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Pharmacist-led medication review targeted by an automated prioritisation tool in primary care patients prescribed 15 or more chronic medicines: a pragmatic cluster-randomised study

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Abstract

Introduction. Medication review can improve prescribing, but evidence for effects on unplanned hospital care is inconsistent, particularly among patients with very high medication burden, and services lack the capacity to review every such patient.

Aim. To evaluate adding a targeted pharmacist-led medication review and individualised report to usual care supported by VIGIA (Viewer of Potentially Inappropriate Therapeutic Groups), an automated prioritisation tool available in both arms.

Method. Pragmatic, open-label, cluster-randomised study in ten primary care units in Andalusia, Spain. Adults with at least 15 active chronic prescriptions in February 2022 were ranked by VIGIA, and the 422 highest-priority patients per arm were selected. The 830 patients (419 intervention; 411 control) were analysed according to their unit's allocated arm, after 14 exclusions. The primary outcome was change in unplanned hospital care episodes over 12 months. A cluster-level sensitivity analysis was added post hoc.

Results. The pharmacist component was delivered in full: all 419 intervention patients were reviewed and received an individualised report, and physician review of the report was documented for 100 (23.9%). No statistically significant between-group difference was detected in the primary outcome (+ 0.10 episodes; 95% confidence interval − 0.23 to + 0.44; p = 0.591). The post hoc cluster-level estimate was similar but less precise (+ 0.09; −0.36 to 0.54; p = 0.663). No statistically significant between-group differences were detected in secondary outcomes; medicine counts, VIGIA alerts and the inappropriateness index decreased within both arms.

Conclusion. Automated prioritisation made it feasible to deliver a targeted pharmacist review to an entire cohort with extreme medication burden. A reduction in unplanned hospital care was not demonstrated when individualised pharmacist reports were added to VIGIA-supported usual care, and the confidence interval does not exclude a clinically relevant benefit or harm. Physician review of the report was documented for a minority of patients, and acceptance and implementation of recommendations were not recorded. Baseline imbalance, post-allocation selection and only ten randomised units limit causal interpretation.

Trial registration. Not registered.

Impact statements

Automated prioritisation and detection of medication-related problems made it feasible for primary care pharmacists to review an entire cohort with extreme medication burden under routine conditions, but issuing a report did not ensure that it reached a prescribing decision.

Pharmacist-led review programmes should record prospectively, for each report, its receipt and review by the physician and the acceptance and implementation of each recommendation; without these records,

effects on clinical outcomes cannot be interpreted.

Introduction

Polypharmacy is heterogeneous and has no universal definition; numerical thresholds are common, but the number of medicines alone does not establish whether a regimen is appropriate [1]. Its prevalence increases with age, and it is associated with adverse events, healthcare use and mortality [2-5]. Patients prescribed 15 or more chronic medicines form a group with extreme medication burden, whose prioritisation also requires consideration of clinical risk and potential medication-related problems.

Systematic reviews indicate that multidisciplinary polypharmacy interventions improve prescribing appropriateness more consistently than clinical outcomes, while effects on hospitalisation and emergency care remain uncertain [6, 7]. Cluster-randomised trials in primary care and other settings show a similar pattern: changes in prescribing without a clear, reproducible reduction in hospital use [8-10]. The relevant question is therefore not only whether pharmacists can identify problems, but whether their recommendations reach the prescriber, are considered and implemented, and change clinical outcomes.

Guidance on medication management in polypharmacy offers limited operational detail, and pharmacist-led reviews vary widely in how they are delivered [11, 12]. Pharmacist-prescriber collaboration and prescriber acceptance condition the implementation of recommendations [13, 14]. Because service capacity is limited, review cannot be offered to every patient with polypharmacy: in our area, even restricting it to patients prescribed 15 or more chronic medicines left more patients than pharmacists could review. Evidence from routine practice on programmes combining automated prioritisation, pharmacist review and structured communication with the prescriber remains limited, particularly from primary care studies measuring clinical outcomes.

The RINGPOL project (Risk of Hospital Admission in Patients with Polypharmacy), a collaboration between primary care and hospital pharmacy, developed VIGIA (VIsor de Grupos terapéuticos potencialmente InAdecuados; Viewer of Potentially Inappropriate Therapeutic Groups), a web-based tool that orders patients using variables associated with hospital admission in the literature and flags predefined medication-related problems, so that pharmacist time is spent confirming and communicating problems rather than searching for them. In this study, clinicians in both arms could access VIGIA, whereas only the intervention arm received an individualised pharmacist report. The study therefore evaluated the incremental effect of a targeted pharmacist review and communication programme over usual care supported by the same prioritisation tool.

Aim

To evaluate the effect of adding a targeted pharmacist-led medication review and individualised report to usual care with access to VIGIA on unplanned hospital care over 12 months, and to describe its effects

on healthcare use, medication appropriateness and programme implementation, in primary care patients with high medication burden.

Methods

Design, setting and randomisation

This was a pragmatic, open-label, multicentre, cluster-randomised study in the Jerez-Costa Noroeste y Sierra de Cádiz Healthcare Management Area, Andalusia, Spain. The unit of randomisation was the primary care clinical management unit; the unit of observation was the patient. All ten units referring patients to Hospital Universitario de Jerez were included and allocated 1:1 using EPIDAT 4.1, centrally and before patient selection, yielding five units per arm. Blinding was not feasible. Reporting was informed by CONSORT 2025, its cluster and pragmatic extensions, and TIDieR [15-18].

Participants and selection

In February 2022, the regional prescribing system identified 1,732 adults in participating units with at least 15 active prescriptions of 180 days or longer, excluding medical devices: 653 in control and 1,079 in intervention units. Within each arm, patients were ranked once by the combination of predicted admission risk and pharmacotherapeutic inappropriateness generated by VIGIA; no minimum risk threshold was an eligibility criterion. The 422 highest-priority patients per arm were selected, so the fixed-number procedure sampled 64.6% of eligible control and 39.1% of eligible intervention patients, which may have contributed to baseline imbalance in the two ranking variables; identifying participants after cluster allocation is a recognised source of selection bias [19]. Patients who did not consent, were no longer assigned to a participating unit, had died before intervention or had undergone pharmacist review in the previous six months were excluded.

Baseline variables were re-extracted at each patient's index date: the pharmacist report date in the intervention arm and 18 September 2022, the midpoint of the intervention period, in the control arm. Four to ten months after selection, some patients no longer met the threshold; eligibility was not reapplied, but under a decision documented before analysis, patients with fewer than 10 active medicines at the index date were excluded as no longer representing the target population. Fourteen patients met this criterion (three intervention; eleven control; range 0 to 9 medicines) and were excluded, leaving 830. Among these, the number of active medicines at the index date ranged from 10 to 33 (mean 18.4), and 57 (6.9%) had fewer than 15.

Intervention and comparator

Between June and December 2022, eight primary care pharmacists reviewed each intervention patient's active medicines, health problems, clinical information and VIGIA alerts, which covered therapeutic duplication, anticholinergic burden, therapeutic cascades, medicines of low therapeutic value and QT-prolonging medicines. Pharmacists confirmed the alerts they judged clinically relevant, added other

problems identified during review, and generated one individualised report per patient with optimisation recommendations, available to the responsible physician through the prescribing module and recorded in the electronic health record. Physicians retained responsibility for accepting and implementing recommendations.

Control-unit physicians had access to VIGIA and its prioritisation information but received no individualised pharmacist report, so the comparator was usual care reinforced by the same prioritisation tool. Reducing medication burden was a health-service objective in both arms. Implementation measures were the numbers of intervention patients with a pharmacist report and with documented physician review, the medication-related problems communicated, and physician-level engagement; acceptance and implementation of recommendations were not recorded.

Outcomes and data sources

The primary outcome was the number of unplanned hospital care episodes per patient over 12 months, defined as unplanned admissions plus hospital emergency department visits without admission. Secondary outcomes were the two components separately, primary care contacts (excluding primary care emergency visits, reported separately), primary care emergency visits, hospital outpatient contacts, planned admissions and stay days, numbers of active and chronic medicines, predicted admission risk, and the inappropriateness index and its five components. Predicted admission risk is the admission risk score generated by VIGIA (%), an intermediate measure whose inputs include the number of active medicines and therapeutic groups. The inappropriateness index is the sum of the weighted scores of the five VIGIA categories: each category count is multiplied by a coefficient of 1.0 (therapeutic duplications, low therapeutic value medicines) or 0.5 (therapeutic cascades, QT-prolonging and anticholinergic medicines), assigned by research-group consensus; the unweighted total of VIGIA alerts is reported descriptively. Data came from the Diraya electronic health record and corporate prescribing tools.

Healthcare contacts were counted over the 12 months preceding and the 12 months following each patient's index date, and were extracted as one record per patient, care setting, period and contact type, each carrying the number of contacts of that type. Contact outcomes sum these counts rather than counting distinct contact types. Hospital contacts were restricted to outpatient clinic activity, since inpatient and emergency activity is captured by the admission and emergency-visit outcomes.

Sample size

The protocol sample size was calculated to detect a mean between-group difference of 0.35 hospitalisations per patient over 12 months (standard deviation 1.29; two-sided alpha 0.05; 80% power), requiring 221 patients per arm. Correction for a design effect of 1.59 (mean cluster size 60; intracluster correlation 0.01) gave 703 patients and, assuming 20% losses, the protocol set a target of 843 patients, which was rounded to 844 to allocate 422 per arm.

Statistical analysis

Continuous variables were described using mean (standard deviation) or median (interquartile range), and categorical variables using frequency and percentage. Normality was assessed with the Anderson-Darling test and homoscedasticity with the Fligner-Killeen test. Within-group pre-post comparisons used paired t, Wilcoxon signed-rank, McNemar or Stuart-Maxwell tests as appropriate; in the prespecified individual-level analysis, between-group comparisons used individual post-minus-pre changes with independent t or Mann-Whitney U tests. The 830 patients were analysed according to their unit's allocated arm, after the 14 exclusions described. The dataset records outcomes at two fixed evaluation points and holds no date of death, so follow-up could not be truncated for patients who died, who were analysed on the same 12-month basis as the rest.

Because allocation occurred by unit, post hoc cluster-level sensitivity analyses were performed after the individual-level results were known. For each outcome, the mean individual change from baseline was calculated in each unit; the five intervention means were compared with the five control means using an unweighted, equal-variance two-sample t test with eight degrees of freedom. This cluster-summary method preserves the randomised unit but is imprecise with only ten units and does not adjust for baseline covariates or unequal cluster sizes [20]. A one-way random-effects analysis of variance estimated the intracluster correlation for the follow-up primary outcome. Unit-level data are provided in Online Resource 1.

A post hoc exploratory analysis was conducted because of the limited implementation of the intervention: physician review of the pharmacist report was not documented for 76.1% of intervention patients, which may have hindered detection of a potential effect in the primary analysis. The 100 intervention patients with documented physician review were therefore compared with 100 control patients matched one-to-one by propensity score on baseline characteristics (Online Resource 1), to explore the potential effect of the intervention under conditions closer to its intended delivery. Because patients were selected after randomisation, this analysis is subject to selection bias and cannot establish a causal effect. Documented physician review does not necessarily imply acceptance or implementation of the recommendations or subsequent changes in treatment.

Only the individual-level analysis was prespecified; the cluster-level and exploratory analyses are post hoc.

Use of generative artificial intelligence

During manuscript preparation (August to November 2026), the authors used ChatGPT (OpenAI) and Claude (Anthropic) to support methodological consistency checks, the post hoc cluster-level calculations and language editing. All outputs were reviewed and verified by the authors against the source data and the original publications, and AI-generated outputs were not treated as scientific evidence. The authors take full responsibility for the integrity and final content of the manuscript.

Ethics approval

The Research Ethics Committee of Cádiz issued a favourable opinion with minor pending comments before patient selection, and its final favourable report, after those corrections, on 26 May 2022 (protocol AP-0192-2021-C2-F2; PEIBA 2665-N-21; registration 231.21). All participants provided written informed consent before inclusion.

Results

Study population and implementation

Of 1,732 eligible patients, 422 were selected per arm; 14 were excluded at the index date, leaving 830 in ten clusters: 419 intervention and 411 control (Fig. 1). Cluster size ranged from 57 to 119 patients in control units and from 31 to 143 in intervention units (mean 83). Pharmacists reviewed all 419 intervention patients and generated an individualised report for each, communicating 1,532 medication-related problems (mean 3.66 per patient), of which 239 lay outside the five VIGIA categories. Physician review of the report was documented for 100 (23.9%). Twenty-one patients died during follow-up (8 intervention; 13 control).

Uptake was concentrated in a minority of clinicians: of the 62 responsible physicians, 30 (48.4%) never opened the tool and 43 (69.4%) reviewed no report, while the five most active accounted for 55 of the 100 documented reviews.

Baseline characteristics

Baseline characteristics are shown in Table 1. The intervention arm had higher predicted admission risk (44.03% versus 38.14%; $p < 0.001$) and inappropriateness index (2.19 versus 1.95; $p = 0.001$). These were the ranking variables, and the imbalance is compatible with the unequal sampling fractions created by selecting the same number from different-sized source populations.

Table 1 Baseline characteristics of the primary analysis population

Variable	Control (N = 411)	Intervention (N = 419)	p
Sex (male), n (%)	164 (39.90)	142 (33.89)	0.073
Age (years), mean (SD)	73.95 (11.48)	74.37 (11.32)	0.511
Hospital ED visits, mean (SD)	1.00 (1.45)	1.09 (1.59)	0.670
Planned hospital admissions, n (%)			0.134 †
0	352 (85.64)	377 (89.98)	
1	51 (12.41)	38 (9.07)	
2	8 (1.95)	4 (0.95)	
Unplanned hospital admissions, n (%)			0.746 †
0	344 (83.70)	358 (85.44)	
1	49 (11.92)	50 (11.93)	
2	13 (3.16)	8 (1.91)	
3	4 (0.97)	2 (0.48)	
4	1 (0.24)	1 (0.24)	
Predicted admission risk (%), mean (SD)	38.14 (20.32)	44.03 (19.97)	<0.001
Total medicines, mean (SD)	18.21 (3.16)	18.56 (3.25)	0.122
Chronic medicines, mean (SD)	16.26 (3.08)	16.71 (3.28)	0.072
Inappropriateness index (weighted), mean (SD)	1.95 (1.38)	2.19 (1.36)	0.001
QT-prolonging medicines, n (%)			0.051 †
0	293 (71.29)	265 (63.25)	
1	99 (24.09)	131 (31.26)	
2	19 (4.62)	22 (5.25)	
3	0 (0.00)	1 (0.24)	

Values are mean (SD) or n (%). Continuous variables are presented as mean (SD) for comparability with Tables 2–4; their p values are from Mann-Whitney U tests. Categorical variables were compared with chi-squared tests unless otherwise indicated; †, Fisher's exact test. Admissions and ED visits refer to the 12 months before the index date. ED, emergency department; SD, standard deviation.

Primary outcome

Unplanned hospital care episodes showed no significant within-group change and no between-group difference (Table 2). Mean change was 0.00 in the intervention group (p = 0.827) and −0.11 in the control group (p = 0.314), a between-group difference of +0.10 episodes (95% confidence interval −0.23 to +0.44; p = 0.591). Neither component differed significantly.

Table 2 Primary outcome and components over 12 months in the primary analysis population

Outcome	Group	Baseline mean (SD)	Follow-up mean (SD)	Change	p	Between-group difference; p
Unplanned hospital care episodes	Intervention	1.27 (1.87)	1.27 (1.98)	0.00	0.827	+0.10 (95% CI −0.23 to +0.44); 0.591
	Control	1.22 (1.82)	1.11 (1.70)	−0.11	0.314	
Unplanned hospital admissions	Intervention	0.18 (0.49)	0.18 (0.51)	0.00	0.952	+0.02; 0.962
	Control	0.22 (0.57)	0.20 (0.50)	−0.02	0.646	
Hospital ED visits	Intervention	1.09 (1.59)	1.09 (1.69)	−0.01	0.857	+0.08; 0.459
	Control	1.00 (1.45)	0.91 (1.42)	−0.09	0.224	

Change is follow-up minus baseline. The between-group difference is intervention-group change minus control-group change, calculated from unrounded values, and is displayed once per outcome. p values and the primary confidence interval are individual-level estimates without cluster adjustment; 95% confidence intervals for the components are given in Online Resource 1. CI, confidence interval; ED, emergency department; SD, standard deviation.

The post hoc cluster-level analysis gave mean changes of −0.026 across intervention units and −0.115 across control units, an unweighted between-arm difference of +0.089 episodes (95% confidence interval −0.362 to +0.539; p = 0.663), similar to the individual-level estimate but less precise. The intracluster correlation for the follow-up primary outcome was −0.0007, compatible with zero.

Secondary outcomes

No healthcare-utilisation outcome showed a significant between-group difference at individual level (Table 3). Primary care activity was high in both arms, at about 21 to 23 contacts per patient per year, without significant within-group change.

Table 3 Secondary healthcare-utilisation outcomes over 12 months

Outcome	Group	Baseline mean (SD)	Follow-up mean (SD)	Change	p	Between-group difference; p
Primary care contacts	Intervention	20.95 (16.26)	21.81 (18.92)	+0.85	0.170	+0.41; 0.835
	Control	22.40 (15.91)	22.84 (17.86)	+0.44	0.364	
Hospital outpatient contacts	Intervention	1.16 (1.39)	1.08 (1.48)	−0.09	0.220	+0.01; 0.839
	Control	1.36 (1.52)	1.27 (1.52)	−0.09	0.274	
Primary care emergency visits	Intervention	1.32 (3.22)	1.29 (3.33)	−0.02	0.680	+0.07; 0.205
	Control	1.05 (1.53)	0.96 (1.52)	−0.09	0.246	
Planned hospital admissions	Intervention	0.11 (0.34)	0.14 (0.42)	+0.03	0.244	+0.05; 0.227
	Control	0.16 (0.42)	0.14 (0.41)	−0.02	0.488	
Planned hospital stay days	Intervention	0.34 (2.36)	0.52 (3.66)	+0.18	0.975	+0.16; 0.266
	Control	0.31 (1.55)	0.33 (2.36)	+0.02	0.254	

Change is follow-up minus baseline. The between-group difference is intervention-group change minus control-group change, calculated from unrounded values, and is displayed once per outcome. 95% confidence intervals for all secondary outcomes are given in Online Resource 1. Contact outcomes report the number of contacts, not the number of distinct contact types; primary care contacts exclude primary care emergency visits, which are reported separately. Stay days followed the Andalusian Minimum Basic Data Set manual: one day when the patient is hospitalised at the census hour (00:00) and zero days when admission and discharge occur on the same date. Planned stay days are highly skewed: most patients had no change and means are driven by a few long stays, which explains a mean change of +0.18 with a within-group p value of 0.975. p values are individual-level estimates without cluster or multiplicity adjustment. SD, standard deviation.

Medicine use and appropriateness improved within both arms without between-group differences (Table 4). Total medicines fell by 1.42 in intervention patients and 1.52 in controls (difference +0.10; p = 0.773), and VIGIA alerts fell from 2.78 to 2.47 per intervention patient and from 2.44 to 2.23 per control patient (difference −0.10; p = 0.473). Chronic medicines, therapeutic duplications, anticholinergic and low-value

medicines, predicted admission risk and the inappropriateness index also decreased in both arms; therapeutic cascades and QT-prolonging medicines did not change consistently.

Table 4 Secondary medication-use and appropriateness outcomes over 12 months

Outcome	Group	Baseline mean (SD)	Follow-up mean (SD)	Change	p	Between-group difference; p
Predicted admission risk (%)	Intervention	44.03 (19.97)	39.83 (19.39)	−4.20	<0.001	−0.71; 0.845
	Control	38.14 (20.32)	34.65 (19.72)	−3.48	<0.001	
Total medicines	Intervention	18.56 (3.25)	17.14 (5.05)	−1.42	<0.001	+0.10; 0.773
	Control	18.21 (3.16)	16.70 (5.61)	−1.52	<0.001	
Chronic medicines	Intervention	16.71 (3.28)	15.44 (4.69)	−1.27	<0.001	+0.10; 0.834
	Control	16.26 (3.08)	14.89 (5.09)	−1.37	<0.001	
Therapeutic duplications	Intervention	1.22 (1.19)	1.05 (1.13)	−0.16	<0.001	−0.02; 0.970
	Control	1.11 (1.22)	0.98 (1.23)	−0.14	<0.001	
Therapeutic cascades	Intervention	0.23 (0.48)	0.22 (0.49)	−0.01	0.703	−0.04; 0.240
	Control	0.18 (0.46)	0.20 (0.48)	+0.03	0.098	
Low therapeutic value medicines	Intervention	0.39 (0.58)	0.34 (0.57)	−0.05	0.007	−0.01; 0.671
	Control	0.34 (0.55)	0.30 (0.52)	−0.04	0.043	
QT-prolonging medicines	Intervention	0.42 (0.60)	0.41 (0.63)	−0.02	0.334	−0.01; 0.840
	Control	0.33 (0.56)	0.33 (0.55)	0.00	0.803	
Anticholinergic medicines	Intervention	0.52 (0.70)	0.45 (0.68)	−0.06	0.011	−0.01; 0.536
	Control	0.47 (0.63)	0.42 (0.63)	−0.05	0.024	
VIGIA alerts, total (unweighted)	Intervention	2.78 (1.64)	2.47 (1.68)	−0.30	<0.001	−0.10; 0.473
	Control	2.44 (1.64)	2.23 (1.71)	−0.21	0.002	

Outcome	Group	Baseline mean (SD)	Follow-up mean (SD)	Change	p	Between-group difference; p
Inappropriateness index (weighted)	Intervention	2.19 (1.36)	1.94 (1.38)	−0.26	<0.001	−0.06; 0.415
	Control	1.95 (1.38)	1.75 (1.42)	−0.19	<0.001	

Change is follow-up minus baseline. The between-group difference is intervention-group change minus control-group change, calculated from unrounded values, and is displayed once per outcome. 95% confidence intervals for all secondary outcomes are given in Online Resource 1. Predicted admission risk is the admission risk score generated by VIGIA; its inputs include medication variables, so it is an intermediate measure. The inappropriateness index is the sum of the weighted scores of the five VIGIA categories (coefficient 1.0 for therapeutic duplications and low therapeutic value medicines; 0.5 for therapeutic cascades, QT-prolonging and anticholinergic medicines). VIGIA alerts, total, is the unweighted sum of the five categories and is reported descriptively. p values are individual-level estimates without cluster or multiplicity adjustment. SD, standard deviation.

Cluster-level sensitivity analyses

The post hoc cluster-level analyses did not detect statistically significant between-arm differences for any outcome either (p values 0.141 to 0.979). Some secondary estimates changed in magnitude or direction: for unplanned admissions, primary care emergency visits and hospital outpatient contacts, the sign of the difference was reversed (Online Resource 1). These analyses do not correct baseline imbalance or potential selection bias.

Exploratory analysis in patients with documented physician review

In the post hoc exploratory analysis of 100 matched pairs with documented physician review in the intervention patient, no statistically significant differences were detected (Online Resource 1).

Discussion

In this pragmatic cluster-randomised study, adding a targeted pharmacist review and individualised report to usual care with access to the same prioritisation tool did not show a reduction in unplanned hospital care over 12 months. The individual-level difference was + 0.10 episodes per patient (95% CI − 0.23 to + 0.44), and the post hoc analysis of the ten randomised units gave a similar but less precise estimate (+ 0.09; 95% CI − 0.36 to 0.54). These intervals do not establish equivalence or exclude a clinically relevant benefit or harm.

Delivery of the pharmacist component was complete: a review was carried out and a report issued for all 419 intervention patients. However, only 100 (23.9%) had documented physician review, and acceptance

and implementation of recommendations were not recorded. The trial therefore estimates the effect of offering pharmacist reports within the observed care pathway, not the efficacy of a fully implemented collaborative review. This low documented continuity is a relevant operational finding, although the data cannot attribute it solely to prescribers or quantify its contribution to the result.

The study also shows what can be achieved. Automated prioritisation made it operationally possible for eight pharmacists to review an entire cohort of patients prescribed 15 or more chronic medicines, a population so complex that a first structured review is valuable in itself. VIGIA flagged medication-related problems systematically, and pharmacists confirmed and communicated them to prescribers, adding problems outside the automated categories. Evidence on polypharmacy interventions with clinical outcomes in routine primary care is scarce, and this collaboration between primary care and hospital pharmacy contributes to it.

The pattern is consistent with reviews and trials showing more consistent effects on prescribing than on hospital use [6–10], and with recent studies in this journal stressing patient selection, shared clinical information and pharmacist-physician collaboration [21, 22]; differences in population, intervention intensity, prescribing authority and outcomes preclude direct comparison.

The comparator was active: clinicians in both arms could consult VIGIA, and reducing medication burden was a concurrent health-service objective. The contrast therefore evaluates the incremental value of the pharmacist report, not the effect of VIGIA or of review versus no intervention. Within-group improvements may reflect usual care, secular change, regression to the mean or shared access to the tool; they cannot be attributed to the programme, but they show that the targeted measures are modifiable. The fall in predicted admission risk is partly mechanical, since the score's inputs include medication variables that also changed.

Strengths include evaluation under routine conditions in ten primary care units, use of routine clinical data, collaboration between primary care and hospital pharmacy, delivery of reports to the entire intervention cohort and description of use by clinicians. These features show the gap between issuing a recommendation and its incorporation into care.

The main limitations concern design and analysis. The prespecified individual-level analysis did not model cluster allocation, and the post hoc unit-level analysis, with only ten units of unequal size, is imprecise; count outcomes were analysed as change scores, and secondary outcomes without multiplicity adjustment. Selecting patients after allocation with different sampling fractions produced imbalance in the ranking variables [19], and index dates differed between arms. Acceptance and implementation of recommendations were not recorded, and the trial was not registered. Other constraints, such as the lack of dates of death and the exploratory nature of the matched analysis, are described in the Method.

Future studies should select participants before randomisation or apply identical rules within each unit, prespecify cluster- and baseline-adjusted analyses, and use comparable index dates. Process evaluation

should follow each step from report issued to treatment change and clinical follow-up, and measure professional time and fidelity. Integrating the review into a collaborative workflow with defined responsibilities and communication channels is the natural design improvement to test next.

Conclusion

In this pragmatic cluster-randomised evaluation, automated prioritisation made it feasible to deliver a targeted pharmacist review and individualised report to every patient in a cohort with extreme medication burden, with systematic detection of medication-related problems. A reduction in unplanned hospital care over 12 months was not demonstrated when these reports were added to usual care with access to the same tool. Physician review of the report was documented for 23.9% of patients, and acceptance and implementation of recommendations were not recorded. The findings identify the pathway between report and prescribing decision as the priority for future evaluation, and do not demonstrate that pharmacist review or VIGIA is ineffective. These findings call for cautious interpretation.

Declarations

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Data availability. The datasets generated and analysed during the current study are not publicly available because of ethical and data-protection restrictions. Access may be considered on reasonable request to the corresponding author, subject to approval by the Research Ethics Committee of Cádiz and the relevant data custodian.

Ethics approval. The Research Ethics Committee of Cádiz issued a favourable opinion with minor pending comments before patient selection, and its final favourable report, after those corrections, on 26 May 2022 (protocol AP-0192-2021-C2-F2; PEIBA 2665-N-21; registration 231.21).

Consent to participate. Written informed consent was obtained from all participants.

Consent to publish. Not applicable; the manuscript contains no identifiable individual participant information.

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Figures

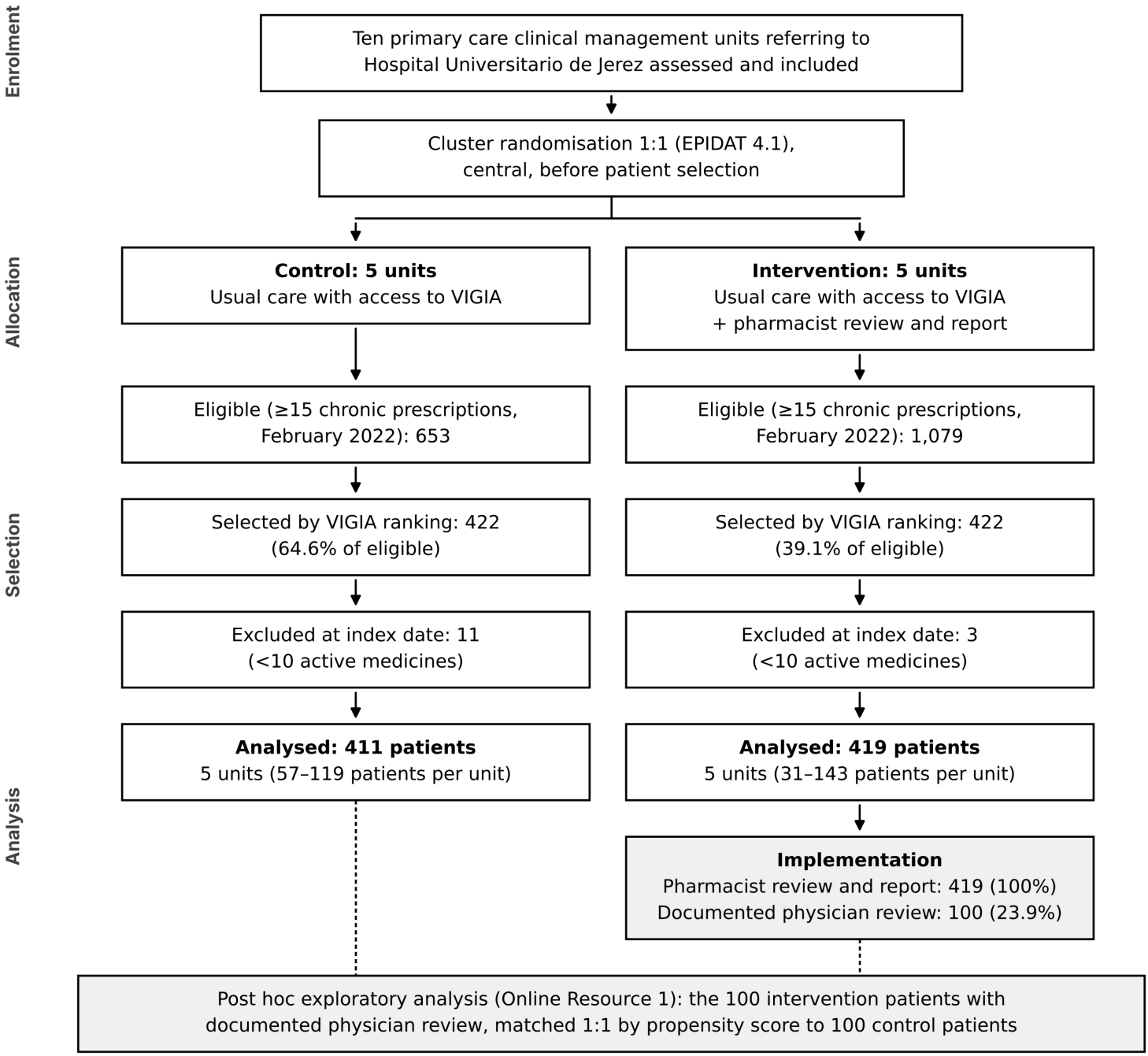


Figure 1

Flow of clusters, participants and justified implementation measures

From 653 eligible control and 1,079 eligible intervention patients, 422 per arm were selected. After 11 control and three intervention exclusions, 411 control and 419 intervention patients were analysed; all 419 received a pharmacist report and 100 had documented physician review.

Supplementary Files

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