

BMJ Open Narrative medicine-based intervention in primary care to reduce polypharmacy: results from the cluster-randomised controlled trial MultiCare AGENDA

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ABSTRACT

Objectives To determine if patient-centred communication leads to a reduction of the number of medications taken without reducing health-related quality of life.

Design Two-arm cluster-randomised controlled trial.

Setting 55 primary care practices in Hamburg, Düsseldorf and Rostock, Germany.

Participants 604 patients 65 to 84 years of age with at least three chronic conditions.

Interventions Within the 12-month intervention, general practitioners (GPs) had three 30 min talks with each of their patients in addition to routine consultations. The first talk aimed at identifying treatment targets and priorities of the patient. During the second talk, the medication taken by the patient was discussed based on a 'brown bag' review of all the medications the patient had at home. The third talk served to discuss goal attainment and future treatment targets. GPs in the control group performed care as usual.

Primary outcome measures We assumed that the number of medications taken by the patient would be reduced by 1.5 substances in the intervention group and that the change in the intervention group's health-related quality of life would not be statistically significantly inferior to the control group.

Results The patients took a mean of 7.0 ± 3.5 medications at baseline and 6.8 ± 3.5 medications at follow-up. There was no difference between treatment and control group in the change of the number of medications taken (0.43; 95% CI -0.07 to 0.93 ; $P=0.094$) and no difference in health-related quality of life (0.03; -0.02 to 0.08 ; $P=0.207$). The likelihood of receiving a new prescription for analgesics was twice as high in the intervention group compared with the control group (risk ratio, 2.043; $P=0.019$), but the days spent in hospital were reduced by the intervention (-3.07 ; -5.25 to -0.89 ; $P=0.006$).

Conclusions Intensifying the doctor-patient dialogue and discussing the patient's agenda and personal needs did not lead to a reduction of medication intake and did not alter health-related quality of life.

Trial registration number ISRCTN46272088; Pre-results.

Strengths and limitations of this study

- The intervention was based on the established concepts of the Chronic Care Model, which was especially designed for the treatment of chronically ill patients, and Narrative Based Medicine, providing a framework for approaching a patient's problems holistically and possibly helping to reduce medication.
- We carefully designed the study with adequate numbers of recruited patients, with general practitioners (GPs) and patients unaware of study endpoints and the data analysis controlled for relevant confounders, allowing for cluster effects and blinding to group assignment.
- There was a slight patient selection bias regarding gender and certain diagnosis groups, but we found no other baseline differences regarding sociodemographic data and no imbalances regarding medication intake.
- However, we cannot rule out that a higher-than-average percentage of motivated and educated GPs and a higher-than-average percentage of co-operative patients, who had been more satisfied with their primary care than other patients, responded to our invitations for study participation.
- Despite the fact that we monitored the implementation of the intervention by telephone or personal visits to the GPs, we had not been able to observe the consultations with the patients and therefore do not know whether the intervention was implemented per protocol and if the GPs in the control group really conducted care as usual or if they focused more on their patients due to their study participation.

INTRODUCTION

Multimorbidity, that is, the coexistence of two or more chronic conditions in one patient, is a frequent condition in the elderly population. Depending on the definition and operationalisation, its prevalence rate is estimated between 50% and 80% in most studies.^{1,2} Many

studies found an association between multimorbidity and adverse patient-related outcomes, for example, higher mortality, limited functioning and reduced health-related quality of life.^{2 3}

Usually, multimorbidity also goes along with polypharmacy, that is, the co-prescription of multiple medications, especially if clinical practice guidelines on all morbidities of a patient are fully applied.^{4 5} Polypharmacy may result in an additional burden to the patient, for example, adverse drug events, fall-related outcomes or hospital admissions.^{6 7} There is some evidence that patients with polypharmacy may benefit from medication withdrawal, especially concerning psychotropic drugs.⁸ However, there are still only few intervention studies addressing the management of multimorbidity,⁹ and the question of how to reduce the number of medications is also still under-researched and unclear.¹⁰

Given the high complexity of multimorbidity including the possible interactions of illnesses and medications in multimorbid patients,^{11 12} there is wide consensus that a patient-centred approach is preferable.^{13 14} Key elements of this approach are shared decision-making between physician and patient, guided by the patient's central values and priorities as well as coordinated interdisciplinary care, based on a biopsychosocial disease concept.^{14 15}

The Chronic Care Model and Narrative Based Medicine provide a framework for such a patient-centred care. The Chronic Care Model consists of the following elements: (1) joint definition of problems by patient and physician; (2) targeting, goal setting and planning; (3) a continuum of self-management training and support services; and (4) active and sustained follow-up by the professional.^{16 17} Narrative Based Medicine assumes that patient's narratives of illness can provide a framework for approaching his problems holistically and, thus, may reveal diagnostic and therapeutic options.^{18 19} Narrative Based Medicine can also help in reducing medication.²⁰

The MultiCare AGENDA study investigated the efficacy of a multifaceted intervention based on these concepts. It aimed at improving the doctor–patient dialogue and identifying the patient's agenda and personal needs. The dialogue included a 'brown bag' review. We expected that a more patient-centred communication would be able to disclose the main focus of patient care—which would sometimes have implications for medication use. Our primary hypothesis was that patient-centred communication would lead to a reduction in the number of medications taken without affecting health-related quality of life.

These hypotheses were based on the results of several studies showing that longer consultation times with patients were associated with fewer prescriptions and one study showing a better prescribing quality based on the use of 10 categories of medications.²¹ There is growing evidence that the phenomenon of polypharmacy and inappropriate prescribing has primarily been the result of miscommunication (or even non-communication) during the doctor–patient interaction.^{22 23} Therefore, we

expected that polypharmacy could be reduced through more intensive communication in terms of dedicating more time on the patient and focusing on the patient's perspectives without the support of specific medication tools. Despite the fact that there is mixed evidence concerning the question if inappropriate prescribing could be harmful for the patient,²⁴ researchers advocate that a reduction of the medication load and adherence to essential medications are of great importance, especially in patients with multimorbidity.²⁵

METHODS

Study design

Multicare AGENDA was designed as a cluster-randomised controlled trial in general practice. Cluster randomisation was conducted on the general practitioner (GP) practice level. The study intended to evaluate the efficacy of narrative doctor–patient dialogues in patients with multimorbidity. The narrative intervention was tested against care as usual. We conducted the study in three larger German cities (study centres), that is, Hamburg, Düsseldorf and Rostock.

Setting

The intervention was GP-led and carried out in GP practices. In each study centre, we randomly selected GPs from the register of the Association of Statutory Health Insurance Physicians and invited them to participate in our study by mail. Additionally, we recruited GPs using Internet and print media advertisements.

Participants and eligibility criteria

GPs were eligible for the study if they were willing to participate in the study regardless of randomisation to the intervention or control arm, if they had established an own GP practice for at least 2 years and if they used a practice software that was able to create a list of all their patients based on their ages. We excluded GPs if they had participated in our feasibility study²⁶ or in the MultiCare Cohort Study.²⁷ In group practices, only one GP was allowed to participate in the study.

Each participating GP retrieved a list of his patients who were between 65 and 84 years old and had consulted him within the last completed quarter (ie, 3-month period). Up to 25 patients per practice were randomly selected from this list (using random number tables) and checked for exclusion criteria. Only patients with at least three chronic conditions out of a list of 42 diagnosis groups²⁸ were included in the study.

Patients were excluded if they were hardly known by the GP (ie, ad hoc consultation, had been a patient of this practice for less than 12 months), if they were not able to consent (eg, dementia) or if they were not able to participate in interviews according to the GP (eg, severe psychiatric illness, deafness, insufficient German language skills). Further exclusion criteria were a life expectancy of 3 months or less according to their GP, residence in a

nursing home and participation in other scientific trials at the time of recruitment.

If patients were eligible, they were invited by a letter from their GP to participate in the study. If they were interested, the patients consulted their GP to receive information about the study and signed an informed consent form.

Study registration

Rationale and detailed methods of the study can be found in trial registration (<http://www.isrctn.com/ISRCTN46272088>) and in the published protocol.²⁸

Intervention

We developed and pretested the intervention in a pilot study, which was described in detail in the published protocol.²⁸ The intervention was based on the Chronic Care Model^{16 17} and Narrative Based Medicine.^{18 19} GPs allocated to the intervention arm received three training sessions, each lasting for about 4 hours. Each training session was conducted by at least three of the following study team members: AM and COS (experienced GPs), HK (physician) and IS (sociologist). Training topics were how to perform narrative based doctor–patient dialogues reflecting treatment targets and priorities of the patient and how to perform narrative, patient-centred medication reviews as well as goal setting and attainment regarding care and treatments. Simulated patients^{29 30} were used in the training sessions to practise Narrative Based Medicine.

Within the 12-month intervention time, GPs of the intervention arm held altogether three individual talks with each of their participating patients, which were conducted in addition to routine consultations in the GP's practices at their convenience. Each of these talks was intended to take about 30 min and was based on narratives of the patient prompted by an initial narrative question of the GP.

The first talk carried out after the start of the intervention aimed at identifying the patient's priorities in life (which could be non-medical) and used this information to carve out treatment targets. This talk was stimulated by the GP's question asking how the patient had experienced the last 6 months. After the patient's narrative had ended, the GP could ask for more details about the patient's topics using the order they had been mentioned. If the talk did not produce topics to discuss, the GP could ask if there had been any changes in the patient's health status, if the patient had set goals in his life or if something unexpected had happened. Additionally, the GP could ask the patient to describe what he wished to happen (or not to happen) over the next year.

The focus of the second talk, which was conducted within a couple of weeks afterwards, was on the medication taken by the patient based on a 'brown bag' review³¹ where the patient was asked to bring all the medications he had at home into the practice. At the beginning of this talk, the patient was asked to present his medications and

to tell if he had taken them, how he had taken them and what he thought about them. GPs should not interrupt in order to allow the patient to present his own views. Then, based on this information, the doctor and the patient should discuss and implement changes, if necessary. Specific medication aids were not used.

The third talk, scheduled 12 months after the first, combined the elements of both previous talks and was used to discuss goal attainment, changes in medication and treatment targets for the future. The initial narrative question and additional supportive questions were the same as in the first talk. During the intervention period, all additional treatments and consultations were permitted.

Comparator

GPs of the control group performed care as usual. At the end of the intervention, they were offered to participate in a similar training as given to the intervention group. This offer had been announced before starting the study to counterbalance the possible lower motivation level of GPs randomly assigned to the control arm. The GPs of the control group received the same remuneration as the GPs of the intervention group.

Primary outcome measures

Our primary outcome measures were the number of medications taken at follow-up (adjusted for the number of medications taken at baseline) and the health-related quality of life at follow-up (adjusted for the health-related quality of life at baseline). Regression coefficients represent the outcome change in the intervention group minus the outcome change in the control group.

We assumed that the number of medications taken by the patient would be reduced as a result of the intervention. A minimum difference of 0.5 medications between both groups was defined as clinically relevant. We assumed that a reduction of medication use would not impair health-related quality of life, that is, we expected that the mean change in health-related quality of life in the intervention group would not be statistically significantly inferior to the mean change in the control group.

Secondary outcome measures

The effects of the intervention on the GP's knowledge about the medication taken by the patient, patient satisfaction with GP services, patient empowerment as well as healthcare use are reported as outcome changes between baseline and follow-up adjusted for the baseline values and coded as intervention group minus control group.

Data collection and monitoring of GPs

Members of the study team collected the data in personal interviews. GPs were interviewed at their practices and they were able to validate their answers in the patient medical records. Patient interviews were conducted at the patients' homes. Baseline data were collected between October 2011 and June 2012 and follow-up data between November 2012 and July 2013. Data collection of the

intervention group was performed before the intervention started (baseline) and after it finished (follow-up). Baseline assessments of the control group were conducted after patient recruitment and follow-up assessments 14 months after the baseline interview. During the intervention, each GP was contacted at least twice by telephone or personally visited by a member of the study team (COS) in order to monitor the implementation of the intervention and to get information about potential harms for the patients.

We used data on the patients' age and gender from GP charts and data on education, type of household, patient satisfaction, empowerment and healthcare use from patient interviews. The highest level of attained education was described according to the international Comparative Analysis of Social Mobility in Industrial Nations questionnaire (CASMIN) classification in three groups: (1) inadequately completed general education, general elementary education or basic vocational qualification; (2) intermediate qualification or A level equivalent; and (3) lower or higher tertiary education.³² Patient satisfaction with GP services was measured by the EUROPEAN task force on Patient Evaluations of general Practice care (EUROPEP) questionnaire,³³ which was scored in the subscales 'clinical performance' and 'organisation of care' ranging between 0 and 4 points each. Patient empowerment was assessed with the Health Care Empowerment Questionnaire (HCEQ).³⁴ The scores in the dimensions 'involvement in interactions' and 'involvement in decisions' were determined by the cross-product between motivation for control and perception of control in each item and ranged between 4 and 64 points and 3 and 48 points, respectively. In the EUROPEP and the HCEQ scores, higher values indicated a higher amount of patient satisfaction and empowerment, respectively.

Data on healthcare use were collected using a short form of the Leipzig Supply and Cost Instrument³⁵ covering the number of contacts with outpatient physicians as well as physical, occupational and speech therapy units during the last 3 months. It also includes number and length of hospital stays during the last 6 months. Additionally, the patient interviews contained the Geriatric Depression Scale with a total score range between 0 and 15 points and higher values indicating a higher level of depressive mood.³⁶

The use of medication was assessed as part of the patient interviews by documenting all current medications the patients had at home. The interviewer asked the patient to present the medication packages to obtain maximum information. If product name and drug code were not available, the patient was asked for the medical indication of the medication. The patient's medication was also documented in GP interviews using product names and drug codes. The GP's knowledge about the medication taken by the patient was defined as percentage of level 2 Anatomical Therapeutic Chemical classification system (ATC) codes of the patient's medication correctly identified by the GP. It was calculated using the Jaccard

similarity measure,³⁷ which divides the number of categories with positive agreement by the number of categories with disagreement or positive agreement. Categories with negative agreement are not considered by this coefficient.

Health-related quality of life was measured by the EuroQol group 5 Dimensions questionnaire (EQ-5D)³⁸ value set UK³⁹ and was also recorded as part of the patient interview. The value set UK indicates the value 1.000 for full health, which is reduced by a severity-related subtrahend between -0.081 and -0.350 if any limitations occur and up to five additional subtrahends between -0.036 and -0.386 depending on the severity of limitations in the domains mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Morbidity data were collected in face-to-face GP interviews by a standardised documentation instrument covering a list of 46 chronic conditions. This list was compiled by an interdisciplinary expert group based on the criteria of prevalence and chronicity.⁴⁰

Sample size

We expected a mean reduction of 1.5 medications per patient in the intervention group, a SD of 3.5 medications, an intracluster correlation coefficient of $\rho=0.14$ and a dropout rate of 20%. We defined an $\alpha=0.025$ in order to adjust for multiple testing and a power of 80%. Based on the assumption of 10 recruited patients per practice, a minimum sample size of 594 patients was needed for the first primary outcome. The rationale for our assumptions can be found in the published protocol.²⁸

Concerning the endpoint health-related quality of life, we expected no differences between intervention and control group. With this in mind, we assumed that the mean score of the intervention group at the end of the intervention would be at most half a SD less than the mean score of the control group and we estimated the SD as 0.30. Thus, a minimum sample size of 362 patients was needed to analyse the second primary outcome.

Randomisation

GP practices were randomised to conduct the intervention or to continue with care as usual (control). Randomisation was carried out after patient recruitment and baseline interviews with recruited patients had been completed. Block randomisation was used to provide comparable numbers of patients in the treatment and the control group. The randomisation was stratified by the number of patients recruited per practice (categories: <10 , $10-25$, $26-50$, >50 patients) using a block size of 4 and a ratio of 1:1.

Blinding and allocation concealment

The intervention was led by GPs; therefore, blinding study GPs and their patients was not possible. However, based on the contents of the intervention, the GPs could speculate about the endpoints, but they were not informed by the study team of study hypotheses and primary outcome measures. Assessors who performed

GP and patient interviews could not effectively be blinded because they communicated with GPs and practice personnel. For that reason, we cannot rule out that they had received information about the group assignment of the practice. Randomisation was conducted by BW (Hanover) blinded to names and addresses of the GPs. The statistical analysis was performed by IS (Hamburg) blinded to group assignment of the GPs (ie, intervention or control group).

Statistical methods

Descriptive data were presented as means and SD and as percentages, respectively. We compared the treatment and control group with t-tests in case of continuous variables and χ^2 tests in case of categorical variables. Changes in medication between baseline and follow-up were described for the treatment and control group and analysed by χ^2 tests. These analyses were adjusted for familywise error rate in multiple testing using the Benjamini-Hochberg procedure.⁴¹

We analysed the number of medications taken by the patients at follow-up, the GP's knowledge of the patients' medication, the patient satisfaction with GP services, the patient empowerment as well as the healthcare use (response variables) by multilevel mixed-effects linear regression allowing for random effects at the study centre and GP practice within study centre level. The health-related quality of life at follow-up was not normally distributed. We therefore analysed this response variable using multilevel mixed-effects ordinal logistic regression allowing for random effects at the study centre and GP practice within study centre level. The analyses of all of these response variables were baseline adjusted and controlled for the time between baseline and follow-up. Group assignment in our primary analyses was based on intention to treat, that is, based on the intended group assignment regardless of fulfilling the protocol.

Sensitivity analyses were conducted with the group assignments 'as treated', that is, based on the treatment the patients received de facto, and 'per protocol', that is, including only practices fulfilling the protocol regarding the intended group assignment and excluding practices that did not. We also conducted additional exploratory analyses adjusted for age, gender, type of household, education, depression and chronic diseases in different statistical models.

Furthermore, the change of medication profiles over the study period was analysed using multilevel mixed-effects logistic regression allowing for random effects at the study centre and GP practice within study centre level and controlled for age, gender and time between baseline and follow-up. To support the discussion, ORs from these analyses were recalculated into risk ratios as risk ratios do not depend on the prevalence of a condition and are therefore easier to interpret.⁴²

Due to the two primary endpoints, Bonferroni correction was applied to our analyses of the primary outcomes to adjust for multiple comparisons, that is, we defined an

α -level of 2.5% (ie, $P \leq 0.025$) as statistically significant. For all additional analyses, we defined an α -level of 5% (ie, $P \leq 0.05$) as statistically significant. Ordinal logistic regression analyses were performed using Stata V.14.2. All other statistical tests were conducted using Stata V.12.1.

Patient involvement

In order to understand the patients' health problems and healthcare needs, we conducted qualitative in-depth interviews with 19 patients during the development of the intervention.^{43 44} Additionally, we conducted standardised telephone interviews with the participating patients during our feasibility study and analysed transcripts of the patients' consultations with their GPs during our pilot study.²⁶ The patient perspective obtained from these data was used in the study design, formulation of hypotheses and interpretation of study results.

RESULTS

Participant flow

Sampling and response rates are shown in [figure 1](#). We checked 4028 patients for inclusion and exclusion criteria. A total of 1358 patients were eligible for study participation and contacted for informed consent. Moreover, 663 (48.8%) of these patients agreed to participate in our study. However, before the baseline assessment, 13 patients dropped out of the study because they had either died, their health status had severely deteriorated, they had changed their GP or they had participated in other scientific studies without their GPs' knowledge.

A total of 650 patients from 55 practices were randomised to the treatment and control group. All these patients completed the baseline assessment. From the control and the intervention group, 6.2% and 8.0%, respectively, were lost to follow-up. All in all, 305 patients from 27 practices in the control group and 299 from 28 practices in the intervention group participated in the study and completed the follow-up assessment.

Baseline and follow-up data

We found no differences between the intervention and control group regarding the characteristics of GPs and practices (cf. [table 1](#)). On average, the intervention group had a 65 days longer period between baseline and follow-up assessment. Additionally, the control group had a significantly higher proportion of female patients than the intervention group (58.7% vs 50.5%), but there were no differences in age, type of household and education. The data from the depression screening, and number of chronic conditions were also similar between the groups (cf. [table 2](#)).

Regarding the primary and secondary outcome measures at baseline and follow-up, there were no differences between the groups except for slightly better baseline values in the intervention group regarding the EUROPEP—Organisation of Care subscale (3.2 points vs 3.0 points) and the GP's knowledge of the patients'

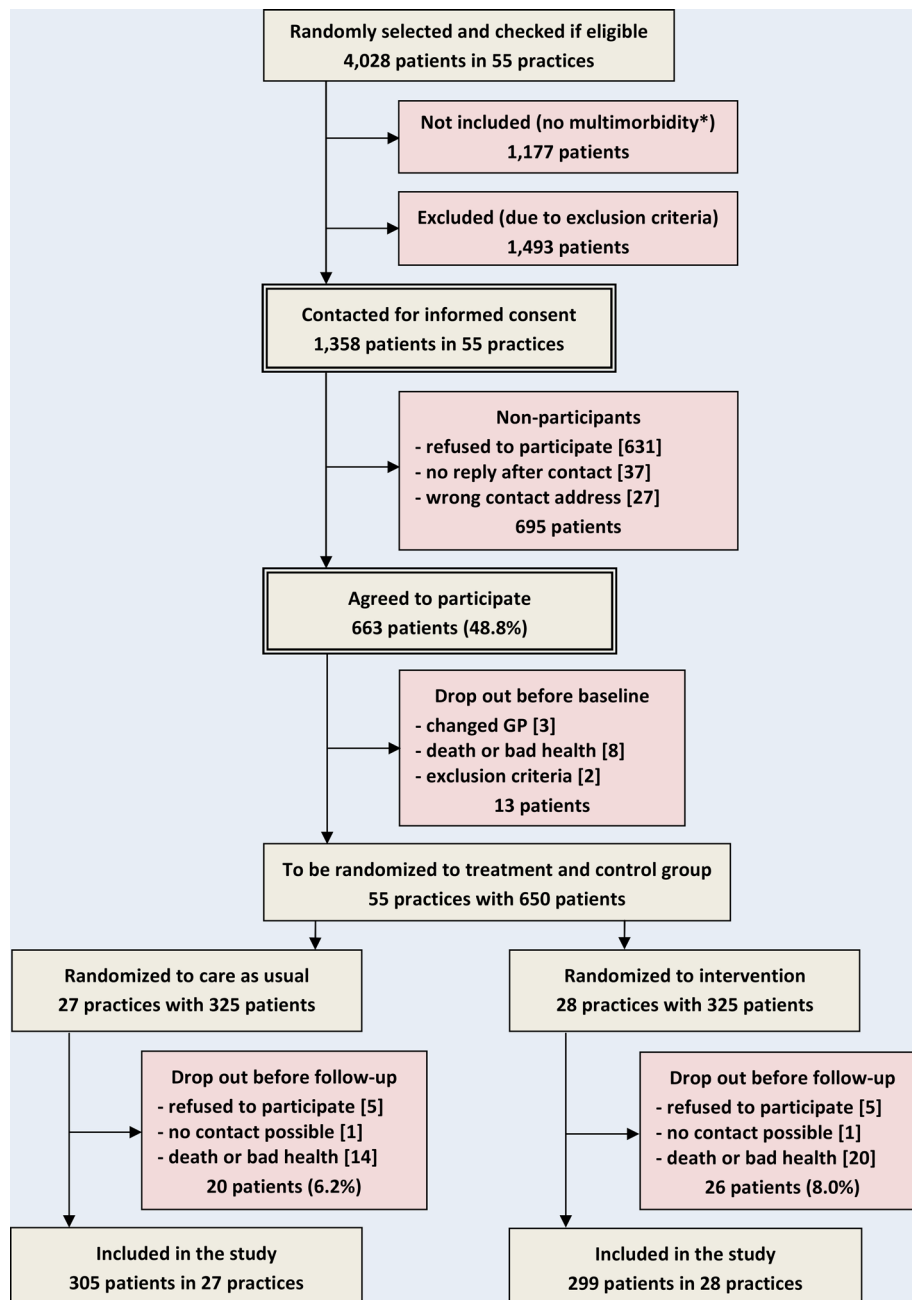


Figure 1 Sampling and response rates of patients. *‘Multimorbidity’ is defined as at least 3 out of 42 ICD-10-based diagnosis groups. ICD, International Classification of Diseases.

medication (66.6% vs 61.1%) (cf. table 3). The medications taken differed only regarding more patients in the control group using active ingredients classified by the level 2 ATC codes ‘A11—vitamins’ (11.5% vs 6.4%) and ‘M09—other musculo-skeletal system’ (1.3% vs 0) (cf. table 4).

Effects on primary outcomes

The effect of our intervention on the outcomes can be found in table 5. There was no statistically significant difference between the treatment and the control group in the change of the number of medications. The intra-cluster correlation coefficient (ICC) of the number of medications was 0.00 (95% CI 0.00 to 0.00) on the study

centre level and 0.03 (0.00 to 0.13) on the practice level. Sensitivity analyses ‘as treated’ and ‘per protocol’ showed similar results.

Our additional exploratory analyses revealed that the change in the number of medications taken by the patient remained statistically non-significant when step-wise adjusted for age, gender, type of household, education, Geriatric Depression Scale score and 46 chronic diseases. Regarding health-related quality of life, there was no significant difference between the treatment and control groups. The ICC of health-related quality of life was 0.01 (0.00–0.13) on the study centre level and 0.03 (0.01–0.17) on the practice level.

Table 1 Characteristics of general practitioners (GPs) and practices

	Care as usual (n=27)	Intervention (n=28)	P
Age at baseline: mean±SD	50.8±6.9 years	48.2±5.0 years	0.117
Gender			
Female	51.9 %	42.9 %	0.504
Male	48.2 %	57.1 %	
Specialty of GP			
Family medicine	74.1 %	64.3 %	0.432
Internal medicine	18.5 %	39.3 %	0.090
No specialty	7.4 %	3.6 %	0.531
No of physicians working in practice	2.0±1.2	2.1±0.9	0.903
No of patients treated in practice per quarter	1457±817	1404±673	0.792

n, number of observations.

Effects on secondary outcomes

There were no effects of the intervention on patient satisfaction, patient empowerment and the GP's knowledge about the medication taken by the patient. However, healthcare use developed differently between groups. Compared with the control group, the amount of contacts with GPs increased in the intervention group (+0.51 contacts in the last 3 months), whereas the amount

of physical, occupational or speech therapy (−1.38 units in the last 3 months) and the days spent in hospital (−3.07 days in the last 6 months) decreased (cf. [table 5](#)).

Potential harms

[Figure 2](#) shows a comparison between the treatment and the control group regarding the change of medication profiles during the study period. There was a significant increase in the frequency of treatment with active ingredients in the ATC groups C08 (ie, calcium channel blockers), M01 (ie, anti-inflammatory and antirheumatic agents), N02 (ie, analgesics) and N06 (ie, psychoanaleptics) in the intervention group compared with the control group. After adjustment for age, gender and the time between baseline and follow-up, most of these differences disappeared. However, the difference in newly prescribed analgesics remained statistically significant after adjustment for these variables, showing that the likelihood of receiving a new prescription for analgesics was twice as high in the intervention group compared with the control group (risk ratio, 2.043; P=0.019). Beyond this finding, which could be interpreted as a negative side effect of the study, the GPs reported no adverse events of the intervention.

DISCUSSION

Principal findings

MultiCare AGENDA was conducted to examine if additional GP consultations structured by the Chronic Care

Table 2 Patients' sociodemographic data, health status and time between baseline and follow-up

	Care as usual (n=305)	Intervention (n=299)	P
Age at baseline: mean±SD	73.5±5.0 years	73.3±4.8 years	0.679
Gender			
Female	58.7%	50.5%	0.043
Male	41.3%	49.5%	
Type of household			
Living in private home alone	40.0%	30.4%	0.082
Living in private home with spouse	55.1%	64.6%	
Living in private home with family members	1.3%	3.0%	
Living in private home with other persons	0.3%	0.3%	
Living in assisted living facility	2.6%	1.3%	
Living in retirement home	0.7%	0.3%	
Education (CASMIN classification)			
Low	54.4%	56.2%	0.479
Medium	29.8%	25.8%	
High	15.7%	18.1%	
No of chronic diseases (based on a list of 46): mean±SD	8.4±3.5	8.7±4.3	0.335
Geriatric Depression Scale score: mean±SD	2.2±2.7	2.1±2.4	0.566
Time between baseline and follow-up: mean±SD	376±27 days	441±66 days	<0.001

CASMIN, Comparative Analysis of Social Mobility in Industrial Nations questionnaire; n, number of observations.

Table 3 Primary and secondary outcomes measures at baseline and follow-up

	Care as usual (n=305)	Intervention (n=299)	P
Medications taken by the patient : mean±SD			
At baseline	7.0±3.5 (n=304)	7.1±3.5	0.715
At follow-up	6.8±3.5 (n=304)	7.3±3.4	0.086
EQ-5D score (value set UK): mean±SD			
At baseline	0.69±0.28 (n=302)	0.67±0.30	0.455
At follow-up	0.70±0.28 (n=303)	0.68±0.32 (n=298)	0.473
EUROPEP—Clinical Performance score: mean±SD			
At baseline	3.1±0.72 (n=284)	3.1±0.69 (n=277)	0.353
At follow-up	2.9±0.72 (n=268)	3.0±0.71 (n=260)	0.465
EUROPEP—Organisation of Care score: mean±SD			
At baseline	3.0±0.71 (n=267)	3.2±0.56 (n=244)	0.003
At follow-up	3.0±0.63 (n=263)	3.1±0.55 (n=240)	0.483
HCEQ—Involvement in Interactions score: mean±SD			
At baseline	36.1±9.3 (n=303)	37.1±9.2 (n=294)	0.176
At follow-up	37.6±9.2 (n=301)	37.4±9.0 (n=292)	0.821
HCEQ—Involvement in Decisions score: mean±SD			
At baseline	24.3±8.1	23.9±8.2	0.542
At follow-up	24.5±8.3 (n=302)	23.3±8.5 (n=298)	0.065
GP's knowledge of active ingredients taken (%): mean±SD			
At baseline	61.1±26.2 (n=304)	66.6±25.6 (n=298)	0.009
At follow-up	64.2±27.2 (n=302)	66.4±28.0	0.338
Contacts with GPs: mean±SD			
At baseline	2.6±3.9	2.3±2.0	0.153
At follow-up-	2.1±2.3	2.4±2.1	0.081
Contacts with other outpatient physicians: mean±SD			
At baseline	2.2±2.4	2.1±2.3	0.665
At follow-up	2.0±2.6	2.2±3.2	0.539
Physical, occupational or speech therapy units: mean±SD			
At baseline	1.6±4.7	1.8±5.0	0.669
At follow-up	3.0±8.0	2.3±5.7	0.205
Days spent in hospital: mean±SD			
At baseline	2.0±6.9	2.6±8.7	0.412
At follow-up	3.5±12.1	2.6±8.3 (n=298)	0.258

EUROPEP, EUROpean task force on Patient Evaluations of general Practice care questionnaire; EQ-5D, EuroQol group 5 Dimensions questionnaire; GP, general practitioner; HCEQ, Health Care Empowerment Questionnaire; n, number of observations.

Model and Narrative Based Medicine could reduce polypharmacy without affecting the patients' health-related quality of life. In our study, this approach did not prove to be effective. This might be attributed to patient-related or GP-related barriers to medication discontinuation. For example, a systematic review of 21 articles, published after the beginning of our study, described patient-reported barriers to deprescribing due to patient disagreement with the appropriateness of cessation, absence of a planned process for cessation, negative influences on the patient to cease the medication and the patient's fear

of cessation.⁴⁵ Furthermore, a systematic review of additional 21 studies identified prescriber-related barriers, such as missing problem awareness, inertia combined with a low perceived value of medication discontinuation, provider's low self-efficacy in regard to alter prescribing patterns and problems with the feasibility of altering the medication in routine care environments.⁴⁶

The lack of efficacy of our study might also stem from the fact that the participating GPs were unaware of study endpoints and polypharmacy was not explicitly addressed. The additional consultations in the intervention group

Table 4 Frequency of medications taken by the patients in the treatment and control group at baseline

ATC	Medication	Care as usual (n=304)	Intervention (n=299)	P*
C09	Angiotensin inhibitor	68.8%	65.2%	0.356
C07	Beta-receptor blocker	48.0%	55.2%	0.079
B01	Antithrombotical agents	51.0%	50.8%	0.970
C10	Antilipemics	47.4%	42.1%	0.197
A02	Ulcer therapeutics	28.0%	32.8%	0.198
C03	Diuretics	25.7%	25.8%	0.979
A10	Antidiabetics	21.1%	23.4%	0.486
H03	Thyroid therapeutics	23.0%	21.1%	0.562
M01	Antiphlogistics/anti-inflammatory	21.7%	21.4%	0.927
N02	Analgesics	20.7%	22.1%	0.686
C08	Calcium antagonists	22.4%	19.1%	0.317
R03	Antiasthma medication	16.1%	14.4%	0.553
C01	Cardiac therapeutics	12.5%	16.7%	0.142
N06	Psychoanaleptics	14.8%	14.1%	0.792
G04	Urological drugs	11.8%	14.7%	0.298
S01	Ophthalmic drugs	13.5%	12.4%	0.684
M04	Gout agents	9.9%	9.0%	0.725
N05	Psycholeptics	9.5%	9.0%	0.829
A11	Vitamins	11.5%	6.4%	0.027
A12	Minerals	10.9%	7.0%	0.099
H02	Corticosteroids (systemic)	4.6%	5.7%	0.548
N04	Anti-parkinson drugs	3.6%	6.7%	0.088
A06	Laxatives	5.3%	4.7%	0.743
R05	Cough and cold preparations	4.9%	5.0%	0.963
N03	Antiepileptics	5.6%	3.3%	0.182
A03	Spasmolytics	4.3%	4.0%	0.871
M02	Anti-inflammatory agents (topical)	3.0%	4.4%	0.364
C02	Antihypertensives	3.0%	4.4%	0.364
M05	Osteoporosis agents	2.6%	4.0%	0.343
G03	Sexual hormones	2.6%	3.7%	0.462
B03	Antianaemic combinations	3.6%	2.3%	0.357
R01	Rhinological drugs	2.3%	3.7%	0.321
J01	Antibiotics	2.6%	2.7%	0.973
N07	Antivertiginous and addiction	3.0%	2.3%	0.636
D07	Corticosteroids (dermatological)	2.3%	2.3%	0.975
R06	Antihistamines	2.6%	1.7%	0.417
C05	Vasoprotectives	3.0%	1.0%	0.085
L02	Hormone antagonists	1.3%	2.0%	0.507
A07	Antidiarrheals	1.6%	1.3%	0.756
R02	Throat and pharynx therapeutics	0.7%	2.0%	0.148
D01	Antifungals (topical)	1.3%	1.3%	0.981
D11	Other dermatological preparations	1.3%	1.3%	0.981
L04	Immunosuppressants	0.7%	1.0%	0.640
M03	Muscle relaxants	1.0%	0.3%	0.324
M09	Other musculo-skeletal system	1.3%	0	0.047

*Statistically significant change ($P \leq 0.05$ Benjamini-Hochberg adjusted for 45 statistical tests).
 ATC, Anatomical Therapeutic Chemical classification system.

Table 5 Effect of the intervention on primary and secondary outcomes: results from multilevel mixed-effects linear regression* and multilevel mixed-effects ordinal logistic regression† analyses (n_{study centres}=3; n_{practices}=55; n_{patients}=602)

	Model 1			Model 2			Model 3		
	β	95% CI	P	β	95% CI	P	β	95% CI	P
Primary outcomes									
No of medications (intention to treat)	0.43	-0.07 to 0.93	0.094	0.53‡	0.01 to 1.06	0.046	0.43‡	-0.07 to 0.93	0.095
No of medications (as treated)	0.45	-0.05 to 0.95	0.079						
No of medications (per protocol)	0.48	-0.03 to 1.00	0.067						
EQ-5D value set UK (intention to treat)	0.34	-0.05 to 0.74	0.091						
Secondary outcomes									
EUROPEP—Clinical Performance score	0.01	-0.11 to 0.13	0.916						
EUROPEP—Organisation of Care score	-0.05	-0.18 to 0.08	0.416						
HCEQ—Involvement in Interactions score	-0.33	-1.82 to 1.15	0.662						
HCEQ—Involvement in Decisions score	-0.29	-1.70 to 1.12	0.685						
GP's knowledge of the patients' medication (%)	1.17	-6.76 to 9.10	0.772						
Contacts with GPs	0.51	0.12 to 0.90	0.010						
Contacts with other outpatient physicians	0.43	-0.13 to 0.99	0.134						
Physical, occupational or speech therapy units	-1.38	-2.73 to -0.04	0.044						
Days spent in hospital	-3.07	-5.25 to -0.89	0.006						

Model 1: baseline-adjusted, controlled for age, gender and time between baseline and follow-up and allowing for random effects of study centres and GP practices within study centres;

Model 2: Model 1 additionally controlled for household type and education; Model 3: Model 2 additionally controlled for Geriatric Depression Scale score and 46 chronic diseases.

*Analyses of primary outcome 'number of medications' and secondary outcomes.

†Analyses of primary outcome 'EQ-5D value set UK'.

‡Statistically significant increase in model fit compared with nested model (results from likelihood ratio test).

EUROPEP, EUROPEAN task force on Patient Evaluations of general Practice care questionnaire; EQ-5D, EuroQol group 5 Dimensions questionnaire; GP, general practitioner; HCEQ, Health Care Empowerment Questionnaire.



Figure 2 Changes of medication in treatment and control group between baseline and follow-up. Example reading of C09 angiotensin inhibitor: 5.4% of intervention group patients and 3.3% of control group patients took an angiotensin inhibitor at baseline but had discontinued this medication at follow-up. At the same time, 3.3% of control group patients and 4.4% of intervention group patients did not have an angiotensin inhibitor at baseline but had obtained this medication at follow-up. *Statistically significant difference ($P \leq 0.05$ Benjamini-Hochberg adjusted for 45 statistical tests). O, change in intervention group; X, change in control group.

resulted in an increase of the number of analgesics. Our intervention might therefore have supported the identification and treatment of unrecognised health problems, such as chronic pain, which are sometimes difficult to detect in routine care.⁴⁷ Additionally, the intervention resulted in a reduction of the physical, occupational and speech therapy units and the days spent in hospital. These findings can be interpreted as an improvement in health-care due to a more intensive GP care and knowledge of the problems of the patient.

However, it has to be taken into account that our study has shown no change in the intervention groups's health-related quality of life compared with the control

group. Prescribing a high number of medications can have many reasons, including health status and socio-demographic factors, such as age, race or education. An additional important factor is the use of health-care,⁴⁸ including the number of consultations in primary care,^{49 50} which had increased as part of the intervention in our study. For this reason, our intervention might have contributed to an oversupply of medications in the multimorbid population.

Comparison with the literature

Other approaches aiming at reducing polypharmacy are more specifically related to the outcome than the

approach of our study, for example, withdrawal of specific classes of medications, medication reviews by physicians or pharmacists with the explicit aim of deprescribing, audit and feedback, educational approaches and interventions based on multidisciplinary teams.⁶

A systematic review of 2012 identified four pharmacist-based, four physician-based and two multidisciplinary-based interventions to reduce polypharmacy. Eight of these 10 studies showed a significant reduction in the number of medications.⁵¹ For example, in a study on 160 residents of a nursing home, who used 16.6 medications on average, a physician medication review was conducted based on updated Beers Criteria and the Epocrates online drug–drug interaction programme. This intervention resulted in a mean reduction of 1.1 medications per patient.⁵²

These results were confirmed by a more recent systematic review of 2016 on 116 deprescribing trials. The study concluded that deprescribing was feasible but difficult to implement. In the systematic review, mortality was significantly reduced only in randomised studies of patient-specific interventions. Therefore, the authors stressed the importance of an individualised approach on the reduction of polypharmacy.⁵³ However, in another systematic review, the authors concluded that it was still unclear how best to organise and implement strategies in order to reduce inappropriate polypharmacy or have an impact on clinically relevant endpoints in patients with polypharmacy.⁵⁴

Strengths and weaknesses

Strengths of our study are related to the study design with adequate numbers of recruited patients, the GPs and patients being unaware of study endpoints and the data analysis controlled for relevant confounders, allowing for cluster effects and blinding to group assignment. However, our study results do not necessarily provide evidence against the effectiveness of a narrative chronic care intervention to reduce polypharmacy in primary care. There are three factors related to the study design that may also account for the lack of effectiveness.

First, we trained and monitored the GPs in the intervention group to conduct the narrative-based intervention and we instructed the GPs in the control group to continue with care as usual. Despite the fact that we monitored the implementation of the intervention by telephone or personal visits to the GPs, we had no possibility to observe the consultations with the patients. For this reason, we do not know if the intervention had been implemented per protocol. Furthermore, we also do not know if the GPs from the control group really had conducted care as usual or whether they had focused more on their patients due to their study participation.

Second, there might be a selection bias in our GP population if a higher-than-average percentage of motivated and educated GPs responded to our invitations for study participation. This bias might even have increased because we had randomly selected GPs from the official

physician register in statutory healthcare and through Internet and print media advertisements.

Thirdly, the missing efficacy of our study might also result from the fact that our study did not explicitly address oversupply and misuse of certain classes of medications, but aimed at identifying and addressing unmet needs of patients as well. This problem has been discussed in literature. For example, in a systematic review of the literature, Hajjar *et al* stated that polypharmacy might not be reduced if intervention studies simultaneously addressed overuse and underuse of medications as both effects might even out each other.⁴⁸ Regarding the secondary outcomes, it needs to be noted that healthcare costs could not be quantified in Euros in the short form of the Leipzig Supply and Cost Instrument, but instead are expressed as use of healthcare providers.

There are also some limitations related to the representativeness of the study. The population was recruited among patients with multimorbidity who visited their GPs during the study period. Thus, non-users of general practice services were not included. Furthermore, we obtained a response rate of 48.8%, which means that more than half of the eligible population refused to participate in the study. However, on average, we recruited two patients more per practice than expected and the sample included 56 patients more than planned. As with most population-based healthcare research, selection bias towards cooperative patients who may have been more satisfied with their primary care than other patients cannot be excluded. Besides a slight patient selection bias regarding gender and certain diagnosis groups, we found no other baseline differences regarding sociodemographic data and no bias regarding medication intake.

CONCLUSIONS

This is the first cluster-randomised controlled trial investigating the effects of a multifaceted intervention based on the Chronic Care Model and Narrative Based Medicine on the number of medications taken and health-related quality of life. Intensifying the doctor–patient dialogue and discussing the patient’s agenda and personal needs did not lead to a reduction of medication intake nor did it alter health-related quality of life. Exploratory analyses show that the additional consultations in our intervention group probably have not been without any effect, but may have resulted in an increase of the medication load, especially regarding analgesics. Future interventions addressing both oversupply and undersupply of medications should therefore be accompanied by measures preventing an inappropriate prescription of medications.

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Ethics approval The study was approved by the Ethics Committee of the Medical Association of Hamburg in July 2011 (Approval No. PV3788).

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Data sharing statement Data are not available for other researchers.

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