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RESEARCH ARTICLE

The efficacy of a medication review programme conducted in an emergency department

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Abstract

Background Older age and inappropriate prescribing is related to a greater rate of emergency department visits and hospitalisations. *Objective* To assess the efficacy of an interprofessional collaboration programme in which a review of the medication of older patients seen in the emergency observation unit was carried out. *Setting* Emergency departments at four Spanish hospitals. *Method* Randomised, controlled study. Patients over 65 years of age presenting to the emergency department were randomised to a control or an intervention group. In the intervention group, a pharmacist reviewed the patients' chronic medication and identified any potentially inappropriate prescriptions based on the STOPP/START criteria. Each case was discussed with the emergency specialist and a recommendation to modify the treatment was sent to the general practitioner. *Main outcome measure* Rate of emergency visits and hospital admissions. *Results* The adjusted rate ratio of emergency visits and hospital admissions was 0.808 (95% CI 0.617 to 1.059) at 3 months, 0.888 (95% CI 0.696 to 1.134) at 6 months and 0.954 (95% CI 0.772 to 1.179) at 12 months. There was a statistically significant reduction at 3 months in two of the hospitals that participated in the study [adjusted rate ratio at 3 months was 0.452 (95% CI 0.222 to 0.923) in hospital 3 and 0.567 (95% CI 0.328 to 0.983) in hospital 4]. *Conclusion* Overall, the intervention did not reduce the number of emergency visits and hospital admissions. However, a significant effect was observed in centres were a high acceptance rate of treatment recommendations was achieved.

Keywords Clinical pharmacy · Emergency department · Medication review · Potentially inappropriate prescriptions · Primary care · Spain · STOPP/START criteria

Impacts on practice

- Medication review programmes conducted in emergency departments, in order to reduce emergency visits and hospitalization, require further investigation.
- Medication review programmes conducted in emergency departments may be beneficial when a good coordination between hospital and primary care is achieved and treatment recommendations to optimise drug therapy made in the emergency department are accepted by the general practitioner.

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Introduction

The aging of the population in recent years has led to an increase in the number of patients with chronic diseases, drug use and drug-related adverse events. Several studies have shown that age is related to a greater risk of adverse drug events (ADEs) and drug-related emergency department (ED) visits and hospitalisations [1–3].

In addition, preventability of ADEs has also been found to be greater in older patients. Older adults frequently receive potentially inappropriate prescriptions (PIPs), which are defined as prescriptions of drugs whose potential risks outweigh their potential benefits. Several authors have studied their prevalence in different healthcare settings but very disparate results have been obtained (from 20 to 79%) [1, 4–7].

One of the most commonly used strategies to reduce PIPs is the implementation of medication review (MR) programmes. MR is a critical and structured assessment of a patient's drug therapy with the purpose of optimising its effectiveness and safety [8, 9]. Different types of programmes have been defined according to their complexity and the most comprehensive ones have been shown to reduce the number of hospitalisations [9].

MR programmes can be performed in different healthcare settings. One of the settings in which they have been studied to a lesser extent is the ED, despite the fact that there are several arguments in favour of this. First, ADEs account for a high number of emergency visits [10–14] and therefore, taking a good medication history is essential to assess the possible iatrogenic origin of the acute episodes of patients presenting to the ED. If an ADE is identified, then chronic medication must be modified to prevent future emergency visits. Second, medication reconciliation is necessary in the ED to prevent unintentional medication changes during transitions of care and to ensure adequate continuity in healthcare. The first step for medication reconciliation is to perform a good medication history, which is also the first step for MR. This process is complex and time-consuming and can be optimised if medication reconciliation and MR are done in the same setting at the same time [15]. Finally, EDs have a wide experience in multidisciplinary management of patients and the inclusion of pharmacists in ED teams has been acknowledged and is considered necessary by different health professionals and scientific associations, who assign them a key role in the management of chronic medication [16–19].

The lack of an ongoing and effective communication between healthcare settings is one of the obstacles encountered for the performance of MR programmes, namely between hospital EDs and primary care services.

Aim of the study

The objective of this study was to assess the influence on the number of all-cause emergency visits and hospital admissions (EVHA) of an interprofessional collaboration programme between ED specialists, hospital pharmacists and general practitioners (GPs), through which a review of the medication of older patients with chronic diseases seen in the emergency observation unit was carried out.

Ethics approval

All the procedures performed in the study were in accordance with the ethical standards of the institution and the national research committee and with the 1964 Helsinki declaration and its later amendments. Thus, according to national guidelines, the study was submitted to the Spanish Medicines Agency that classified the project as a Clinical Study that required the approval of the Clinical Research Ethics Committee of the coordinating site (resolution 2/6/2014). The study was approved with number code EPA24/2013.

An informed consent was obtained from all individual participants included in the study.

Method

This was a multicentre, randomised, controlled study in patients over 65 years of age presenting to the ED of the participating sites and seen in the observation unit. Patients had to have been taking at least one outpatient drug for a chronic disease defined as a condition that had lasted more than 6 months. The design of the study and exclusion criteria have been published previously [20].

The period of inclusion was 9 months (October 2014–June 2015). Patients were followed-up for 12 months.

The intervention consisted of the implementation of an interprofessional collaboration programme between hospital pharmacists, emergency specialists and GPs. The pharmacists reviewed the medications patients were taking prior to the emergency visit and assessed their appropriateness based on the STOPP/START criteria, version 2 [21]. Data collected are shown in Fig. 1. When PIPs were identified according to these criteria, the pharmacist discussed these patients' cases with the study emergency specialist. The emergency specialists confirmed that the PIPs were correctly identified based on the patients' clinical data. Then, the pharmacists and emergency specialists agreed upon the recommendation to be made to the GPs to correct the PIPs.

Fig. 1 Data chart collection

Nº	GROUP (control/intervention)	GENDER	ORIGIN(home/nursing home)
HOSPITATALISED (yes/no)		DISCHARGED DATE	

INCLUSION CRITERIA: Aged < 65 y (yes/no) 1 o more outpatient drug (yes/no)

EXCLUSION CRITERIA (yes/no)

Patients seen by the psychiatry unit of the emergency department.
Patients followed by the palliative care department.
Situations preventing communication.
Lack of written source documents on the patient's chronic treatment, unless the treatment received by the patient can be physically verified.
Patients with chronic diseases followed at a private (not publicly funded) healthcare centre.

COMORBIDITIES (yes/no)	CLINICAL DATA (at admission)
Diabetes mellitus	Blood preassure
Liver disease	Heart rate
Malignancy (leukemia, lymphoma, solid tumor with metástasis)	Creatinine clearance
AIDS	LVEF in patient with COPD
Congestive heart failure	pO 2
Chronic kidney disease	Sa O2
Myocardial infarction	Uric acid
COPD	Na
Peripheral vascular disease	K
Cerebrovascular accident or transiet isquemic disease	Ca
Dementia	
Hemiplegia	
Connective tissue disease	
Peptic ulcer disease	
Other medical/social conditions:	
Housebound	
Experiencing falls	
Anxiety	
Major depression	
Urinary incontinence	
Chronic constipation	
Restless Legs Syndrome	
Pain (moderate/severe)	
Symptomatic orthostatic hypotension	

CHRONIC MEDICATION

Drug	DOSAGE	PIP (yes/no)	STOPP/START CRITERIA	OTHER DRP

THERAPEUTIC RECOMMENDATION
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……
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……

Prior to study initiation, each participating site established its own communication protocol with the primary care facilities, This protocol was approved by the management board of each site. All GPs were informed prior to the initiation of the study (Table 1) [20].

If in the course of this review and of the clinical interview, drug-related problems (DRPs) were spontaneously identified that were not included in the STOPP/START criteria, these were also amended using the same communication protocol. They were recorded as covariates following Climente's classification [22].

Patients in the control group received standard medical and pharmaceutical care. Chronic medication taken by the patients was recorded, but medication review or systematic

Table 1 Communication protocols between hospitals and primary care

Hospital	Approved communication protocol per hospital
1	An email with the treatment recommendations is sent by the hospital pharmacist to the GP. This email is coded to protect patient identity. When GP receives the email, he/she asks for the password to download the document with the treatment recommendations. If, after a few days, the GP has not requested the password, the hospital pharmacist contacts the GP by phone Alternatively, the treatment recommendations are included in the discharge report provided to the patient. When the patient returns to primary care centre for follow-up, the discharge report is provided to the GP
2	Treatment recommendations are entered into the electronic clinical record. At this site, a single electronic clinical record is used by primary care and hospital care. Additionally, the patient is given an appointment by the emergency specialist for a follow-up visit with the GP upon discharge
3	Treatment recommendations are entered into the primary care electronic clinical record. Additionally an email with the recommendations is sent by the hospital to the pharmacist working in the primary care centre, who the contacts the GP
4	A discharge report with the treatment recommendations is provided to the patient. When the patient goes to primary care centre for the follow-up visit, the discharge report is provided to the GP Alternatively, an email with the treatment recommendations is sent by the hospital to the pharmacist working in the primary care centres, who then contacts the manager of the primary care centre. The manager discusses the recommendations with the GP

identification of PIPs based on the STOPP/START criteria was not performed.

In the intervention group, the patients' clinical records were reviewed by the pharmacists 1 month after making the recommendations to the GPs in order to assess if the recommendations had been followed. Patients were followed for a year after enrolment in the study. During this time, visits to the ED and hospitalisations were registered, but no further interventions were done, i.e. MR and treatment modification recommendations were only done in the first visit to the ED. Information regarding ED visits and hospitalisations was obtained by searching the health care database of each hospital.

The main outcome measure was the number of all-cause emergency visits and hospital admissions (EVHA) per patient-year. The rate of all-cause EVHA was established at 3, 6 and 12 months following enrolment. An overall analysis and an analysis stratified by site were performed.

To calculate sample size, it was assumed that an 18% absolute reduction of EVHA would result from eliminating PIPs [23] and that 60% of the recommendations made to the GP would lead to the correction of PIPs [24]. By applying this reduction, a 95% confidence level, a 5% accuracy for the observation method and an 80% statistical power, it was estimated that 555 patients were required. Assuming a 20% drop-out rate, the calculated sample size required to conduct the study was 666 patients.

Patients were randomly assigned to either the control or the intervention group. A complete randomisation by hospital and by intervention group was performed [20].

The association between the number of EVHA and the intervention was analysed using a negative binomial regression. Rate ratios of EVHA per 100 patient-day in the intervention and control groups and their 95% confidence intervals were calculated. Statistical significance was determined using Wald's test. An adjusted multivariate negative binomial regression analysis was developed using the following predictor variables: intervention, age, gender, Charlson index [25], number of drugs, hospital and origin (nursing home or home).

Data were analysed on an intention-to-treat basis. This included all randomised patients who met the inclusion criteria and did not die before the recommendation could be sent to the GP.

Results

Four sites took part in the study and 666 patients were enrolled. One patient was withdrawn because its case had been duplicated. Of the remaining 665 patients, 342 were assigned to the control group and 323 to the intervention group. Nine patients assigned to the control group and 15 to the intervention group died prior to hospital discharge and therefore recommendations about their treatment were not sent to their GP.

In addition, 3 patients randomised to the control group and 7 patients to the intervention group were withdrawn before follow-up started because they did not meet all the inclusion criteria (Fig. 2).

Patients enrolled in the control and the intervention groups showed similar characteristics for most of the variables recorded. Significant differences were seen only in the number of drugs patients received and in the percentage of patients hospitalised, i.e. patients who met criteria for hospital admission and who were not directly discharged from the ED. Patient characteristics are detailed in Table 2.

581 PIPs were identified, of which 465 were notified to the GPs together with a recommendation to revise them (Fig. 3). In addition, 317 DRPs not identified by STOPP/START criteria were spontaneously identified, of which 263 were notified to the GPs. 48 DRPs were related to problems

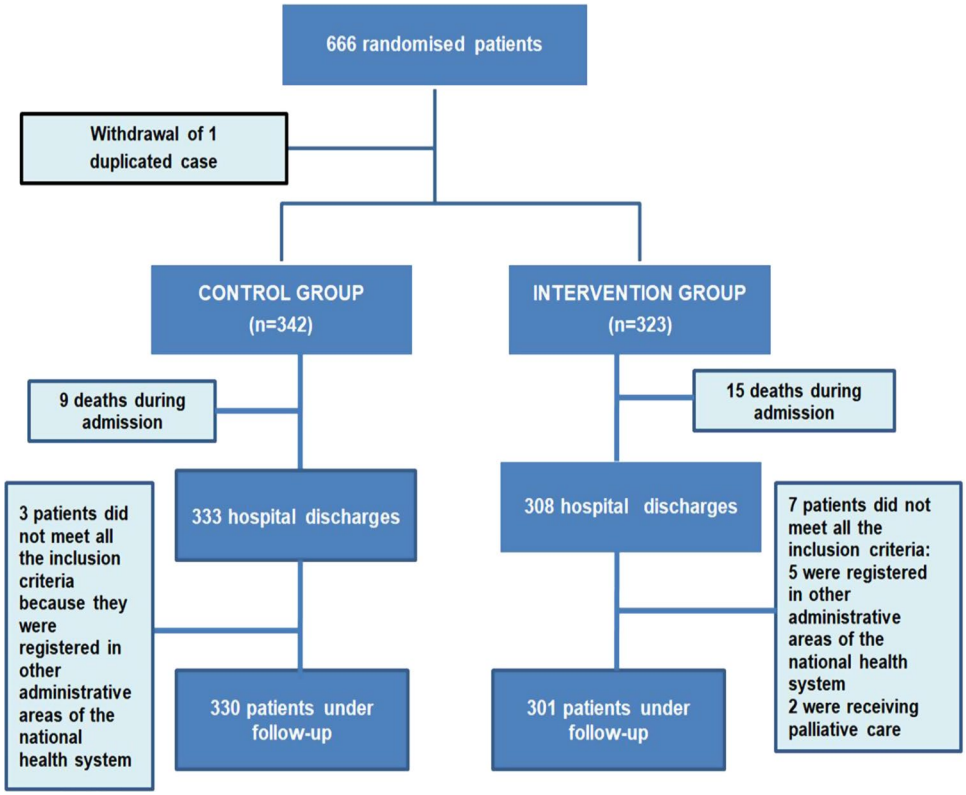

Fig. 2 Flow diagram of patients through the study

Table 2 Characteristics of patients enrolled in the study

Patients characteristics	Control group (n = 342)	Intervention group (n = 323)	*P*
Gender			0.614
Female	183 (53.5%)	167 (51.6%)	
Male	159 (46.5%)	156 (48.4%)	
Age: mean (SD)	78.2 (7.82)	78.99 (7.59)	0.129
Origin[a]			0.445
Home	327 (95.6%)	313 (97.5%)	
Healthcare facility	13 (3.8%)	7 (2.2%)	
Age-adjusted Charlson index: mean (SD)	2.85 (2.3)	3.05 (2.15)	0.077
Number of drugs: median (IQR)[b]	8 (5)	9 (6)	0.008
Hospitalised patients[c]	148 (43.3%)	169 (52.5%)	0.018

SD standard deviation, *IQR* interquartile range

[a]Refers to patient's usual residence

[b]Refers to the number of drugs that patients were receiving in the outpatient setting for a chronic condition, defined as any condition lasting over 6 months

[c]Refers to patients that were hospitalized after being attended in the emergency department and included in the study

with medication adherence or drug administration and were discussed directly with the patients. The remaining 116 PIPs and 6 DRPs were identified in patients who were finally not followed-up, either because they died before discharge from hospital or because they did not meet the inclusion criteria.

In the overall analysis, there were no significant statistical differences in the rate of EVHA between the control group and the intervention group throughout the study. Results are shown in Table 3.

In the multivariate analysis, the adjusted EVHA rate ratio of the intervention group versus the control group was not statistically significant either (see Table 4). The number of drugs turned out to be a risk factor for EVHA at 3, 6 and 12 months, while the adjusted Charlson index was found to

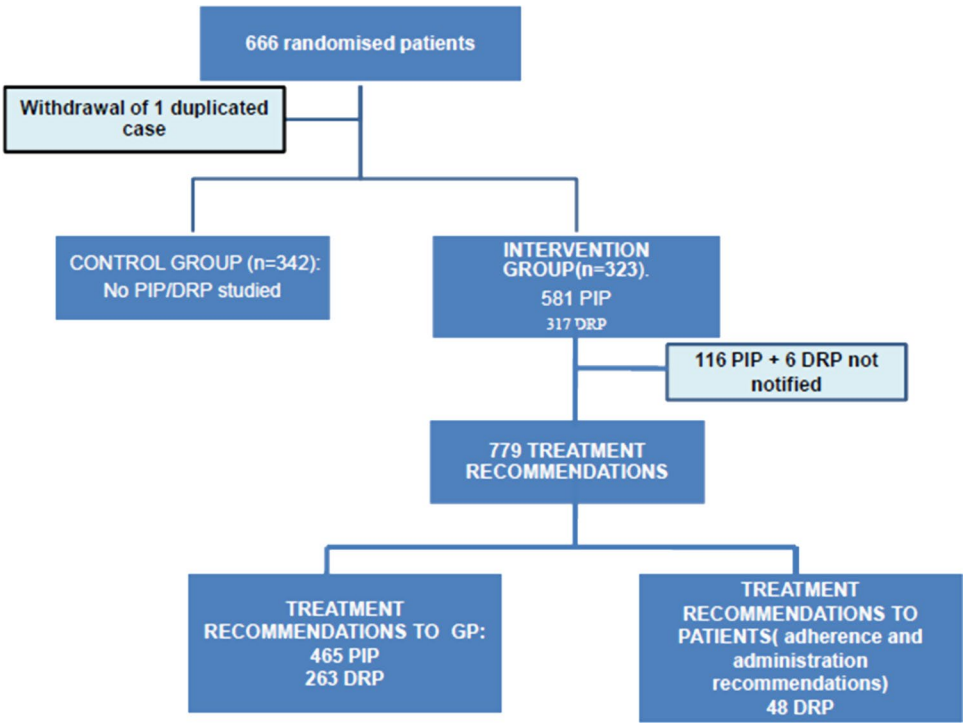

Fig. 3 Flow diagram of potentially inappropriate prescriptions and drug related problems identified and treatment recommendations sent

be significant only at 12 months, but for shorter periods it did not have an impact on EVHA.

The results of adjusted analysis stratified by site at 3 months are shown in Table 5. Sites 3 and 4 showed a significant reduction in the adjusted rate ratio of EVHA in the intervention group compared with the control group (0.452 (95% CI 0.222 to 0.923) at site 3 and 0.567 (95% CI 0.328 to 0.983) at site 4). The percentage of acceptance, by the GP, of the recommendations made by the hospital to correct PIPs and solve DRPs was greater at these sites.

There were no significant differences between sites in the analysis stratified by site at 6 and 12 months.

Discussion

Overall, the MR performed in the setting of an interprofessional collaboration programme for patients over 65 years of age presenting to the ED did not lead to a reduction in the rate of EVHA throughout the follow-up period. However, the analysis stratified by site showed that the programme was successful at 3 months in certain sites.

Other authors have assessed the benefit of MR programmes in EDs.

In a randomised clinical trial, Okere et al. [26] evaluated a collaboration programme between hospital pharmacists and emergency specialists. Pharmacists interviewed patients presenting to the ED, reviewed and reconciled the medication and, unlike the present project, provided drug information and carried out counselling activities at the time of hospital discharge. The programme included information and recommendations sent to the GP regarding drug therapy. Three months after the intervention, there was an increase in the number of patients visiting the GP following discharge from the ED. However, there were no significant differences in the number of emergency visits between groups.

Shaw et al. [27] assessed the results from a care unit for older patients in an ED where a hospital pharmacist with specialised geriatric training had joined the emergency team. One of the activities performed by the pharmacist was the review of chronic medication of the patients visiting the unit. The study was a retrospective cohort analysis in which the rates of emergency visits, hospitalisations and mortality were compared at 30 and 90 days between patients seen at the general ED, patients seen at the older patient unit and patients seen at the older patient unit where there was a pharmacist. The presence of a pharmacist did not improve the rates of emergency visits, hospitalisations, or mortality.

Thus, the evidence available when this project was started did not provide conclusive results regarding the benefit of chronic MR by teams in EDs including physicians and pharmacists. In this multicentre trial, the results stratified per hospital show that the benefits resulting from these programmes depend on the conditions under which they are performed.

In this project, the main tool used to reduce PIPs was a MR based on the STOPP/START criteria. The application of these criteria is simple and they can even be included in

Table 3 Rate of emergency visits and hospital admissions

	Rate of EVHA per 100 patient-day		EVHA rate ratio (intervention/control) (95% CI)
	Intervention group (n = 323)	Control group (n = 342)	
3 months[a]			
Global data[b]	1.1	1.3	0.857 (0.652 to 1.126)
Site 1 (n = 285)	1.5	1.4	1.138 (0.772 to 1.678)
Site 2 (n = 89)	0.9	1.3	0.790 (0.380 to 1.642)
Site 3 (n = 166)	0.9	1.3	0.564 (0.293 to 1.086)
Site 4 (n = 125)	1.7	1.1	0.613 (0.347 to 1.083)
6 months[a]			
Global[b]	1	1.1	0.917 (0.715 to 1.176)
Site 1 (n = 285)	1.2	1.2	1.086 (0.749 to 1.574)
Site 2 (n = 89)	0.9	0.9	1.004 (0.503 to 1.902)
Site 3 (n = 166)	1	1.2	0.753 (0.415 to 1.302)
Site 4 (n = 125)	0.7	0.9	0.742 (0.449 to 1.227)
12 months[a]			
Global[b]	1	1.1	0.954 (0.766 to 1.187)
Site 1 (n = 2585)	1.2	1.2	1.019 (0.744 to 1.395)
Site 2 (n = 89)	0.7	0.8	1.042 (0.564 to 1.927)
Site 3 (n = 166)	1.2	1.3	0.895 (0.541 to 1.480)
Site 4 (n = 125)	0.6	0.8	0.815 (0.517 to 1.286)

Site 1: Príncipe de Asturias University Hospital; Site 2: Son Llàtzer Hospital; Site 3: Manacor Hospital; Site 4: Jerez Hospital

EVHA emergency visits and hospital admissions

$P > 0.05$ for all comparisons

[a]Refers to time at which the main outcome measure (number of all-cause emergency visits and hospital admissions (EVHA)) were measured; i.e. at 3 and 6 months and 12 months after the intervention

[b]Global data refers to data from all patients included in the four sites

computer assisted prescription programs. Therefore, a positive result based on PIP detection using this method would have been highly useful in the healthcare practice. In other contexts, outside EDs, MR of older patients with the involvement of a pharmacist has shown to provide a clinical benefit. However, it is unclear whether this is due to the reduction of PIPs [4, 9, 28]. This suggests that MR based on the detection of PIPs in older people may not be the most effective method of optimising treatment and reducing admissions.

Thus, MR in the EDs based not only on the detection of PIPs but also on the detection and resolution of other drug-related problems may result in a clinical benefit.

This hypothesis is consistent with a recent publication on emergency visits due to adverse drug events in the US [3]. In that study, only 3.4% of emergency visits were due to PIPs (defined according to the BEERS criteria). The authors reflect on the convenience of continuing prioritising the reduction of PIPs as a strategy to improve the safety of medications in older patients and advocate for other types of strategies. For example, they found in their study that antidiabetic agents were involved in one of every eight emergency visits due to ADE. New diabetes treatment guidelines advise to increase the recommended glycaemic level in older patients at risk of hypoglycaemia. Therefore, a strategy centred on the adherence to this recommendation could be more useful.

One interesting finding of this study is that at sites where the intervention showed a benefit at 3 months, the efficacy was lost after a longer follow-up. In a recent meta-analysis evaluating the effectiveness of pharmacist-led medication reconciliation programmes, Mekonnen [29] obtained similar results. Most studies evaluated in this systematic review included reconciliation and MR programmes. In the subgroup analysis, a clinical benefit was found only in studies with a shorter follow-up period. This is interesting because in many countries policymakers are investing in MR programmes aimed at improving the quality and safety of medication use. A key question which needs further investigation is the optimal frequency of MRs.

Our study has certain limitations. The main outcome in this study was the number of all-cause EVHA. This outcome is objective, clinically relevant and easy to measure. However, MR programmes have demonstrated greater benefits in the reduction of drug-related EVHA. The meta-analysis conducted by Mekonnen et al. [29], showed a relative risk of 0.72 (95% CI 0.57–0.92) in all cause ED visits, a relative risk of 0.81 (95% CI 0.7–0.95) in all cause hospital readmissions and a larger effect in drug-related emergency visits and hospital readmissions (RR = 0.33; 95% CI 0.2–0.53). Gillespie et al. [28] found a positive relationship between the number of PIPs and drug-related readmissions, but not with all cause hospital admissions. Thus, this study could have produced more complete findings if drug-related emergency visits and hospital admissions had been measured.

Finally, it is a study in which a high degree of coordination with the primary care services was required for the intervention to be effective. A pragmatic design was chosen whereby each site decided what the best communication protocol between the hospital ED and the primary care facilities was. This avoided a rigid study design which would be

Table 4 Multivariate analysis of the rate ratio of emergency visits and hospital admissions at 3, 6 and 12 months

Variable	EVHA rate ratio at 3 months (exposure/no exposure); 95% CI	EVHA rate ratio at 6 months (exposure/no exposure); 95% CI	EVHA rate ratio at 12 months (exposure/no exposure); 95% CI
Intervention	0.808 (0.617 to 1.05)	0.888 (0.696 to 1.134)	0.954 (0.772 to 1.179)
Charlson index	1.047 (0.982 to 1.116)	1.054 (0.994 to 1.118)	1.074 (1.019 to 1.132)*
Gender Male	1.154 (0.878 to 1.517)	1.082 (0.844 to 1.388)	1.180 (0.949 to 1.468)
Age	1.004 (0.986 to 1.022)	1.000 (0.984 to 1.016)	1.000 (0.984 to 1.016)
Origin[a] Healthcare facility	1.042 (0.494 to 2.198)	1.084 (0.539 to 2.178)	1.320 (0.728 to 2.393)
No. of drugs[b]	1.062 (1.022 to 1.104)*	1.060 (1.023 to 1.098)*	1.060 (1.027 to 1.093)*
Site 1 (n = 285)	1	1	1
Site 2 (n = 89)	0.720 (0.476 to 1.091)	0.749 (0.515 to 1.091)	0.665 (0.479 to 0.923)
Site 3 (n = 166)	0.625 (0.442 to 0.885)	0.779 (0.569 to 1.067)	0.841 (0.637 to 1.109)
Site 4 (n = 125)	0.529 (0.359 to 0.781)	0.592 (0.418 to 0.838)	0.596 (0.443 to 0.801)

Site 1: Príncipe de Asturias University Hospital; Site 2: Son Llàtzer Hospital; Site 3: Manacor Hospital; Site 4: Jerez Hospital

*Statistically significant

[a]Refers to patient's usual residence

[b]Refers to the number of drugs that patients were receiving in the outpatient setting for a chronic condition, defined as any condition lasting over 6 months

Table 5 Acceptance of recommendations and EVHA adjusted rate ratio per site at 3 months

Acceptance %	EVHA adjusted rate ratio at 3 months (intervention/control)
Site 1	
27%	1.047 (95% CI 0.710 to 1.544)
Site 2	
31%	0.888 (95% CI 0.431 to 1.829)
Site 3	
52%	0.452 (95% CI 0.222 to 0.923)*
Site 4	
53%	0.567 (95% CI 0.328 to 0.983)*

Site 1: Príncipe de Asturias University Hospital; Site 2: Son Llàtzer Hospital; Site 3: Manacor Hospital; Site 4: Jerez Hospital

Acceptance %: percentage of therapeutic recommendations that were followed by general practitioner. EVHA adjusted ratio at 3 months: rate of all-cause emergency visits and hospital admissions (EVHA) per patient-year measured 3 months after the intervention

*Statistically significant

difficult to reproduce once the study ended. However, it had the disadvantage of having a different level of coordination at each site. In order to minimise this effect, a randomisation stratified by site was used. In addition, the participating sites were requested to send to the coordinating site their communication protocol with the primary care services approved by the site prior to the start of the study, in order to ensure that an analysis of the best method of communication had been done. Despite this, the results regarding the level of acceptance of recommendations show that there were important differences in communication effectiveness. Part of the rationale for this project was the awareness of the existence of a communication barrier between primary care services and specialised care, as well as a cultural barrier to team work among healthcare professionals in both settings. The sites that achieved a reduction in the number of EVHA obtained at least a 50% level of acceptance of the recommendations made by the ED, which was a much higher level of acceptance than the one obtained at the sites in which the intervention was shown to be ineffective. It can be hypothesized that MR performed in the ED will be effective as long as an effective communication line is established with the primary care services. It is of interest to note that technological tools used to improve communication such as the use of a unique electronic clinical record for primary and hospital care, which was available at site 2, did not result in a better percentage of acceptance of the recommendations. Conversely, the inclusion of treatment recommendations in the discharge report and the participation of pharmacists working in primary care centres turned out to be more effective.

Conclusion

The interprofessional collaboration programme between ED specialists, hospital pharmacists and GPs did not reduce the number of EVHA Further studies are needed to investigate whether these programmes can be effective if an adequate level of coordination is achieved with the primary

care services and if the MR is not based exclusively on the application of explicit criteria for the detection of potentially inappropriate prescriptions but also on the detection and resolution of other drug-related problems.

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