Improving Appropriate Prescribing For Geriatric Patients Using a Clinical Decision Support System

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ABSTRACT

Purpose: *Polypharmacy is a known risk factor for potentially inappropriate prescribing. Recently there is an increasing interest in clinical decision support systems (CDSS) to improve prescribing. The objective of this study was to evaluate the impact of a CDSS, with the START-STOPP criteria as main content in the setting of a geriatric ward. Endpoints were 1) appropriateness of prescribing and 2) acceptance rate of recommendations.*

Methods: *This prospective study comparing the use of a CDSS with usual care involved patients admitted to geriatric wards in two teaching hospitals in the Netherlands. Patients were included from January to May 2017. The medications of 64 patients in the first six weeks was assessed according to the current standard, whereas the medications of 61 patients in the second six weeks were also assessed by using a CDSS. Medication appropriateness was assessed with the Medication Appropriateness Index (MAI).*

Results: *The medications of 125 patients (median age 83 years) were reviewed. In both the usual care group and the intervention group MAI scores decreased significantly from admission to discharge (within group analyses, $p<0.001$). This effect was significantly larger in the intervention group ($p<0.05$). MAI scores at discharge in the usual care group and the intervention group were respectively 9.95±6.70 and 7.26±5.07. The CDSS generated 193 recommendations, of which 71 concerned START criteria, 45 STOPP criteria, and 77 potential interactions. Overall, 31.6% of the recommendations were accepted.*

Conclusion: *This study shows that a CDSS to improve prescribing has additional value in the setting of a geriatric ward. Almost one third of the software-generated recommendations were interpreted as clinically relevant and accepted, on average one per patient.*

Keywords: clinical decision support system, polypharmacy, elderly, geriatric

INTRODUCTION

Polypharmacy, the use of five medications or more, is a growing problem among older patients[1], especially because it is a risk factor for potentially inappropriate prescribing[1,2]. Whereas polypharmacy is associated with multimorbidity the purpose of the medications is to improve the patients' health. However, interactions and negative health outcomes can occur, such as hospital admissions and adverse drug events[1,3,4,5]. Therefore, more awareness is needed for potentially inappropriate prescribing.

Several strategies have demonstrated effectiveness in reducing the potentially negative outcomes of polypharmacy[6]. Two of the most widely used strategies include using screening tools such as the Screening Tool of Older Persons' Prescriptions (STOPP) and Screening Tool to Alert to Right Treatment (START)[7]. The STOPP criteria consists of a list of potentially inappropriate medications, which are associated with adverse drug events. The START criteria are used to assess potential prescribing omissions. Recent randomized controlled trials have shown the efficacy of the STOPP/START criteria for improving medication appropriateness in older hospitalized patients[8] and for reducing the incidence of adverse drug reactions and medication costs in acutely ill older adults[9]. Another frequently described intervention is the use of geriatric assessments and systematic medication reviews by pharmacists[10-12]. Medication reviews improve prescribing and shorten the length of hospital stay, but are time consuming and costly[11,12]. Despite all these strategies, the negative effects of polypharmacy remain.

In recent years there is growing interest in the use of clinical decision support systems (CDSS) to assist prescribing[13,14]. In Ireland, a randomized controlled trial showed that a structured medication review supported by the use of a CDSS significantly reduced the incidence of adverse drug reactions in older patients with multimorbidity compared to standard pharmaceutical care and improved the appropriateness of prescribed medications[15,16]. However, these systems have not been applied to the medications of patients admitted to a geriatric ward, where specialists with a lot of knowledge of

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polypharmacy work. Therefore, it is unclear what the potential beneficial effect from a CDSS is in the setting of a geriatric ward.

The aim of this study was to determine whether computer systems, in this case a CDSS that combines the START/STOPP criteria and the clinical interactions and contraindications mentioned in a Dutch drug database[17], improve the appropriateness of prescribing compared with the usual care for patients on a geriatric ward. This database comprises all medications that are available in the Netherlands. All their features, for example, their interactions, contraindications and possible doses are registered in this database.

METHODS

Study design

Patient selection and data collection procedure

This study was designed as a 12-week prospective study, comparing the use of a CDSS with usual care (Figure 1). The research population consisted of patients admitted to the geriatric wards of two teaching hospitals in the Netherlands, the Medical Center Slotervaart hospital in Amsterdam and the Jeroen Bosch Hospital in Den Bosch. The patients were included from mid-January 2017 to May 2017. During 12 weeks, the first six newly admitted patients of the week were included in both hospitals if they met the inclusion criteria. Inclusion criteria were age 65 years or older and polypharmacy at admission. We defined polypharmacy as the use of five medications or more. Exclusion criteria were a hospital stay of less than 48 hours, a life expectancy of less than 3 months, and geriatric trauma patients. Patients included in the study were not included a second time if they were readmitted during the study period.

Usual care

During the first 6 weeks, patients were included in the usual care group. Usual care consisted of a comprehensive geriatric assessment. Medication was reviewed by at least one geriatrician during the hospital stay. Patients and their medication were discussed during the grand rounds, which was attended by at least two geriatricians and a pharmacist or clinical pharmacologist. When the decision is made to change medications, the responsible physician makes sure these alterations are made during the stay of the patient.

The Clinical Decision Support System (CDSS)

In weeks 8 to 13 patients were included in the intervention group. There was a 1-week interval between patient inclusion, to ensure that the physicians were not influenced by CDSS recommendations during the inclusion of the usual care group and to avoid a learning effect. The intervention group received usual care as described above, plus the patient's physician was given advice generated by the CDSS. A stand-alone web-based CDSS was developed to support healthcare professionals when carrying out a medication review. It is based on STOPP and START (version 2, Dutch version) criteria combined with information from a Dutch drug database about licensed medicines, including information about pharmacovigilance for each product[7,17-19].

The CDSS made use of the medical history, medication list, age, blood pressure, and estimated glomerular filtration rate (eGFR) recorded in the patient's digital medical record. Medical conditions were classified according to the World Health Organization (WHO) International Classification of Diseases, version 10 (ICD-10). Drugs were classified according to the WHO Anatomical Therapeutic Chemical (ATC) classification system[20,21]. These data were entered into the CDSS by a junior researcher, a final phase medical resident.

All the recommendations generated by the CDSS were given verbally to the physicians during the grand rounds, by the junior researcher. The physicians, together with a pharmacist or clinical pharmacologist, decided whether the recommendations were relevant for the patient or not. Recommendations about vaccinations were ignored, since in the Netherlands vaccinations are part of nonhospital treatment programs.

The CDSS separately

In addition, the effect of the CDSS alone was investigated for all patients, including the usual care group, recommendations were created. The recommendations for the usual care groups were not shared with the physicians and thus did not affect patient care. New hypothetical medications lists were made, after accepting all the recommendations created by the CDSS. In case of an alarming recommendation with effect on the patient's health, the physician of the patient would be informed. If the CDSS recommended stopping one of two medicines, the first option was stopped. The newly created medication lists were then used to calculate the MAI scores for the sole CDSS group.

Outcomes

The primary outcome was the appropriateness of prescribing, as assessed with the Medication Appropriateness Index (MAI), a validated tool to assess polypharmacy[22,23]. The MAI consists of 10 questions you have to answer for each medicine. Each medicine is being scored, the higher the score the less appropriate is the prescription. The definitive MAI score is obtained by summing up all the scores of individual medications of one patient. The medication lists were imported into a document without patient information. Secondary outcomes were the rate of acceptance of recommendations generated by the CDSS and the differences in scores for individual MAI items.

Data collection

Data were collected from the medical records of the included patients by the junior researcher. At baseline the following data were collected: medical history, Charlson comorbidity index, medication used, reason of admission, age, sex, living situation (independent, nursing home), medical history, number of medicines, cognitive function (diagnosis in medical history), fall

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risk (one or more falls during the last 6 months), functional status/activities of daily living dependence, blood pressure, pulse, basic laboratory findings (international normalized ratio (INR), renal function) and possible side effects if mentioned in the medical records. The medications used by most patients before hospital admission were independently confirmed by a pharmacist or by the physician on the ward. Discharge data concerned actual medication, number of medicines, blood pressure, pulse, and laboratory findings (INR, renal function).

The medication lists at admission and at discharge were used to calculate the MAI scores. Two experienced geriatricians calculated the MAI scores separately. In case of inter-rater differences, there was discussion until agreement. Inter-rater calculations were not made. The patients were blinded and only the medical history, age and kidney function were shown. The summated MAI scores were registered and used for statistical analyses.

Ethical considerations

The Medical Ethics Committee of the Medical Center Slotervaart Amsterdam did not consider the study to fulfill the criteria of the Dutch Law on Medical Research (WMO), which means that informed consent was not needed. The study was registered under number P1705. The Dutch Society of Medical Education Ethics Review Board approved the conduct of the study. (NERB dossier number 996).

Statistics and power calculation

The baseline characteristics of the study population were analyzed with descriptive statistics, using means and standard deviations where appropriate. To compare differences in baseline characteristics between the usual care and intervention groups, as well as the two hospitals, an independent, two-sided t-test was used for the continuous, normally distributed traits. A chi-square test was used for the categorical variables. For all tests statistical significance was assumed at $p<0.05$.

A repeated measures ANOVA was used to analyze the summed MAI scores of the usual care group versus the intervention group. Effect sizes were calculated, using a partial eta squared. The values $\eta^2 = >0.26$ were considered as a large, $\eta^2 = >0.13$ as a medium, and $\eta^2 = >0.02$ as a small effect[24].

The differences between individual MAI items at admission and at discharge were assessed using a paired t-test. Also, here a $p<0.05$ was considered as statistically significant. Statistical analyses were performed with the statistical package SPPS version 24.0 (IBM, Armonk, New York, United States).

Power calculation

The power calculation was based on a previous study by O'Sullivan et al showing a reduction in MAI score from 15 (IQR 7-21) to 12 (IQR 6-18)[16]. With a double sided, $\alpha=0.05$, and $\beta=0.20$, it was calculated that at least 24 cases would be needed per group in order to compare the two groups.

RESULTS

Inclusion

Figure 2 shows the patient selection. Of 224 patients assessed, 130 met the inclusion criteria. Most patients were excluded because of a life expectancy of less than 3 months. Five patients who were initially included died unexpectedly or had a changed life expectancy and were discharged with palliative care. Thus, the data of 125 patients were analyzed: 64 patients (51.2%) in the usual care group and 61 (48.8%) in the intervention group (figure 2); 57 patients (45.6%) were admitted to the Medical Center Slotervaart Hospital and 68 patients (54.4%) to the Jeroen Bosch Hospital.

Baseline characteristics

Table 1 shows the baseline characteristics of the usual care and the intervention groups. There were no significant differences between the two groups. The baseline characteristics of patients admitted to the two hospitals differed in the proportion of men and women ($p=0.049$) and also in the number of medicines at admission ($p=0.025$). However, these characteristics were equally divided between the usual care and intervention groups. The two populations had comparable MAI and Charlson Comorbidity Index (CCI) scores.

Main results: effect of the intervention

Figure 3 shows the main results. The MAI scores were significantly different in the usual care group and the intervention group($p=0.046$ $F(1, 123)=4.072$). At admission, the MAI score (mean ± SD) of the usual care group was 13.98±9.29 and that of the intervention group was 14.56±11.39; at discharge, these scores were 9.95±6.70 and 7.26±5.07, respectively. While the MAI score decreased significantly in both groups (both $p<0.001$), the decrease was greater in the intervention group ($p=0.046$).

Calculation of the effect sizes revealed a large effect of usual care ($\eta^2=0.285$) and a smaller additional effect of the intervention ($\eta^2=0.032$). Thus, usual care contributed substantially to the decrease in MAI scores, with a smaller additional effect of the intervention.

The effect of accepting all the recommendations from the CDSS

Figure 3 shows the comparison of accepting all the computer recommendations without physician interpretation or consideration of clinical factors versus the usual care or intervention care. The MAI score decreased from 13.98±9.29 to 12.39±7.56 ($p=0.001$). The usual care group had a decline of an additional 2.44 points, this is significantly more than with the CDSS alone ($p<0.001$). The use of the CDSS alone has less effect on appropriate prescribing than usual care.

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Acceptance rate

The CDSS generated 193 recommendations, of which 71 involved START criteria, 45 STOPP criteria, and 77 interactions. Overall, 61 recommendations (31.6%) were considered clinically relevant and accepted, which was an average of one accepted advice per patient. The most-often accepted recommendations concerned interactions (n=39). This could mean that one of the interacting medicines was stopped or monitored more appropriately, for example in case of anticoagulants.

Of the accepted START criteria (n=10), 4 concerned starting an ACE inhibitor and 5 starting vitamin D or calcium carbonate. The STOPP criterion most frequently accepted was stopping ferrous fumarate.

Different MAI criteria

The scores of most MAI criteria were significantly better at discharge, with the exception of the practicality of advice. That was evaluated by assessing if a medication was prescribed in a user-friendly way, for example by dosing once daily or in a single tablet regimen. Alternative medications were not considered at that moment. Although it seemed as if there were more impractical medications at discharge than at admission, this difference was not statistically significant.

DISCUSSION

We found that a CDSS can be valuable on a geriatric ward to raise awareness for potentially inappropriate prescribing. We also found that the existing procedure for reviewing medications was effective. Usual care had the largest effect on appropriate prescribing, with a smaller additional effect of the CDSS. The use of a CDSS alone had a minor, not clinically relevant, effect on MAI scores, less than achieved with usual care. It demonstrates its role as a support system for clinicians and cannot replace physician competency in prescribing.

O'Sullivan et al. found a CDSS to be an effective tool in improving appropriate prescribing,[15,16]. with MAI scores decreasing from 15 (IQR: 7-21) at admission to 12 (IQR:6-18) at follow-up[16]. We found that MAI scores decreased by 4.03 points with usual care alone, with an additional decrease of 2.69 points when the CDSS was used alongside usual care. The larger decrease in MAI scores found in our study might be due to differences in study population. We included patients on geriatric wards whereas O'Sullivan et al included patients on different wards, but excluded patients on intensive care, psychiatry, and geriatric wards. Even though they included patients aged 65 years and older, they did not focus on geriatric patients specifically. And because polypharmacy is common among geriatric patients, they are more likely to have potentially inappropriate prescriptions. Another explanation could be the fact that in our study the CDSS-generated recommendations were assessed for clinical relevance by geriatricians and pharmacists, whereas in the study of O'Sullivan et al this was done by the attending medical team, which probably had less pharmaceutical experience. Lastly, in our study the CDSS recommendations were verbally during the grand rounds, whereas in the study of O'Sullivan et al recommendations were communicated by the research pharmacist in writing, which might not have been read.

There are also patient factors that can have effect on the MAI scores. An example is when a patient is admitted with an acute kidney insufficiency. Some medications might not have the right dose at that moment. This might cause a bigger difference in MAI score before and after hospital admission. However, the CDSS might help to determine what medications can cause harm at that moment.

Implications

The results of this study could have clinical implications. Given the negative healthcare effects of polypharmacy, it is important to find the best strategies to improve prescribing. Our study illustrated that the usual care provided by geriatricians and pharmacists significantly improved appropriate prescribing. We also showed that the use of the CDSS, as a supportive tool, further improved appropriate prescribing. A junior researcher entered information into the CDSS, which took 10-15 minutes per patient, because ATC- and ICD-10 codes were connected manually. This was rather time consuming. However a prototype specifically developed for the study was used. Clearly the CDSS would need an update for practical use in a hospital or to be implemented in the prescribing system and longer use of a CDSS improves time efficiency [26].

In our study the effect of the CDSS was modest in the wards, which is also explained by the strong focus on rational prescribing in the institutions in which the study was conducted. When used by in experienced physicians, a CDSS could also cause harmful decisions.

Strengths and limitations

A major limitation is the way recommendations were reported, which was verbally. By verbally reporting the recommendations, dialogue and discussions are created. Many of the recommendations are also flagged by our electronic prescribing system. However, these alerts are often ignored because prescribers tend to stop reading the alerts and just quickly scroll through them[25]. When such alerts are ignored, a major interaction can be missed. The most-often accepted recommendations in our study concerned interactions. Owing to the relatively small number of included patients, we did not make a list of the most prevalent interactions, START and STOPP criteria. This might explain why they were accepted more often. For future research it would be valuable to test the effect of verbally communicating recommendations to an electronically created advice.

The MAI itself also has limitations. While it is a very valuable tool to evaluate polypharmacy and especially possible inappropriate medications, however it does not cover potential

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prescribing omissions. Calculating the MAI score can be time consuming, because ten questions have to be answered about all medications. Prior to that, the physician has to collect the complete and correct medical history of a patient and the current medications. It requires knowledge about interactions, costs and dosages of medications. Furthermore, the score does not help in modifying medications and does not provide alternative medicines[23]. The exact relation between a lower MAI score and patient outcomes is still unclear and has to be studied.

This study was the first to examine the application of a CDSS in a hospital setting and involving older patients on polypharmacy. Some study limitations should be considered when interpreting findings. Although the MAI score decreased substantially, the clinical relevance of this decrease is not known. This should be investigated in later studies. Even though the MAI score decreased overall, it increased in 22 patients (17.6%) – in 16 patients (25%) in the usual care group and in 8 patients (13.1%) in the intervention group. The MAI score increased by 1–11 points in the usual care group and by 1–2 points in the intervention group. Even though our research population was large enough, it was still limited. This makes it hard to perform statistical analyses and draw conclusions on subgroups.

Conclusion

We found that a CDSS can increase the attention for potentially impropriate prescribing on a geriatric ward, during a grand round, when recommendations are presented verbally. Almost one third of the CDSS-generated recommendations were considered clinically relevant and implemented, on average one accepted advice per patient. This effect was small, possibly because physicians working on geriatric wards already have a good knowledge of appropriate prescribing and their close cooperation with the pharmacists/pharmacologists. Whether a CDSS would have a greater effect when used by inexperienced prescribers or on wards where polypharmacy is less common remains to be studied.

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Analysis and interpretation of data: van den Hanenberg, Poetsema, Keijsers, Tichelaar, van Agtmael
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Consent to participate and ethics approval: This study falls outside the scope of the Dutch Law on Medical Research (WMO), as declared by the ethical review board

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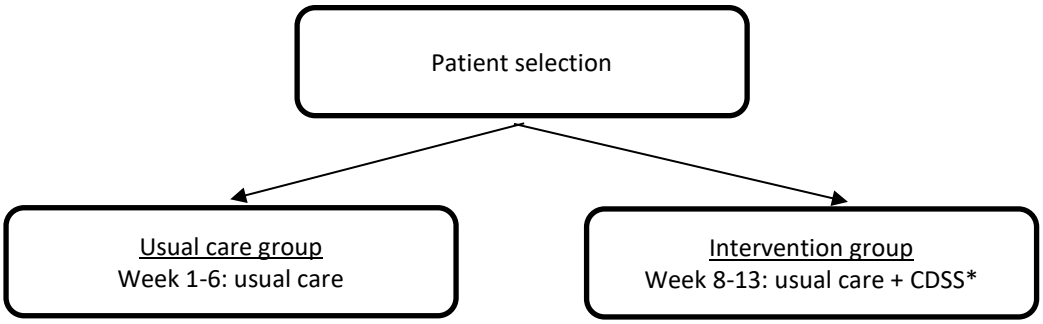
Figure 1. Study design



*CDSS: clinical decision support system result incorporated bij experts

Figure 2. Flowchart patient selection

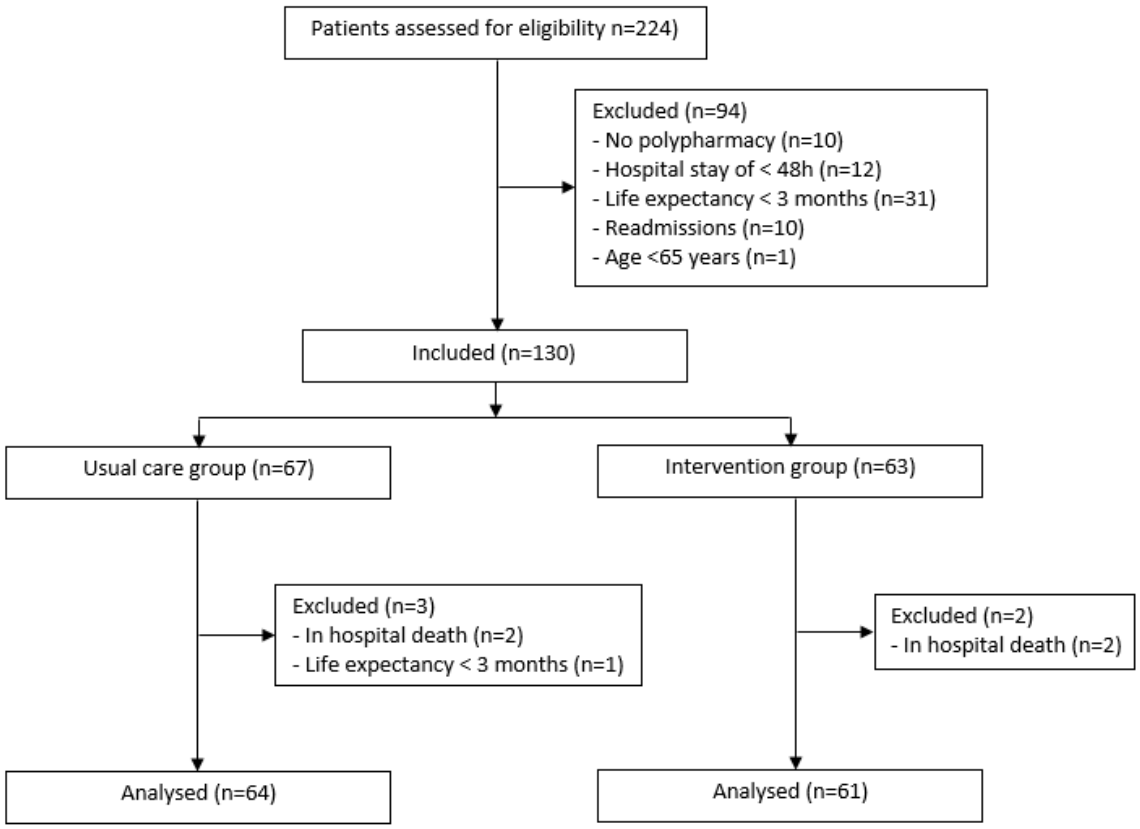
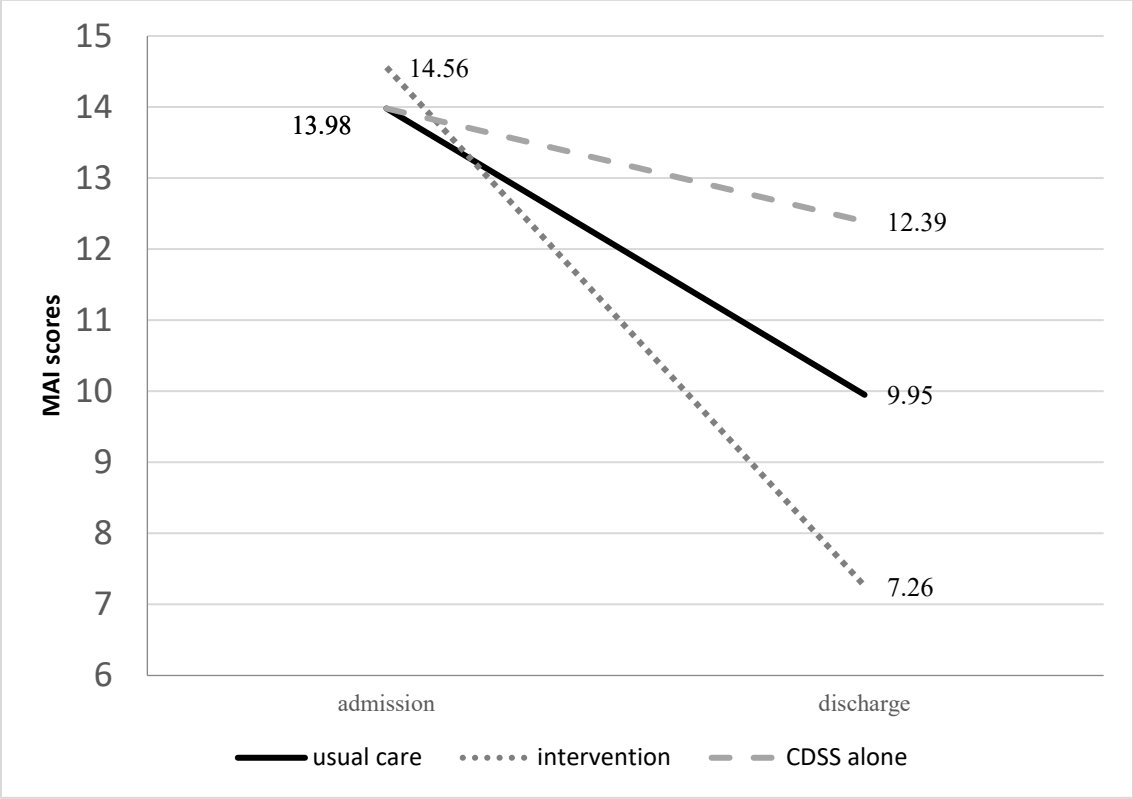


Figure 3. Differences in Medication Appropiate Index (MAI)



MAI scores between the usual care group, intervention group and the CDSS alone group at admission and discharge. *A lower score is a better outcome.*

Table 1. Baseline characteristics

	Usual care group (n=64)	Intervention group (n=61)	p-value
Age Mean ± SD, years	83.0 ± 6.9	83.6 ± 7.0	0.591
Gender: (%)			
- Female	37 (58)	39 (64)	0.483
- Male	27 (42)	22 (36)	
Charlson comorbidity index Mean ± SD	2.50 ± 1.47	2.56 ± 1.73	0.842
Cognition: [n (%)]			
- No cognitive problems	14 (22)	22 (36)	0.243
- Mild cognitive impairment	15 (23)	17 (28)	
- Dementia	28 (44)	17 (28)	
- Other etiology	4 (6)	2 (3)	
- Unknown	2 (3)	3 (5)	
Way of living [n (%)]			
- Alone	32 (50)	40 (66)	0.187
- With partner/family	22 (34)	13 (21)	
- Nursing home	10 (16)	8 (13)	
ADL[1] help [n (%)]			
- Yes	49 (77)	41 (67)	0.187
- No	14 (22)	20 (33)	
Fall risk [n (%)]			
- Yes	37 (58)	36 (59)	0.974
- No	26 (41)	25 (41)	
Side effects [n (%)]			
- Yes	17 (27)	20 (33)	0.420
- No	47 (73)	41 (67)	
Number of medicines ± SD	9.97 ± 3.28	9.62 ± 4.09	0.602
Renal function [n (%)]			
- eGFR >60 ml/min/1,73m^2	28 (44)	26 (43)	0.078
- eGFR 30-59 ml/min/1,73m^2	24 (38)	31 (51)	
- eGFR <29 ml/min/1,73m^2	12 (19)	4 (7)	
Hypertension [n (%)]			
- no hypertension (<140/90)	35 (55)	34 (56)	0.099
- 140-160/90	11 (17)	18 (30)	
- hypertension (>160/90)	18 (28)	9 (15)	
MAI[2] score at admission Mean ± SD	13.98 ± 9.29	14.56 ± 11.39	0.758

[1] = activities of daily life, [2]= Medication Appropriateness Index

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