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Original Research

A pharmacist-led follow-up program for patients with established coronary heart disease in North Norway – a randomized controlled trial

Beate H. GARCIA, Trude GIVERHAUG, June U. HØGLI, Frode SKJOLD, Lars SMÅBREKKE.

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ABSTRACT[*]

Objectives: The aim of the study was twofold; 1) to develop a clinical pharmacist-led 12 month lasting follow-up program for patients with established coronary heart disease (CHD) discharged from the University Hospital of North Norway, and 2) to explore the impact of the program with regards to adherence to a medication assessment tool for secondary prevention of CHD and change in biomedical risk factors.

Methods: A total of 102 patients aged 18-82 years were enrolled in a non-blinded randomized controlled trial with an intervention group and a control group. The intervention comprised medication reconciliation, medication review and patient education during three meetings; at discharge, after three months and after twelve months. The control group received standard care from their general practitioner. Primary outcomes were adherence to clinical guideline recommendations concerning prescription, therapy goal achievement and lifestyle education defined in the medication assessment tool for secondary prevention of CHD (MAT-CHDSP). Secondary outcomes included changes in the biomedical risk factors cholesterol, blood pressure and blood glucose.

Results: Ninety-four patients completed the trial, 48 intervention group patients and 46 controls. Appropriate prescribing was high, but therapy goal achievement was low in both groups. Overall adherence to MAT-CHDSP criteria increased in both groups and was significantly higher in the intervention group at study end, 78.4% vs. 62.0%, p<0.001. The difference was statistically significant for the documented lifestyle advices in intervention group patients. No significant improvements in biomedical risk factors were observed in favor of the intervention group.

Conclusions: The study showed an increased guideline adherence in both study groups. This indicates that attention to clinical practice guideline recommendations in itself increases adherence – which may be a clinical pharmacist task. A larger adequately powered study is needed to show a significant difference in biomedical risk factor improvements in favor of the intervention. Amendments to the follow-up program are suggested before implementation in standard patient care can be recommended.

Keywords: Pharmaceutical Services; Medication Reconciliation; Pharmacists; Coronary Disease; Randomized Controlled Trials as Topic; Norway

[*] **Beate Hennie GARCIA**. Cand Pharm & PhD. Hospital Pharmacy of North Norway; & Department of Pharmacy, University of Tromsø. Tromsø (Norway). beate.garcia@uit.no

Trude GIVERHAUG. Cand Pharm & PhD. Regional Drug Information Center of North Norway & University Hospital of North-Norway. Tromsø (Norway). trude.giverhaug@unn.no

June Utnes HØGLI. Master of Pharmacy. Department of Pharmacy, University of Tromsø. Tromsø (Norway). june.utnes@uit.no

Frode SKJOLD. Master of Statistics. Department of Pharmacy, University of Tromsø, Tromsø (Norway). frode.skjold@uit.no

Lars SMÅBREKKE. Cand Pharm, MPH & PhD. Department of Pharmacy, University of Tromsø. Tromsø (Norway). lars.smabrekke@uit.no

INTRODUCTION

Coronary heart disease (CHD) is the leading cause of death world-wide, and the major biomedical risk factors being high blood pressure (BP), high blood cholesterol, smoking, unhealthy diet, physical inactivity, diabetes, advancing age and genetic disposition.[1] Death rates due to CHD are decreasing in most developed countries, but are still a major public health concern.[2] Clinical practice guidelines are cornerstones for quality improvement, and are constantly developed to support clinicians, health personnel and patients regarding choice of therapy and monitoring.[3-5] Adherence to clinical practice guidelines has been shown to reduce morbidity, mortality and overall treatment costs in patients with CHD.[6,7] Still, non-adherence to guidelines and achievement of therapeutic goals are inadequate in this patient group.[1,7-10]

Pharmaceutical care programs developed and implemented by clinical pharmacists have improved the quality of care in both ambulatory care and hospitalized patients with various chronic diseases.[11] Considering the substantial body of literature showing benefits of pharmacist involvement in managing risk factors related to CHD, pharmacist-led follow-up programs of this patient group are scarce. The best described programs are developed in the United States and the United Kingdom[12-14], where pharmacists have been recognized as health care practitioners since the 1990s.[15] The largest European program within secondary prevention of CHD (CHDSP), the nurse-coordinated, multidisciplinary, EuroAction program, was initiated in 2002 by the European Society of Cardiology as a reaction to alarming results of large European surveys on CHDSP.[16,17] EuroAction has focused upon prescribing of appropriate drugs, achievement of therapy goals, and changes in lifestyle behavior. Results from nine European countries indicate that the program has a significant effect on lifestyle changes, waist circumference, systolic and diastolic BP, and fasting blood glucose.

In previous studies, we have identified a significant potential for improvement in patients with established CHD discharged from our hospital, especially regarding achievement of therapy goals, follow-up on unachieved therapy goals and documentation of lifestyle recommendations.[18,19] The aim of the present study was to design a pharmacist-led follow-up program, and to explore its influences on adherence to clinical practice guidelines as well as changes in biomedical risk factors relevant for CHDSP.

METHODS

Study design

The study was a non-blinded, randomized controlled trial with an intervention group (IG) and a control group (CG). The study site was the University Hospital of North Norway (UNN), a 650-bed teaching hospital. UNN is the leading health care provider in the area of North Norway, and serves about 465,000 inhabitants with respect of procedures like percutaneous coronary interventions and coronary bypass.[20]

Study subjects, enrolment and randomization

Patients were recruited from the cardiology ward at UNN during 205 days in the period February 1, 2009 to June 30, 2010 (18 months). Only patients with established CHD were eligible for inclusion. This was defined by a diagnosis of present or previous myocardial infarction, angina pectoris, coronary stent implantation or bypass operation, ascertained by International Statistical Classification of Diseases and Related Health Problems (ICD) code in medical records. Other inclusion criteria included: age 18 to 80 years, self-administration of medications at home, and registered home address within one of the three closest communities to the hospital, i.e. Tromsø, Balsfjord and Karlsoey. Patients were excluded if they were already included in another ongoing clinical studies at the ward[21], if they had terminal cancer or if they already received pharmaceutical care at the heart-failure clinic.

The clinical pharmacist working at the ward identified eligible patients every morning by reviewing patient lists when it was present at the ward. She then informed the patients about the study and invited them to participate. Patients were allocated to intervention group (IG) or control group (CG) in a 1:1 relationship applying an online randomization procedure, stratifying on gender.[22] We informed patients instantly about randomization results, as they were going to meet the clinical pharmacist at hospital discharge.

Sample size

Sample size calculation was based on results from our pilot study revealing that 22% of patients discharged from UNN after elective PCI had achieved a blood pressure (BP) lower than 130/80 mmHg.[18] This particular guideline recommendation was chosen due to its low adherence and consequently its improvement potential. A 80% power to detect an increase in BP goal achievement from 20% to 40% in IG patients only, required a sample size of 101 patients in each group, assuming 10% loss.

Standard care

Patients allocated to the CG received standard care from the hospital and general practitioners (GPs). If patients experience a cardiac event (MI, bypass, PCI) for the first time, the hospital physician refers them to the hospital for follow-up approximately three months after the event. For some patients replaced by a two-day patient-school for CHD including physiotherapy, training, consultation with cardiologist, and lectures about CHD disease, CHD medications, lifestyle modifications and secondary prevention. It is a GP task to follow-up effect and safety of medications in addition to monitoring the disease. Patients experiencing an MI for the second, third time or more may be followed by their GP only, if no complications occur. No one provide standardized pharmaceutical care to any of these patients.

The clinical pharmacist intervention (the follow-up program)

In addition to standard care, patients allocated to the IG received follow-up from the clinical pharmacist at three points of time: 1) at hospital discharge, 2) three months after hospital discharge and 3) twelve months after discharge. The first meeting was held at the ward, the latter at the hospital pharmacy. The clinical pharmacist arranged follow-up meetings by phone approximately two weeks before due date. The Pharmacist and patient tasks during follow-up meetings are described in Figure 1. Briefly, the follow-up comprised traditional medication reconciliation, clinical medication therapy reviews, and patient education concerning medications, lifestyle behaviour and risk reduction. The latter was performed in the spirit of motivational interviewing, which is described as collaborative, evocative and honouring of patient autonomy.[23] There was no strict protocol for these tasks, but the clinical pharmacist used hospital records to prepare for meetings. The pharmacist did not have the authority to make dose adjustments or other medication amendments, but recommendations were communicated to, and/or discussed with, the patients' GPs and the patients themselves, both by phone and by letter.

Data collection

The following data was collected from predefined electronic patient records: demographics, family history of CHD, medical history relevant for CHD, medication at hospital admission and discharge, systolic and diastolic BP at admission and discharge, serum total cholesterol, serum low-density lipoprotein (LDL) cholesterol, blood glucose, glycated hemoglobin (HbA1c), body weight, height, waist circumference, body mass index (BMI), and any documented instructions concerning medications, life-style and/or follow-up issues given to patients during hospitalization and/or submitted to the next health care level.

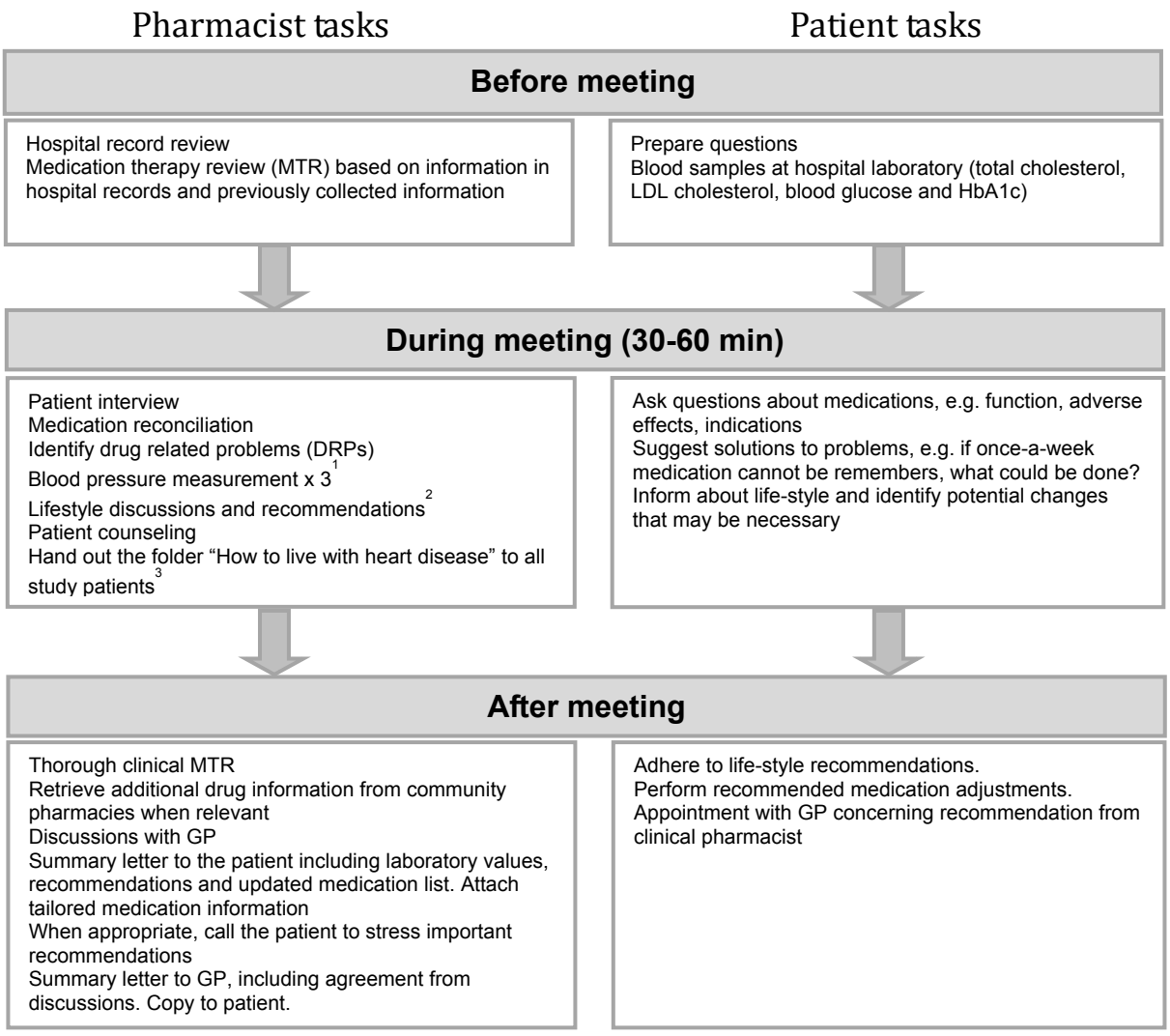

Figure 1. Pharmacist and patient tasks during meetings in the follow-up program for patients with established coronary heart disease led by a clinical pharmacist. Meetings were held at discharge, 3 months post-discharge and 12 months post-discharge.

GP, general practitioner; HbA1c, glycated hemoglobin; LDL, Low-density lipoprotein.

1) A calibrated GE Dinamap Pro 300 Patient Monitor and the correct sized cuff were utilized. A standardized three-time measurement procedure was where the average blood pressure was denoted and used for clinical evaluation.
2) Discussion/information on diet and preparation of food, exercise advices. When patients wanted to stop smoking, they were much encouraged and were referred to the Norwegian's authorities smoking cessation programs found at the webpage www.slutta.no or to the 'smoking telephone' (a free phone-line where you meet professional personnel advising you on smoking cessation). When appropriate, the CP suggested choices of food and preparation of food and exercise. On request, or when needed, the CP printed lifestyle recommendations from the webpage of the Norwegian heart association and Norwegian diabetes association and handed out to patients (www.hjerte.no or www.diabetes.no)
3) Published by the National Association for Heart and Lung Diseases (LHL). The folder includes information concerning heart disease, the most normal clinical procedures in relation to CHD, the most common drugs and lifestyle recommendations. Only handed out at the first meeting.

Before each follow-up meeting with the clinical pharmacist, blood samples for analysis of serum total and LDL cholesterol, blood glucose and HbA1c were drawn at the hospital ambulatory facilities. Sampling and analyzing methods were equal to those used for hospitalized patients at UNN. BP was by protocol measured by the clinical pharmacist, trained by a nurse, using standardized equipment.[24,25] Twelve months after inclusion, we summoned CG patients for follow-up meetings in order to collect the same laboratory and BP data as IG patients. After data collection and medication reconciliation to verify medication list, medication therapy reviews and patient education was supplied also to CG patients. Information regarding the life-style criteria was based on what occurred during follow-up (documented by the pharmacist), information in electronic patient records, and information from patients themselves.

The MAT-CHDSP

The MAT-CHDSP is a medication assessment tool (MAT) based on clinical therapy guidelines issued by the European Society of Cardiology. It comprises 21 review criteria related to appropriate prescribing, therapy goal achievement and life-style advices in

CHDSP.[18] A review criterion can be answered YES (adherence) or NO (non-adherence) according to whether the conditions defined by the standard are met or not. One of the strengths with the MAT methodology is the acknowledgement of justified reasons for non-adherence, which is applied 'justified non-adherence' (NOj) in cases where this is documented. Adherence to MAT criteria is calculated as the number of criteria where the standard can be answered YES divided by the number of applicable criteria, i.e. where the standard is answered YES, NO, NOj or where information is insufficient to answer the standard (IDs). Face and content validity of the MAT-CHDSP, together with its reliability and feasibility, have been shown excellent.[18]

Outcome measures

The primary outcome was adherence to the MAT-CHDSP criteria, both overall (all criteria together) and single criteria. Criterion 6 was omitted because it was outdated. Criterion 14 was omitted because data could not be found in patient records at hospital. Secondary outcomes comprised the biomedical risk factors; total and LDL cholesterol, BP, blood glucose and HbA1c.

Reliability measures

We explored the reliability of MAT-CHDSP applications by Cohen's Kappa statistics, expressing agreement between two observers. A kappa-value 0.75 or greater was considered excellent agreement.[26] The second observer (also a pharmacist) applied the MAT-CHDSP criteria at 12 months, using the clinical pharmacist's patient profiles as information source. The profiles comprised information on medications (after medication reconciliation), medical history, biomedical measure and documentation of lifestyle advices. The clinical pharmacist's personal notes were excluded. The second observer was blinded to study group allocation.

Data analysis

We managed and analysed data using Microsoft® Office Excel 2002 and SPSS® 16.0 for Windows. PASS® was used for sample size calculations. Continuous variables are expressed as mean with standard deviation (SD) and categorical variables as percentages. Two-sample comparisons were conducted using the Student's t-test for continuous normally distributed variables and the Paired

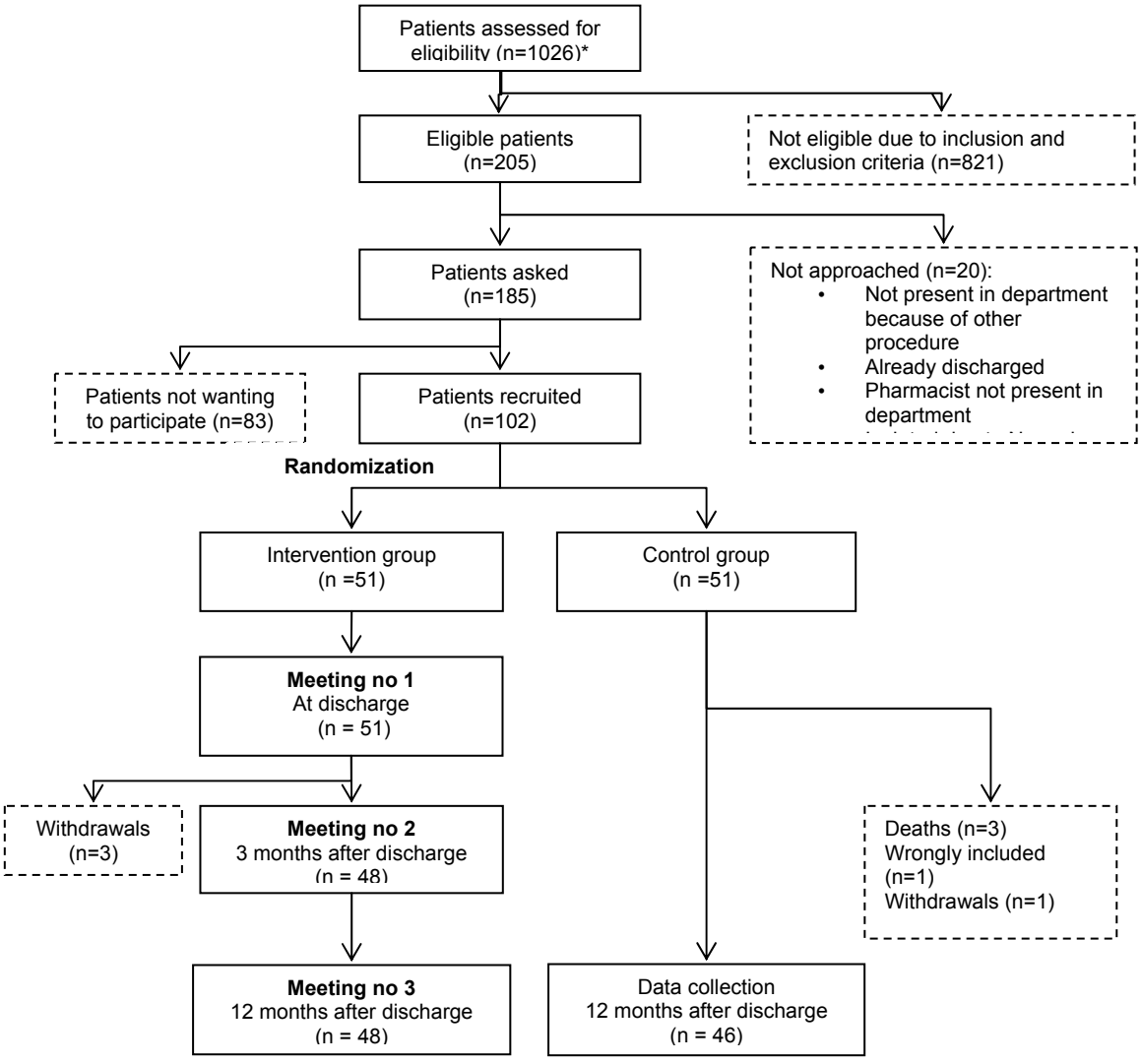

Figure 2, Patient flow during the randomized controlled trial
*Patient were assessed for eligibility during 205 days.

Table 1. Patient characteristics for the intervention group (n = 48) and the control group (n = 46)

Variable	Intervention group	Control group
Gender, no. (%)		
Male	35 (72)	33 (72)
Age, years		
Mean (SD)	63.9 (9.0)	63.4 (9.9)
Min, max values	46, 81	44, 82
BMI, kg/m^2 (n=44)		
Mean (SD)	28.6 (6.2)	28.9 (4.8)
Min, max values	20, 54	22, 48
Smoking status, no. (%)		
Yes, no.	7 (15)	11 (24)
Ex, no.	16 (33)	12 (26)
Never, no.	24 (50)	21 (46)
Comorbidities, no (%)		
Congestive Heart failure (EF<45%)	12 (25)	9 (20)
Diabetes mellitus (type I and II)	8 (17)	8 (17)
Blood pressure ≥ 130/80 mmHg	27 (56)	31 (67)
Main procedure during hospitalization, no. (%)		
PCI with stent implantation	12 (25.0)	18 (39.1)
Coronary bypass	12 (25.0)	5 (10.9)
Medical therapy only	24 (50.0)	23 (50.0)

All P-values concerning differences between the two groups are > 0.05. Variables are given as geometric mean (percent of total participants of intervention/ control group) or mean ± standard deviation (SD), BMI; body mass index, PCI; percutaneous coronary intervention

sample t-test for continuous variables within the same group. Comparisons of proportions were carried out using the Pearson chi-square or Fisher's exact test, as appropriate. To test for differences in the change of adherence from baseline to study end in the two groups, we used Normal approximation to the binomial distribution. We used the individual sample t-test to compare the difference in mean change from baseline to 12 months in biomedical values between the study groups. A two-sided p-value of <0.05 was considered statistically significant.

Ethical considerations

The Regional Committee for Medical Research Ethics (REK) North Norway approved the study on January 8, 2009. All included patients supplied written and informed consent. The study is registered at www.clinicaltrials.gov (study number NCT01115608).

RESULTS

Study participants

About half of the eligible patients did not want to participate. Inclusion was stopped before the estimated sample size was achieved, because of the predefined enrolment period. Finally, 102 patients were recruited, and 51 were randomized to each study group. Eight patients (7.8%) were lost to follow-up, see Figure 2. A total of 48 IG patients and 46 CG patients were subjected for analysis. The study groups did not differ significantly, see Table 1.

Adherence to MAT-CHDSP criteria

Overall adherence (adherence to all criteria) increased in both groups from baseline to 12 months, and was significantly higher in IG patients compared to CG patients at study end, p<0.001, see Table 2. This difference was mainly caused by the significant difference in adherence to the life-style criteria (no 19-21) in the MAT-CHDSP criteria (p<0.001).

Prescription of antiplatelet medications was high both at baseline and at 12 months, see criteria 1-4 in Table 2. All cases of non-adherence to aspirin prescribing among IG patients at 12 months were justified; this was not the case in the three CG patients. More than 90% of patients in both groups were prescribed a statin at baseline and at 12 months, see criterion 5 in Table 2. At 12 months, the two IG patients not prescribed a statin had a justified reason, which was not the case for the two CG patients not prescribed a statin. At baseline, a β-blocker was prescribed in >70% of patients in both groups, see criterion 9 in Table 2. From baseline to 12 months, adherence decreased by respectively 10.4% and 2.2% in IG and CG patients. This decrease was justified in IG patients, but not in CG patients. In both IG and CG patients, prescription of an angiotensin-converting enzyme (ACE)-inhibitor or an angiotensin receptor II blocker (ARB) was higher in eligible patients with left systolic ventricular dysfunction (LSVD) compared to eligible patients with diabetes mellitus (criterion 12 and 13 in Table 2). More eligible IG patients with diabetes mellitus type 2 were prescribed and ACE-inhibitor or an ARB at 12 months compared to baseline. This difference was not significant.

Therapy goal achievement for total and LDL cholesterol and BP was relatively low at baseline, and it did not increase significantly in any groups from baseline to 12 months (criterion 7 and 10, Table 2). In patients with unachieved therapy goals for cholesterol and BP at baseline, about 40-50% of the patients in both groups were discharged without any therapy amendment or instructions to the next caregiver in order to achieve therapy goals (criteria 8 and 11, Table 2). About 50% of patients with blood glucose >7 mmol/L at hospital admittance were discharged without a second measurement of blood glucose or HbA1c (criterion 16, Table 2).

Table 2. Adherence to MAT-CHDSP criteria at baseline and 12 months after hospital discharge in the 48 intervention group patients (912 applicable criteria) and the 46 control group patients (874 applicable criteria)

Criterion focus#		Adherence Intervention group (IG)						Adherence Control group (CG)						p-value
		Baseline			12 months			Baseline			12 months			
In patients with established coronary heart disease		No.		%	No.		%	No.		%	No.		%	
1	Aspirin prescription	46	/48	**95,8**	43	/48	**89,6**	42	/46	**91,3**	42	/46	**91,3**	0,011
2	Clopidogrel prescription if contraindications/intolerance to aspirin	-	/0	**-**	1	/2	**50,0**	1	/2	**50,0**	0	/1	**0**	NS
3	Clopidogrel prescription if MI or unstable AP, but no coronary stent implantation	2	/2	**100**	-	-	**-**	1	/1	**100**	-	-	**-**	
4	Clopidogrel prescription if PCI with stent implantation	14	/14	**100**	-	-	**-**	20	/20	**100**	-	-	**-**	
5	Statin prescription	47	/48	**97,9**	46	/48	**95,8**	42	/46	**91,3**	44	/46	**95,7**	NS
7	Total cholesterol ≤ 4.5 mmol/L and LDL cholesterol ≤ 2.5 mmol/L	13	/47	**27,7**	13	/48	**27,1**	16	/42	**38,1**	19	/45	**42,2**	NS
8	Therapy amendments§ if unachieved therapy goals for cholesterol	19	/32	**59,4**	-	-	**-**	15	/25	**60,0**	-	-	**-**	
9	ß-blocker prescription	35	/48	**72,9**	30	/48	**62,5**	38	/46	**82,6**	37	/46	**80,4**	NS
10	SBP ≤ 130 mmHg and DBP ≤ 80 mmHg	17	/48	**35,4**	20	/48	**41,7**	16	/46	**34,8**	19	/46	**41.3**	NS
11	Therapy amendments§ if unachieved therapy goals for SBP and DBP	11	/27	**40,7**	-	-	**-**	13	/31	**41,9**	-	-	**-**	
12	ACE inhibitor or ARB prescription if LVSD (ejection fraction < 45 %)	12	/12	**100**	12	/12	**100**	7	/9	**77,8**	8	/9	**88.9**	NS
13	ACE inhibitor or ARB prescription if DM with hypertension or nephropathy	6	/8	**75,0**	7	/8	**87,5**	4	/8	**50,0**	5	/8	**62,5**	NS
15	... documentation of blood glucose measurements < 7.0 mmol/L at hospital admission	33	/48	**68,8**	40	/48	**83,3**	33	/46	**71,7**	40	/46	**87,0**	NS
16	... documentation of a new blood glucose and/or HbA1c measurement if first measurement ≥ 7.0 mmol/L	7	/16	**43,8**	-	-	**-**	9	/17	**52,9**	-	-	**-**	-
17	... documentation of smoking cessation advice in smokers	4	/7	**57,1**	8	/8	**100**	6	/11	**54,5**	5	/9	**55.6**	NS
18	... documentation of weight, height, BMI and/or waist circumference	21	/48	**43,8**	47	/48	**97,9**	12	/46	**26,1**	43	/46	**93.5**	NS
19	... documentation of weight reduction advice if overweight (BMI ≥ 30 kg/m2)	2	/7	**28,6**	10	/11	**90,9**	0	/4	**0**	0	/13	**0**	< 0,001
20	... documentation of dietary advice	4	/48	**8,3**	47	/48	**97,9**	8	/46	**17,4**	8	/46	**17.4**	< 0,001
21	... documentation of physical activity advice	6	/48	**12,5**	47	/48	**97,9**	11	/46	**23,9**	11	/46	**23.9**	< 0,001
Overall		299	/556	**53,8**	371	/473	**78,4**	294	/538	**54,6**	281	/453	**62,0**	< 0,001

Criteria 6 and 14 were omitted. ¤ Adherence is calculated as the number of criteria where the standard can be answered 'YES' divided by the number of applicable criteria, i.e. where the standard is answered YES, NO, NO-justified or where information to answer the standard is insufficient. §Increased dose, change of drug and/or addition of drug.* P-values reflect both change from baseline to study end as well as difference in between groups at study end.ACE, angiotensin converting enzyme; AP, angina pectoris; ARB, angiotensin II receptor blocker; BMI, body mass index; CI, Confidence interval; DM, diabetes mellitus; DPB, diastolic blood pressure; LDL, low-density lipoprotein; LVSD, left ventricular systolic dysfunction; NS, Not significant; PCI, percutaneous coronary intervention; SBP, systolic blood pressure.

Applicability

For both study groups, insufficient data to decide whether the qualifying statement was applicable (IDq) mostly affected baseline applications of criterion 19 due to lack of information on body weight and height or BMI. This was less prominent at 12 months. Applicability decreased from 61% at baseline to 51% at study end in both groups. This was because criteria 8, 11 and 16 could not be applied at study end, as they are designed for application after e.g. a hospital stay, to identify whether medication amendments have been appropriately conducted. More details on applicability, justified non-adherence and insufficient data can be retrieved by contacting the authors.

Biomedical risk factors and therapy goal achievement

No intervention approach or data collection instrument presented any major difficulties during the study. Biomedical measures at baseline and at study end did not differ significantly between the groups (p>0.05), see Table 3. No improvements in biomedical measures from baseline to study end were observed for IG patients, but a significant

Table 3. Biomedical values for the intervention group (n = 48) and the control group (n = 46) throughout the study

	Intervention group						Control group			
	Baseline		3 months		12 months		Baseline		12 months	
LDL cholesterol (mmol/L)										
Mean (SD)	3.0	(1.14)	2.7	(0.87)	2,8	(0.94)	*3.1*	*(1.20)*	*2.5*	*(0.81)*
Min, max	1.5	6.4	0.7	4.9	1.0	6.1	1.2	5.8	1.3	5.4
Total cholesterol (mmol/L)										
Mean (SD)	4.9	(1.28)	4.7	(1.06)	4.8	(1.12)	5.1	(1.40)	4.5	(0.91)
Min, max	2.9	8.2	2.2	7.3	2.6	8.5	2.8	8.0	3.0	7.3
Blood glucose, (mmol/L)										
Mean (SD)	6.8	(2.89)	6.2	(2.46)	6.5	(2.36)	7.5	(3.54)	7.0	(3.6)
Min, max value	3.4	17.3	3.4	15.6	3.8	15.5	4.0	20.0	3.9	23.5
HbA1c (%)										
Mean (SD)	6.5	(1.04)	6.4	(0.99)	6.2	(0.99)	6.5	(1.35)	6.2	(0.93)
Min, max	5.2	8.6	5.2	9.9	5.0	10.4	5.4	9.7	4.5	9.7
Systolic blood pressure (mmHg)										
Mean (SD)	134.0	(18.9)	135.1	(19.2)	135.2	(19.3)	141.9	(20.9)	135.4	(19.8)
Min, max	103	178	84	177	92	197	100	188	96	178
Diastolic blood pressure (mmHg)										
Mean (SD)	79.2	(10.5)	79.3	(12.2)	77.2	(10.1)	79.2	(11.9)	77.7	(10.3)
Min, max	60	112	53	105	53	98	55	100	57	96

All P-values concerning differences in between groups at baseline and from baseline to 12 months are > 0.05, except the P-value for the difference between mean baseline values and mean 12 month values for low-density-lipoprotein (LDL) cholesterol in the control group, where P = 0.009 (italic). Variables are given as geometric mean (percent of total participants of intervention/ control group) or mean ± standard deviation (SD); LDL, Low-density lipoprotein; HbA1c, glycosylated haemoglobin.

improvement in LDL cholesterol was observed for CG patients (p=0.009), see Table 3. Even though no significant improvement in BP was observed in any group, three more patients in both groups had achieved their BP therapy goals at study end compared to baseline, see criterion 10, Table 3.

Reliability of MAT-CHDSP application

Inter-observer agreement tests on 12 months data showed excellent reproducibility of MAT-CHDSP application with a κ-value of 0.91 (95 % CI; 0.89, 0.94).[26]

DISCUSSION

We have developed a pharmacist-led follow-up program for post-discharged patients with established CHD proved functional, both clinically and logistically. To our knowledge, no similar program has been described in the literature. The low lost-to-follow-up rate in addition to a high satisfaction identified by qualitative interviews, indicates that the intervention was appreciated by the patients.[27] High patient satisfaction has also been shown by others studying patient satisfaction with pharmaceutical care.[28-30]

We found that overall adherence to guideline recommendations defined in the MAT-CHDSP increased in both groups. This indicates that focus on guideline adherence in itself may increase adherence and consequently improve therapy. Our study shows that this can be a pharmacist task. Although no significant increase in biomedical measures could be observed in favour of IG patients, we identified a higher documentation of justified reasons for non-prescription of guideline recommended medications aspirin, statins and beta-blockers in IG patients compared to CG patients at study end. At study end, we also observed higher prescription of ACE-inhibitors or ARBs in eligible IG patients with diabetes mellitus type 2 compared to CG patients at study end. Due to small numbers, these differences were not statistical significant, but indicates that the MAT-CHDSP can function as a follow-up tool to be applied in clinical practice. It also underlines the clinical pharmacist's impact on documentation, which is essential in health care.

A high prescription rate of guideline recommended medications was observed in both groups at baseline and study end, which is higher than observed in other studies.[1,7-10] Achievement of therapy goals was low in both study groups, which clearly supports findings from other studies arguing for introducing successful interventions to improve patient care for these patients.[31-36] Other studies have shown that the clinical pharmacist can have a significant positive impact in direct care for CHD patients, both concerning lipid- and BP management, appropriate prescribing, smoking cessation and guideline adherence.[31-36]

There are two major limitations of this study. First, the study was underpowered to detect potential differences between the study groups. We based our sample size calculations on a low adherence for BP therapy goal achievement of 20%, but the initial adherence in our study was higher. In addition, the adherence increase throughout the study was similar in both study groups. The lost-to follow-up rate was low, but did not compensate for this. Second, the MAT-CHDSP may be unsuitable to measure change in actual care. It is possible that the major sources of improvements were in the documentation of care, not the provision of care. This may again explain the apparent lack of beneficial clinical effects from the follow-up program. Additionally, the impact of lifestyle advices depend on several factors, such as the quality of the advices, the patient's ability to understand the information, and patient adherence. It is necessary to control these factors in order to decide on the influence of lifestyle counselling on the biomedical outcomes.

Other elements that may have contributed to the inability to demonstrate a benefit in favour of the

intervention group include the following: First, prescription rates (i.e. adherence to criteria 1-5, 9, 12 and 13) were high in both groups at baseline, and consequently, the opportunity to increase appropriate prescribing was low. Second, selection bias may have been introduced by the voluntarily study participation. The randomization process was successful, resulting in comparable study groups, but the included patients may be different from those who refused participation. Also, our study population was recruited as they were hospitalized due to a coronary event, for which the severity of the event itself may have had an impact on medication adherence and lifestyle. This may have diluted a potential effect of the intervention. Third, Hawthorn effects may have led to improvements in adherence and biomedical measures among CG patients that would not have been seen outside the study. This may consequently have diluted any effect that could have been attributable to the intervention.[37] This is supported by the fact that CG patients expressed disappointment after the randomization process. In addition, clinicians and GPs were aware of the study and may have changed behaviour. However, this is not supported by the low therapy goal achievement at study end. Fourth, GPs were sometimes reluctant to make changes concerning medications initiated at the hospital, and hence did not always effectuate recommendations from the clinical pharmacist. This is not a new dilemma, and it has been shown that the GPs consider it inappropriate to take responsibility for the patients in about 50% of all discharges.[38] Unfortunately, we were do not have reliable measures on the proportion of recommendations that were actually accepted by the GPs, as we were relying on patient information during follow-up. Pharmacist prescriptive authority, which is routine in the UK and US, may have counteracted this.[39]

In order to explore a possible benefit of the follow-up program, a larger study is necessary. In addition, we suggest the following improvements of the program itself:

1. A closer collaboration with the prescriber to facilitate discussions and effectuate recommendations more rapidly. This has been described as a key feature in similar programs (13). In hospitals, this may be feasible if the clinical pharmacist is part of the ambulatory follow-up team. In primary care, a 'hot line' to the GP's office could be established, or the clinical pharmacist could be situated at the GP's office.
2. Conduct the first medication reconciliation and medication therapy reviews before hospital discharge, including appropriate approaches to solve drug-related problems, make medication amendments and communicate amendments to the next care level. This may counteract the GPs' resistance to amending medications initiated at the hospital,
3. Prescriptive authority for the clinical pharmacist according to agreed algorithms may facilitate dose titration and therapy goal achievement. This could reduce the number of extra appointments with the GP and be economically favourable.
4. More frequent follow-up meetings initially may facilitate a more aggressive medication titration and rapid achievement of therapy goals. In the Euro Action program, patients met every week during the sixteen-week program, and also attended group workshops and a supervised exercise class.[40]

CONCLUSIONS

This is to our knowledge the first description of a twelve-month lasting follow-up program for post-discharged patients with CHD led by a clinical pharmacist. The program was successful concerning logistics and patient experiences. In both study groups at baseline, we observed a high prescription proportion of guideline recommended medications, a relatively low achievement of therapy goals, and an inadequate follow-up on unachieved therapy goals. During the study period, adherence to review criteria defined in the MAT-CHDSP increased in both groups. Even though no significant improvement of biomedical measures was observed in favor of the intervention group, the increased focus on adherence to guideline recommendations improved adherence to the MAT-CHDSP for both groups. This may in itself be an argument for such a follow-up program. Even though not significant, our study indicates that the clinical pharmacist may increase documentation of justified reasons non-prescription of guideline-recommended medications as well as increase appropriate prescription of ACE inhibitors and ARBs in eligible patients with diabetes mellitus type II. A larger, adequately powered study is warranted to explore the full benefit of the follow-up program. In addition, adjustments to the program, including a closer collaboration with the prescriber, is crucial.

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CONFLICT OF INTEREST

The authors declare that they have no conflicts of interest to disclose.

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PROGRAMA FARMACÉUTICO DE SEGUIMIENTO PARA PACIENTES CON ENFERMEDAD CORONARIA ESTABLECIDA EN EL NORTE DE NORUEGA – ENSAYO CONTROLADO ALEATORIZADO

RESUMEN

Objetivos: El objetivo del presente estudio fue doble: 1) desarrollar un programa de seguimiento farmacéutico de 12 meses de duración para pacientes con enfermedad coronaria establecida (CHD) dados de alta del Hospital Universitario de Noruega del Norte, y 2) explorar el impacto del programa en relación a un instrumento de evaluación para la prevención secundaria de CHD y cambios en los factores de riesgo biomédicos.

Métodos: Se incluyeron en un estudio controlado aleatorizado no cegado un total de 102 pacientes de 18-82 años. La intervención consistió en reconciliación de la medicación, revisión de la medicación, y educación del paciente en tres encuentros: al alta, después de 3 meses y después de 12 meses. El grupo control recibió los cuidados habituales de su médico general. Los *outcomes* primarios fueron la adherencia a las guías de práctica clínica relativa a la prescripción, la consecución de los objetivos terapéuticos y los hábitos de vida definidos en el instrumento de evaluación de la prevención secundaria de CHD (el MAT-CHDSP). Los *outcomes* secundarios incluían cambios en los factores biomédicos de riesgo, como colesterol, presión arterial y glucemia.

Resultados: 94 pacientes completaron el ensayo, 48 en el grupo intervención y 46 controles. La prescripción adecuada fue elevada, pero la consecución de los objetivos terapéuticos fue baja en ambos grupos a lo largo del estudio. La adherencia total a los criterios del MAT-CHDSP aumentó en ambos grupos, y fue significativamente mayor en el grupo intervención al final del estudio, comparado con el control (78.4% vs. 60.2%, respectivamente, $p<0.001$). La diferencia fue estadísticamente significativa para los estilos de vida aconsejados en los pacientes del grupo intervención. No se observaron cambios significativos en los factores biomédicos de riesgo a favor del grupo intervención.

Conclusiones: El estudio mostró un aumento de adherencia a las guías en ambos grupos. Esto indica que la atención a las recomendaciones de las guías de práctica clínica por sí mismo aumenta la adherencia – lo que podría ser una tarea del farmacéutico. Se necesita un estudio mayor y con más poder para mostrar una diferencia significativa en la mejoría a favor de la intervención de los factores biomédicos de riesgo. Pueden recomendarse modificaciones a los programas de seguimiento que mejoren la implantación en los cuidados normales de los pacientes.

Palabras clave: Servicios farmacéuticos; Reconciliación de Medicamentos; Farmacéuticos; Enfermedad Coronaria; Ensayos Clínicos Controlados Aleatorios como Asunto; noruega

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