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A multi-intervention approach on drug therapy can lead to a more appropriate drug use in the elderly. LIMM-Landskrona Integrated Medicines Management

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Abstract
Rationale, aims and objectives To evaluate if an integrated medicines management can lead to a more appropriate drug use in elderly inpatients.
Method The study was an intervention study at a department of internal medicine in southern Sweden. During the intervention period pharmacists took part in the daily work at the wards. Systematic interventions aiming to identify, solve and prevent drug-related problems (DRPs) were performed during the patient's hospital stay by multidisciplinary teams consisting of physicians, nurses and pharmacists. DRPs identified by the pharmacist were put forward to the care team and discussed. Medication Appropriateness Index (MAI) was used to evaluate the appropriateness in the patients' drug treatment at admission, discharge and 2 weeks after discharge. In total 43 patients were included, 28 patients in the intervention group and 25 patients in the group which was used as control.
Results For the intervention group there was a significant decrease in the number of inappropriate drugs compared with the control group ($P = 0.049$). Indication, duration and expenses were the MAI-dimensions with most inappropriate ratings, and the drugs with most inappropriate ratings were anxiolytics, hypnotics and sedatives.
Conclusion This kind of systematic approach on drug therapy can result in a more appropriate drug use in the elderly.

Introduction
Inappropriate use of drugs is a common cause of health care contacts, and systematic reviews show that adverse drug reactions (ADR) are the cause of 5% (0.2–41%) of admissions to hospital [1–3]. Further, ADR are the 4th–6th most common cause of death in American hospitals [1], and the majority of them can be avoided [1,3]. In the elderly as much as 90% of ADR can be avoided. Swedish studies show similar results [4–6]. These problems do not only occur in outpatients. Reviews show that 1–24% of all patients acquire ADR during their hospital stay [1]. Using drugs in an inappropriate way is also expensive, and for every dollar spent on drugs in American nursing homes, it costs 1.33 dollars to take measures against problems directly related to drug use [7]. Drugs are important in the treatment of elderly patients, and in Swedish nursing homes patients have been reported to use on average 8.8 drugs [8]. An American study on elderly inpatients showed that 42% of the patients were prescribed at least one drug without valid indication and that 47% of the patients were prescribed drugs with inappropriate duration [9]. Studies have also shown a relationship between the number of drugs prescribed and inappropriate

drug use [9,10]. As the number of elderly is increasing and therefore also the drug use, inappropriate drug use will probably be a growing problem.

In order to measure prescribing appropriateness, Medication Appropriateness Index (MAI) was developed in 1992 [11,12]. This is an instrument that combines implicit and explicit criteria when determining a drug's appropriateness to an individual [11]. It consists of 10 dimensions: indication, effectiveness, dosage, correct directions, practical directions, drug–drug interactions, drug–disease interactions, duplication, duration and expense; and it has been validated for evaluating drug therapy in the elderly [12]. A weighing scheme has been developed where each drug can receive a score from 0 (no inappropriate ratings) to 18 (only inappropriate ratings) [12]. A patient MAI-score can then be determined by summing the MAI-medication scores for all the patient's medications [13]. MAI has been proved, by tests of inter-rater agreement, to be a reliable method in evaluating drug therapy appropriateness [11,14].

To optimize the drug treatment for an individual, a systematic approach is necessary. In Northern Ireland, an integrated medicine management (IMM) service has been developed, which involves pharmaceutical care at admission, during the hospital stay and at discharge [15]. A randomized study showed that patients receiving the IMM service had a significantly shorter length of hospital stay, decreased rate of readmission over a 12-month follow-up period and an increased time to readmission [15]. Our research group has earlier put together and developed systematic and validated instruments for use in pharmaceutical care practice including medication reconciliation at admission and discharge. A medication interview scheme has been put together, using validated instruments, to assess the correctness of the medication list at admission, the patient's knowledge about the drug treatment, the patient's attitudes towards disease and drug treatment {believes about medication questionnaire, specific BMQ [16] and patient compliance (Morisky 4-item scale) [17]}. To individualize and monitor a patient's drug treatment during hospital stay, a model containing checklists for the pharmacist and for the care team has been developed and used at Lund University hospital. Patients' knowledge of their drug treatment is incomplete. To improve this, drug information leaflets containing information on the drug with a possibility to clearly determine the patient goal with the treatment have been developed. Finally, a medication report at discharge has been constructed in order to provide the patient and the general practitioner with information on changes in the patient's drug therapy [18].

After taking part of the model produced in Lund, the department of internal medicine at Landskrona hospital, in the southern Sweden, was interested in introducing clinical pharmacy services as a support to the medical team in order to improve the quality of drug treatment. A condition for introducing the clinical pharmacy services was to scientifically evaluate the model and after receiving financial support the project started in September 2005. In this study we have evaluated if an IMM in the elderly can lead to a more appropriate drug use according to MAI.

Methods

Study design

This is a prospective study and the intervention group was compared with a control group where patients were included at the same wards prior to the intervention period. In the control group, 25 patients were included from mid-November 2005 until mid- January 2006, and 28 patients were included in the intervention group from 1 March 2006 to mid-May 2006. Patients were included continuously and systematically during the study periods.

The evaluation of the ethics committee at Lund University was that no formal approval was necessary.

Size of study population and calculation of power

In a study at a geriatric outpatient clinic (n = 25) in USA with similar interventions, the mean (SD, standard deviation) MAI-score per person was reduced from 11.1 (5.9) to 3.6 (2.8) ($P < 0.0001$) [19]. Student's *t*-test gives that an improvement from 11.1 to 3.6 and with a SD of 5.9; 11 patients per group were needed. Based on this power calculation, the minimum difference in MAI-scores that could be detected was a difference of 7.5. We believed that smaller differences also were valuable for the patients. Therefore by including at least 25 patients in each group we were able to detect differences in MAI-scores from 4.8 and more. As Lam *et al.* presented their results as median and SD we were bound to use *t*-test in the power calculation even though we would have preferred Wilcoxon.

Setting and study population

The study was performed at the department of internal medicine at Landskrona hospital in southern Sweden. The clinic comprises three wards with 61 beds in total.

Patients 65 years or older, admitted to the medical clinic, were eligible for inclusion. The pharmacist gave the patients oral and written information about the project, and at acceptance the patient was asked to give written consent to participate in the study. When it was not possible to communicate with the patient, a next of kin was asked instead. Patients in terminal stage of their disease were excluded for ethical reasons. Because of practical reasons, it was not possible to include all patients. Therefore the selection of patients was done by a specific scheme. For both the control group and the intervention group, inclusion to measure MAI-scores was stopped when, at minimum, the first 25 patients had been included. The pharmacist had no prior knowledge of the patients' medical history at the time of inclusion.

Interventions

During the intervention period the pharmacists took part in the daily work at the three wards and performed interventions during the patients' hospital stay as described below:

- Patient interview.
- Check of symptoms.
- Patient medication review checklist.
- Systematic medication care plan.
- Drug information leaflets.
- Evaluation of the medication report.

The interview was performed systematically at admission and helped identify the correct medication list, problems with compliance, knowledge and attitudes to the drug therapy. As an instrument to detect possible ADR and/or need for new drug therapy, the patients' symptoms were checked at admission. The medication review checklist was used systematically to evaluate the patient's drug treatment and detect drug-related problems (DRPs) (DRPs according to Cipolle, Strand, and Morely [20]), and a systematic medication care plan was created in which DRPs and changes in drug therapy were noted. The care plan was updated continuously and was decided on by the team.

The DRPs identified by the pharmacist were put forward to the care team and discussed. The pharmacist's advice on drug treatment was noted as well as the response from the physician. If the patient started on a new drug treatment during the hospital stay, drug

information leaflets were provided, and the pharmacist took part in informing the patient about the new drug. At discharge the pharmacist evaluated the medication report, written by the physician, according to a specific scheme so that information on all changes in drug therapy together with a correct drug chart was included.

Measures

The MAI-scores were systematically determined by the pharmacists at admission, discharge and 2 weeks after discharge (by contact over the telephone) according to the specific instructions for MAI [11]. First, one of two pharmacists determined MAI-scores for each patient. One of the pharmacists decided on one third of the MAI-classifications, and the other pharmacist was responsible for two-thirds of the classifications. Then both pharmacists went through all MAI-scores together to reach consensus. This method of rating MAI-scores has been used elsewhere [21]. Inappropriate medicines were then grouped into different therapeutic classes according to the Anatomic Therapeutic Chemical Classification System published by World Health Organization [22]. Figure 1 describes how MAI-scores and the number of drugs with at least one inappropriate rating were compared between the groups.

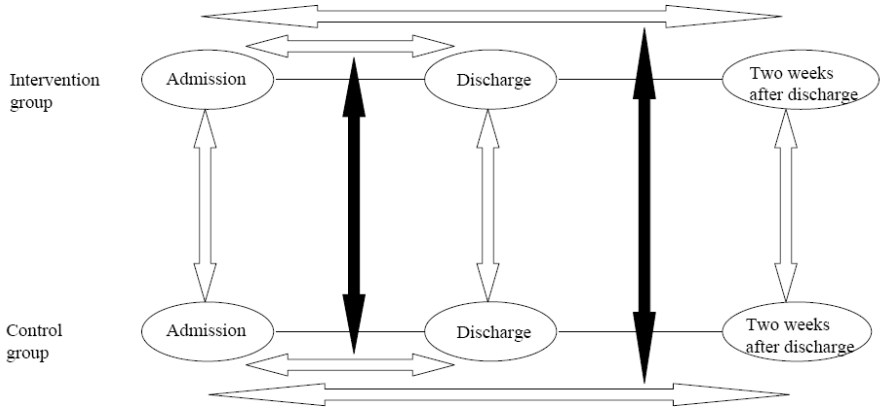

Figure 1 Time of measurement of MAI – descriptive and comparative. MAI-scores and the number of drugs with at least one inappropriate rating were compared at these times. White arrows are representing the comparison of the actual MAI-score and the number of drugs with at least one inappropriate rating between the groups and the black arrows represents the difference within each group compared between the groups. MAI, Medication Appropriateness Index.

Data analyses

Computer software R version 2.5.1 (R Foundation for Statistical Computing, Vienna, Austria) was used for all statistical analyses. When comparing MAI-score per drug at admission, discharge and 2 weeks after discharge, an average MAI-score per drug per patient was used. The Wilcoxon Mann–Whitney Rank Sum Test was used for analyses on MAI-scores. When analysing number of drugs with (and without) inappropriate ratings, the Poisson regression test was used. The R COIN procedure (Asymptotic Linear by-Linear Association Test) was used to compare changes in the number of drugs with at least one inappropriate rating per patient between admission, discharge and 2 weeks after discharge. Data analyses were performed as 'intention-to-treat' analyses, and Last Observation Carried Forward was used for missing observations.

Results

Patients in the control group were slightly older and had more drugs on average than patients in the intervention group, as seen in Table 1. During the hospital stay one patient in the control group and four patients in the intervention group were lost because of death or change of clinic. From discharge to the follow-up, one additional patient per group dropped out.

Table 1 Descriptive data for the control group and the intervention group

Factors	Intervention group (n = *28*)	Control group (n = *25*)
Age, mean (SD)	82 (6)	84 (6)
Sex (female)	61%	64%
Drugs at admission continuous (SD)	7.9 (3.4)	8.3 (4.4)
Drugs at admission on demand (SD)	1.0 (1.2)	1.4 (1.3)
Drugs at discharge continuous (SD)	7.5 (3.1)	8.0 (3.7)
Drugs at discharge on demand (SD)	1.5 (1.5)	1.3 (1.6)

SD, standard deviation

Medication Appropriateness Index – summated scores and number of drugs with at least one inappropriate rating

Medication Appropriateness Index-score per patient

For the intervention group, there was a decrease in the mean (SD) MAI-score per patient from 11.5 (12.4) at admission to 6.36 (10.3) at discharge and 6.79 (9.95), 2 weeks after discharge. Corresponding data for the control group were 18.8 (12.9), 17.5 (15.0) and 18.3 (14.0). Patients in the control group had significantly higher MAI than the intervention group at admission (P = 0.009), at discharge (P = 0.0002) and at 2-week follow-up (P = 0.0004). There were no significant differences in the change in mean MAI-score between the groups during the hospital stay (P = 0.085) or during the period from admission to 2 weeks after discharge (P = 0.087).

Medication Appropriateness Index-score per drug

There was a decrease in MAI-score per drug for the intervention group, from 1.21 (1.04) at admission to 0.67 (0.81) at discharge and 0.72 (0.78) 2 weeks after discharge. Corresponding data for the control group were 1.90 (0.76), 1.66 (1.15) and 1.66 (1.10). Patients in the control group had significantly higher mean MAI per drug per patient (P = 0.002) at admission than patients in the intervention group. At discharge and 2-week follow-up, patients in the intervention group had lower mean MAI per drug per patient, P = 0.0005 and P = 0.0008 respectively. There were no differences in the change in mean MAI-score between the groups during hospital stay (P = 0.335) or from admission to 2 weeks after discharge (P = 0.326).

Number of drugs with at least one inappropriate rating

In addition to MAI-scores per patient and per drug, we were interested in the number of drugs with at least one inappropriate rating. The control group had significantly more drugs with at least one inappropriate rating at admission compared with the intervention group (P = 0.014). A significant difference at discharge was also seen, and the intervention group had fewer drugs with at least one inappropriate rating (P = 0.000003). Two weeks after discharge, the difference remained (P = 0.000006). Figure 2 shows the number of drugs with at lest one inappropriate rating at admission, discharge and 2 weeks after discharge for all patients in the control group and in the intervention group. There was also a difference between the groups in the number of drugs without inappropriate ratings at discharge (P = 0.049) and 2 weeks after discharge (P = 0.031), where the intervention group had more drugs without inappropriate ratings. This difference was not seen at admission. No differences in total number of drugs were seen at any time.

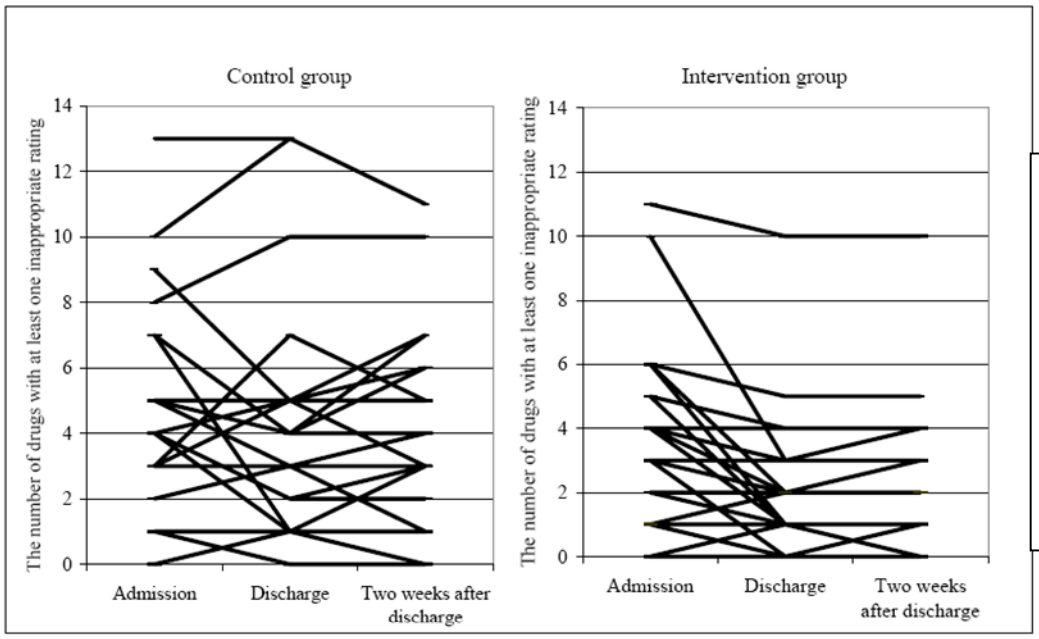

Figure 2 The number of drugs with at least one inappropriate rating at admission, discharge and 2 weeks after discharge shown for each patient in the control group and the intervention group. The number of drugs with at least one inappropriate rating are shown for each patient in both groups (control group $n = 25$, intervention group $n = 28$). Some patients have the same number of drugs with at least one inappropriate rating; therefore the number of lines is not equal to the number of patients in each group.

We used Poisson regression to analyse what affected the number of drugs with at least one inappropriate rating at discharge and found that it was dependent on number of drugs with inappropriate ratings at admission and whether the patient was in the control group or the intervention group. We were also interested in how the number of drugs with at least one inappropriate rating per patient changed from admission to discharge. This was performed using the Asymptotic Linear-by-Linear Association Test. As shown in Table 2 there were significantly more patients in the intervention group with no change or decrease in the number of drugs with inappropriate ratings than in the control group. This was also seen when analysing data like per protocol $P = 0.032$. Changes in the number of drugs without inappropriate ratings and the total number of drugs were not significant. However, when comparing the change in the number of drugs with at least one inappropriate rating in the control group with the change in the intervention group, there was no significant difference between the groups. On individual level there was a spread from increase of four drugs with at least one inappropriate rating to decrease with seven drugs with at lest one inappropriate rating during the hospital stay. Figure 3 illustrates the change in the number of drugs with at least one inappropriate rating and the number of patients for each level.

Table 2 Comparison of the number of patients in each group with increase, no change and decrease in the number of drugs with at least one inappropriate rating

	Intervention group (n = *28*)	Control group (n = *25*)
Increase	2	8
No change	10	7
Decrease	16	10
	$P = 0.049$	

Observations at admission and discharge are compared.

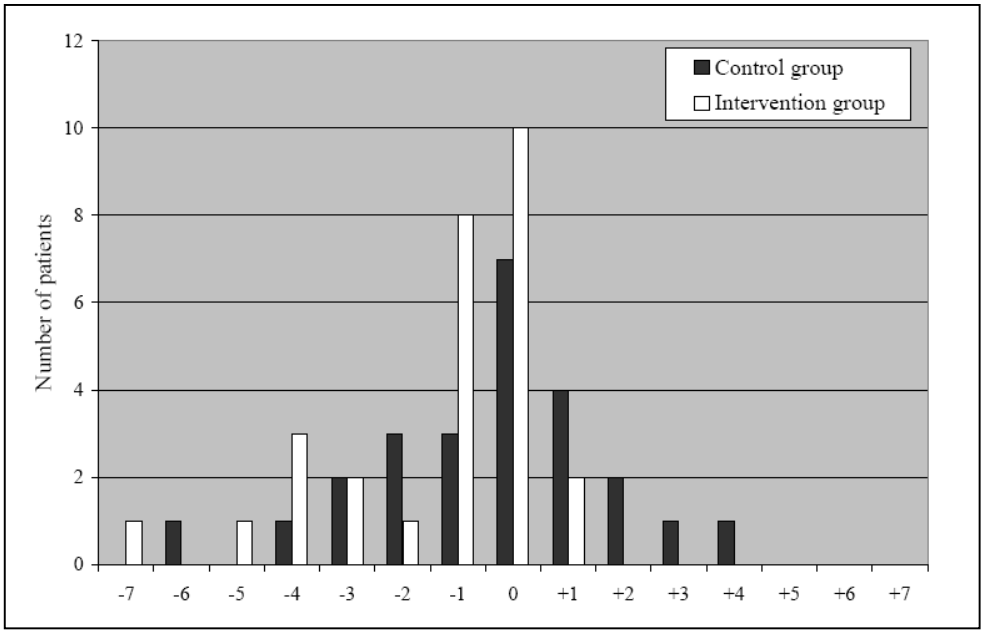

Figure 3 The change in number of drugs with at least one inappropriate rating, admission compared with discharge shown for the control and the intervention group.

Medication Appropriateness Index-dimensions with inappropriate ratings

Some of the MAI-dimensions received more inappropriate ratings than other as shown in Table 3. Our intention was to show results as intention to treat; however, Table 3 shows per protocol data. As drug therapy changes during hospital stay, it is difficult to decide on a value for the drug at admission when the therapy started during hospital stay. We therefore examined drugs at admission and drugs at discharge. The dimensions with most inappropriate ratings were indication, duration and expense. A similar pattern was seen for patients with at least one inappropriate rating per MAI-dimension.

Table 3 Description of drugs with inappropriate ratings for each MAI-dimension

	Intervention group			Control group		
MAI-dimension	Admission (n = *243*) (%)	Discharge (n = *211*) (%)	After 2 w (n = *203*) (%)	Admission (n = *231*) (%)	Discharge (n = *235*) (%)	After 2 w (n = *219*) (%)
Indication	17	10	11	29	24	27
Effectiveness	2	2	2	4	5	5
Dosage	9	1	2	7	8	10
Correct directions	1	0	0	2	0	0
Practical directions	0	0	0	3	2	1
Drug-drug interaction	0	0	0	2	1	1
Drug-disease interaction	9	8	7	9	7	6
Duplication	1	1	0	4	3	3
Duration	20	11	12	29	27	29
Expense	25	15	16	34	31	33
In total	39	23	23	51	44	46

Table 4 shows the percentage of the patients with at least one inappropriate rating for each dimension. The dimensions with most inappropriate ratings were indication, duration and expense for the control group. In the intervention group drug–disease interaction was as frequent in inappropriate ratings as the other three. At admission, 96% of the patients in the control group and 86% of the patients in the intervention group had at least one drug with an inappropriate rating.

Table 4 Description of patients with at least one inappropriate rating for each MAI-dimension

	Intervention group			Control group		
MAI-dimension	Admission n (%)	Discharge n (%)	After 2 w n (%)	Admission n (%)	Discharge n (%)	After 2 w n (%)
Indication	15 (54)	11 (39)	13 (46)	22 (88)	20 (80)	20 (80)
Effectiveness	4 (14)	4 (14)	4 (14)	9 (36)	10 (40)	10 (40)
Dosage	13 (46)	4 (14)	6 (21)	13 (52)	15 (60)	18 (72)
Correct directions	2 (7)	0 (0)	0 (0)	4 (16)	1 (4)	1 (4)
Practical directions	0 (0)	0 (0)	0 (0)	5 (20)	4 (16)	3 (12)
Drug-drug interaction	0 (0)	0 (0)	0 (0)	3 (12)	2 (8)	3 (12)
Drug-disease interaction	16 (57)	15 (54)	13 (46)	13 (52)	12 (48)	9 (36)
Duplication	3 (11)	2 (7)	2 (7)	5 (20)	5 (20)	5 (20)
Duration	18 (64)	13 (46)	15 (54)	22 (88)	21 (84)	21 (84)
Expense	22 (79)	16 (57)	18 (64)	22 (88)	22 (88)	21 (84)
In total	24 (86)	22 (79)	22 (79)	24 (96)	24 (96)	22 (88)

The control group comprises 25 patients and the intervention group 28 patients

Some medication classes were more frequently than others involved inappropriate ratings. To describe the most hazardous medication classes per MAI-dimension, the drugs involved in inappropriate ratings at admission in the control group and in the intervention group are summarized in Table 5. Psycholeptics were involved in inappropriate ratings for several dimensions, and among them it was mostly anxiolytics, hypnotics and sedatives that were used inappropriately.

Table 5 Medication class responsible for most inappropriate ratings per MAI-dimension at admission to hospital

MAI-dimension	Medication class	% of the inappropriate ratings that the medication class was responsible for n (%)
Indication	N05 – Psycholeptics	19/107 (18)
Effectiveness	R05 - Cough and cold preparations	4/14 (29)
Dosage	C03 – Diuretics	11/38 (29)
Correct directions	R03 - Drugs for obstructive airway diseases	4/8 (50)
Practical directions	N05 – Psycholeptics	3/7 (43)
Drug-drug interaction	B01 - Antithrombotic agents, C03 - Diuretics, L02 - Endocrine therapy, N02 -Analgesics, N05 – Psycholeptics	1/5 (20)[a]
Drug-disease interaction	N05 – Psycholeptics	13/43 (30)
Duplication	N05 – Psycholeptics	4/13 (31)
Duration	N05 – Psycholeptics	18/116 (16)
Expense	N05 – Psycholeptics	19/140 (14)

The drugs are grouped in medication class according to the 2nd level (therapeutic subgroup) in the ATC-system (WHO Collaborating Centre for Drug Statistics Methodology, World Health Organ Tech Rep Ser. 2006; (933):1-119, back cover).[a] For drug-drug interactions there was one inappropriate rating for each of the five medication classes noted.

Discussion

The patients in the intervention group significantly improved their MAI-scores and their number of drugs with inappropriate ratings. This was not seen in the control group. We believe that the improvement in the intervention group was due to our intervention based on an integrated medicines management approach with a process and focus for identification, resolution and prevention of DRPs. Other studies have also shown decrease in MAI-scores after interventions based on pharmaceutical care [13,23–25].

The first studies on MAI-scores used summarized scores (MAI-score per patient and MAI-score per drug) to compare the appropriateness in drug treatment. During our study period, other articles were published looking at the number of drugs with at least one inappropriate rating per patient. We found this to be more accurate in describing use of

inappropriate drugs as the correctness in summating ordinal data and then using the summa score as if it is at continuous variable is questionable. Therefore we included the number of drugs with at least one inappropriate rating in our analysis, either a drug is inappropriate or it is not. MAI-dimensions with the most inappropriate ratings were found to be indication, duration and expense (when indication receives an inappropriate rating, duration, and expense also automatically receives inappropriate ratings). This is similar to the results seen in a Danish study [26]. Other studies have shown these dimensions to be correct directions, practical directions and expense [27]. When developing the MAI, indication and effectiveness were the dimensions considered to be most important [12]. We found great room for improvement in drug therapy as most patients received at least one drug with inappropriate ratings (at admission, 96% of the control group and 86% of the intervention group had at least one drug with inappropriate ratings). This was also found elsewhere [9,26,27].

The advantage of MAI is that it combines implicit (judgement based) and explicit (criterion-based) criteria. Many indexes only use explicit criteria (i.e. Beers' criteria [28]) and do not take into account factors for the individual patient. In MAI implicit criteria give a more accurate opinion of the drug's appropriateness in the individual. The quality indicators from the Swedish National Board of Health and Welfare only use explicit criteria [29]. On the other hand, MAI is time consuming, and the raters spend approximately 10 minutes evaluating the appropriateness of each drug [11]. Another disadvantage of MAI is that it does not assess underprescribing, so it must be combined with other tools in order to provide the patient with a complete drug therapy.

High MAI-scores has been shown to relate to hospital admission and unscheduled ambulatory or emergency care visits [30]. An increase in MAI-scores was related to more emergency department visits and hospital readmissions [31]. However, a recent review article showed mixed and contradictory evidence regarding inappropriate prescribing and adverse patient outcomes (mortality, use of health care services, adverse drug events and quality of life) [32]. Therefore it is difficult to know the impact of the decrease in the number of drugs on health outcomes.

This kind of systematic approach on drug therapy resulted in a significantly more appropriate drug use in the elderly. As the elderly use many drugs and are more sensitive to side effects, a more appropriate drug treatment could be of great importance for their well-being.

Limitations of the study

The study is not a randomized study. We could not randomize per patient as the intervention was a systematic team approach. Neither could we have a control ward at the clinic as the staff was not permanent in one ward and also as the funding was for service at all wards at the clinic. Using another department of internal medicine as control was not an alternative because of lack of resources and problems with heterogeneity and limitations in the statistical comparisons because of few clusters. Instead, we used a control group where patients were included prior to the interventions in order to have a group to compare the intervention group with. There have been no changes in organization, staffing or routines during the study period that can explain the positive outcomes from the study.

The intervention group and the control group differed at admission, as the control group had a more inappropriate drug treatment, according to the MAI. This could have led us to underestimate the effect of our interventions as the room for improvement was smaller in the intervention group than in the control group.

Future needs

There is a need for studies on cost–effectiveness and effects on patient's quality of life. The intervention that is described in this study could be more thoroughly evaluated in a qualitative study. There is also a need for studies that compare different kinds of interventions in this field.

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References

1. Lazarou, J., Pomeranz, B. H. & Corey, P. N. (1998) Incidence of adverse drug reactions in hospitalized patients: a meta-analysis of prospective studies. *The Journal of the American Medical Association*, 279 (15), 1200–1205.
2. Einarson, T. R. (1993) Drug-related hospital admissions. *The Annals of Pharmacotherapy*, 27 (7–8), 832–840.
3. Beijer, H. J. & de Blaey, C. J. (2002) Hospitalisations caused by adverse drug reactions (ADR): a meta-analysis of observational studies. *Pharmacy World & Science: PWS*, 24 (2), 46–54.
4. Bergman, U. & Wiholm, B. E. (1981) Drug-related problems causing admission to a medical clinic. *European Journal of Clinical Pharmacology*, 20 (3), 193–200.
5. Mjorndal, T., Boman, M. D., Hagg, S., Backstrom, M.,Wiholm, B. E., Wahlin, A. & Dahlqvist, R. (2002) Adverse drug reactions as a cause for admissions to a department of internal medicine. *Pharmacoepidemiology and Drug Safety*, 11 (1), 65–72.
6. Odar-Cederlöf, I., Oskarsson, P., Öhlén, G., Tesfa, Y., Bergendal, A., Helldén, A. & Bergman, U. (2008) Adverse drug reaction as a cause of admission to hospital. Common drugs are responsible for the vast majority, according to a cross-sectional study (In Swedish: Läkemedelsbiverkan som orsak till inläggning på sjukhus. Vanliga medel står för merparten, visar tvärsnittsstudie.). *Lakartidningen*, 2008 (105), 890–893.
7. Bootman, J. L., Harrison, D. L. & Cox, E. (2089) 1997) The health care cost of drug-related morbidity and mortality in nursing facilities. *Archives of International Medicine*, 157 (18), 96,
8. Schmidt, I. K. & Fastbom, J. (2000) Quality of drug use in Swedish nursing homes. A follow-up study. *Clinical Drug Investigation*, 20 (6), 433–446.
9. Hanlon, J. T., Artz, M. B., Pieper, C. F., Lindblad, C. I., Sloane, R. J., Ruby, C. M. & Schmader, K. E. (2004) Inappropriate medication use among frail elderly inpatients. *The Annals of Pharmacotherapy*, 38 (1), 9–14.
10. Steinman, M. A., Landefeld, C. S., Rosenthal, G. E., Berthenthal, D., Sen, S. & Kaboli, P. J. (2006) Polypharmacy and prescribing quality in older people. *Journal of the American Geriatrics Society*, 54 (10), 1516–1523.
11. Hanlon, J. T., Schmader, K. E., Samsa, G. P., Weinberger, M., Uttech, K. M., Lewis, I. K., Cohen, H. J. & Feussner, J. R. (1992) A method for assessing drug therapy appropriateness. *Journal of Clinical Epidemiology*, 45 (10), 1045–1051.

12. Samsa, G. P., Hanlon, J. T., Schmader, K. E., Weinberger, M., Clipp, E. C., Uttech, K. M., Lewis, I. K., Landsman, P. B. & Cohen, H. J. (1994) A summated score for the Medication Appropriateness Index: development and assessment of clinimetric properties including content validity. *Journal of Clinical Epidemiology*, 47 (8), 891–896.
13. Hanlon, J. T., Weinberger, M., Samsa, G. P., Schmader, K. E., Uttech, K. M., Lewis, I. K., Cowper, P. A., Landsman, P. B., Cohen, H. J. & Feussner, J. R. (1996) A randomized, controlled trial of a clinical pharmacist intervention to improve inappropriate prescribing in elderly outpatients with polypharmacy. *The American Journal of Medicine*, 100 (4), 428–437.
14. Fitzgerald, L. S., Hanlon, J. T., Shelton, P. S., Landsman, P. B., Schmader, K. E., Pulliam, C. C. & Williams, M. E. (1997) Reliability of a modified Medication Appropriateness Index in ambulatory older persons. *The Annals of Pharmacotherapy*, 31 (5), 543–548.
15. Scullin, C., Scott, M. G., Hogg, A. & McElnay, J. C. (2007) An innovative approach to integrated medicines management. *Journal of Evaluation in Clinical Practice*, 13 (5), 781–788.
16. Horne, R. & Weinman, J. (1999) Patients' beliefs about prescribed medicines and their role in adherence to treatment in chronic physical illness. *Journal of Psychosomatic Research*, 47 (6), 555–567.
17. Morisky, D. E., Green, L.W. & Levine, D. M. (1986) Concurrent and predictive validity of a self-reported measure of medication adherence. *Medical Care*, 24 (1), 67–74.
18. Midlov, P., Holmdahl, L., Eriksson, T., Bergkvist, A., Ljungberg, B., Widner, H., Nerbrand, C. & Hoglund, P. (2008) Medication report reduces number of medication errors when elderly patients are discharged from hospital. *Pharmacy World and Science: PWS*, 30 (1), 92–98.
19. Lam, S. & Ruby, C. M. (2005) Impact of an interdisciplinary team on drug therapy outcomes in a geriatric clinic. *American Journal of Health-System Pharmacy*, 62 (6), 626–629.
20. Cipolle, R., Strand, L. M. &Morley, P. C. (1998) Pharmaceutical Care Practice. New York: McGraw, Hill.
21. Spinewine, A., Dumont, C.,Mallet, L. & Swine, C. (2006) Medication Appropriateness Index: reliability and recommendations for future use. *Journal of the American Geriatrics Society*, 54 (4), 720–722.
22. (2005) ATC Classification Index with DDDs 2006. Oslo: WHO Collaborating Centre for Drug Statistics Methodology.
23. Schmader, K. E., Hanlon, J. T., Pieper, C. F., *et al*. (2004) Effects of geriatric evaluation and management on adverse drug reactions and suboptimal prescribing in the frail elderly. *The American Journal of Medicine*, 116 (6), 394–401.
24. Spinewine, A., Swine, C., Dhillon, S., Lambert, P., Nachega, J. B., Wilmotte, L. & Tulkens, P. M. (2007) Effect of a collaborative approach on the quality of prescribing for geriatric inpatients: a randomized, controlled trial. *Journal of the American Geriatrics Society*, 55 (5), 658–665.
25. Crotty, M., Halbert, J., Rowett, D., Giles, L., Birks, R.,Williams, H. & Whitehead, C. (2004) An outreach geriatric medication advisory service in residential aged care: a randomised controlled trial of case conferencing. *Age and Ageing*, 33 (6), 612–617.
26. Bregnhoj, L., Thirstrup, S., Kristensen, M. B., Bjerrum, L. & Sonne, J. (2007) Prevalence of inappropriate prescribing in primary care. *Pharmacy World and Science: PWS*, 29 (3), 109–115.
27. Schmader, K., Hanlon, J. T.,Weinberger, M., Landsman, P. B., Samsa, G. P., Lewis, I., Uttech, K., Cohen, H. J. & Feussner, J. R. (1994) Appropriateness of medication prescribing in ambulatory elderly patients. *Journal of the American Geriatrics Society*, 42 (12), 1241–1247.
28. Beers, M. H. (1997) Explicit criteria for determining potentially inappropriate medication use by the elderly. An update. *Archives of International Medicine*, 157 (14), 1531–1536.

29. Fastbom, J., Bernsten, C., Schmidt, I., *et al*. (2003) *Indicators for Evaluation of the Quality in Drug Use in the Elderly – Suggestions by The National Board of Health and Welfare (In Swedish: Indikatorer för utvärdering av kvaliteten i äldres läkemedelsterapi – Socialstyrelsens förslag).* Stockholm: The National Board of Health and Welfare.
30. Schmader, K. E., Hanlon, J. T., Landsman, P. B., Samsa, G. P., Lewis, I. K. & Weinberger, M. (1997) Inappropriate prescribing and health outcomes in elderly veteran outpatients. *The Annals of Pharmacotherapy*, 31 (5), 529–533.
31. Crotty, M., Rowett, D., Spurling, L., Giles, L. C. & Phillips, P. A. (2004) Does the addition of a pharmacist transition coordinator improve evidence-based medication management and health outcomes in older adults moving from the hospital to a long-term care facility? Results of a randomized, controlled trial. *The American Journal of Geriatric Pharmacotherapy*, 2 (4), 257–264.
32. Spinewine, A., Schmader, K. E., Barber, N., Hughes, C., Lapane, K. L., Swine, C. & Hanlon, J. T. (2007) Appropriate prescribing in elderly people: how well can it be measured and optimised? *The Lancet*, 370 (9582), 173–184.