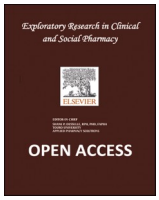
Exploratory Research in Clinical and Social Pharmacy 13 (2024) 100390

Contents lists available at ScienceDirect

Exploratory Research in Clinical and Social Pharmacy

journal homepage: www.elsevier.com/locate/rcsop



Primary care pharmacist-led medication review in older adult patients in coordination with general practitioners: an observational retrospective cohorts study

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ARTICLE INFO

Keywords:
Polymedication
Medication review
Primary care pharmacist
Inappropriate prescribing
Medication-related problems

ABSTRACT

Background: Polypharmacy and risk of potentially inappropriate prescribing (PIP) in older adult are being continuously increased. Including a primary care pharmacist (PCP) in the healthcare team is associated with lower rates of medication-related problems (MRPs).
Objectives: To determine the impact (in terms of variation of PIP, MRPs and polymedication) of treatment reviews (TR) carried out by the PCP by comparing two cohorts: standard TR *vs* coordinated TR with prescribing General Practitioners (GP). To assess possible health outcomes in both groups 6 months post-TR.
Methods: This is an observational study of two retrospective cohorts (2018 to 2020). All patients who met the inclusion/exclusion criteria were analyzed. Patients ≥65 years, who underwent complete TR by the PCP were included. Patients in a situation of exitus at the time of TR and those who underwent a partial TR were excluded. Control group cohort consisted of patients who underwent standard TR, and intervention group cohort consisted of those who underwent TR coordinated with GP. Sociodemographic, clinical and pharmacological variables were analyzed.
Results: 181 patients were enrolled. Mean age 84.4 ± 7.2 years, 78.5% women. Variables (GP-coordinated *vs* standard TRs) pre-post: decrease in drugs/patient 1.9 (95%CI: 1.4–2.4) *vs* 0.6 (95%CI: 0.2–1.3), $p < 0.05$; decrease in MRPs/patient 3.1 (95%CI: 2.8–3.4) *vs* 1.0 (95%CI: 0.6–1.4), $p < 0.05$; decrease in PIP/patient 2.0 (95% CI: 1.6–2.2) *vs* 0.6 (95% CI: 0.2–0.9), $p < 0.05$. Health outcomes: there was significant difference in average primary-care visits/patient 1.3 ± 0.5 *vs* 2.2 ± 1.8, $p < 0.05$.
Conclusions: Multidisciplinary interventions between PCP and GP, together with a systematic approach to TR can improve the quality of pharmacotherapy in the elderly. Prospective large follow-up studies are needed to demonstrate a positive trend in health outcomes.

1. Introduction

The elderly population has a higher prevalence of chronic diseases that often result in concurrent treatment with multiple medications and, consequently, a higher risk of potentially inappropriate prescribing (PIP) compared to younger populations.[1]

In Spain, the prevalence of polypharmacy in the primary care (PC) setting is close to 50% in people over 65 years of age.[2] A recent study carried out in Spain showed that the excessive polymedication (≥ 10 drugs) for at least six months has increased tenfold and these increments are observed at all ages, especially in those over 80-year-old.[3]

Interventions aimed at the polymedicated patient have been shown to be effective in reducing the number of PIP, improving the quality of prescribing or reducing medication-related problems (MRPs), although there is little evidence about their impact on patient health.[4] Various approaches are needed to manage these problems. One of them is oriented towards collaborative work by the entire healthcare team, in which clinical pharmacists are included in the management of patients'

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https://doi.org/10.1016/j.rcsop.2023.100390
Received 20 October 2023; Received in revised form 22 November 2023; Accepted 1 December 2023
Available online 3 December 2023

pharmacotherapy. In fact, several studies have found that including a pharmacist as a member of the healthcare team was associated with a substantially lower rate of MRPs.[5–8] In this sense, the primary care pharmacist (PCP) is a health professional integrated into primary health care services. The fundamental role of PCP focuses on improving the safety, effectiveness and efficiency of the use of medicines and medical devices at the individual and population level, facilitating clinical decision-making by professionals.[9] The definition of 'medication review', approved in 2018 by the Pharmaceutical Care Network Europe, involves detecting MRPs and recommending interventions.[10] Precisely, treatment review is a function defined and included both in the PCP Portfolio of Services[9] and in the PCP Professional Competencies Map.[11]

Therefore, the main objective of the present study is to determine the impact of PCP treatment reviews (TR), by comparing a model of 'standard TR' carried out by the PCP with a model of 'coordinated TR' between the PCP and the General Practitioner (GP) in terms of variation of PIP, MRPs, polymedication, and rate of acceptance of PCP recommendations. This comparison will allow to assess possible health outcomes in both groups 6 months post-TR.

2. Material and methods

2.1. Design and study population

This is an observational study of two retrospective historical cohorts (2018 to 2020). Patients recruited belonged to five health centres of the Northwest Healthcare Directorate of Madrid. All patients who met the inclusion/exclusion criteria were analyzed: patients aged 65 years or older, who underwent complete TR by the PCP as part of standard practice were included. Patients in a situation of *exitus* at the time of TR and those who underwent a partial TR report (focal review) were excluded. The control group cohort consisted of patients who underwent standard TR by the PCP. The intervention group cohort consisted of patients who underwent TR coordinated with the prescribing GP. Processes in both cohorts were conducted according to a series of defined phases, similar to a PDCA (*Plan - Do - Check - Act*) cycle. The activities included in each of the cohorts, which differentiate and define the intervention carried out, are listed in Table 1.

2.2. Variables and intervention

The main source of information was the PC Electronical Health Report, which includes access to external reports from Specialized Care and to the Electronic Prescription, where both the updated treatment and the patient's historical prescriptions are available. The pharmacotherapeutic review reports prepared by the PCP and the local review registry database were also used.

The following study variables were defined:

- Sociodemographic variables: age, gender, place of origin (home patient/nursing-home institutionalised patient).
- Clinical variables: *n* chronic pathologies, Charlson comorbidity index score,[12] *n* hospital admissions, *n* emergency department visits, *n* PC visits, and mortality (for any reason, or MRPs-related) in the period from the time of the TR report to 6 months later.
- Pharmacological variables: *n* drugs/patient, *n* PIP/patient and *n* MRPs/patient pre-TR and post-TR. Difference in drugs/patient, PIP/patient and MRPs/patient pre-post TR in both cohorts. N recommendations issued by the PCP. Medical acceptance rate of recommendations. Active drugs and therapeutic subgroups implicated in PIP and identified MRPs. PIP and MRPs were identified according to the PCP's treatment review methodology that is applied in routine practice our setting: PIP was quantified according to STOPP/START V2[13,14] and Beers Criteria 2019[15]; and MRPs, according to the classification of SEFAP - *Spanish Society of Primary Care Pharmacists* - medication review algorithm.[16]

Table 1
Activities carried out in each of the study groups, in sequential order of application in the TR process.

Stage of the cycle PDCA	Activity carried out	Control Group	Intervention Group
PLAN	- Initial face-to-face meeting between the GP, PCP (and nursing-home doctor, if applicable) to establish the target group of patients to be reviewed and to explain the PDCA cycle		Yes
	- Explanation of the complete TR process according to the *Spanish Society of Primary Care Pharmacists* (SEFAP) TR algorithm.		Yes
	- Detection of patient candidates for TR	Yes	Yes
DO	- Collection of demographic, clinical and pharmacotherapeutic data through EHRs	Yes	Yes
	- Detection of MRPs and PIP	Yes	Yes
	- Preparation of the TR report by the PCP according to the *Spanish Society of Primary Care Pharmacists* (SEFAP) TR algorithm, with recommendations for pharmacological treatment.	Yes	Yes
	- Sending the TR report to the prescribing doctor by telematic means (email, internal mail integrated in the EHR).	Yes	Yes
	- Communication to the prescribing doctor of the appropriate therapeutic alternatives according to the particular circumstances of the patient, after sending the TR report a few days before the sharing meeting, *via* telematic means (email, internal mail integrated in the EHR).		Yes
CHECK	- Meeting to share and discuss, in person, GP, PCP (and nursing-home doctor, if applicable), each of the TR reports prepared by the PCP.		Yes
ACT	- Acceptance or non-acceptance by the PCP of the recommendations and modification of the requirements in the Prescription Module if applicable	Yes	Yes
	- Subsequent feedback on the changes made to each patient's Prescription Module.		Yes

TR: treatment review; GP: General Practitioner; PDCA: *Plan-Do-Check-Act* cycle; EHR: Electronic Health Record; MRPs: Medication-Related Problems; PIP: Potentially Inappropriate Prescription; PCP: Primary Care Pharmacist.

2.3. Statistical analyses

Qualitative variables are presented with frequency distribution and percentage. Quantitative variables are summarised with mean and standard deviation (SD). The association between qualitative variables was performed with the *Chi-square* test. Comparison of means was performed using the *Student's t*-test, after performing Levene's test of homogeneity of variances, if the variables follow a normal distribution in the groups to be compared; and for asymmetric variables, the non-parametric *Mann-Whitney U* test was used. In the correlation analyses of quantitative variables, *Pearson's* correlation was used in case of normality, or *Spearman's* correlation, otherwise. The impact of the intervention was estimated with the variation in MRP, PIP and polymedication, before and after. To assess the differences between both review models, the *Student's t*-test for related samples was applied if normality was accepted, or the *Wilcoxon* non-parametric test otherwise. The statistical analyses were carried out using SPSS v26.0 software. A value of $p < 0.05$ was considered statistically significant.

2.4. Ethical aspects

The study was approved by the Research Ethics Committee on Medicines Research of the Hospital Universitario Ramón y Cajal of Madrid and by the Local Research Commission of the Northwest Healthcare Directorate of Madrid. Data processing was carried out in compliance with international data protection standards, as well as with the current Spanish legislation (Organic Law 3/2018, 5th December, on Personal Data Protection), and European Regulation (2016/679 of the European Parliament and of the Council of 27 April 2016 on General Data Protection Regulation).

3. Results

3.1. Baseline population characteristics

Of the 188 patients who made up the initial sample, the study finally consisted of 181 patients: 3 were patients who died before the review was performed; 2 were patients who underwent TR but no report was issued because no associated MRPs or PIP were found; and 2 were patients who moved to another Autonomous Community prior to TR.

The mean age of the patients was 84.4 (SD: 7.2) years, with a distribution by gender mostly female (78.5%). A 64.1% of patients were institutionalised in social healthcare centres. All patients had a Charlson index (CI) score >3, with a calculated mean CI value of 7.2 (SD: 2.1) (range 3–15).

Study participants had a mean of 7.1 (SD: 2.3) chronic pathologies (range 2–14). The most frequent ATC-10 (*Anatomical Therapeutic Chemical* classification system) pathologies were those corresponding to 24% of Group I (circulatory system), 17.4% of Group E (endocrine, nutritional and metabolic), and 14.9% of Group M (musculoskeletal system).

The total number of drugs chronically consumed by the patients was 2176, with a mean of 12 (SD: 3.7) drugs/patient (range 5–23). A total of 69.6% of patients were taking at least 10 drugs chronically and 26.5% were taking ≥15 drugs. There was no association between patient age and number of drugs ($p = 0.487$), and no differences were observed with respect to gender ($p = 0.755$). However, a positive correlation was observed between the number of drugs and the number of chronic pathologies ($p < 0.01$, $r = 0.529$), or the CI score ($p < 0.01$, $r = 402$).

All patients presented at least one MRP, with a baseline mean of 4.4 (SD:1.7) MRP/patient. The most frequently detected MRPs were appropriateness (36.9%) and safety (36.8%), and to a lesser extent indication (21.7%), efficiency (3.0%) and effectiveness (1.5%). The distribution of the MRPs detected is shown in Fig. 1 (Supplementary Data Section).

Fig. 2 (Supplementary Data Section) shows the proportion of recommendations issued by the PCP to MRPs, with the most common recommendation being 'deprescription' followed by 'dosage adjustment'.

A total of 50.2% of all drugs prescribed were found to be involved in one MRP. Of these, the 5 most frequently affected by a MRPs were paracetamol (8.2%), lorazepam (6.6%), quetiapine (5.3%), escitalopram (3.9%) and trazodone (3.4%). The pharmacological groups mostly involved were Group N (nervous system) with a 59.3% of the total; in second place, Group A (digestive system and metabolism) with a 13.5%; in third place, Group C (cardiovascular system) with a 12.5%.

In relation to PIP (STOPP/START criteria & Beers criteria), the mean baseline PIP was 2.9 (SD: 1.7) PIP/patient. There was no correlation between patient age and *n* PIP ($p = 0.553$). There was also no difference with respect to gender ($p = 0.149$).

In the correlation analyses, there was a positive association between *n* MRPs and *n* chronic pathologies ($p < 0.01$, $r = 0.279$) or *n* drugs ($p < 0.01$, $r = 0.601$); and a positive association between *n* PIP and *n* chronic pathologies ($p < 0.01$, $r = 231$) or *n* drugs ($p < 0.01$, $r = 0.476$).

3.2. PCP intervention

TR following the coordinated model was performed on 115 patients (63.5%), and with the standard model on 66 patients (36.5%). The characteristics of each cohort according to the type of TR are detailed in Table 2.

The inferential analyses with respect to the TR model applied is shown in Table 3.

In relation to health outcomes, Table 4 shows the results obtained in terms of proportions of admissions, emergency department visits and PC visits (total and those due to MRP) before 6 months post-TR. The proportion of patients who died in the 6 months post-TR is also shown.

4. Discussion

The present study shows that multidisciplinary interventions between GP and PCP, together with a systematic approach to TR, can render positive results and generate positive impact on the improvement of the quality of pharmacotherapy of elderly patients, in terms of reduction of polymedication, *n* MRPs, *n* PIP and use of health resources.

A significant reduction was observed in all variables in the coordinated model when compared with the standard model. The rate of acceptance by the GP of the recommendations issued by the PCP in its TR report was also significantly higher in the coordinated model.

This type of intervention is feasible in clinical practice and can be extrapolated and reproduced systematically. These results are consistent with other studies carried out in the PC setting,[17–21] which show a reduction of PIP when the pharmacist is integrated into the multidisciplinary team.

The mean number of drugs consumed per patient was similar to that of Stuhec et al.[21] (13.8 drugs/patient); but higher compared to the PHARM-C trial[22] (8.4 drugs/patient), the REMEI trial[23] (10.8 drugs/patient) and the MultiPAP study[24] (7.4 drugs/patient).

The PHARM-C[22] clinical trial indicates that the proportion of patients with PIP decreased by 13.7% (95%CI: 9.3–18.2) more in the intervention group conducted by the pharmacist than in the control group, and the mean number of PIP/patient decreased by 0.43 (95%CI: 0.32–0.54) more in intervention group *vs* control. The current study showed even greater reductions: 0.6 (95%CI: 0.2–0.9) in the standard TR model, and 2 (95%CI: 1.6–2.2) in the coordinated TR model.

The REMEI[23] group trial concludes that the evaluation of pharmacotherapy in elderly patients by the pharmacist in the PC setting, in coordination with the physician, significantly reduced the number of PIP/patient compared to the control group.

In terms of the health outcomes, a statistical significance was obtained in the reduction of number of visits to PC for any cause within 6

Table 2
Characteristics of the population, according to type of review.

	GP-coordinated TRs *n* = 115 (63.5%)	Standard TRs *n* = 66 (36.5%)	p
Mean age, years ± SD	85.9 ± 7.0	81.7 ± 6.9	**< 0.05**
Gender, *n* (%)			0.647
Female	89 (77.4%)	53 (80.3%)	
Male	26 (22.6%)	13 (19.7%)	
Origin, *n* (%)			**< 0.05**
Home patient	15 (13.0%)	50 (75.8%)	
Institutionalised	100 (87.0%)	16 (24.2%)	
Chronic pathologies, mean ± SD	7.3 ± 2.4	6.7 ± 1.9	0.117
Charlson index, mean ± SD	7.4 ± 1.9	6.8 ± 2.3	**< 0.05**
Drugs/patient, mean ± SD	11.5 ± 3.6	13.0 ± 3.6	**< 0.05**
MRPs/patient, mean ± SD	4.2 ± 1.7	4.7 ± 1.6	0.062
PIP/patient, mean ± SD	2.9 ± 1.7	2.8 ± 1.6	0.625

TR: treatment review; MRPs: Medication-Related Problems; PIP: Potentially Inappropriate Prescription.

Table 3
Comparison of the number of drugs, MRPs, PIP, and percentage of reports accepted by the GP; before and after the intervention, in both TR models.

	GP-coordinated TRs	Standard TRs	p
n Drugs/patient, mean ± SD			
Before TR	11.5 ± 3.6	13.0 ± 3.6	
After TR	9.6 ± 3.0	12.4 ± 3.4	
Difference (95% CI)	1.9 (1.4–2.4)	0.6 (0.2–1.3)	**< 0.05**
n MRPs/patient, mean ± SD			
Before TR	4.2 ± 1.8	4.7 ± 1.6	
After TR	1.1 ± 1.1	3.7 ± 2.0	
Difference (95% CI)	3.1 (2.8–3.4)	1.0 (0.6–1.4)	**< 0.05**
n PIP/patient, mean ± SD			
Before TR	2.9 ± 1.7	2.8 ± 1.5	
After TR	0.9 ± 0.9	2.2 ± 1.5	
Difference (95% CI)	2.0 (1.6–2.2)	0.6 (0.2–0.9)	**< 0.05**
TR reports accepted by GP			
n	99	29	
% (95% CI)	86.1 (78.4–91.8)	43.9 (31.7–56.7)	**< 0.05**

TR: treatment review; MRPs: Medication-Related Problems; PIP: Potentially Inappropriate Prescription; GP: General Practitioner.

Table 4
Comparative health outcomes (hospital admissions, emergency department visits, primary care visits and deaths) 6 months after TR in both TR models.

	GP-coordinated TRs	Standard TRs	p
Patients admitted to hospital, n (%)	**21 (18.3%)**	**10 (15.2%)**	0.593
Total number of patient admissions	23	16	
Average admissions/patient ± SD	1.1 ± 2.0	1.6 ± 1.3	0.667
Number of MRP-related hospital admissions, n (%)	2 (8.7%)	3 (18.8%)	0.154
Average days of admissions ± SD	7.5 ± 4.6	5.2 ± 4.2	0.111
Patients with Emergency visits, n (%)	**34 (29.6%)**	**16 (24.2%)**	0.441
Total number of Emergency visits	51	31	
Average of Emergency visits/patient ± SD	1.5 ± 0.8	1.9 ± 1.1	0.607
Number of MRP-related emergency visitis, n (%)	4 (7.8%)	4 (12.9%)	0.334
Patients with PC visits, n (%)	**46 (40.0%)**	**43 (65.2%)**	**<0.05**
Total number of PC visits	58	94	
Average PC visits/patient ± SD	1.3 ± 0.5	2.2 ± 1.8	**<0.05**
Number of MRP-related PC visitis, n (%)	2 (3.4%)	10 (10.6%)	0.157
Exitus 6 months post-TR, n (%)	**7 (6.1%)**	**3 (4.5%)**	0.662

TR: treatment review; PC: Primary Care; MRP: Medication-Related Problems.

months post-TR, in favour of the GP-coordinated group. There was also a trend towards a reduction in hospital admissions, emergency visits and PC visits (all MRP-related) in the GP-coordinated group. No significant difference was found between both cohorts in mortality 6 months post-intervention, as in the PHARM-C[22] and REMEI[23] prospective trials, in which no statistically significant differences is observed in morbidity and mortality in the intervention groups, compared to the control groups.

In line with our results, a recent systematic review and meta-analysis[25] including 14 randomized clinical trials that evaluated the effect of different pharmaceutical interventions on PIP outcomes in elderly patients concludes that the incidence of PIP, *n* PIP/person, *n* drugs used, and 30-day readmission rate are significantly lower in the pharmaceutical intervention groups. On the other hand, although mortality and number of falls are lower in the study groups than in the control groups, these differences are not statistically significant, as has been observed in previous studies[26] and our own analysis of health outcomes.

Some limitations should be point out. The pharmacotherapeutic review of the PCP did not include the patient clinical assessment,[27] wherefore a percentage of recommendations not accepted by the clinician were found. Moreover, it should be noted the limitation posed by the retrospective design of the study itself, as the possible lack of information in some cases, in the clinical history records, which is designed strictly for healthcare follow-up. As this was an observational retrospective cohort study, all patients who met all the inclusion and exclusion criteria during the study period were taken into account for the analysis. No sample size calculation was performed beforehand, and for this same reason, we obtained an imbalance between the number of GP-coordinated TRs and standard TRs. However, one of the strengths of our study is the fact that it has been carried out under real conditions and with not very restrictive selection criteria, this collaborative model can be applied and reproduced systematically in other regions and/or healthcare settings. Our study was based on recognized PIP screening criteria. In this regard, authors of recent updated version 3 of STOPP/START explicit criteria to define clinically important PIP in older people, conclude that although these kinds of criteria cannot replace clinical judgment in individual cases, they may serve to guide physician prescribing and deprescribing practices.[28] The fact that our evaluation was carried out in comparison with a control group allows to reaffirm the strength of the results obtained. In addition, a systematic methodology[16] has been followed in the review process, which has enabled the TRs to be standardised.

5. Conclusion

Finally, the systematic TRs carried out by the PCP in a model coordinated with the GP had a positive impact in improving the quality of the pharmacotherapy of the elderly patient in the PC setting, in terms of reductions in polymedication, *n* MRPs and *n* PIP, compared to standard TR practice. In addition, the GP-coordinated model provided higher rates of acceptance of treatment recommendations issued by the PCP. Prospective large follow-up studies are needed to demonstrate a positive trend in health outcomes.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Disclosures

We confirm that this work is original and has not been published elsewhere, nor is it currently under consideration for publication elsewhere. A part of the study findings was presented at European Geriatric Medicine Society (EuGMS) Congress, held in Helsinki from September 20th to 22nd 2023.

CRediT authorship contribution statement

M.C. Herrero Domínguez-Berrueta: Conceptualization, Data curation, Investigation, Writing – original draft, Writing – review & editing, Methodology. **M. Muñoz-García:** Conceptualization, Supervision, Validation, Writing – review & editing. **E. Delgado-Silveira:** Conceptualization, Validation, Writing – review & editing, Supervision. **S. Martín-Aragón:** Conceptualization, Supervision, Validation, Writing – review & editing. **A. Gangoso Fermoso:** Methodology, Validation, Writing – review & editing.

Declaration of Competing Interest

The authors declare no conflict of interest.

Acknowledgements

The authors would like to sincerely thank every person who has been part of the multidisciplinary team for making this study possible. The authors address their thanks above all to the team from the Northwest Healthcare Directorate of Madrid.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.rcsop.2023.100390.

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