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Combined intervention programme reduces inappropriate prescribing in elderly patients exposed to polypharmacy in primary care

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Abstract

Purpose To evaluate the effect of a combined or a single educational intervention on the prescribing behaviour of general practitioners (GPs). The primary endpoint was effect on inappropriate prescribing according to the Medication Appropriateness Index (MAI).

Methods General practitioners were randomised to either (1) a combined intervention consisting of an interactive educational meeting plus feedback on participating patients' medication, (2) a single intervention with an interactive educational meeting or (3) a control group (no intervention). Elderly (>65 years) patients exposed to polypharmacy (≥ 5 medications) were identified and approached for inclusion. Data on medications prescribed over a 3-month period were collected, and the GPs provided detailed information on their patients before and after the intervention. A pre- and post-MAI were scored for all medications. **Results** Of the 277 GPs invited to participate; 41 (14.8%) volunteered. Data were obtained from 166 patients before

and after the intervention. Medication appropriateness improved in the combined intervention group but not in the single intervention group. The mean change in MAI and number of medications was -5 [95% confidence interval (CI) -7.3 to -2.6] and -1.03 (95% CI -1.7 to -0.30) in the combined intervention group compared with the group with the educational meeting only and the no intervention group. **Conclusions** A combined intervention consisting of an interactive educational meeting plus recommendations given by clinical pharmacologists/pharmacists concerning specific patients can improve the appropriateness of prescribing among elderly patients exposed to polypharmacy. This study adds to the limited number of well-controlled, randomised studies on overall medication appropriateness among elderly patients in primary care. Important limitations to the study include variability in data provided by participating GPs and a low number of GPs volunteering for the study.

Keywords Aged · Intervention ·
Medication appropriateness index · Polypharmacy ·
Primary health care

The trial is not registered in a publicly available database of clinical trials. The trial was conducted in a period prior to June 1, 2007.

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Introduction

As the world's population ages, the number of patients exposed to polypharmacy is increasing [1–3]. The increased number of medications used by a patient correlates with poorer compliance, increased risk of drug–drug interactions and adverse drug reactions (ADRs) and increased economic burden [4–9].

A substantial proportion of the ADRs leading to hospitalisation are considered preventable as they are caused by inappropriately prescribed medications [10–15].

Many studies have shown that inappropriate prescribing is a common problem among the elderly in different settings. The scale of the problem is difficult to assess due to limitations associated with the selection of a standard and publication bias [16–18]. Improving medication use would have important financial and public health benefits, and many attempts have been made to find methods of improving the quality of prescribing in various settings [19–21]. However, only a limited number of well-controlled studies have examined the effect of different strategies on prescribing quality in primary care. None of these examined the effect on all medications taken by participating patients [22].

The purpose of the study was to investigate whether a combined intervention consisting of an interactive educational meeting for general practitioners (GPs) plus recommendations on specific patients registered with those GPs would improve the overall appropriateness of prescribing compared to an interactive educational meeting alone or no intervention.

Methods

This was a randomised, controlled intervention study carried out within the framework of primary health care in Copenhagen County, Denmark.

Participants

Each GP with a single-handed practice in the County of Copenhagen ($n=277$) was sent a letter inviting him/her to participate in the study; 41 GPs (14.8%) ultimately volunteered.

Each GP was asked to recruit six patients who were randomly selected by the authors from a list produced by the county of Copenhagen of all the elderly polypharmacy patients registered with the GP. Eligibility criteria included: (1) aged 65 years and older; (2) taking five or more regularly scheduled medications over a 3-month period prior to recruitment according to a database used to record the drug subsidy system of Danish pharmacies; (3) capable of giving informed consent. In all, 303 patients were approached; 212 gave informed consent and data on 166 of these 212 patients were collected before and after the intervention period. The derivation of the study population is shown in Fig. 1.

Data collection

For each patient, 3 months of prescription data were collected before and after the intervention, respectively. Based on these data, the GPs were asked to provide

information on the patients' medical history. Detailed information on all subsidised and non-subsidised medications used by the patients were recorded on standard forms. These forms contained questions on the indication for use (illnesses, symptoms, laboratory findings etc.), medications previously used for the same indication, reasons for medication changes, expected treatment effect, follow-up method, start of treatment, expected duration, results of latest follow-ups, dose (reason for sub-optimal dose if applicable) and instructions given to the patients.

The GPs were contacted for clarification regarding missing information. If data were not obtainable, it was decided to rate the item as 'appropriate'. Only medications prescribed by or known to the patients' own GPs were included. Topical, dermatological medications and medications not used regularly were not analysed. Medications were classified according to the Anatomical Therapeutic Chemical Classification System (ATC).

Interventions

The GPs were randomised to the following three 'intervention' groups according to a computer-generated randomisation list prepared by a consultant statistician (Fig. 2):

1. a combined intervention consisting of an interactive educational meeting on the subject of polypharmacy in the elderly plus feedback on participating patients' medication,
2. a single intervention with an interactive educational meeting, or
3. a control group.

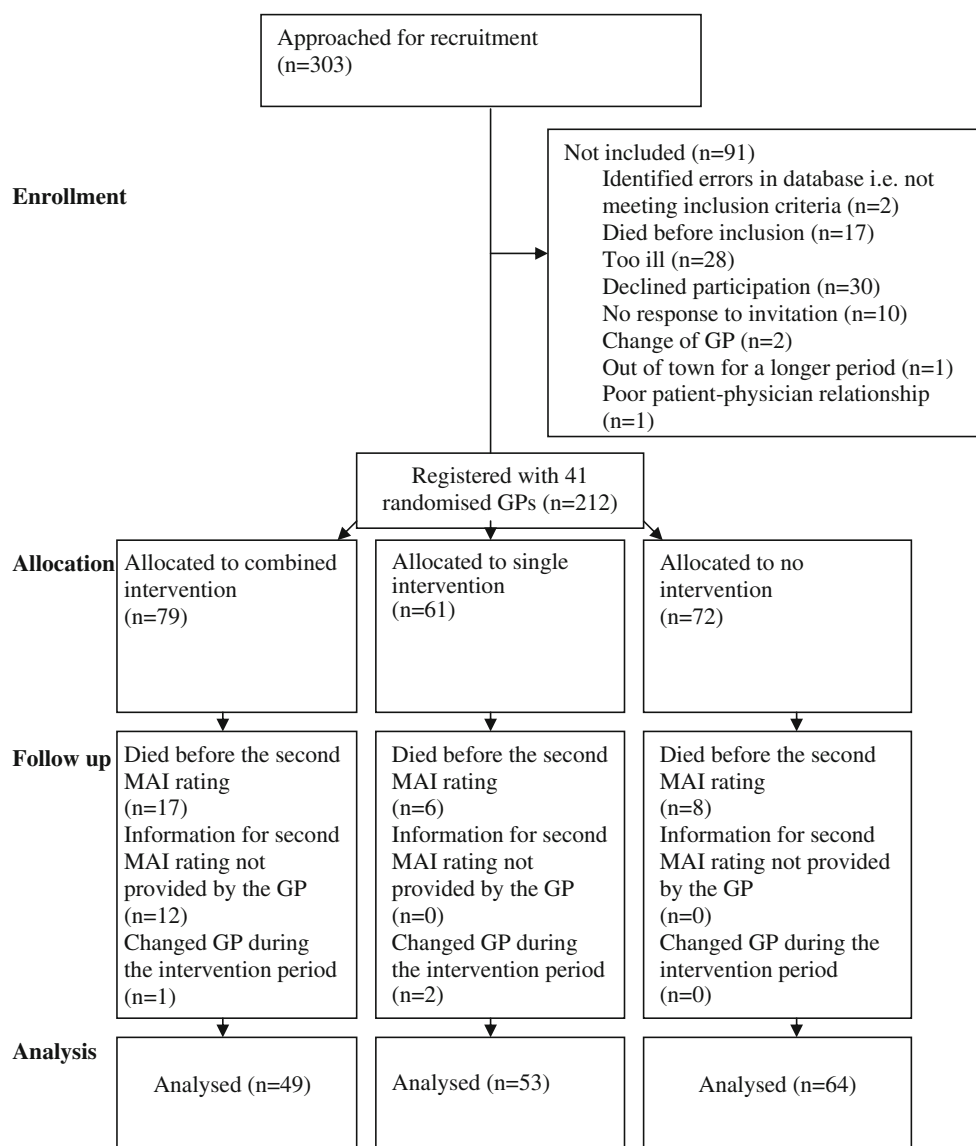
The GPs were informed about the group assignment after baseline data had been collected.

Main outcome measures

The appropriateness of prescribing was measured by using the Medication Appropriateness Index (MAI). This index was chosen because it addresses and quantifies many relevant elements of drug prescribing. One of two groups of evaluators scored the MAI before and after the intervention for every medication used by the patients. Post-intervention ratings were scored approximately 1 year after the baseline rating. The evaluator groups were blinded to the intervention group of the GPs and to the identity of the patients and GPs; however, age and gender of the patients were known.

The MAI incorporates explicit criteria and uses implicit instructions. It consists of ten criteria rated for each medication: (1) indication, (2) effectiveness, (3) dosage, (4) directions correctness, (5) directions practicality, (6) drug–drug interaction, (7) drug–disease interaction, (8)

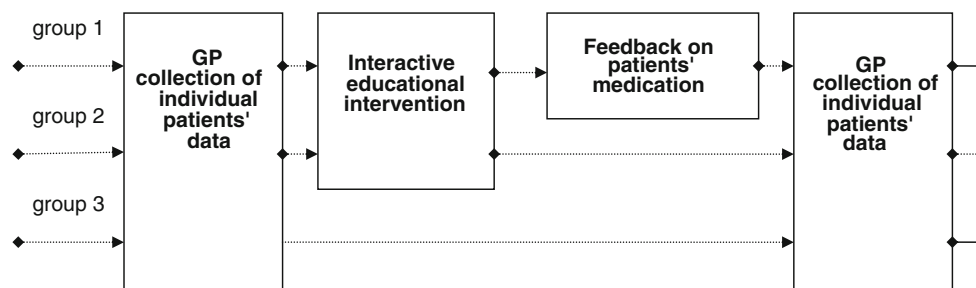
Fig. 1 Derivation of the study population. *GP* General practitioner, *MAI* Medication Appropriateness Index



duplication, (9) duration and (10) expense. The evaluator groups rated whether a criterion was ‘appropriate’, ‘marginally appropriate’ or ‘inappropriate’. A weighted MAI score was calculated for each medication (see [Appendix](#)), and a MAI score per patient was calculated by summing weighted MAI scores for all medications used by the patient. Thus, the patient MAI score depended on the

number of medications taken by the patient and the MAI score per medication. A MAI score per GP was calculated by taking the mean patient MAI for the patients of that particular GP. Due to the results of an earlier study indicating better intra- than inter-rater reliability when rating the MAI, it was decided that whenever possible the same group should rate the same patients before and after

Fig. 2 Flowchart of the interventions



the intervention. All combinations of medications were controlled for potential interactions, which were defined as class 1 or class 2 interactions according to the top 100 drug interactions described by Hansten and Horn [23]. Other interactions deemed to be clinically important to the specific patient were rated as inappropriate.

In the rating of criterion 10, the price of the medication, a medication was rated as inappropriate if there was an alternative of equal utility that was more than 25% cheaper than the medication chosen. As Denmark has a system of automatic generic substitution at pharmacies unless the GP opposes substitution by means of a written note on the prescription itself, we mainly concentrated on analogue alternatives.

The treatment of the patients was also assessed from the information provided by the GPs. A patient was considered to be under-treated if the assessors judged that a new medication should be added in order to follow best practice of treatment for a specific disease.

Interventions

Following randomisation, GPs in both intervention groups participated in an interactive educational meeting on the subject of polypharmacy and appropriateness of prescribing. The meeting included background information on the causes and consequences of polypharmacy, areas of concern in the treatment of the elderly and group discussions on patient cases. The GPs in the combined intervention group also received written recommendations targeting medication problems identified while rating the MAI. Afterwards, the GPs were contacted by telephone by a senior clinical pharmacologist (JS) to discuss any uncertainties concerning the recommendations given, and the GPs were asked to send a written feedback on the implementation of the recommendations.

The GPs in the single intervention group and the control group received no advice on medication problems in this intervention study. After the study was completed, GPs in these groups were given written recommendations based on the variables identified during the scoring of the MAI and asked to give feedback on implementation.

The two different interventions were chosen in order to evaluate the effect of both a relatively inexpensive intervention (educational meetings alone) and a more expensive intervention (educational meeting and feedback with recommendations) on GPs.

Statistical analysis

To assess the comparability of continuous variables between study groups at baseline we used the Kruskal–Wallis test and median test. Dichotomous variables were

compared using the chi-square test. The Wilcoxon signed rank test was used to test for significant changes in patient MAI and number of medications in the intervention groups. The effect of the interventions on patient MAI and number of medications per patient was estimated by linear regression analyses. We used the 95% confidence interval (CI) and adjusted for number of medications and patient MAI at baseline. SPSS software (SPSS, Chicago, IL) was used for all analyses. Power calculations for the primary outcome measure assumed a difference in change in patient MAI of 3 between groups, a standard deviation (SD) of 7, an alpha of 0.05, and a power of 80%. The estimates for mean and standard deviations were obtained from previous studies using MAI. A sample size of 86 per group was required. To allow for a drop-out rate of 17% estimated from a similar study, a sample size of 100 patients per group was required.

As participation in the project was expected to be time-consuming, the number of GPs involved was determined by a desire not to overburden the individual GP.

Results

Characteristics of the 212 patients included in the study are shown in Table 1. For the combined and single intervention groups, the mean age of the patients was 77.1 and 75.4 years, respectively, and for the control group, the mean age was 77.0 years. Most patients were female in all three groups (68.4, 62.3 and 66.7%, respectively). There were no significant differences between the patients of the three groups in terms of the characteristics reported in Table 1.

In terms of patient MAI at baseline and number of medications at baseline, there was a tendency for patients in the combined intervention group to have a higher MAI and to be exposed to more medications at baseline than those patients in the single intervention group and the control group. The difference was significant for baseline MAI but not for number of medications. Nevertheless, it was decided to control for both parameters in the analyses.

Overall, data were collected for 166 of the 212 randomised patients (78%). More patients died in the combined intervention group than in the single intervention group and control group (17 vs. six and eight, respectively), and more physicians in the combined intervention group omitted to submit patient information after the intervention (for 12 vs. 0 and 0 patients, respectively) than in the other groups.

Characteristics of the GPs are shown in Table 2. For all parameters relating to GP activities, except the number of patients registered with the GP, there was a tendency for the values for GPs in the combined intervention group to be higher than those for GPs in the single intervention and control groups.

Table 1 Patient characteristics at baseline

Patient characteristics at baseline	Combined intervention (<i>n</i> =79)	Single intervention (<i>n</i> =61)	Control (<i>n</i> =72)
Gender (% female)	68.4	62.3	66.7
Age (years)			
Mean (\pm SD)	77.1 (\pm 6.9)	75.4 (\pm 7.0)	77.0 (\pm 7.8)
Median (range)	77 (65–90)	74 (65–97)	76 (65–92)
Patient MAI at baseline			
Mean (\pm SD)	10.8 (\pm 7.7)	9.1 (\pm 8.5)	9.8 (\pm 7.9)
Median (range)	10 (0–33)	5 (0–33)	9 (0–32)
Number of medications at baseline			
Mean (\pm SD)	8.0 (\pm 2.8)	7.2 (\pm 2.9)	7.7 (\pm 3.0)
Median (range)	7 (1–17)	7 (3–17)	7 (3–16)

MAI, Medication Appropriateness Index; SD, standard deviation

Only the difference in the parameter *number of consultations* was significant.

The effect of the interventions on mean patient MAI, mean number of medications and number of patients under treatment are shown in Table 3.

The patient MAIs before the intervention for the combined intervention, single intervention and control groups were 11.2, 7.5 and 9.3, respectively, and the post-patient MAIs were 6.0, 8.2 and 10.1, respectively. Regression analysis showed that the estimated difference for the combined intervention group was a 5-point (95% CI -7.3 to -2.6) improvement in MAI score. Part of this change in patient MAI can be explained by the baseline variables alone. However, the difference in MAI is still significant after these variables had been controlled.

The change in number of medications in the combined intervention group consisted of a significant decrease of -1.03 (95% CI -1.7 to -0.30).

Pre-intervention, 21 patients assessed to be under-treated: six in the combined intervention group, ten in the

single intervention group and five in the control group; post-intervention, these were four, 12 and 11 patients, respectively. Only six patients were assessed as being under-treated at both ratings. Of these latter patients, none were in the combined intervention group, three were in the single intervention group and three were in the control group.

Tables 4 and 5 show that improvements were seen for all MAI criteria and therapeutic groups in the combined intervention group.

Discussion

The results from this study demonstrate that a combined intervention consisting of an interactive educational meeting for GPs and feedback to GPs on participating patients' medication by clinical pharmacologists and a clinical pharmacist can improve medication appropriateness in elderly patients exposed to polypharmacy. Furthermore,

Table 2 Characteristics of the GP at baseline

Characteristics of the GP at baseline	Combined intervention (<i>n</i> =15)	Single intervention (<i>n</i> =12)	Control (<i>n</i> =14)
Gender (% female)	33.3	41.4	28.6
Age (years)	51.6 (\pm 8.3)	51.1 (\pm 5.7)	51.9 (\pm 6.7)
Number of patients in project	5.3 (\pm 1.1)	5.1 (\pm 1.2)	5.1 (\pm 1.4)
Percentage of patient drop outs	34 (\pm 36)	12 (\pm 21)	11 (\pm 10)
Number of patients registered in practice	1592 (\pm 354)	1423 (\pm 300)	1598 (\pm 359)
Number of patients registered > 65 years, exposed to >4 medications according to database	38 (\pm 16)	33 (\pm 15)	31 (\pm 18)
Number of consultations over a 3-month period	1436 (\pm 467)	1061 (\pm 305)	1119 (\pm 290)
Number of telephone consultations over a 3-month period	983 (\pm 410)	804 (\pm 312)	963 (\pm 470)
Number of home visits over a 3-month period	39 (\pm 26)	38 (\pm 25)	27 (\pm 15)
Mean MAI score per GP at baseline	10.7 (\pm 3.9)	9.0 (\pm 5.5)	9.7 (\pm 3.3)

Values are the mean \pm SD

Table 3 Pre- and post- intervention values of patient MAI, number of medications and number of patients under treated

Variables	Combined intervention (<i>n</i> =49)			Educational meeting (single intervention) (<i>n</i> =53)			Control (<i>n</i> =64)		
	Before	After	Change	Before	After	Change	Before	After	Change
Patient MAI score	11.2	6.0	5.1	7.5	8.2	−0.7	9.3	10.1	−0.8
Number of medications	7.9	7.0	0.9	6.8	7.3	−0.5	7.5	7.7	−0.2
Number of patients under treated	6	4	2	10	12	−2	5	11	−0.6

the combined intervention resulted in a significant decrease in the mean number of medications taken by the patients.

Studies undertaken with the objective of improving prescribing appropriateness have mainly concentrated on hospital and nursing home settings [22]. Even though some studies have been targeted at GPs, the majority have concentrated on specific indicators and narrow therapeutic areas, and only a few well-controlled studies have examined the effect on overall prescribing quality. An exception is a study carried out by Allard et al., who failed to demonstrate a significant effect—measured as the change in the number of potentially inappropriate prescriptions—of mailing recommendations to the GPs concerning the medications of specific patients [24]. These researchers also found no effect on the number of medications prescribed. The authors explained the lack of effect on the fact that they used a single intervention aimed at the GPs, which is a very plausible explanation considering the number of papers published relating to the effect of interventions in general. Several authors of reviews on the area have found that multifaceted interventions seem to be more effective than single interventions [25–29]. Indeed, our study failed to show any effect of the single intervention, the interactive educational meeting.

A combined intervention including feedback on participating patients' medication given by clinical pharma-

cologists/pharmacists is more costly and time consuming than educational meetings alone. An estimate of the time needed to assess the MAI is needed in order to decide whether the intervention is cost effective and worthwhile. In addition, the time spent by GPs and/or others on collecting individual patient data and the time spent on communicating recommendations should be included in the estimate. It was not within the objective of this study to evaluate the cost effectiveness. However, according to Hanlon et al. [32], their research assistant required approximately 45 min to prepare each medical information abstract utilised by the raters, and the raters spent approximately 10 min evaluating the appropriateness of each medication. In our study, we estimated that GPs needed 1 h per patient, before and after the intervention, respectively, in order to collect and communicate patient details; however, feedback from several GPs indicated that more time was spent per patient.

More patients in the combined intervention group than in the single intervention and control group died during the intervention study (17 vs. six and eight, respectively), and more GPs from the combined intervention group omitted to submit patient information after the intervention (12 vs. 0 and 0, respectively). The latter is probably explained by the fact that the GPs in the combined intervention group had already received the recommendations for patients, as part of

Table 4 Inappropriate prescribing distributed over MAI criteria pre- and post-intervention

MAI criteria	Combined intervention		Educational meeting		Control	
	Before (<i>n</i> =632) <i>n</i> (%)	After (<i>n</i> =341) <i>n</i> (%)	Before (<i>n</i> =437) <i>n</i> (%)	After (<i>n</i> =384) <i>n</i> (%)	Before (<i>n</i> =552) <i>n</i> (%)	After (<i>n</i> =493) <i>n</i> (%)
Indication	77 (12.2)	25 (7.3)	51 (11.7)	36 (9.4)	72 (13.0)	60 (12.2)
Effectiveness	34 (5.4)	13 (3.8)	30 (6.9)	14 (3.6)	34 (6.2)	31 (6.3)
Dosage	51 (8.1)	17 (5.0)	23 (5.3)	27 (7.0)	35 (6.3)	31 (6.3)
Correct directions	9 (1.4)	1 (0.3)	1 (0.2)	1 (0.3)	1 (0.2)	1 (0.2)
Practical directions	8 (1.3)	2 (0.6)	4 (0.9)	10 (2.6)	9 (1.6)	6 (1.2)
Drug-drug interaction	4 (0.6)	0 (0.0)	4 (0.9)	3 (0.8)	2 (0.4)	1 (0.2)
Drug-disease interaction	54 (8.5)	19 (5.6)	36 (8.2)	24 (6.3)	50 (9.1)	40 (8.1)
Duplication	19 (3.0)	4 (1.2)	14 (3.2)	13 (3.4)	17 (3.1)	11 (2.2)
Duration	105 (16.6)	37 (10.9)	73 (16.7)	53 (13.8)	89 (16.1)	81 (16.4)
Expense	189 (29.9)	82 (24.0)	114 (26.1)	111 (28.9)	137 (24.8)	164 (33.3)

Table 5 Inappropriate prescribing distributed over therapeutic groups pre- and post-intervention

Therapeutic group (code)	Combined intervention		Educational meeting		Control	
	Before	After	Before	After	Before	After
	(n=632) n (%)	(n=341) n (%)	(n=437) n (%)	(n=384) n (%)	(n=552) n (%)	(n=493) n (%)
Alimentary tract and metabolism (A)	30 (4.7)	7 (2.1)	16 (3.7)	12 (3.1)	13 (2.4)	18 (3.7)
Blood and blood forming organs (B)	13 (2.1)	5 (1.5)	12 (2.7)	15 (3.9)	10 (1.8)	9 (1.8)
Cardiovascular system (C)	91 (14.4)	47 (13.8)	53 (12.1)	49 (12.8)	49 (8.9)	76 (15.4)
Genito-urinary system and sex hormones (G)	5 (0.8)	2 (0.6)	4 (0.9)	6 (1.6)	5 (0.9)	5 (1.0)
Systemic hormonal prep., exclusive sex hormones (H)	4 (0.6)	2 (0.6)	3 (0.7)	2 (0.5)	5 (0.9)	6 (1.2)
Musculo-skeletal system (M)	25 (4.0)	7 (2.1)	12 (2.7)	15 (3.9)	23 (4.2)	20 (4.1)
Nervous system (N)	59 (9.3)	22 (6.5)	38 (8.7)	34 (8.9)	66 (12.0)	53 (10.8)
Antiparasitic products (P)	10 (1.6)	5 (1.5)	4 (0.9)	2 (0.5)	8 (1.4)	9 (1.8)
Respiratory system (R)	31 (4.9)	13 (3.8)	29 (6.6)	19 (4.9)	20 (3.6)	15 (3.0)
Others (O)	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

the intervention, at the time of the second submission, whereas GPs in the single intervention and control groups did not receive the recommendations until after submission. Their incentive to submit the information concerning the patients was, therefore, greater. More people in the combined intervention group died, possibly because the patients in this group were sicker and exposed to more medications at baseline. The mean patient MAI and number of medications used were 12.7 and 9.5 at baseline for patients in the combined intervention group who died, whereas the corresponding numbers were 10.0 and 7.0, respectively, for all patients at baseline. The possibility exists that the higher number of deaths in the combined intervention group is a chance finding or that detrimental recommendations were given; however, the recommendations were given by well-qualified and experienced clinical pharmacologists based on available information regarding the individual patient, the disease and the treatment.

The study was conducted among GPs in Copenhagen County; however, only 14.8% of the invited GPs volunteered. This could have implications regarding the results of the study or jeopardise the generalisability of the study. It is likely that GPs volunteering for such a study may be different from those GPs who did not participate in terms of their readiness to accept a second opinion on their prescribing behaviour and to accept changes. This would result in a larger intervention effect than would be generally expected. On the other hand, it is also likely that GPs volunteering were better at prescribing and therefore would not object to a second opinion, whereas GPs who recognise their own prescribing deficiencies would not volunteer in order not to feel exposed/reprimanded. This, in contrast, could result in a higher baseline performance and less room for improve-

ment and, consequently, a decreased chance of demonstrating an intervention effect.

We suspect that many GPs did not sign up for this study because they expected it to be time consuming and to continue over a longer period of time. In addition, many GPs are likely not interested in second opinions on their prescribing behaviour. However, the reasons for non-participation were beyond the scope of this study.

This study has a number of potential limitations. The first limitation relates to the collection of data on which we based the MAI ratings. For logistical reasons, we did not collect data directly from the medical records of the GPs. The GPs themselves abstracted data from their medical records and submitted the information needed on standard forms. This allowed the GPs to intentionally or unintentionally modify patients' data and, consequently, the level of appropriateness prior to the intervention could have been overestimated. Both the GPs in the control group and those in the intervention groups were asked to subtract and submit data from participating patients. It is very likely that the Hawthorne effect occurred, resulting in an effect in both intervention groups and the control group which reduced the apparent effect of the intervention. In fact, Soumerai et al. who provided a critical analysis of the experimental literature on the subject of improving drug prescribing in primary care, wrote: "*interestingly, several of the control groups in the randomised studies exhibited positive trends in prescribing habits as well*", which indicates that this is a common problem in such studies [30].

Another limitation relating to the data collection is that the quality and quantity of the data received from the 41 participating GPs varied considerably. Differences in data quality probably left some room for interpretation. We decided to take a conservative approach and rate items as

appropriate in the case of missing data. This probably also resulted in an overstatement of prescribing appropriateness.

A third limitation is that only medications prescribed by the patients' own GPs and non-prescription medications that the GPs knew of were included in this study. Other studies have indicated that the number of physicians involved in a patient's care is associated with more inappropriate prescribing. However, in Denmark general practice has a gatekeeper role. As a result, the GP receives notifications from hospitals, nursing homes and specialists regarding patients' treatment, and prescriptions are generally renewed by the patient's GP. Furthermore, in connection with this study, we carried out a pilot study where data from 141 of the patients also participating in this study were collected from a database allowing differentiation between medications prescribed by the patients' own GPs and medications prescribed by other physicians and hospitals. The conclusion drawn from that study was that medications used by patients exposed to polypharmacy were primarily prescribed by the patients' own GPs and that medications prescribed by other physicians were mainly renewals of medication prescriptions.

A final limitation related to the use of the MAI is that this index does not measure the clinical outcomes; therefore, the clinical significance of the ratings is not established.

Our study adds to the limited number of well-controlled, randomised studies on the overall medication appropriateness among elderly patients in primary care. Contrary to the study done by Allard et al., we found that an educational intervention aimed at modifying the prescribing behaviour of GPs did have an effect on medication appropriateness. Furthermore, due to limitations in our data collection method, the observed improvement is actually likely to be an under-estimate of the effectiveness of the intervention. Our combined intervention also had an effect on the mean number of medications taken by the patients, which is encouraging as the number of medications taken by a patient is correlated to the risk of experiencing an ADR.

Future studies should establish the clinical significance of improvement in the MAI, evaluate sustained effect of interventions and include patients more actively. Potential GP or patient barriers to enacting recommendations should be addressed, and economic implications should be studied.

Ethics approval Due to an exception to the 'Act on Patients' legal rights and entitlements in Denmark', the Danish National Board of Health instead of the ethics committee approved the protocol.

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Conflict of interest None.

Appendix

In rating the Medication Appropriateness Index, weights of 3 were given to inappropriate ratings for *indication* and *effectiveness*, 2 for *dosage*, *direction correctness*, *drug–drug interactions* and *drug–disease interactions* and 1 for *direction practicality*, *therapeutic duplication*, *duration* and *cost*. The weighted MAI score can range from 0, which indicates no prescribing problems, to 18 if all criteria are rated as inappropriate. A score of 0 was given for all criteria rated as appropriate or marginally appropriate. For more information on the MAI, other references should be consulted [31–33].

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