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Original Research

Process- and patient-reported outcomes of a multifaceted medication adherence intervention for hypertensive patients in secondary care

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Abstract

Background: Adherence to antihypertensive medications is suboptimal. Hospital pharmacist interventions including motivational interviewing (MI) might assist in improving adherence in patients with hypertension. For an intervention to be useful, it is important to have tools that can easily identify potential adherence problems.

Objectives: To evaluate process outcomes and patient- and pharmacist-reported outcomes of a pharmacist adherence intervention for hypertensive patients treated in hospital outpatient clinics. Secondly, to determine the agreement between two different adherence metrics: an adherence questionnaire used in the intervention and a prescription-based measure.

Methods: The development of the intervention was based on adherence and behavioral theories and evidence of effective interventions. This included a focused medication review, a patient interview, and follow-up telephone calls. Two tools were used to identify adherence problems: The Drug Adherence Work-up (DRAW) tool and an adherence questionnaire. Process data included drug-related problems (DRPs) with recommendations to the physicians, medication- and lifestyle problems identified at the patient interview, actions taken and time spent on the intervention.

Results: In total, 91 DRPs in 8 categories generated recommendations to the physicians; 56 recommendations were generated at the medication review and 35 at the patient interview. At the interview, 421 problems were identified, of which 60% were medication-related and 40% lifestyle-related. In connection with the interview, 528 actions were taken within 8 different categories. MI was a central technique applicable for most problems and was employed in nearly all patients (94%). About half of the patients reported increased focus on lifestyle change, and 21–39% reported increased knowledge, confidence and skills in relation to their medication as well as better quality of life. The pharmacists found that the

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intervention elements were meaningful pharmacist tasks, and that the DRAW tool was easy to use and helped them focus on addressing reasons for non-adherence. The mean total time spent by the pharmacist per patient was 2 h 14 min (SD 40 min).

Conclusions: A pharmacist-led, multifaceted, tailored adherence intervention was feasible for identifying and addressing a wide range of potential adherence and lifestyle problems. Among the intervention procedures, MI was a central technique, applicable in most types of problems. The questionnaire showed relatively little value for identifying non-adherence. The intervention was well accepted both by the pharmacists and the patients, thereby increasing the likeliness of successful implementation in routine practice.

Keywords: Hypertension; Medication adherence; Motivational interviewing; Pharmacy services; Hospital

Introduction

Treatment of hypertension significantly reduces the risk of cardiovascular event and stroke.[1] In clinical practice, however, hypertension can be difficult to control, and poor adherence to treatment is the most important cause of uncontrolled blood pressure (BP).[2] In patients with hypertension, a high level of adherence is associated with lower risk of hospitalization, and medical costs tend to be lower.[3] Given that only 50–60% of patients treated for hypertension are considered "good compliers",[4,5] there is a potential for substantial health gains through improved adherence.

The problem of non-adherence is multidimensional, driven by myriad practical and behavioral factors.[6] Interventions to improve adherence to antihypertensive agents therefore need to adopt multiple approaches, including technical, behavioral, cognitive and emotional elements in combination to address the reasons for non-adherence.[7–9] Still, even the most effective interventions have shown only modest effect on adherence.[7,8]

Due to the paucity of effective interventions, novel, cognitive-based behavioral change techniques have emerged. Among these, motivational interviewing (MI) is the most widely recognized one for improving long-term medication adherence.[10] MI is a non-judgmental, patient-centered counseling style to address behavioral, medical and psychosocial issues.[11] MI is designed to explore and resolve ambivalence to health behavioral change by mobilizing the patients' intrinsic values (autonomy) and helping them to discover their own resources and solution (self-efficacy). For hypertensive patients, a limited number of studies mostly focusing on primary care have shown promising results for MI in enhancing medication adherence.[12–18]

Another approach, with growing evidence of effect, is to supplement the traditional team of doctors and nurses with a clinical pharmacist particularly focusing on patients' drug-related problems and adherence behavior.[19–22]

A critical step for a clinical intervention to be useful is that potential adherence problems can be easily and validly identified. Asking the patient about adherence or using adherence questionnaires are feasible instruments.[23,24] However, the questionnaire chosen[25] and the manner in which patients are asked[24] are of decisive importance for the response. A recently developed tool, the DRug Adherence Work-up (DRAW©) tool, with questions based on current evidence of determinants of non-adherence, has shown promising results for identifying and addressing multiple reasons for non-adherence.[26,27]

So far, no pharmacist intervention using MI has targeted patients with hypertension treated in specialty care clinics in hospital settings. Accordingly, an adherence intervention was designed for this novel setting combining pharmacists integrated in team-based care, MI and interventions that had separately been shown to be effective in improving medication adherence. In an attempt to identify adherence problems, use of an adherence questionnaire validated in the target group, Danish patients with hypertension,[28] was combined with a modified version of the DRAW tool. When a new pharmacist intervention like this is developed, it is important to evaluate process and implementation variables such as acceptability, adoption and feasibility.[29] These variables can reveal valuable information of possible modification that may optimize and smoothen successful implementation.

The current study had two aims:

1) To evaluate process outcomes and patient- and pharmacist-reported outcomes of a pharmacist adherence intervention for hypertensive patients treated in hospital outpatient clinics.

2) To determine the agreement between two different adherence metrics, an adherence questionnaire used in the intervention and a prescription-based measure.

Methods

This trial report describes a pharmacist adherence intervention including three main elements: a focused medication review, a patient interview and follow-up telephone calls (Fig. 1).

The study includes evaluation of process outcomes, patients' and pharmacists' experiences with the intervention and a validation of a questionnaire used in the intervention.

Intervention strategy

The pharmacist intervention was designed as a multifaceted and patient-oriented intervention to address multiple reasons for non-adherence. The intervention included three main elements, all conducted by pharmacists: a focused medication review, an MI-based patient interview and at least two follow-up telephone calls (Fig. 1). The elements included have either alone or in combination shown effect for improvement of adherence in patients with hypertension.[7–9] The strategy for the intervention was to distinguish between different types of non-adherence according to the theories of intentional and non-intentional adherence,[30] the necessity-concern framework[31] and the World Health Organization model of five dimensions of adherence covering social/economic factors and factors related to therapy, patient, condition and health care system.[2]

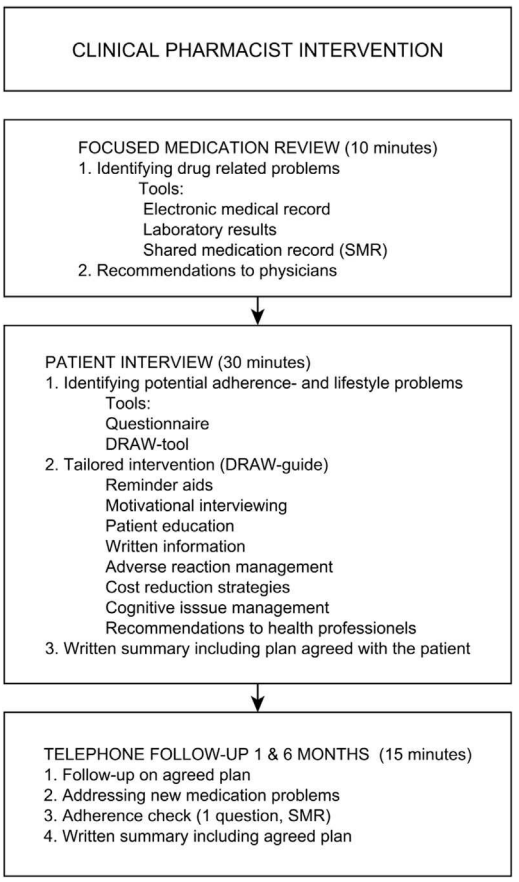

Fig. 1. Elements of the clinical pharmacist intervention. DRAW tool: Drug Adherence Work-up tool.

The medication review focused on identifying drug-related problems (DRPs) of antihypertensive and lipid-lowering agents with a potential of affecting adherence, and it followed the well-defined procedure developed by Strand et al.[32] Written guidelines containing potential DRPs with suggested recommendations were designed to ensure a standardized approach to DRP identification. Information sources used were the EMR, laboratory results and the shared medication record (SMR), which provides a shared overview of medication at transition of care. The SMR hosts information on all active, prescribed medications and pharmacy records of medication redeemed to each inhabitant in Denmark within the preceding 24 months.[33,34] Advice on DRPs was provided to the physician in charge either at a face-to-face meeting, by telephone or written in the medical records along with a notification in the record system to the physician concerned. If relevant, the DRPs were also discussed with the patient during the interview.

The aim of the patient interview was to identify and address potential adherence- and lifestyle problems in close cooperation with the patient. The dialog and behavioral counseling in the interview session was based on the concept of MI[11] and the Transtheoretical Model,[35] which asserts that behavioral change occurs in a temporally ordered series of stages. Relatives were allowed to participate in the interview. After the interview, the patients received a written summary of the interview including their own goals and a list of jointly agreed actions to be taken. To ensure standardization and to guide the pharmacist in assessing the multiple reasons for non-adherence, two tools were used: a medication adherence questionnaire validated in Danish users

of antihypertensive medication in primary care[28] and an adapted version of the DRAW tool.[26] The purpose of the adherence questionnaire was to provide a quick overview of possible adherence problems to the pharmacist. The questionnaire was filled out before the interview was initiated. The questionnaire contained 18 items grouped into four scales central for identifying adherence problems labeled as follows: patient's systolic BP, unintentional non-adherence, intentional non-adherence and concern about medications.[28] A 5-point, Likert-type scale was used for all items except one. The questionnaire scales have been validated against prescription register data and electronic monitoring containers.[28]

The DRAW tool including the DRAW guide was developed to help pharmacists assess and address multiple reasons for non-adherence.[26] The DRAW guide contains suggested actions to address each reason identified during the interview. The tool was modified by adding questions and actions about attitude towards medicine, additional (unknown) medications and lifestyle changes. The DRAW tool functioned as an interview guide, and all 14 questions were required to be asked. Patients' narratives about medication were generated by the first two questions and typically used as opening questions, but a fixed order was not required. The tool also contained two questions to the pharmacists addressing non-adherence related to cognitive issues and instrumental activity of daily living. The suggested actions in the DRAW guide are shown in Fig. 1 and described in detail in the Appendix.

The pharmacist interviewed the patient by telephone one month and six months after the hospital visit. The rationale for choosing one month was to have enough time for actions to be implemented and six months because adherence often decreases at that time.[8] Additional follow-up telephone calls were performed between the two scheduled telephone calls, if agreed necessary. A semi-structured interview format was used. The patient was screened for non-adherence (data not collected) by checking the SMR and asking a validated question, "How many times in the last week have you missed your medications"?[36] The agreed plan from the previous interview was followed up, and additional actions to be taken were planned, if necessary. The patient was asked about practical use of medication, adverse reactions and changes in medication since last interview. After the telephone calls, the patients received a written summary and a list of agreed actions to be taken. At the last follow-up, the patient's satisfaction and experience with the intervention were explored.

Five clinical pharmacists employed at the hospital pharmacy at Odense University Hospital carried out the intervention. Before the study, all clinical pharmacists participated in a 3-day external course in aspects of MI[11] and one day of internal training. The training was interactive with practice sessions incorporated. Additionally, the pharmacists were trained in the specific procedures developed for the study and knowledge of hypertension, risk factors, lifestyle support and medication adherence. To ensure consistency of the intervention, patient interviews were audiotaped and reviewed three times during the study. The recording was coded and evaluated by the consulting pharmacist and a second pharmacist by using a modified version of The MI Treatment Integrity (MITI) Code system 3.0.[37,38]

Inclusion of participants

Patients with hypertension were included from two endocrinology outpatient clinics and one cardiology outpatient clinic at Odense University Hospital, Denmark. Patients were eligible if they were 18 years or older and were prescribed at least one antihypertensive agent. They were excluded if they lived in a care home, received dose-dispensed medicine from a pharmacy, had medicine dispensed by a home nurse, had terminal illness, had conditions that precluded patient interview, e.g. dementia, or lived outside the Region of Southern Denmark. Lists of scheduled visits were electronically generated two weeks prior to clinic days, and from these lists the researcher identified eligible patients by reviewing each patient's electronic medical record (EMR). Patients were mailed written information and an invitation to participate in the study. At the clinic, the pharmacist provided oral information and if the patient wished to participate, informed consent was obtained. The Regional Scientific Ethical Committee for Southern Denmark and the Danish Data Protection Agency approved the study.

Data collection, outcomes and assessments

Data on age, sex, diagnosis, hospital setting, BP, risk factors and prescribed medication were collected from the patients' EMR and a local database hosting information on diabetes patients.

Refill data were obtained from the Odense University Pharmacoepidemiological Database (OPED).[39] The register covers all prescriptions for reimbursed medicine redeemed at Danish pharmacies by inhabitants in the Region of Southern Denmark. Medication adherence of antihypertensive agents was calculated using the medication possession ratio (MPR) measure[40] defined as the amount of drug available from refills during the observation period relative to the amount prescribed. Patients were considered adherent if they switched within drug classes and the estimate was adjusted accordingly. MPRs for each of the patient's antihypertensives were averaged to derive the regimen-MPR. A time-window of 12 months was used in the analysis. Prescriptions with a duration crossing the end of the observation period were truncated accordingly. The MPR was capped at 1.0 as rates exceeding 1.0 were regarded as full adherence rather than over-medication. The MPR estimate was refined in two ways as described by Vollmer et al[41]: (1) expanding the denominator to the entire follow-up period (in contrast to using the period from first to last dispensing) and (2) accounting for medications that individuals possessed at the start of the follow-up period. Non-adherence was defined as a regimen-MPR less than 0.80.

Process data collected at baseline included DRPs with recommendation to the physicians generated at the medication review and the interview, medication- and lifestyle problems identified at the interview, actions taken and time spent on each element of the intervention. Number of actions and time spent were also collected at the time of follow-up telephone calls. Pharmacist-reported and patient-reported experiences were collected at the end of intervention.

DRPs identified at the medication review and the interview resulting in recommendations to the physicians were categorized into eight categories using an adapted version of the classification described by Strand et al[32] together with suggested actions. Information of physicians' accept of the recommendations were collected from the patients' EMR. Problems and actions recorded from the interview were both categorized into eight categories.

Patients' satisfaction and experience with the intervention were examined at the 6-month telephone call using nine questions that included aspects of change in medication behavior (confidence, skills and knowledge), lifestyle and quality of life. Three- or 5-point, Likert-type scales were used for the items except for the final open-ended question that requested further comments.

The five clinical pharmacists reported their experiences from participation in the study at termination by answering a questionnaire that included items about training, relevance of the intervention components, collaboration with the physicians and usefulness of the DRAW tool. A 4-point, Likert-type scale was used for the items. Comments and suggestions for improvement of the intervention could be added by using free text.

Responses to the adherence questionnaire were categorized into seven non-adherence scales; the four central scales (described in the 'Intervention strategy' section), and three scales based on the number of answers indicating non-adherence. For a patient to be classified as non-adherent according to the three latter scales, at least one, two or three answers were to indicate non-adherence. Answers indicating non-adherence were for 17 of the 18 items defined as the two most extreme rates on the 5-point Likert-type scales or answering "yes" to the question whether latest systolic BP was above 140 mm Hg. Numbers of adherent/non-adherent patients from the seven scales of the questionnaire were compared with the numbers obtained from prescription refill records in two-by-two tables, and the agreement between the methods was calculated and analyzed. Predictive values, sensitivity and specificity were calculated for the scales using prescription refill records as reference ("gold standard").

Statistical analysis

Data were analyzed using Stata, Version 13. Results were reported in number and percentage for categorical variables and mean (standard deviation) or median (interquartile range) for continuous variables. Pharmacist intervariability in relation to problem types and actions were compared using chi-squared tests. Kappa statistics were used to compare the questionnaire and the refill measurements of adherence.

Results

Characteristics of the participants and the intervention

From December 2012 to July 2013, 240 hypertensive patients, considered eligible, were invited

to participate in the study. At the clinic encounter, 12 patients did not fulfill the in- and exclusion criteria, 59 declined to participate and 13 did not show up at the clinic. The remaining 156 patients (65%) received the intervention. Seven patients discontinued the intervention; one patient died, one patient discontinued antihypertensive treatment, four patients dropped out and one patient was lost to follow-up. Four of these patients discontinued the intervention before the one-month follow-up call. Between the two scheduled calls, one, two and three additional telephone calls were done to 30, 3 and 1 patient, respectively. The median number of patients per pharmacist was 36 (range 19–41). The mean time spent (SD) on the focused medication review, patient interview and telephone calls were 10 (5) minutes, 35 (10) minutes and 15 (7) minutes, respectively. For completed intervention, the mean total time the pharmacists spent per patient was 2 h 14 min (SD 40 min) and ranged from 65 min to 5 h 25 min.

The median age of the patients was 62 years (Table 1). The majority of patients were men (60%) and had other medical conditions (92% of the patients had diabetes and 81% had dyslipidemia). Ninety percent of the patients were overweight and 47% were obese (BMI $>$ 30 kg/m^2).

Among 125 patients with BP measures, 63% had uncontrolled BP, defined as higher than 140/90 mm Hg or 130/80 mm Hg in diabetics. Twenty patients were excluded from the assessment of adherence, as they had no refill of antihypertensive agents during the 12-month pre-study observation period. Among the remaining 136 patients, 20.6% were non-adherent (regimen-MPR $<$ 0.80) (Table 1).

Recommendations on drug-related problems

The focused medication review generated 56 recommendations on DRPs to the physicians, and during the patient interviews, an additional 35 were made. The type and acceptance rate of all 91 DRPs among 64 patients are shown in Table 2. Physicians accepted 64% of the recommendations, 4% were refused and 32% gave no response. The most common DRP was reconciliation errors (58%), which also had a low rate of acceptance (58%). When reconciliation errors were left out, the acceptance rate was 71%. The agents most commonly involved were renin angiotensin agents (23), diuretics (20), statins (19) and calcium antagonists (17) while beta-blockers were most rarely involved (2). The most frequent recommendations to the physicians after reconciliation (50) were to adjust dose (10), discontinue therapy (9), change therapy (8), or change to combination therapy (6).

Problems identified during the patient interview and actions taken

In total, 421 problems were identified during the patient interview of which 60% were related to medication and 40% to lifestyle (Tables 3 and 4).

Among the 421 problems, 87% were identified by 8 of the 16 DRAW tool questions (Table 3). In nearly all patients (98.7%), at least one problem was identified, while at least two and three problems were recognized in 85.2% and 53.8% of the

Table 1
Demographic and clinical characteristics of study participants

Variable (n = 156)	n (%)
Men	94 (60.3)
Age, median (IQR)	62 (54–68)
Systolic blood pressure mm Hg, mean (SD)[a]	136.1 ± 14.0
Diastolic blood pressure mm Hg, mean (SD)[a]	78.1 ± 9.9
Medications	
Diuretics	36 (23.1)
Calcium antagonists	73 (46.8)
Beta-blockers	42 (26.9)
Renin-angiotensin agents	143 (91.7)
Number of medications, median (IQR)	
Antihypertensive agents	2 (1–2)
Total number of unique medications	7 (5–9)
Non-adherent (regimen-MPR $<$ 0.8)[b,c]	28 (20.6)
Comorbidity	
Diabetes	143 (91.7)
Cardiovascular disease	46 (29.5)
Dyslipidemia	126 (80.8)
Cerebrovascular disease	12 (7.7)
Renal disease	21 (13.5)
Risk factors	
High alcohol consumption[d]	6 (3.8)
Smoker	30 (19.2)
BMI $>$30 kg/m^2	73 (46.8)

IQR: interquartile range; MPR: mediation possession ratio.

[a] Blood pressure analysis (n = 125).

[b] MPR analysis (n = 136).

[c] Average MPR for antihypertensive agents.

[d] Weekly consumption, women $>$14 drinks, men $>$21 drinks.

Table 2
Number of DRPs identified at medication reviews or at interviews resulting in recommendations to physicians. Acceptance rates of the recommendations

Type	*N*	%	% accepted
Complex dose regimen	11	12	64
Adverse drug reactions	9	10	78
Inappropriate dose	7	8	100
No indication/double prescribing	5	5	60
Need for additional drug therapy	4	4	50
Inappropriate drug	1	1	0
Drug interactions	1	1	100
Reconciliation errors	53	58	58
Total	91	100	64

patients. The mean (SD) number of problems addressed per patient was 2.7 (1.2). Except for lifestyle problems, the frequency with which the different types of problems were identified varied markedly among the pharmacists (Table 4).

Medication problems most frequently addressed were medication concern and belief, medication management and adverse reaction accounting for 22%, 14% and 11% of the total number of problems (Table 4). Among the 169 lifestyle problems addressed, the majority concerned exercise (31%) followed by diet (27%), weight reduction (26%) and smoking cessation (11%).

In connection with the interview, 528 actions were implemented for the 156 patients, i.e. mean (SD) of 3.4 (1.9) per patients, ranging among the pharmacist from 2.7 to 4.6 actions per patient. MI ($n = 315$) was the most frequent action (60%) and was exercised in nearly all patients (94%). The frequency for using patient education, adverse reaction management and drug regimen simplifying as actions varied significantly between the pharmacists (Table 4).

MI was used for all types of problems but most frequently for lifestyle change (150/315), concerns and beliefs about medication (92/315) and medication management (38/315). Patient education was most frequently used for lifestyle (21/86), concerns and beliefs about medication (20/86) and medication management (20/86). Written information was mainly used for lifestyle problems (24/28) and reminder aids mainly for medication management (21/23). Adverse reaction management was, apart from adverse reactions (20/28), used for concerns and beliefs about medication (8/28).

Actions taken at follow-up telephone calls

In total, 647 actions were taken during 335 follow-up telephone calls. MI was the most frequent action (74%) followed by patient education (14%) and adverse reaction management (4%). New actions were taken for 94% and 99% of the patients who completed the 1-month ($n = 152$) and 6-month ($n = 149$) telephone call. At the telephone calls at one month, six months, and at additional calls in-between ($n = 34$), the mean number (SD) of actions per patient was 1.8 (1.0), 2.1 (1.5) and 2.1 (1.1), respectively.

Patient-reported experiences

Nearly all patients reported satisfaction with participation in the study, and the majority of the patients had a positive view on the clinical pharmacist (Table 5). About half of the patients reported increased focus on lifestyle changes, and 39% of the patients reported increased knowledge about their medications. Approximately, one quarter of the patients had experienced an increased confidence with medication use, better skills for correct use of medications and better quality of life. The written summaries were very useful or somewhat useful for 71% of the patients.

Pharmacist-reported experiences

All five pharmacists found that the intervention elements were meaningful pharmacist tasks, and all agreed that the DRAW tool was easy to use and helped them focus on addressing reasons for non-adherence. They all reported that their competence had improved by being a part of the project and that they had been very properly or somewhat properly trained to deliver the intervention. Two pharmacists felt a high level of acceptance in the collaboration with the physicians while three pharmacists felt some level of acceptance. Two of the pharmacists found that using the DRAW tool at times made the dialog "stiff" as all questions were to be asked. All pharmacists found that the one month timespan between the patient interview and the first telephone call was appropriate, although one pharmacist stated, "it would be better if the use and time of follow-up telephone calls was based on individual need".

Response to the adherence questionnaire

The response to the 18 items of the questionnaire is shown in Table 6. When applying the seven non-

Table 3
Problems identified at the patient interview using the Modified Drug Adherence Work-up (DRAW©) Tool. Suggested actions with reference to the DRAW guide (Appendix)

	Patient interview ($n = 156$)	Problems identified, *n* (type)	Suggested actions (DRAW guide)
1	How do you feel about taken medications/Which thoughts do you have about medications?	72 (Medication concern and belief)	Motivational interviewing. Reinforcement of positive statements **C1 C2**
2	Please tell me how you take your medications every day?	26 (Medication management (MM))	Assess adherence; identify any problems; add to their knowledge
3	What are the pros and cons of handling your medication in this way?	4 (MM)	**A1 A2 B1 B2 D F**
4	Do you take other drugs herbal medicine) than those listed in the electronic medical record (EMR)?	21 (Drugs not listed in EMR)	Identify any problems; add to their knowledge **B1 B2 F**
5	Do you feel like you have too many medications or to many doses per day?	18 (Complex regimen)	Reduce number of meds per day by stopping/changing medications; Simplify regimen **A1 A2 C1 D F**
6	Do you sometimes forget to take your medication on routine days?	19 (MM)	Reminder aids, alarm or specialized packaging, SMS-service etc. Rule out anticholinergic meds
7	Do you forget on non-routine days such as weekends or when traveling?	5 (MM)	**A1 A2 E1 E2 F**
8	Do you have a concern that you medication is **not** helping you?	14 (Medication concern and belief)	Patient education; Motivational interviewing
9	Do you feel that you **do not** need this medication?	0	**B1 B2 C1**
10	Have you had any side effects?	44 (Adverse reactions)	Switch medications; symptom management; adjust regimen; Motivational interviewing. **B1 B2 C1 C2 F**
11	Are you concerned about side effects?	7 (Medication concern and belief)	
12	Is the cost of this medication too much?	13 (Costs)	Switch to less costly medication; cost reduction strategies **D F**
13	Are there other issues about the medication you want to talk about?	4 (Lifestyle) 3 (MM) 1 (Complex regimen) 1 (Adverse reaction) 1 (Self-monitoring)	Motivational interviewing **C1**
14	Are there any issues that you have considered in relation to your disease? (e.g. *stop smoking, diet*)	165 (Lifestyle) 3 (Self-monitoring)	Motivational interviewing. Add to their knowledge **B1 B2 C1**
	Pharmacist		
15	At any time during the interview, did you sense an issue about decrease in cognitive function?	0	Rule out anticholinergic. Referral to medications assistance **A1 A2 E1 E2 F**
16	Is there a limitation on instrumental activities of daily living that can affect adherence or use of adherence aids?	0	

adherence scales to the cohort of patients, the scale "high BP" showed the highest prevalence (31.2%) followed by the "medication concern" scale (18.2%) (Table 7). The lowest prevalence was found for unintentional non-adherence, i.e. 3.2%. For the scales based on one, two and three answers indicating non-adherence, the prevalence was 44.2%, 13.6% and 8.4%, respectively.

Table 4
Problems identified and actions taken after the patient interview. Pharmacist intervariability in relation to problems identified and actions taken

	N	%	Patients with problem/action %		
			All	Range pharmacists	*p*-Value[a]
Problem ($n = 421$)					
Lifestyle	169	40.1	75.6	65.8–80.5	0.60
Medication concerns and beliefs	93	22.1	59.6	31.8–68.3	0.03
Medication management	57	13.5	36.5	5.3–50.0	0.02
Adverse reactions	45	10.7	28.8	9.8–44.4	0.02
Drugs taken not listed in EMR	21	5.0	13.5	0.0–26.3	0.03
Complex regimen	19	4.5	12.2	4.5–22.2	0.24
Costs	13	3.1	8.3	2.6–15.8	0.49
Self-monitoring	4	1.0	2.6	0.0–5.6	0.37
Action ($n = 528$)					
Motivational interviewing	315	59.7	93.6	84.2–100.0	0.09
Patient education	86	16.3	43.6	18.2–65.9	<0.01
Recommendations for physicians	35	6.6	18.6	10.5–27.8	0.26
Adverse reactions management	28	5.3	17.3	2.4–47.4	<0.01
Written information	28	5.3	16.0	9.1–21.1	0.74
Reminder aids	23	4.4	13.5	5.3–18.2	0.47
Simplifying dose regimen	9	1.7	5.8	0.0–14.6	0.02
Cost reduction	4	0.8	2.6	0.0–10.5	0.13

Patients ($n = 156$); Pharmacist ($n = 5$); EMR = electronic medical record.
[a] Chi-squared test comparing pharmacist intervariability.

Comparison of adherence as assessed by prescription refill records and by the questionnaire

Among the 136 patients with adherence measures from prescription data, one had not filled out the questionnaire due to impaired vision. Data from the remaining 135 patients were used for comparison of the two adherence metrics. The agreement between the refill method and the different adherence categories of the questionnaire are shown in Table 8. The highest agreement occurred with the "medication concern" scale

Table 5
Patients' experiences and satisfaction with participation in the study

$N = 149$	Better	The same	Worse		
	n (%)	*n* (%)	*n* (%)		
Did participating in the study change your:					
Confidence with medication use	40 (27)	109 (73)	0		
Skills about medication use	31 (21)	118 (79)	0		
Knowledge about your medications	58 (39)	90 (60)	1 (0.7)		
Focus on change of lifestyle	70 (47)	78 (52)	1 (0.7)		
Quality of life	34 (23)	113 (76)	2 (1.3)		
Your view on the clinical pharmacist	Positive	Neutral	Negative		
	126 (85)	22 (15)	1 (0.7)		
Satisfaction with participation in the study	Very satisfied	Satisfied	Neither satisfied nor dissatisfied		
	94 (63)	46 (31)	9 (6)		
Were the summaries useful?	Very	Somewhat	Less	Not at all	Not relevant
$N = 131$	34 (26)	59 (45)	16 (12)	12 (10)	9 (7)

Table 6
Responses to adherence questionnaire

No.	$N = 154$	*n* (%)	*n* (%)	*n* (%)	*n* (%)	*n* (%)
		Yes	No	Don't no		
1	Were you high blood pressure more than 140 mm Hg at latest measure?	48 (31)	80 (52)	26 (17)		
		Always	Often	At times	Rarely	Never
2	I take my blood pressure (BP) meds exactly as instructed	142 (92)	7 (5)	2 (1)	1 (1)	2 (1)
3	I generally forget to take my BP meds	2 (1)	3 (2)	41 (27)	107 (69)	1 (1)
4	I forget to take my BP meds when I am not at home	1 (1)	1 (1)	8 (5)	35 (23)	109 (71)
5	I forget to take my BP meds when I am busy[a]	0	2 (1)	9 (6)	29 (19)	113 (73)
6	I have difficulties remembering to take my BP meds[b]	1 (1)	2 (1)	6 (4)	22 (14)	121 (79)
7	I stop taking my BP meds for a while	1 (1)	1 (1)	2 (1)	6 (4)	144 (94)
8	I take less of my BP meds than instructed	1 (1)	0	0	1 (1)	152 (99)
9	I take more of my BP meds than instructed[a]	0	0	0	0	153 (99)
10	I Decide to miss out a dose	1 (1)	1 (1)	1 (1)	8 (5)	143 (93)
11	I stop taking my BP meds when I feel my blood pressure is under control	0	1 (1)	1 (1)	2 (1)	150 (97)
12	I stop taking my BP meds if I do something else to improve my blood pressure (e.g. exercise)	0	0	0	1 (1)	152 (99)
13	I stop taking BP meds if I believe they don't work[a]	0	1 (1)	2 (1)	0	151 (98)
		Not at all sure	Not sure	Maybe	Almost sure	Very sure
14	I will take my meds as instructed, if taking BP meds long-life, concerns me	4 (3)	4 (3)	0	8 (5)	138 (90)
15	I will take my meds as instructed, if I experience adverse reactions	6 (4)	10 (6)	24 (16)	31 (20)	83 (54)
16	I will take my meds as instructed, if I am concerned about becoming dependent of my BP meds	4 (3)	3 (2)	12 (8)	18 (12)	117 (76)
17	I will take my meds as instructed, if the BP meds make me tired	2 (1)	6 (4)	12 (8)	16 (10)	118 (77)
18	I will take my meds as instructed, if the BP meds make me dizzy	4 (3)	11 (7)	14 (9)	22 (14)	103 (67)

[a] $N = 153$.
[b] $N = 152$.

and the "two answers" scale, which had kappa values of 0.27 and 0.25, respectively. The sensitivity of the latter was slightly higher than the "medication concern" measure (92.5% vs. 88.8%) and the specificity was slightly lower (28.6% vs. 35.7%). The values for predictive of adherence and non-adherence were more than 80% and 45%, respectively, for both tests. The lowest agreement with the refill method was seen with the systolic BP item ($k = 0.04$) and the intentional adherence scale ($k = 0.06$).

Discussion

An individualized, multifaceted adherence intervention was developed for patients with hypertension with a strong focus on the patient's own resources. The intervention was built on solid theoretical foundations and existing evidence of effective interventions, and both are considered essential for development of successful complex programs.[42] Other variables that are important to evaluate before implementation in larger

Table 7
Questionnaire responses distributed across seven different non-adherence scales

Non-adherence scales ($N = 154$)	Non-adherent	
	N	%
1. Systolic BP > 140 mm Hg[a]	48	31.2
2. Unintentional Non-adherence[b]	5	3.2
3. Intentional Non-adherence[c]	6	3.9
4. Concern about medications[d]	28	18.2
5. Answers ≥1 indicating non-adherence[e]	68	44.2
6. Answers ≥2 indicating non-adherence[e]	21	13.6
7. Answers ≥3 indicating non-adherence[e]	13	8.4

[a] Question no. 1 = yes. Nos. of the questions are shown in Table 6.

[b] 1 of question no. 2 = rarely/never or questions no. 3–6 = always/often.

[c] 1 of questions no. 7–13 = always/often.

[d] 1 of questions no. 14–18 = not at all sure/not sure.

[e] Indication of non-adherence: question no. 1 = yes, question no. 2 = rarely/never or questions no. 3–13 = always/often, questions no. 14–18 = not at all sure/not sure.

populations are acceptability, feasibility, adoption and cost of the intervention.[29]

According to the process evaluation, the intervention was feasible for identifying and addressing various potential adherence- and lifestyle problems. The patients were satisfied with participation in the study, and the acceptance seemed good as only a few patients did not complete the intervention. The patient evaluation suggests that the intervention had an influence on patients' empowerment to manage their medication and even on their quality of life. The sample size and the lack of a control group, however, limits the results and patient-reported outcomes should be explored with validated methods in further studies.

Another positive benefit was that the pharmacists identified DRPs in 41% of the patients. Most suggestions were accepted by the physicians, indicating that the intervention is useful for optimizing therapy. The mean acceptance rate was 64% (Table 2) which is similar to the high rates seen in other studies where pharmacists were in contact with patients and had face-to-face meetings with physicians for decision-making about DRPs.[43] A large part of the DRPs were identified during the patient interviews emphasizing that medication review without patient contact is less effective.[44]

The intervention was carried out by clinical pharmacists. Pharmacists are trained in addressing medication management, potential interactions and adverse reactions, and making use of pharmacists trained in adherence counseling in team-based care is an established model for effective adherence intervention.[19–22] The pharmacists found that the intervention tasks matched their professional skills but a main challenge was to establish a good collaboration with the physician. The clinics had no prior experience with pharmacist collaboration. Before the study, the pharmacists were presented to the physicians by mailed, written information and posters, but not all the pharmacists had met the physician face-to-face before initiation of the study; hence, a run-in phase might have strengthened the interpersonal relationship. Regular participation of the clinical pharmacists in meetings with teams for discussion of care as well as regular meetings during the study with feedback to the physicians about progress and experiences are other means of strengthening the implementation.[45]

The pharmacists found the DRAW tool very useful for identifying specific reasons for non-adherence. This is similar to what was found by Doucette when developing the tool.[26] Usefulness of the tool was also reported in a recent large evaluation where the tool was used in 5–10-min encounters.[27] In the evaluation, the users reported that time limitation and required additional efforts from both patients and pharmacists were potential barriers for incorporating the tool into busy workflows. Our encounters were considerably longer; however, time barriers were not reported. Some of the pharmacists found that using the DRAW tool made the dialog more "stiff" at times as all questions were to be asked. The majority of the problems (87%) were identified from half of the DRAW items suggesting that the DRAW tool could be shortened with minimal consequences for the ability to identify problems. A shorter DRAW tool would be time-saving with the potential of a more cost-effective and more user-friendly intervention and should be further explored.

A potential limitation in using the DRAW tool as a manual is that it might violate MI itself by the pharmacist setting the agenda rather than the patient.[11] Manually guided MI has been associated with smaller effect size.[46] To avoid this, narrative techniques were used to identify the key issues most important for the patient. A major strength of manuals is that they facilitate standardization.

Table 8
Agreement between adherence as assessed by an adherence questionnaire and adherence as assessed by prescription data. Predictive values, sensitivity and specificity of the questionnaire

Adherence scales ($n = 135$)	Refill methods		Agreement %	Kappa	Sensitivity	Specificity	PPV	NPV
	Adherent *n*	Non-adherent *n*						
1. Systolic blood pressure> 140 mm Hg								
Adherent	77	19	64	0.04	72.0	32.1	80.2	23.1
Non-adherent	30	9						
2. Unintentional non-adherence								
Adherent	105	25	80	0.13	98.1	10.7	80.8	60.0
Non-adherent	2	3						
3. Intentional non-adherence								
Adherent	104	26	79	0.06	97.2	7.1	80.0	40.0
Non-adherent	3	2						
4. Concern about medications								
Adherent	95	18	78	0.27	88.8	35.7	84.1	45.5
Non-adherent	12	10						
5. Answers ≥1 indicating non-adherence								
Adherent	65	13	59	0.10	60.7	53.6	83.3	26.3
Non-adherent	42	15						
6. Answers ≥2 indicating non-adherence								
Adherent	99	20	79	0.25	92.5	28.6	83.2	50.0
Non-adherent	8	8						
7. Answers ≥3 indicating non-adherence								
Adherent	103	22	81	0.23	96.3	21.4	82.4	60.0
Non-adherent	4	6						

PPV: positive predictive value, NPV: negative predictive value.

Without a manual, an even greater variability might have been seen in relation to problems and actions addressed by the pharmacists. Dissimilar categorization, personal preferences or the nature of the intervention being individualized may also explain the variability.

The intervention elements are quite general, and translation to other outpatient settings and chronic medication users could be easily done. Cost-effectiveness studies and larger controlled studies to assess the intervention effect on clinical outcomes are warranted prior to a routine implementation. However, a similar multifaceted pharmacist intervention was found to be cost-neutral even though the pharmacist spent twice as much time on each patient than in the current study.[19] For follow-up, we used telephone contact, which allows individualized personal interaction at minimal cost without the time and transportation barriers associated with clinic visits.

Most adherence intervention studies using MI in hypertensive patients[12–18] have demonstrated a positive outcome on adherence and/or BP.[12–16] Similar to our study, two studies were pharmacist-led[15,18] and three studies used multicomponent interventions.[12,15,18] The interventions differed considerably in choice of profession delivering the intervention, intensity, training in MI and the components used (medication review, reminders, medication management, dose aids, follow-up visit or telephone calls, BP self-monitoring, arranging family adherence support, patient education/information and feedback on pill count/refill data).[12,15,18] Primary care was the main focus of most studies[13,15–18]; two studies included patients from both primary and hospital clinics[12,14] and one was performed in hospital outpatient clinics in Jordan.[16] The latter intervention was a 3-month, high-intensive, nurse-led intervention including seven MI sessions. To our knowledge, this is the

first study on a pharmacist-led, MI-based adherence intervention targeting hypertensive patients in a hospital setting. Contrary to this study, most of the MI studies only included patients with indication of poor adherence, such as poor BP control or poor refill adherence.[12,13,15,18] However, a considerable part of the patients in our study had probably a potential risk of poor adherence as the majority of them had uncontrolled BP. Polypharmacy was also present, which is a well-known predictor of non-adherence.[6] As opposed to this, severe comorbidity (92% of the cohort had diabetes) is known to positively affect adherence.[6,47] Predictors should, however, be used with caution for targeting non-adherence.[6] Instead, validated self-report tools and objective assessments methods are recommendable for identifying non-adherence.[6]

Among more than 40 adherence scales,[25] preference was given to one particular scale validated in a population similar to the population in the study.[28] This scale was able to differentiate among various non-adherence behaviors. The prevalence of intentional and non-intentional adherence was 3% and 4%, respectively, which is lower than the prevalence found for other scales.[30,48,49] A recent study has suggested that non-intentional adherence is overestimated if the influence of concern about medication is neglected.[49] In accordance with this, the questionnaire included a medication concern scale, which together with the "two answers" scale showed the best agreement with the refill measures. Sensitivity and specificity for the two scales were about 90% and 30%. This is comparable to the well-established Morisky scale with sensitivity and specificity of 73% and 36% when tested against prescription refill records.[25] In general, the agreement between classification methods was slight to fair, with kappa values below 0.3. The low specificity of the questionnaire scales and the fairly low agreement with pharmacy refill data suggest that the questionnaire only has little value for identifying non-adherence. As the adherence questionnaire was not a core component, i.e. an essential and indispensable element of the intervention,[45] this element can be omitted possibly without affecting the effect of the intervention.

In recent years, many health care systems are moving towards easier access to electronic pharmacy data. Such data provide an objective and readily available source of adherence information.[50] This is also the case in Denmark where the SMR has recently been implemented.[33] When this study was conducted, it was not fully implemented and reliable for precise estimation,[51] but henceforth, when data can be processed and delivered to both patients and providers in a timely and processed manner, electronic data will definitely play an important role in improving adherence both in daily practice and in clinical research.

Conclusion

The study showed that a pharmacist-led, multifaceted, tailored adherence in a hospital setting was feasible for identifying and addressing a wide range of potential adherence and lifestyle-related problems. Among the intervention procedures, MI was a central technique, applicable in most types of problems.

Among the scales of the questionnaire, the" medication concern" scale and the "two answers" scale demonstrated the best agreement with the refill measures. The specificity for the two scales was low, and the agreement with refill data were fairly low suggesting the questionnaire only has little value for identifying non-adherence.

The intervention was well accepted both by the pharmacists and the patients and the intervention elements are quite general, which all increases the likeliness of successful implementation in routine practice. Cost-effectiveness studies and results from larger controlled studies on the intervention effect on clinical outcomes are warranted prior to a routine implementation.

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Appendix

DRAW©-guide

DRAW© guide – modified		
A	**A1 Reminder aids** Day/time pill containers, SMS service, cell phone alarm, medication calendar, apps, mnemonic rule (for more options see notes). Toolbox: Reminders aids for demonstration.	**A2 Simplifying regimen** Use combination drugs when possible* Use long acting drugs where possible* Reducing number of medications*
B	**B1 Patient education** Addresses any identified knowledge deficiencies e.g. area dealing with medication, blood pressure, disease, health system, self-management. Refrain from reiterating that their physician ordered it. Positive reinforcement of the benefits sounds better than being told about the negative outcomes from non-adherence. Toolbox: Cardiovascular risk assessment tool	**B2 Written information** Toolbox: Educational material about antihypertensive and lipid-lowering medications, adherence, hypertension and lifestyle issues.
C	**C1 Motivational interviewing (MI)** MI addresses concerns about the effectiveness, necessity or adverse reactions of the medications. Also useful for change of lifestyle. 1. Use open-ended question and listen well to understand their concerns and problems. 2. Explore ambivalence and evoke change talk by using OARS (open-ended questions, affirm, reflective listening, and summarize) and tools such as wheel of changes, scaling-questions and balance sheets. Indicators of change talk are their DESIRE, their ABILITY, their REASONS and their NEED to make change. Reinforce their change statements. 3. Ask and listen for their COMMITMENT and TAKING STEPS to make changes. When you hear these, they are motivators or action to encourage. If you ask for permission you can present different possibly steps for the patient, but it is the patient's choice, whether he/she find them useful. 4. Make summaries of the patient's motivation for change, possibilities and future steps. Toolbox: The decisional balance schedule, the visual analog scale and stage of change sheet.	**C2 Adverse reactions/symptom management** Consider if the symptoms are consistent with adverse reactions of the medications the patient is taken. Consider if the symptoms need to be treated or if there is a need to make a change in treatment (change drug, dose reduction*).
D	**Cost reduction strategies** Generic substitution Therapeutic interchange* Reducing number of medications* Use of combination drug when possible* Tablet splitting (if possible and appropriate)	
E	**E1 Cognitive issues** Rule out that anticholinergics (antihistamines, tricyclic antidepressants, antipsychotics) could be contributing to cognitive memory decline. Consider a substitute for the anticholinergic medication*. Consider if the patient should have	**E2 Instrumental activities of daily living (IADL)** Considering the type of adherence aid with regard to visual restriction, having trouble reading or having difficulty in opening the pack.

(*continued on next page*)

(*continued*)

DRAW© guide – modified	
	assistance from visiting nurse, relatives or dose dispensing and discuss it with the health personnel at the department.
F	***Medicines Recommendation for the physician/nurse**
	Marked issues and drug interactions