

stelden. Een voorbeeld is het advies aan de huisarts om het geneesmiddelgebruik van een patiënt na ziekenhuisontslag extra in de gaten te houden bij een verminderde nierfunctie.

In het proces van *medication reconciliation* dient de patiënt actief betrokken te worden. Om de informatiebehoefte van patiënten te onderzoeken, werden 31 patiënten geïnterviewd vlak voor ontslag uit het ziekenhuis (hoofdstuk 3.2). Deze patiënten kregen minimaal één geneesmiddel voor langere tijd voorgeschreven. Patiënten bleken verschillende informatiebehoeften te hebben. De meeste patiënten wilden vooral basisinformatie ontvangen: het doel van het geneesmiddel, de dosering en het gebruik. Sommige patiënten wilden geen informatie en anderen vermeldden dat informatie over bijwerkingen hun houding tegenover medicijngebruik negatief zou kunnen beïnvloeden. Patiënten hadden een voorkeur voor een combinatie van mondelinge en schriftelijke informatie over hun medicijnen. Dit onderzoek toonde aan dat de voorlichting moet worden aangepast aan de individuele behoeften van de patiënt.

In Nederland wordt veelal de medicatiehistorie van de openbare apotheek gebruikt als informatiebron. De medicatie die thuis werd gebruikt, kan met de informatie van de openbare apotheek voortgezet worden in het ziekenhuis. Echter, de historie in de openbare apotheek kan incompleet of incorrect zijn. Patiënten kunnen bijvoorbeeld hun medicatie in meerdere apotheken ophalen of zij kunnen hun medicatie anders gebruiken dan is voorschreven. Er werd daarom onderzocht wat de bijdrage van de patiënt is aan *medication reconciliation* (hoofdstuk 3.3). Het aantal en het type interventies bij ontslag werden geteld. De interventies hadden tot doel om geneesmiddelgerelateerde problemen te voorkomen. De ziekenhuisapotheek beoordeelde bij 262 patiënten het aantal interventies vóór het gesprek met de patiënt (gebruikmakend van de medicatiehistorie van de openbare apotheek) en na het ontslaggesprek (gebruikmakend van de informatie van de patiënt zelf).
Medication reconciliation bleek zonder het ontslaggesprek te leiden tot minimaal één interventie bij 87% van de patiënten (gemiddeld: 2,7 interventies per patiënt). Na het gesprek bleek bij 97% van de patiënten minimaal één interventie vastgelegd te zijn (gemiddeld: 5,3/patiënt). De ontslagmedicatie werd na het gesprek alsnog gewijzigd omdat de patiënt aangaf welke medicijnen nog nodig waren en hoe ze gebruikt werden. Het herstarten van thuismedicatie en doseringsaanpassingen waren de meest voorkomende interventies. Patiënten gaven ook aan welke problemen zij hadden bij het medicatiegebruik. Dit onderzoek toonde aan dat de inbreng van de patiënt een belangrijke bijdrage leverde aan *medication reconciliation*.

Medication reconciliation is tijdrovend, wat leidt tot hogere arbeidskosten. Aan de andere kant kunnen de medicatiekosten dalen. Immers, met *medication reconciliation* wordt de therapie geëvalueerd, wat kan leiden tot het staken van onnodige geneesmiddelen. Bij de 262 patiënten beschreven in hoofdstuk 3.3 werden de arbeidskosten van *medication reconciliation* vergeleken met de medicatiekosten na ziekenhuisontslag (hoofdstuk 3.4). De arbeidskosten waren €41 per patiënt. Ten gevolge van *medication reconciliation* werd medicatie weer omgezet naar de medicatie die thuis werd gebruikt, bijvoorbeeld het vervangen van een duurder origineel geneesmiddel door een goedkoper generiek geneesmiddel dat thuis werd gebruikt. De farmacotherapie werd ook geoptimaliseerd, bijvoorbeeld het staken van een onnodig geneesmiddel. Deze interventies bespaarden samen €97 per patiënt na zes maanden. In totaal werd per patiënt €56 (€97 minus €41) bespaard. Dit onderzoek toonde aan dat *medication reconciliation* kosten bespaart.

Openbare apotheken dienen eventuele nieuwe informatie over ontslagmedicatie te verwerken in hun patiëntendossier. Zij kunnen er dan voor waken dat een bewust gestopt geneesmiddel per ongeluk door een andere zorgverlener wordt herstart. In een onderzoek (hoofdstuk 3.5) werd het effect van handleidingen op de volledigheid van patiëntendossiers in openbare apotheken onderzocht. In de controleperiode kregen openbare apothekers bij ziekenhuisontslag een medicatieoverzicht toegestuurd vanuit het ziekenhuis. In de interventieperiode kregen de apotheken tevens een handleiding toegestuurd. De handleiding gaf aan hoe openbare apotheken medicatiewijzigingen, allergieën en contra-indicaties konden opslaan in hun informatiesysteem. Na twee weken werden de gegevens van de openbare apotheek opgevraagd en vergeleken met de informatie die bij ontslag was toegestuurd. Er werd beoordeeld of medicatiewijzigingen volledig waren vastgelegd; dat wil zeggen of het duidelijk was welke medicatie was gewijzigd. Ook werd beoordeeld of allergieën en contra-indicaties vastgelegd werden. Medicatiewijzigingen werden iets beter vastgelegd in de interventieperiode (47% van de medicatiewijzigingen in de controleperiode versus 56% in de interventieperiode. Het vastleggen van allergieën en contra-indicaties verbeterde niet. Dit onderzoek toonde aan dat openbare apotheken niet altijd alle ontslag informatie vastlegden. Daarnaast bleek een handleiding alleen onvoldoende om de vastlegging te verbeteren.

Deel 4: evaluatie van een transitiezorg programma

Om de transitie van ziekenhuis naar thuis te optimaliseren werd een transitiezorg programma, COACH, ontworpen. De informatie uit eerdere onderzoeken zoals beschreven in dit proefschrift (deel 2 en 3) werd gebruikt om het programma te ontwikkelen. In hoofdstuk 4.1 is het protocol voor het onderzoek naar het effect van het COACH programma beschreven. Voor dit onderzoek kwamen alle patiënten in aanmerking die opgenomen waren op de afdeling interne geneeskunde en die tenminste één geneesmiddel voor

langere tijd gebruikten. Patiënten deden niet mee indien zij geen toestemming gaven, geen medicatie meer bleken te gebruiken bij ziekenhuisontslag, overgeplaatst werden naar een andere afdeling, ziekenhuis of instelling, geen scholing konden ontvangen of overleden. Het COACH programma werd uitgevoerd door een ziekenhuisapotheek team en bestond uit drie onderdelen. Als eerste werd *medication reconciliation* uitgevoerd bij ziekenhuisopname en –ontslag. Ten tweede kreeg de patiënt bij ziekenhuisontslag voorlichting over zijn ontslagmedicatie, de medicatiewijzigingen en het medicatiegebruik. Tot slot werd de informatie over ontslagmedicatie gecommuniceerd aan de volgende zorgverlener.
De belangrijkste uitkomstmaat was het percentage patiënten met een ongeplande heropname binnen zes maanden na ontslag. Andere uitkomsten waren het aantal interventies om geneesmiddelgerelateerde problemen te voorkomen, de therapietrouw van de patiënt, het geloof in het belang van medicatie en de tevredenheid van de patiënt.

In hoofdstuk 4.2 is de evaluatie van het COACH programma beschreven. In de controleperiode (gebruikelijke zorg) deden 341 patiënten mee en in de interventieperiode (COACH programma) 365 patiënten. De patiënten uit de controleperiode en interventieperiode waren niet vergelijkbaar. De patiënten uit de interventieperiode hadden meer aandoeningen die tevens ernstiger waren. In de controleperiode werd 27% van de patiënten ongepland heropgenomen in het ziekenhuis. In de interventieperiode bleek 33% ongepland heropgenomen te zijn. Na het introduceren van het COACH programma werd dus een (niet-significante) toename van 13% (95% betrouwbaarheidsinterval: -7 – 33) ongeplande ziekenhuisheropnames gezien.
Bij alle patiënten waren interventies uitgevoerd om geneesmiddelgerelateerde problemen te voorkomen (gemiddeld aantal interventies: 10 per patiënt). Voorbeelden van interventies waren het herstarten van thuismedicatie, het aanpassen van de dosering aan de nierfunctie of het stoppen van niet benodigde medicatie. Er werd geen effect gezien op therapietrouw en het belang van medicatie. Patiënten waren meer tevreden over de voorlichting verzorgd door de apotheek ten opzichte van de arts (69% arts versus 87% apotheek). De resultaten van het COACH programma waren vergelijkbaar met de resultaten van het systematische literatuuronderzoek, hoofdstuk 2.1. Het COACH programma had invloed op minder harde uitkomsten, namelijk geneesmiddelgerelateerde problemen en de tevredenheid van patiënten. Er werd geen afname van ongeplande ziekenhuisheropnames gezien.

Meer en meer worden programma's ontwikkeld om transitiezorg te organiseren. Door de toenemende kosten van de gezondheidszorg en beperkte middelen zijn onderzoeken naar kosten steeds belangrijker geworden. In hoofdstuk 4.3 is de economische evaluatie van het COACH programma ten opzichte van de controleperiode beschreven. Als

uitkomstmaten werden ongeplande ziekenhuisheropnames en de kwaliteit van leven (QALY= quality-adjusted life-years) onderzocht. Voor dit onderzoek werden patiënten gevraagd om gedurende drie maanden kostendagboeken bij te houden. In de dagboeken legden zij vast hoe vaak ze gebruik hadden gemaakt van de gezondheidszorg na ontslag, hoeveel hulp zij hadden ontvangen en of zij konden werken na ziekenhuisontslag. In dit onderzoek vulden 168 patiënten dagboekjes in tijdens de COACH periode en 151 tijdens de controleperiode. Het aantal patiënten met een ongeplande ziekenhuisheropname verschilde niet significant in de drie maanden na ontslag (21% COACH versus 21% controle, gecorrigeerde 95% betrouwbaarheidsinterval voor het verschil: -9 – 9). Ook was er geen significant verschil in QALY's (0,15 versus 0,17, gecorrigeerde 95% betrouwbaarheidsinterval voor het verschil: -0,0170 – 0,0001). Totale kosten voor patiënten in het COACH programma (€6845 per patiënt) verschilde niet statistisch met de controle (€7952 per patiënt). Het gecorrigeerde verschil in kosten tussen de groepen was -€1160 (95% betrouwbaarheidsinterval voor het verschil: -3168 – 847). Op basis van deze resultaten bleek het COACH programma niet kosteneffectief.

Deel 5: discussie

In deel 5, de algemene discussie, zijn diverse onderwerpen in een breder perspectief geplaatst. Onderwerpen die aan bod kwamen waren de methode van onderzoek om patiëntveiligheid te verhogen en de methodologie van de diverse onderzoeken gepresenteerd in dit proefschrift. Aanbevelingen voor de klinische praktijk en toekomstig onderzoek werden toegelicht.

CONCLUSIE

Er kan worden geconcludeerd dat transities in de zorg kunnen leiden tot medicatiefouten. Dit proefschrift toonde aan dat *medication reconciliation* leidde tot vele interventies om geneesmiddelgerelateerde problemen te voorkomen. Dit leidde echter niet tot een afname van het aantal ongeplande ziekenhuisheropnames. Dit kan onder andere veroorzaakt worden doordat er onvoldoende samenwerking is tussen het ziekenhuis en de zorgverleners in de thuissituatie. Transitiezorg kan niet alleen vanuit het ziekenhuis georganiseerd kan worden. Zorgverleners zullen moeten samenwerken en relevante gegevens moeten documenteren om de patiëntveiligheid te verhogen. Alleen dan kan transitiezorg leiden tot continuïteit van zorg en dus beter afgestemde zorg in de keten.

When eating a fruit, think of the person who planted the tree.

(Vietnamese proverb)

Love does not claim possession, but gives freedom.

(Rabindranath Tagore: poet, 1861-1941)

Be yourself; everyone else is already taken.

(Oscar Wilde: writer and poet, 1854-1900)

Arabic translation of quotes and design by Everitte Barbee

PART

7

From ‘acknowledgements’ to ‘about the author’

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