University of Groningen

Non-dispensing pharmacists' actions and solutions of drug therapy problems among elderly polypharmacy patients in primary care

Hazen, Ankie C M; Zwart, Dorien L M; Poldervaart, Judith M; de Gier, Johan J; de Wit, Niek J; de Bont, Antoinette A; Bouvy, Marcel L

Published in:
Family practice

DOI:
[10.1093/fampra/cmy114](https://doi.org/10.1093/fampra/cmy114)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2019

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Hazen, A. C. M., Zwart, D. L. M., Poldervaart, J. M., de Gier, J. J., de Wit, N. J., de Bont, A. A., & Bouvy, M. L. (2019). Non-dispensing pharmacists' actions and solutions of drug therapy problems among elderly polypharmacy patients in primary care. *Family practice*, 36(5), 544-551.
<https://doi.org/10.1093/fampra/cmy114>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Epidemiology

Non-dispensing pharmacists' actions and solutions of drug therapy problems among elderly polypharmacy patients in primary care

Ankie C M Hazen^{a,*}, Dorien L M Zwart^a, Judith M Poldervaart^a,
Johan J de Gier^b, Niek J de Wit^a, Antoinette A de Bont^c and
Marcel L Bouvy^{d,e}

^aDepartment of General Practice, Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht University, Utrecht (UMCU), the Netherlands, ^bDepartment of Pharmacotherapy, Epidemiology and Economics, University of Groningen, Groningen, the Netherlands, ^cErasmus School of Health Policy and Management, Erasmus University, Rotterdam, the Netherlands and ^dDepartment of Pharmaceutical Sciences, Utrecht University, Utrecht, the Netherlands.

*Correspondence to Ankie C M Hazen, Department of General Practice, Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht, Universiteitsweg 100, STR 6.131, 3584 CG, Utrecht, PO Box 85500 3508 GA Utrecht, the Netherlands; E-mail: ankiehazen@hotmail.com

Abstract

Objective. To evaluate the process of clinical medication review for elderly patients with polypharmacy performed by non-dispensing pharmacists embedded in general practice. The aim was to identify the number and type of drug therapy problems and to assess how and to what extent drug therapy problems were actually solved.

Method. An observational cross-sectional study, conducted in nine general practices in the Netherlands between June 2014 and June 2015. On three pre-set dates, the non-dispensing pharmacists completed an online data form about the last 10 patients who completed all stages of clinical medication review. Outcomes were the type and number of drug therapy problems, the extent to which recommendations were implemented and the percentage of drug therapy problems that were eventually solved. Interventions were divided as either preventive (aimed at following prophylactic guidelines) or corrective (aimed at active patient problems).

Results. In total, 1292 drug therapy problems were identified among 270 patients, with a median of 5 (interquartile range 3) drug therapy problems per patient, mainly related to overtreatment (24%) and undertreatment (21%). The non-dispensing pharmacists most frequently recommended to stop medication (32%). Overall, 83% of the proposed recommendations were implemented; 57% were preventive, and 35% were corrective interventions (8% could not be assessed). Almost two-third (64%) of the corrective interventions actually solved the drug therapy problem.

Conclusion. Non-dispensing pharmacists integrated in general practice identified a large number of drug therapy problems and successfully implemented a proportionally high number of recommendations that solved the majority of drug therapy problems.

Key words. Ageing, medical errors/patient safety, multidisciplinary care, observational (cross-sectional) research, pharmacology/drug reactions, primary care.

KEY MESSAGES

- Optimizing pharmacotherapy requires expertise and integral drug management
- Nondispensing pharmacists identified and solved a high number of drug problems
- The most frequent intervention was stopping medication

Introduction

Drug therapy problems, defined as an event or circumstance that actually or potentially interferes with an optimum outcome of medication therapy for a specific patient (1), are associated with drug-related morbidity and mortality (2,3). In the Netherlands in 2013, 48.779 acute hospitalizations of elderly patients were related to medication, of which half were potentially preventable (4). Poor communication between health care professionals can contribute to drug therapy problems, highlighting the need for better collaboration between GPs and pharmacists to improve pharmaceutical care (2,5).

Since most of the pharmacotherapy is either initiated or repeated in general practice, systematic implementation of clinical medication reviews in primary care is recommended to timely identify and solve drug therapy problems (6,7). A clinical medication review is defined as a structured critical assessment of the patient's medication by pharmacist, GP and the patient, aiming to optimize medication effect and to prevent adverse events (8).

Although clinical medication reviews are demonstrated to be effective in identifying drug therapy problems, there is conflicting evidence regarding their effectiveness to solve them (7,9–12). This can partly be explained by the extensiveness of performed medication reviews, ranging from a superficial 'medication use review' to a full 'clinical medication review' (10) and partly by the relatively poor implementation of recommendations resulting from clinical medication reviews (7,13–15). Several barriers have been identified for the low uptake of these recommendations, such as geographical distance between pharmacists and GPs, poor interprofessional communication and limited access for pharmacists to patients' medical records (16).

Non-dispensing pharmacists embedded in general practice can help to overcome these barriers (17). The non-dispensing pharmacists involved in this study were extensively trained to provide integrated pharmaceutical care. As full-time member of the general practice team, they primarily focused on performing clinical medication reviews, on patient consultations about specific medication therapy problems and on education for GPs as well as for other members of the primary care team. In particular, they were not involved in the dispensing of medication—the traditional role of pharmacists. This is an innovative care model in the Netherlands, where community pharmacists have many competing responsibilities next to pharmaceutical care.

Various models with different levels of integrated pharmaceutical care have been studied in the UK (18,19), North America (20–23) and Australia (24,25), showing that integration of a non-dispensing pharmacist generally increases the implementation rate of recommendations during the process of clinical medication review (15,24). However, it is unknown whether the better uptake of these recommendations actually solves the drug therapy problems. In a multicenter study, we evaluated the process of clinical medication review for elderly patients with polypharmacy performed by non-dispensing pharmacists embedded in general practice. The aim was to identify the number and type of drug therapy problems among elderly patients with polypharmacy in primary care and to assess how and to what extent drug therapy problems were actually solved after an intervention by the non-dispensing pharmacist.

Method**Design**

An observational cross-sectional study was conducted in the Netherlands between June 2014 and May 2015 at nine primary care practices with non-dispensing pharmacists and GPs providing integrated care. The study was part of a larger intervention study, which aimed to evaluate the effect of integration of non-dispensing pharmacists in general practices on the quality and safety of pharmacotherapy (26).

Setting and participants

The participating general practices were multidisciplinary health care centres in both urban and suburban settings, with five to nine (part-time) GPs employed and a total number of registered patients varying between 3700 and 11 700 per general practice. Nine non-dispensing pharmacists participated in this study, two male and seven female, aged between 24 and 39 years; all obtained their Pharmacy Degree at Dutch universities. Their work experience in community pharmacy varied between 1 and 12 years. The non-dispensing pharmacists participated in a 15-month Clinical Pharmacy Training Program to advance their consultation and interprofessional collaboration skills. The design and findings of this training program are described elsewhere (27). The non-dispensing pharmacists had their own consultation room in the practice and had full access to the patient's medical record.

Intervention: clinical medication reviews

The non-dispensing pharmacists' main focus was conducting clinical medication reviews among patients considered to be at risk of adverse drug events: elderly patients (age ≥ 65 years) with polypharmacy (use of ≥ 5 chronic medications).

The medication review started with a semi-structured interview with the patient in which the non-dispensing pharmacist identified the patient's experiences, needs and concerns about medication (step 1, [Supplementary Figure S1](#)). These were integrated with the medical records to determine potential drug therapy problems (step 2, [Supplementary Figure S1](#)). In the next three steps of the clinical medication review, the non-dispensing pharmacist developed a pharmaceutical care plan in collaboration with the patient and the GP, including recommendations to stop, start or switch medication, to adjust dosages or to improve adherence to medication. The recommendations were implemented and monitored, mainly by the non-dispensing pharmacist. The average time to complete all stages of a clinical medication review performed by the non-dispensing pharmacists in our study is ~ 100 – 120 minutes ([Supplementary Figure S1](#)).

Data collection

We used convenience sampling of patient data during 3 weeks, as we wanted to minimize the administrative burden for the non-dispensing pharmacists. The research team selected three data collection weeks, in July 2014, December 2014 and May 2015, and instructed each of nine non-dispensing pharmacists to complete an online data

form about the last 10 consecutive patients during that week who completed all stages of the clinical medication review. Thus, in total, they would collect 270 patients who had a medication review. The data form gathered detailed information about the type and number of drug therapy problems, type of medication, the extent of implementation of the proposed recommendations and the number of drug therapy problems that were solved. Recommendations were categorized in preventive interventions (aimed at following prophylactic guidelines) or corrective interventions (aimed at active patient problems, such as side effects) (Supplementary Table S1). Also, information was collected about the reasons why recommendations were not implemented and about the number of follow-up consultations with the non-dispensing pharmacist required to implement recommendations. Data were coded based upon the Systematic Tool to Reduce Inappropriate Prescribing (7). This tool consists of five steps and is part of the Dutch multidisciplinary guideline on polypharmacy. Step two is a structured pharmaceutical analysis, in which drug therapy problems can be identified according to seven categories that we used for the coding of our data (Supplementary Figure S1). Based upon practice experience with performing medication reviews and existing literature on this topic, we added an eight category: additional monitoring required.

To ensure consistency and accuracy of coding, all data were manually checked by an independent research assistant, and discrepancies were resolved by the principal investigator of this study (AH). For the patients of data collection weeks 2 and 3 ($n = 180$), the pharmaceutical care plan, patient's medical history, laboratory results and consultation notes from the patients' electronic medical records were available for follow-up. This additional information was used to verify whether drug therapy problems were actually solved. Also, only for the patients of data collection weeks 2 and 3, we were able to collect data on gender. Due to a technical error in the online data form, data on related medication were missing for 70 patients in data collection week 1.

Outcomes

Outcomes were (i) type and number of drug therapy problems, related medication and recommendations; (ii) the percentage of recommendations that were implemented and (iii) the percentage and type of drug therapy problems that were solved. Recommendations were marked into either preventive or corrective interventions. A recommendation was considered implemented when the GP endorsed the recommendation personally or after approval by the non-dispensing pharmacist or practice nurse. A drug therapy problem was considered solved when an active problem no longer existed or when a potential problem was successfully anticipated on (Supplementary Table S1).

Analyses

Analyses were performed using SPSS for Windows Version 21.0 to calculate baseline characteristics and outcomes on the number of drug therapy problems, proposed recommendations, the extent of implemented recommendations and the extent of solved drug therapy problems. Results were presented as means (with SD) and median (with interquartile range, IQR).

Results

We collected data about clinical medication reviews of 270 patients. The mean age of patients was 74 years, and 61% was female. The median number of chronic medication and comorbidities was 8 (IQR 5) and 6 (IQR 3), respectively (Table 1).

Table 1. Patient demographics of polypharmacy patients ($n = 270$) who had completed all stages of clinical medication review, selected by the non-dispensing pharmacists between June 2014 and May 2015

	Patients
Gender ^a , n (%)	
Male	70 (39)
Female	110 (61)
Unknown	90
Age, mean (SD)	74 (10)
Chronic medication ^a , median (IQR)	8 (5)
Comorbidities ^a , median (IQR)	6 (3)
Follow-up contacts with non-dispensing pharmacist, median (IQR)	2 (2)
Drug therapy problems	
Median (IQR)	5 (3)
Mean (SD)	4.8 (1.9)
Range	1–12

^a n , number; SD, standard deviation.

^aBased upon information from medical records and pharmaceutical care plan in data collection weeks 2 and 3.

During the reviews, 1292 drug therapy problems were identified, with a median of 5 (IQR 3) per patient (mean 4.8). The drug therapy problems concerned 194 different drugs within 75 different drug classes (29) (Table 2). Overtreatment was most frequently reported (24%) and often correlated to proton-pump inhibitors, antithrombotic agents and diuretics. Obviously, the most associated recommendation was to stop medication (Table 3). Twenty-one percent of the drug therapy problems was related to undertreatment, most frequently related to vitamin D, calcium and lipid-modifying agents. The most associated recommendation was to start medication. Seventeen percent of the drug therapy problems was related to side effects, most frequently related to lipid-modifying agents, beta-blocking agents and angiotensin-converting enzyme inhibitors. The most associated recommendation was to start or switch medication. Interaction and/or contraindication was only limited reported (2%) (Table 3).

In total, 83% of all recommendations were implemented by either the non-dispensing pharmacist (80%), GP (5%), practice nurse (3%), specialist (1%) or combined by different health care providers (11%). Implementation of recommendations often involved follow-up contacts with the non-dispensing pharmacist (median 2, IQR 2) (Table 1). The main reason that prevented implementation of the recommendation was a rejection by the patient (40%), mainly related to the advice to stop the use of proton-pump inhibitors, antidepressants, anxiolytics or analgesics (Supplementary Table S2).

In total, in 78% of the drug therapy problems, the implementation of the recommendations actually solved the drug therapy problem. After stratifying the implemented recommendations ($n = 1070$), we identified 601 preventive interventions (56%) in 259 patients. Almost all preventive interventions were considered solved (91%). We identified 382 corrective interventions (36%) in 182 patients. Sixty-four percent of the corrective interventions solved the patient problem. In 76% of patients ($n = 139$), at least one patient problem was solved. Patient problems related to taking medication, for example, due to swallowing issues, were most successfully solved (91%). Stopping medication to solve an active patient problem, such as a side effect, was successful in 40% of patients (Table 4). Corrective interventions were most commonly related to better pain control with acetaminophen and to reducing side effects of cardiovascular medications, such

Table 2. Medication related to the drug therapy problems identified in 270 polypharmacy patients who had completed all stages of clinical medication review performed by non-dispensing pharmacists in general practice between June 2014 and May 2015^a

Drug class ^b	Drug therapy problem, n (%)								
	Overreatment	Undertreatment	Medication not effective	Side effects	Interaction/contraindication	Incorrect dose	Suboptimal medication use	Monitoring required	Total
A02B drugs for peptic ulcer and GORD	59 (5)	8 (1)	4 (0.3)	6 (1)	1 (0.1)	6 (1)	4 (0.3)	3 (0.2)	91 (7)
A10B blood glucose lowering drugs, excl. insulins	8 (1)	2 (0.2)	1 (0.1)	9 (1)	0 (0)	3 (0.2)	5 (0.4)	1 (0.1)	29 (2)
A11C vitamin A and D	1 (0.1)	42 (3)	4 (0.3)	0 (0)	0 (0)	5 (0.4)	3 (0.2)	1 (0.1)	56 (4)
A12A calcium	3 (0.2)	40 (3)	0 (0)	1 (0.1)	1 (0.1)	4 (0.3)	3 (0.2)	1 (0.1)	53 (4)
B01A antithrombotic agents	18 (1)	6 (1)	3 (0.2)	9 (1)	2 (0.2)	3 (0.2)	4 (0.3)	0 (0)	45 (4)
C03A low-ceiling diuretics, thiazides	7 (1)	4 (0.3)	1 (0.1)	5 (0.4)	1 (0.1)	4 (0.3)	4 (0.3)	7 (1)	33 (3)
C03C high-ceiling diuretics	13 (1)	0 (0)	1 (0.1)	3 (0.2)	0 (0)	1 (0.1)	0 (0)	0 (0)	18 (1)
C07A beta-blocking agents	6 (1)	2 (0.2)	3 (0.2)	14 (1)	0 (0)	3 (0.2)	6 (1)	2 (0.2)	36 (3)
C08C selective calcium channel blockers	4 (0.3)	2 (0.2)	1 (0.1)	12 (1)	0 (0)	2 (0.2)	1 (0.1)	0 (0)	22 (2)
C09A ACE inhibitors	4 (0.3)	6 (1)	2 (0.2)	13 (1)	1 (0.1)	1 (0.1)	4 (0.3)	1 (0.1)	32 (3)
C10A lipid-modifying agents	6 (1)	19 (2)	7 (1)	15 (1)	1 (0.1)	1 (0.1)	5 (0.4)	3 (0.2)	57 (4)
G04C drugs used in benign prostatic hypertrophy	7 (1)	2 (0.2)	6 (1)	3 (0.2)	0 (0)	0 (0)	0 (0)	1 (0.1)	19 (2)
H03A thyroid preparations	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (0.2)	2 (0.2)	5 (0.4)	10 (1)
N02B other analgesics and antipyretics	1 (0.1)	17 (1)	1 (0.1)	4 (0.3)	1 (0.1)	2 (0.2)	1 (0.1)	0 (0)	27 (2)
N05C hypnotics and sedatives	8 (1)	1 (0.1)	2 (0.2)	2 (0.2)	0 (0)	0 (0)	1 (0.1)	0 (0)	14 (1)
N06A antidepressants	12 (1)	2 (0.2)	12 (1)	11 (1)	0 (0)	0 (0)	1 (0.1)	2 (0.2)	40 (3)
R03B other drugs for obstructive airway diseases, inhalants	6 (1)	1 (0.1)	5 (0.4)	2 (0.2)	0 (0)	1 (0.1)	1 (0.1)	1 (0.1)	17 (1)
Total	307 (24)	276 (21)	146 (11)	213 (17)	28 (2)	73 (6)	124 (10)	125 (10)	1292 (100)

Marked in bold: most common correlation between drug class and drug therapy problem.

Percentages <0.5 are reported to one decimal place.

GORD, gastro-oesophageal reflux disease.

^aData on related medication is missing for 70 patients in data collection week 1 due to a technical error in the online data form.

^bDrug class according to anatomical therapeutic chemical class (28).

Table 3. Drug therapy problems identified in 270 polypharmacy patients and related recommendations by non-dispensing pharmacists in general practice between June 2014 and May 2015

Recommendation	Drug therapy problem, <i>n</i> (%) ^a								
	Overtreatment	Undertreatment	Medication not effective	Side effects	Interaction/contraindication	Incorrect dose	Suboptimal medication use	Monitoring required	Total
Stop medication	237 (18)	2 (0.2)	59 (5)	88 (7)	10 (0.8)	0 (0)	11 (1)	0 (0)	407 (32)
Start medication	1 (0.1)	202 (6)	13 (1)	3 (0.2)	1 (0.1)	2 (0.2)	1 (0.1)	1 (0.1)	224 (17)
Switch medication	20 (2)	19 (2)	39 (3)	44 (3)	8 (1)	5 (0.4)	19 (2)	1 (0.1)	155 (12)
Change medication use	6 (1)	4 (0.3)	9 (1)	9 (1)	0 (0)	3 (0.2)	64 (5)	1 (0.1)	96 (7)
Adjust medication dose	35 (3)	15 (1)	10 (1)	41 (3)	3 (0.2)	55 (4)	3 (0.2)	1 (0.1)	163 (13)
Advice/education	7 (1)	13 (1)	9 (1)	15 (1)	5 (0.4)	5 (0.4)	25 (2)	2 (0.2)	81 (6)
Provide monitoring	1 (0.1)	5 (0.4)	5 (0.4)	12 (1)	1 (0.1)	2 (0.2)	1 (0.1)	109 (8)	136 (11)
Refer to healthcare professional	0 (0)	16 (1)	2 (0.2)	1 (0.1)	0 (0)	1 (0.1)	0 (0)	10 (1)	30 (2)
Total	307 (24)	276 (21)	146 (11)	213 (17)	28 (2)	73 (6)	124 (10)	125 (10)	1292 (100)

Marked in bold: The most common correlation between drug therapy problem and recommendation.

^aPercentages <0.5 are reported to one decimal place.

as beta blockers, statins and ACE-inhibitors. For these most common corrective interventions, the outcome assessment of patient's symptoms was tabulated (Table 5).

Due to a technical issue in the data form of data collection week 1, we had insufficient information of 87 implemented interventions (8%) to correctly stratify into either a preventive or corrective intervention.

Discussion

The results of our study demonstrate that medication reviews for elderly patients with polypharmacy performed by non-dispensing pharmacists in general practice result in the detection and resolution of a large number of drug therapy problems. The non-dispensing pharmacists implemented a high proportion of recommendations, covering a wide range of drugs. Follow-up consultations by the non-dispensing pharmacists often resulted in resolution of drug therapy problems, most frequently related to overtreatment and undertreatment. Solving problems that require dose adjustments or stopping of medication proved more challenging than preventive interventions.

To our knowledge, this is the first study that assessed the most common drug therapy problems as identified and solved by non-dispensing pharmacists in general practice. As a member of the general practice team, these pharmacists take integral responsibility for the pharmacotherapy for patients with multimorbidity. Unlike single disease clinics, such as diabetes, cardiovascular and lipid management clinics (30,31), this involves all drug classes, which requires both expert medication knowledge as well as the skills for integral patient management.

Our study demonstrated that the clinical medication review process resulted in a high implementation rate of recommendations. Although our study design was descriptive without control comparison, we think this is an important finding, as most studies on pharmacist-led medication reviews showed considerably lower compliance rates with recommendations (13–15,24,32). The most frequently identified drug therapy problems were—in line with previous studies—overtreatment and undertreatment, which accounted for almost half of all drug therapy problems (45%) (14,29,32,33). This is in line with earlier studies, in which non-adherence and drug selection problems were also frequently reported (14,24,25). Drug therapy problems because of drug–drug or drug–disease interactions were rare, which is probably a reflection of the widespread use of automated clinical risk management systems both in general practice and community pharmacy (34).

In contrast to earlier studies, we found that the most frequent recommendation among elderly was to stop medication. In other studies, the most frequent recommendation was to add pharmacotherapy (24,25,35). Stopping medication can be challenging as it requires a trusted relation between patient and pharmacist. This requires that the non-dispensing pharmacist takes into account the ideas, concerns and expectations of the patient. Our study underlines the need for a patient care oriented role for pharmacists in primary care and the potential to involve them in the evidence-based deprescribing process (36,37).

Overall, the total resolution rate of drug therapy problems by non-dispensing pharmacists in our study was high. We think that a key factor in this was the fact that the non-dispensing pharmacists offered structured follow-up consultations with the patients. Malet-Larrea *et al.* (38) have recently provided evidence showing the clinical benefits of including a follow-up service to clinical medication review. Interestingly, preventive interventions resulted in a higher

Table 4. Implementation of recommendations and drug therapy problems that were solved, stratified by preventive and corrective interventions, of 270 patients who had completed all stages of clinical medication review between June 2014 and May 2015

	Recommendation	Total, <i>n</i> (%)	Recommendation implemented, <i>n</i> (%)	Drug therapy problem solved, <i>n</i> (%)
All interventions	Stop medication	407 (32)	318 (78)	237 (75)
	Start medication	224 (17)	189 (84)	177 (94)
	Switch medication	155 (12)	117 (75)	75 (64)
	Change medication use	96 (7)	90 (94)	76 (84)
	Adjust medication dose	163 (13)	129 (79)	101 (78)
	Advice/education	81 (6)	71 (88)	36 (51)
	Provide monitoring	136 (11)	126 (93)	104 (83)
	Refer to healthcare professional	30 (2)	30 (100)	24 (80)
	Total	1292 (100)^a	1070 (83)	830 (78)^b
Preventive interventions	Stop medication	270 (21)	212 (79)	198 (93)
	Start medication	177 (14)	150 (85)	148 (99)
	Switch medication	60 (5)	41 (68)	34 (83)
	Change medication use	22 (2)	18 (82)	14 (78)
	Adjust medication dose	87 (7)	69 (79)	67 (97)
	Advice/education	28 (2)	25 (89)	11 (44)
	Provide monitoring	88 (7)	79 (90)	71 (90)
	Refer to healthcare professional	7 (1)	7 (100)	5 (71)
	Total	739 (57)	601 (81)	548 (91)
Corrective interventions	Stop medication	122 (9)	94 (77)	38 (40)
	Start medication	42 (3)	36 (86)	28 (78)
	Switch medication	76 (6)	62 (82)	39 (63)
	Change medication use	59 (5)	57 (97)	52 (91)
	Adjust medication dose	59 (5)	46 (78)	24 (52)
	Advice/education	37 (3)	33 (89)	23 (70)
	Provide monitoring	34 (3)	33 (97)	22 (67)
	Refer to healthcare professional	21 (2)	21 (100)	18 (86)
	Total	450 (35)	382 (85)	244 (64)

^aIn 87 cases, insufficient information to categorize the intervention into either preventive or corrective interventions.

^b11 Drug therapy problems were partially solved.

Table 5. Outcome assessment of patient's symptoms of most common drug therapy problems related to corrective interventions

Drug therapy problem (<i>n</i>)	Recommendation to solve drug therapy problem	Recommendation implemented, <i>n</i> (%)	Drug therapy problem solved, <i>n</i> (%)	Outcome assessment of symptoms
Undertreatment acetaminophen (17)	Start (11), dose adjustment (3), switch (1), advice (1), change use (1)	13 (76)	11 (65)	Better pain control
Side effects on statin (15)	Stop (8), switch (4), dose adjustment (2), advice (1)	13 (87)	6 (46)	Muscle pain reduced or disappeared
Side effects on betablocker (14)	Dose adjustment (10), stop (4)	9 (64)	5 (56)	Dizziness, fatigue, nightmares, erectile dysfunction reduced or disappeared
Side effects on ACE-inhibitor (13)	Switch (8), stop (2), change use (2), dose adjustment (1)	11 (85)	4 (36)	Orthostatic hypotension, cough and muscle ache disappeared

resolution rate of drug therapy problems than corrective interventions. We think there are several explanations. First, the problem is probably multifactorial, and a medication adjustment alone is sometimes insufficient. Second, intervening in the prescribing cascade may trigger other problems (e.g. side effects or interactions) or is simply not possible because of a too high risk of other—more serious—events. Third, the patient may be unwilling to accept a medication change. We identified anxiety as a main reason for not following a recommendation, particular in case of medication with an immediate effect, such as analgesics and proton-pump inhibitors. In addition, patients using drugs such as antidepressants and anxiolytics consider these essential for their well-being and are extra reluctant to change. Despite providing structured patient follow-up

by extensively trained non-dispensing pharmacists (27), some active patient problems thus remain challenging to solve.

This study has limitations. First, the observational study design, which lacks a control group, may have compromised the validity of the conclusions and might limit extrapolation. Nevertheless, we think the multicenter study design and the real-life setting allow for conclusions with a more than local impact. Second, the outcomes were primarily based upon self-report by the non-dispensing pharmacists. This might have resulted in social desirable answers. However, an independent research assistant manually checked the self-reports and compared it with the patient's medication list and consultation notes from the patients' electronic medical records. The principal investigator (AH) cross-checked the data. Third, the

extent to which drug therapy problems were solved was mainly based upon patient's self-report. This often did not include validated tools, such as Visual Analogue Scaling, to measure the intensity of pain across a continuum. With our data sources, we were still able to assess whether the drug therapy problem was totally, partially or not solved. In future research, we would recommend that the identification and reporting of drug therapy problems should be performed by an expert panel. Also, the implementation of a tool in digital medical information software to randomly select patients who had completed all stages of clinical medication review would be of benefit.

Conclusions

Solving drug therapy problems in elderly, complex patients with multimorbidity requires pharmaceutical expertise and intense monitoring. We demonstrated that non-dispensing pharmacists embedded in general practice were able to detect and solve a high proportion of drug therapy problems, which frequently resulted in stopping of medication.

Supplementary material

Supplementary material is available at *Family Practice* online.

Declaration

Funding: a research grant was obtained from the Netherlands Organization for Health Research and Development (grant agreement number 80-833600-98-10206). Implementation of non-dispensing pharmacists was financed by an unconditional grant of the Foundation Achmea Healthcare, a Dutch health insurance company (grant number Z456). Funding organizations were not involved in the design of this study or in the decision to submit this manuscript for publication.

Ethical approval: this is a substudy of a larger study (POINT), which was exempted of formal medical-ethical approval by the Medical Ethical Committee University Medical Centre Utrecht (January 2014, reference number 13-432C). All data were anonymized by the non-dispensing pharmacists to protect patient's privacy.

Conflict of interest: none.

References

1. ASHP statement on the role of the pharmacist in patient-focused care. American Society of Health-System Pharmacists. *Am J Health Syst Pharm*. 1995; 52: 1808–10.
2. Gandhi TK, Weingart SN, Borus J *et al*. Adverse drug events in ambulatory care. *N Engl J Med* 2003; 348: 1556–64.
3. Miller GC, Britth HC, Valenti L. Adverse drug events in general practice patients in Australia. *Med J Aust* 2006; 184: 321–4.
4. Sturkenboom MCJM, van den Bemt PMLA, de Smet PAGM, Hek K. <https://www.rijksoverheid.nl/documenten/rapporten/2017/01/31/ein-drapport-vervolgonderzoek-medicatieveiligheid>. Accessed November 12, 2018.
5. Leendertse AJ, Egberts AC, Stoker LJ, van den Bemt PM; HARM Study Group. Frequency of and risk factors for preventable medication-related hospital admissions in the Netherlands. *Arch Intern Med* 2008; 168: 1890–6.
6. Verduijn M, Leendertse A, Moeselaar A, De Wit N, Van Marum R. Multidisciplinaire richtlijn Polyfarmacie bij ouderen. *Huisarts Wet*. 2013; 56: 414–9.
7. Jokanovic N, Tan EC, Sudhakaran S *et al*. Pharmacist-led medication review in community settings: an overview of systematic reviews. *Res Social Adm Pharm* 2017; 13: 661–85.

8. Gilbert AL, Roughead EE, Beilby J, Mott K, Barratt JD. Collaborative medication management services: improving patient care. *Med J Aust* 2002; 177: 189–92.
9. Holland R, Desborough J, Goodyer L *et al*. Does pharmacist-led medication review help to reduce hospital admissions and deaths in older people? A systematic review and meta-analysis. *Br J Clin Pharmacol* 2008; 65: 303–16.
10. Blenkinsopp A, Bond C, Raynor DK. Medication reviews. *Br J Clin Pharmacol* 2012; 74: 573–80.
11. Malet-Larrea A, Goyenechea E, García-Cárdenas V *et al*. The impact of a medication review with follow-up service on hospital admissions in aged polypharmacy patients. *Br J Clin Pharmacol* 2016; 82: 831–8.
12. Hatah E, Braund R, Tordoff J, Duffull SB. A systematic review and meta-analysis of pharmacist-led fee-for-services medication review. *Br J Clin Pharmacol* 2014; 77: 102–15.
13. Kempen TGH, van de Steeg-van Gompel CH, Hoogland P, Liu Y, Bouvy ML. Large scale implementation of clinical medication reviews in Dutch community pharmacies: drug-related problems and interventions. *Int J Clin Pharm* 2014; 36: 630–5.
14. Willeboordse F, Schellevis FG, Chau SH, Hugtenburg JG, Elders PJM. The effectiveness of optimised clinical medication reviews for geriatric patients: opti-med a cluster randomised controlled trial. *Fam Pract* 2017; 34: 437–45.
15. Kwint HF, Bermingham L, Faber A, Gussekloo J, Bouvy ML. The relationship between the extent of collaboration of general practitioners and pharmacists and the implementation of recommendations arising from medication review: a systematic review. *Drugs Aging* 2013; 30: 91–102.
16. Edmunds J, Calnan MW. The reprofessionalisation of community pharmacy? An exploration of attitudes to extended roles for community pharmacists amongst pharmacists and General Practitioners in the United Kingdom. *Soc Sci Med*. 2001; 53: 943–55.
17. Tan EC, Stewart K, Elliott RA, George J. Pharmacist services provided in general practice clinics: a systematic review and meta-analysis. *Res Social Adm Pharm* 2014; 10: 608–22.
18. Krska J, Cromarty JA, Arris F *et al*. Pharmacist-led medication review in patients over 65: a randomized, controlled trial in primary care. *Age Ageing* 2001; 30: 205–11.
19. Zermansky AG, Petty DR, Raynor DK *et al*. Randomised controlled trial of clinical medication review by a pharmacist of elderly patients receiving repeat prescriptions in general practice. *BMJ* 2001; 323: 1340–3.
20. Roth MT, Ivey JL, Esserman DA *et al*. Individualized medication assessment and planning: optimizing medication use in older adults in the primary care setting. *Pharmacotherapy* 2013; 33: 787–97.
21. Sellors J, Kaczorowski J, Sellors C *et al*. A randomized controlled trial of a pharmacist consultation program for family physicians and their elderly patients. *CMAJ* 2003; 169: 17–22.
22. Iserts BJ, Schondelmeyer SW, Artz MB *et al*. Clinical and economic outcomes of medication therapy management services: the Minnesota experience. *J Am Pharm Assoc (2003)* 2008; 48: 203–11.
23. Dolovich L, Pottie K, Kaczorowski J *et al*. Integrating family medicine and pharmacy to advance primary care therapeutics. *Clin Pharmacol Ther* 2008; 83: 913–7.
24. Freeman CR, Cottrell WN, Kyle G, Williams ID, Nissen L. An evaluation of medication review reports across different settings. *Int J Clin Pharm* 2013; 35: 5–13.
25. Tan EC, Stewart K, Elliott RA, George J. Pharmacist consultations in general practice clinics: the pharmacists in practice study (PIPS). *Res Social Adm Pharm* 2014; 10: 623–32.
26. Hazen AC, Sloeserwij VM, Zwart DL *et al*. Design of the POINT study: Pharmacotherapy Optimisation through Integration of a Non-dispensing pharmacist in a primary care Team (POINT). *BMC Fam Pract* 2015; 16: 76.
27. Hazen ACM, de Groot E, Damoiseaux RAMJ *et al*. Design of a 15 months interprofessional workplace learning program to expand the added value of clinical pharmacists in primary care. *Curr Pharm Teach Learn*. 2017 (in press)
28. WHO Collaborating Centre for Drug Statistics Methodology. ATC/DDD Index 2018. https://www.whocc.no/atc_ddd_index/. Accessed November 12, 2018.

29. Milos V, Rekman E, Bondesson Å *et al.* Improving the quality of pharmacotherapy in elderly primary care patients through medication reviews: a randomised controlled study. *Drugs Aging* 2013; 30: 235–46.
30. Wubben DP, Vivian EM. Effects of pharmacist outpatient interventions on adults with diabetes mellitus: a systematic review. *Pharmacotherapy* 2008; 28: 421–36.
31. Santschi V, Chiolerio A, Colosimo AL *et al.* Improving blood pressure control through pharmacist interventions: a meta-analysis of randomized controlled trials. *J Am Heart Assoc* 2014; 3: e000718.
32. Chau SH, Jansen AP, van de Ven PM *et al.* Clinical medication reviews in elderly patients with polypharmacy: a cross-sectional study on drug-related problems in the Netherlands. *Int J Clin Pharm* 2016; 38: 46–53.
33. Kwint HF, Faber A, Gussekloo J, Bouvy ML. The contribution of patient interviews to the identification of drug-related problems in home medication review. *J Clin Pharm Ther* 2012; 37: 674–80.
34. Heringa M, Floor-Schreuderling A, Tromp PC, de Smet PA, Bouvy ML. Nature and frequency of drug therapy alerts generated by clinical decision support in community pharmacy. *Pharmacoepidemiol Drug Saf* 2016; 25: 82–9.
35. Castelino RL, Bajorek BV, Chen TF. Are interventions recommended by pharmacists during home medicines review evidence-based? *J Eval Clin Pract* 2011; 17: 104–10.
36. Reeve E, Shakib S, Hendrix I, Roberts MS, Wiese MD. Review of deprescribing processes and development of an evidence-based, patient-centred deprescribing process. *Br J Clin Pharmacol* 2014; 78: 738–47.
37. Reeve E, To J, Hendrix I *et al.* Patient barriers to and enablers of deprescribing: a systematic review. *Drugs Aging* 2013; 30: 793–807.
38. Malet-Larrea A, Goyenechea E, García-Cárdenas V *et al.* The impact of a medication review with follow-up service on hospital admissions in aged polypharmacy patients. *Br J Clin Pharmacol* 2016; 82: 831–8.