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Multicomponent intervention to tailor prescriptions to patients with dementia in an intermediate care hospital: pre-post quasi experimental study

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Abstract

Objectives In persons with dementia, polypharmacy may be discordant with the goals of care. It is necessary to design interventions that align treatment regimens with the patient's situation, prognosis and preferences. The objectives of this study conducted at an intermediate care were to: i) identify inappropriate prescribing per the main care goal; ii) compare the pharmacotherapy data pre and post a medication review based on the degree of cognitive impairment; iii) assess the implementation of the proposed prescribing recommendations three months after discharge.

Design Pre-post quasi-experimental study.

Setting and participants Patients with dementia discharged from an intermediate care hospital between November 2021 and April 2022.

Methods Demographic, clinical and pharmacotherapy data were evaluated at admission. Medication reviews and interviews with the caregivers were conducted to align pharmacologic therapies with the overall goals of care. At discharge, information on the proposed prescribing recommendations was shared with the primary care team in the discharge summary. Follow up to evaluate implementation of the prescribing recommendations proposed during the medication review was performed at three months.

Results Of the 97 patients included, 94.8% had at least one inappropriately prescribed medication. At discharge, the mean number of chronic medications taken per patient decreased by 29.6%, from 8.05(SD 3.5) to 5.67(SD 2.7) ($p < 0.001$); the anticholinergic burden decreased by 18.6%, from 1.59(SD 1.0) to 1.29(SD 0.9) ($p < 0.001$); and therapeutic complexity decreased by 28.4%, from 29.23(SD 13.8) to 20.94(SD 11.3) ($p < 0.001$). At 3 months implementation of the proposed prescribing recommendations was 90.0%.

Conclusions and implications Admission to an intermediate care hospital provides the ideal setting for a multicomponent intervention, tailoring prescriptions to the patient's overall goals of care and preferences, improving the pharmacotherapy parameters related to side effects, and ensuring that the proposed prescribing recommendations are maintained over the medium term.

Keywords Dementia, Polypharmacy, Inappropriate prescribing, Goals of care, Intermediate care

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Background

The appropriateness of prescribing to include the patient's main care goal (MCG), in a shared decision-making (SDM) setting with the patient and/or their caregiver, is a key element in quality care for patients with dementia given the high prevalence of polypharmacy and the ensuing risk of inappropriate prescribing (IP) [1–3]. Deprescribing, defined as the supervised process of reducing or discontinuing a medication that is inappropriate or no longer needed for the patient's MCG [4], has potential benefits including reducing the incidence of side effects, reducing drug burden, lowering treatment costs and improving the quality of life of both patients and their caregivers [5–7].

People with dementia have a higher burden of comorbid physical and psychological diseases than older people without dementia [8–10]. Caring for patients with multimorbidity requires nuanced approaches that consider the complex interplay of conditions. Prescribing guidelines focus on individual diseases and when applied to patients with multimorbidity, do not provide information on how to prioritize treatment options [11]. As a result, polypharmacy (the use of five or more medications continuously) and excessive polypharmacy (ten or more chronic medications) are common in this population [12–15], leading to an increased risk of IP. In European countries, 60% of older patients with dementia have at least one inappropriate prescription (IP) [16]. IP causes patients to be more likely to experience negative health outcomes, with an increased risk of all-cause mortality, falls, delirium, and hospitalization [17]. The increasing number of articles published on IP in patients with dementia reflects the growing awareness of the need for appropriate prescribing in this population. This is particularly relevant for patients with dementia and comorbidities, especially in regard to high-risk medications and prescribing cascades [16–20].

A comprehensive geriatric assessment (CGA) of a person with dementia allows determining the patient's MCG (prolonging survival, maintaining function or prioritizing symptom control) and the development of patient-centered prescription [21, 22]. Optimizing medication use through patient-centered deprescribing, is a quality indicator in dementia care, as it allows patients to receive treatments that support their goals and avoid those that do not [2, 23].

Medication reviews (MR) are periodically required to assess polypharmacy in patients with dementia [8, 24]. The Patient-Centered Prescription (PCP) model [25, 26] (see additional file 1) is a four-stage systematic process carried out by an interdisciplinary team (geriatrician and nurse who are directly responsible for the care of the patient), and a consultant team (geriatrician and a

clinical pharmacist). This model focuses on determining a patient's MCG, which is based on the CGA, the calculation of the patient's frailty index (VIG-Frail) [27, 28] and the patient's values and preferences. The PCP model is a MR model that applies a mixed methodology using explicit (criterion-based) and implicit (judgment-based) criteria, which allows optimization of the medication regimen for each individual patient. The PCP model [26], as a specific tool for an advanced MR [29] showed its ability to identify IP, reduce polypharmacy, decrease therapeutic complexity as defined by the Medication Regimen Complexity (MRCI) [30], reduce anticholinergic burden (DBI) [31] and improve medication adherence in different profiles of older adults [25, 26, 32–34].

Fragmented health care is a barrier to medication optimization, often resulting in medication-related harm at times of healthcare transitions [3, 35]. Primary care providers positively assess the use of the discharge summary for the communication of prescription decisions made during hospitalization, to justify changes in medication and make follow up recommendations [36]. The transfer of information between the different levels of care regarding changes in medication is essential for the safe and effective management of polypharmacy, especially during transitions of care [24]. Caregivers of patients with dementia should be involved in the SDM process to ensure that the tailoring of the prescription is in line with the patient's preferences and values to ensure a clear understanding of the changes made to the treatment and the reason for them [37–39]. The objectives of the study were to: i) conduct a MR based on the PCP model and identify the amount of IP, taking into account the MCG of patients with dementia discharged from the Psychogeriatric Unit of our intermediate care hospital (ICH); ii) compare the pharmacotherapy data at admission (pre-MR) and at three months post-discharge (post-MR), taking into account the degree of cognitive impairment and the MCG; and iii) evaluate the degree of implementation of the proposals for pharmacological tailoring at three months post-discharge.

Method

Study design and participants

Pre-post quasi-experimental study with no control group, involving 97 patients with a diagnosis of dementia who were discharged consecutively from the Psychogeriatric Unit of our ICH between November 2021 and April 2022, with follow up at 3 months. The exclusion criteria were: inability to provide informed consent, patient or family member declining participation, anticipated length of hospital stay < 72 h, patients in a situation of agony.

Intervention

Medication review and personalized prescribing

When a patient is admitted to the Psychogeriatric Unit, the team directly responsible for the patient's care performs the CGA, which includes calculating the VIG-Frail. This assessment is used to determine the patient's MCG, which is agreed upon with the patient and/or their caregiver during an interview. One week after admission, the responsible team and the consultant team meet to conduct a MR based on the PCP model. During this meeting the interdisciplinary team identifies whether, based on the patient's MCG, there is any IP and makes a consensual proposal to adjust prescription. The proposal for the adjustment of the prescription is implemented during the patient's admission after it is agreed with the patient and/or their caregiver.

Support and engagement

After determining the patient's MCG at admission and following the interdisciplinary team's meeting, the proposal to adjust the patient's medication regimen is agreed upon with the patient and/or primary caregiver following an interview in a SDM environment. Consensus was assessed based on the agreement between the proposals made by the interdisciplinary team and those accepted by the patient and/or caregiver. The patient participates in SDM if they are deemed capable of understanding their situation, prognosis, and expressing their values and preferences. The ability to participate was assessed by the responsible team, which has extensive experience in caring for patients with dementia.

Changes in the discharge summary

At the time of discharge, the patient's MCG and the tailoring of the prescription applied during hospitalization were reflected in the discharge summary, and an electronic prescription was issued.

Measurements

Variables were collected on admission of the patients following a medication review (pre-MR) and three months after discharge (post-MR) from the shared medical record. The variables that were collected were:

Demographic variables: age, sex.

Functional variables: at baseline were collected the Barthel Index (BI) for activities of daily living [40].

Frailty index: measured on admission using the VIG-Frail frailty index [27, 28] VIG-Frail scores were classified as: i) VIG-Frail < 0.20: no frailty; ii) VIG-Frail 0.20–0.35: mild frailty; iii) VIG-Frail 0.36–0.50: moderate frailty; iv) VIG-Frail > 0.50: severe frailty.

Clinical variables: at baseline: i) comorbidity on the age-adjusted Charlson Comorbidity Index [41]; under other morbidities, patients were considered to experience depressive disorder when it was recorded in their medical record or when taking specific medications; ii) geriatric syndromes; iii) degree of cognitive impairment assessed using the Global Deterioration Scale (GDS) [42].

Pharmacotherapy variables: The number of IP was evaluated at the time of admission, in line with the PCP model, and analyzed according to the Anatomical Therapeutic Chemical (ATC) Classification System. The total number of chronic medications, those prescribed and taken continuously by a patient for at least six months, for each patient was collected at admission (pre-MR) and three months after discharge (post-MR). Polypharmacy status was categorized into three levels: i) 0–4: no polypharmacy; ii) 5–9: moderate polypharmacy; iii) ≥ 10 : excessive polypharmacy. Was considered polypharmacy of central nervous system (CNS) if the patient took ≥ 3 drugs [43]. At the 3-month follow up, pre and post polypharmacy status were compared to identify variations in polypharmacy status owing to the MR (decreased, unaltered, or increased) overall and by degree of cognitive impairment. At the pre and post MRs, an analysis was made of the burden of anticholinergic and/or sedative drug use, as measured by the Drug Burden Index (DBI) [21]. Exposure was categorized according to anticholinergic burden score as: i) 0–0.99 low; ii) 1–1.99 moderate; iii) ≥ 2 high. Therapeutic complexity was analyzed using the Medication Regimen Complexity Index (MRCI) tool [30] pre- and post-MR and categorized into three levels: i) 0–19.99 low complexity; ii) 20–39.99 moderate complexity; iii) high complexity if ≥ 40 . After the MR, the DBI and MRCI scores were compared to see whether there had been an increase, no change or decrease overall, according to degree of cognitive impairment. Overall goals of care: The proposed patient's MCG were prolonging survival, maintaining function or prioritizing symptom control. These were established based on a situational diagnosis [44], frailty and the preferences of the patient and agreed upon with the caregiver [37, 45, 46].

Sample size

To determine the sample size, it was estimated that IP in patients with dementia was 60% [16]. With a confidence interval of 95% and a precision of 10%, 97 patients were included. The percentage of replacements was expected to be 4%.

Statistical analysis

The statistical analysis was performed with the IBM SPSS version 29.0 statistical software package. The results of the categorical variables were expressed as absolute and relative frequencies, and those for continuous variables were analyzed using both parametric and non-parametric statistics, depending on the level and distribution of data (as means and standard deviations (SD) or median, Q1 and Q3 and minimum and maximum values). The Chi-Square test (or Fisher's exact test in 2×2 tables) where the expected frequencies were lower than 5 was used for categorical variables; Student's T-test was used to analyze the relationship between normally distributed quantitative and categorical variables; and the Mann–Whitney U test was used for variables that did not have a normal distribution. Statistical tests for paired data: statistical tests for paired data were used to analyze the impact of the intervention: the McNemar test for categorical variables; Student's paired-sample t-test for normally distributed quantitative variables; and the Wilcoxon Test for quantitative variables that were not normally distributed. A p-value less than 0.05 was considered to be statistically significant.

Results

Ninety-seven patients were included, 67% ($n=65$) of whom were women. The mean age was 84.16 years (SD 9.5). Demographic, clinical and pharmacotherapy data at baseline are listed in Table 1. Overall, the patients who were included had moderate disability in the BI with a mean score of 44.43 (SD 27.8). 52.6% ($n=51$) of them had advanced dementia ($GDS > 6C$). As many as 49.5% ($n=48$) of patients had had falls, and 41.2% ($n=40$) suffered from dysphagia. The mean frailty score was 0.47 (SD 0.10), indicating moderate frailty, and 36.1% of patients had advanced frailty. 86.6% of patients had polypharmacy and 25.8% had excessive polypharmacy, with 56% of the patients with excessive polypharmacy having advanced dementia. For 48.5% of the patients, the goal of care was to maintain functional status and for 51.5%, the goal was prioritizing symptom control.

When the MRs based on the PCP model were conducted, it was observed that 94.8% of the patients had one or more IP, with the mean IP per patient being 4.46 (SD 2.82). Of the patients with moderate and advanced dementia, 97.4% and 92.2%, respectively, had one or more IP. When the IP were analyzed according to the ATC classification, it was found that 64.9% of patients had IP for CNS medications and 59.8% of patients had IP for cardiovascular drugs.

In our study, 100% of the proposals for adjusting the prescription were agreed with and accepted by the patient/caregiver.

At the three-month follow up, 16 patients (16.5%) had died. In the pre-post comparative study, the pharmacotherapy data of the 81 patients still alive at the three-month follow up were analyzed. Pre and post pharmacotherapy data were compared overall and according to the degree of cognitive impairment (Table 2). The mean number of chronic medications per patient decreased by 29.6%, from 8.05 (SD 3.5) to 5.67 (SD 2.7) ($p < 0.001$). The mean MRCI score decreased by 28.4%, from 29.23 (SD 13.8) to 20.94 (SD 11.3) ($p < 0.001$), and the mean DBI score decreased by 18.6%, from 1.59 (SD 1.0) to 1.29 (SD 0.9) ($p < 0.001$). The decline in pharmacotherapy parameters was statistically significant both overall and for each degree of cognitive impairment. Figure 1 shows the variations in degree of polypharmacy, DBI and MRCI after applying the PCP model both overall and for each degree of cognitive impairment. With respect to polypharmacy, 45.7% of patients showed a decrease of one or two degrees, while the degree of polypharmacy increased in only 3.7% of patients. 42% of patients went down one or two MRCI categories, while 4.9% went up. As for the degree of DBI, as many as 18.5% of patients showed a decrease of one or two degrees, while 4.9% showed an increase in the degree of DBI ($p < 0.001$).

Pre-MR, CNS polypharmacy was observed in 68.8% of patients as opposed to 51.2% post-MR ($p < 0.001$). At the time of hospital admission, 64.2% of patients had a prescription for neuroleptics, compared to 49.4% after the MR ($p = 0.012$). Pre-MR, 63.7% of patients were taking cardiovascular drugs, compared to 37.5% of patients post-MR ($p < 0.001$).

Of the 81 patients still alive at the three-month follow up, 350 of the total 389 proposed recommendations for changes in prescribing were implemented, which corresponded to 90% of the original proposals ($n=237$ (60.9%) discontinuing medications, $n=70$ (18.0%) dose adjustments, $n=55$ (14.1%) adding new medications and $n=27$ (6.9%) medication changes).

Table 3 shows the types of IP that were analyzed and the proposed optimization of medications at discharge, based on ATC classification. The highest percentage of IP involved the classes of drugs that act on the CNS (37.7%) and those that act on the cardiovascular system (28.7%). The classes of drugs in which recommendations for changes in prescribing were being implemented three months after discharge were: A (alimentary tract and metabolism), B (blood and hematopoietic organs), C (cardiovascular system) and N (nervous system), with rates of 89.5%, 96.2%, 94.8% and 84.9% respectively. It should be noted that these four ATC classes represent 94.3% of the proposed prescribing recommendations that were implemented.

Table 1 Baseline data

Baseline data <i>n</i> = 97		Mean (sd)	Frequency (%)
Demographic data			
Age		84.16 (9.5)	
Sex	Women		65 (67%)
	Men		32 (33%)
Origin	Home		77 (79.4%)
	Nursing home		20 (20.6%)
Ethnia	Caucasian		97 (100.0%)
Clinical, functional, and cognitive data			
Medication management (only patients living at home) (<i>n</i> = 77)			2 (2.6%)
Barthel index (BI)		44.43 (27.8)	
Barthel index (BI)	Independence: BI ≥ 95		2 (2.1%)
	Mild dependence: BI 90–65		26 (26.8%)
	Moderate dependence: BI 60–25		41 (42.3%)
	Severe dependence: BI ≤ 20		28 (28.9%)
Cognitive status	Mild dementia (GDS 4)		7 (7.2%)
	Moderate dementia (GDS 5–6C)		39 (40.2%)
	Advanced dementia (GDS > 6C)		51 (52.6%)
Geriatric syndromes		3.3 (1.6)	
Type of geriatric syndrome	Falls		48 (49.5%)
	Dysphagia		40 (41.2%)
	Pain		13 (13.4%)
	Depressive syndrome		50 (51.5%)
	Insomnia		63 (64.9%)
	Malnutrition		10 (10.3%)
	Constipation		25 (25.8%)
	Pressure ulcers		5 (5.2%)
Charlson Index		3.79 (1.88)	
Frailty index (VIG-frail)		0.46 (0.1)	
Frailty index degrees	No frailty (0–0.19)		1 (1%)
	Mild frailty (0.20–0.35)		9 (9.3%)
	Moderate frailty (0.36–0.50)		52 (53.6%)
	Severe frailty (0.51–1)		35 (36.1%)
Therapeutic goal	Survival		0
	Functionality		47 (48.5%)
	Symptomatic		50 (51.5%)
Pharmacological data			
Number of chronic medications		7.98 (3.4)	
Polypharmacy degree	0–4 medications		13 (13.4%)
	5–9 medications		59 (60.8%)
	≥ 10 medications		25 (25.8%)
MRCI		29.5 (13.84)	
MRCI, degree	Low complexity (0–19.99)		23 (23.7%)
	Moderate complexity (20–39.99)		57 (58.8%)
	High complexity (≥ 40)		17 (17.5%)
DBI		1.50 (0.99)	
DBI, degree	Low DBI (0–0.99)		33 (34%)
	Moderate DBI (1–1.99)		41 (42.3%)
	High DBI (≥ 2)		23 (23.7%)
Inappropriate Prescriptions (IP)		4.46 (2.81)	
IP	0 IP		5 (5.2%)
	1 or more IP		92 (94.8%)
	2 or more IP		87 (89.7%)
	3 or more IP		72 (74.2%)

Abbreviations: *sd* Standard deviation, *GDS* Global Deterioration Scale, *MRCI* Medication regimen complexity index, *DBI* Drug burden index

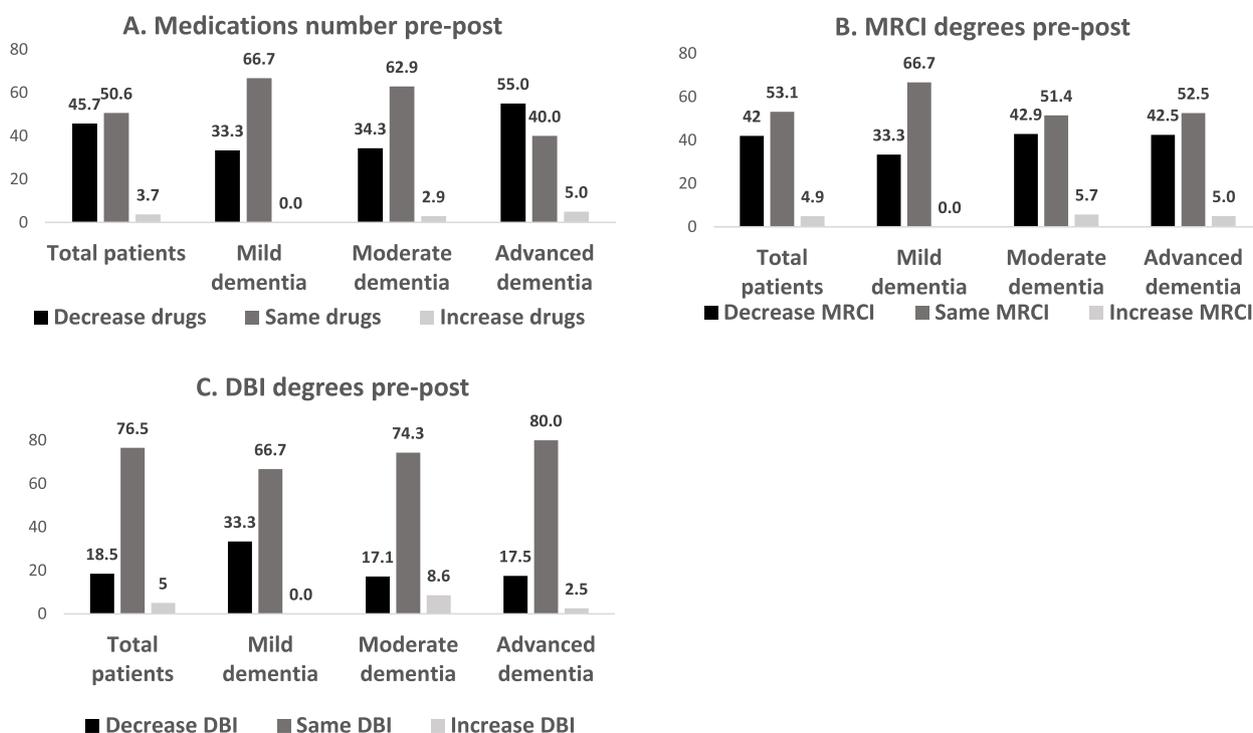


Fig. 1 Modifications in polypharmacy, MRCI, and DBI degrees after the MR according to degree of dementia. MRCI: Medication Regimen Complexity Index; DBI: anticholinergic and or sedative burden; MR: medication review

Table 3 Types of IP based on the Anatomical, Therapeutic, and Chemical (ATC) classification

ATC group	Number of IP identified (n/%)	Number of proposals applied (n)	% of proposals applied
A- Alimentary tract and metabolism	78 (20.53%)	60	89.5%
B-Blood and blood forming organs	26 (7.8%)	25	96.2%
C-Cardiovascular system	96 (28.7%)	91	94.7%
D-Dermatological	1 (0.3%)	1	100%
G-Genitourinary system and hormones	2 (0.6%)	2	100%
H-Systematic hormonal preparations (excluding sex hormones and insulin)	2 (0.6%)	2	100%
J-Anti-infective for systematic uses	2 (0.6%)	2	100%
L-Antineoplastic and immunomodulations agents	0	0	
M-Muusculoskeletal system	2 (0.6%)	2	100%
N-Nervous system	126 (37.7%)	107	84.9%
R-Respiratory system	10 (3.0%)	10	100,00%
S-Sensory organs	0 (0.0%)	0	
V-Various	0 (0.0%)	0	
TOTAL	334	302	90.4%

Discussion

This study demonstrates that MR, based on the PCP model, for people with dementia, multimorbidity, and frailty during hospitalization at an ICH lead to significant

quantitative and qualitative changes in pharmacotherapy prescriptions. These changes were made possible by the participation of an interdisciplinary team, conducting interviews with the patient and/or caregiver to determine

the patient’s MCG in a SDM environment and coordination with the primary care teams through modifications to the discharge summary and the use of electronic prescriptions. The results of this study demonstrate that the recommendations recently proposed by the European Geriatric Medicine Society can be applied to routine clinical practice [24].

Our study identified IP in 94.8% of patients, a higher proportion than that detected in other international studies of older adults with dementia [2, 14, 17, 19] but similar to other studies conducted in our setting [26]. This may occur because the identification of IP in people with dementia has generally been performed using assessment tools or criteria developed for the older population in general, the most commonly used being the Beers and the STOPP/START criteria. In our study, however, MR based on the PCP model and the tailoring of the prescription were performed after taking into account the MCG based on the patient’s own values and preferences, following in-depth interviews with the patient and/or their caregiver. We must also take into account that more than half of the patients met the criteria for advanced dementia and 90% of the patients included had moderate to severe frailty and survival was not the goal of care for any of them. The highest percentage of IP involved the classes of drugs that act on the CNS and the cardiovascular system, results similar to those reported by other studies [14, 19]. As in other studies, implementation of the proposed recommendations was lowest for CNS drugs [26] which indicates the difficulty in making

adjustments in the prescribing of CNS drugs for patients with dementia.

The study showed significant improvement in pharmacotherapy parameters. Polypharmacy, therapeutic complexity and anticholinergic burden are associated with a risk of adverse effects. The PCP model allows results to be optimized both quantitatively and qualitatively. No differences were observed in polypharmacy, anticholinergic burden or therapeutic complexity among the patients based on the degree of cognitive impairment, which indicates that treatments are not personalized taking each individual’s situation into account, but instead are based on general recommendations. Likewise, CNS medication polypharmacy and the number of cardiovascular drugs decreased.

The review conducted three months after discharge found that implementation of the proposed recommendations was 90.0%, a higher rate than that observed in other studies [26]. There may be several underlying reasons for this: first, the methodology of conducting a MR which adjusts prescribing to the patient’s MCG; the information regarding the changes proposed in the discharge summary to justify the changes in the prescription to ensure effective communication with the primary care teams during the care transitions; the issuing of the electronic prescription upon discharge; and the involvement of the caregivers which ensures that interventions are tailored to the patient’s preferences and values and ensures a clear understanding of the changes made in treatment and the reasons for them.

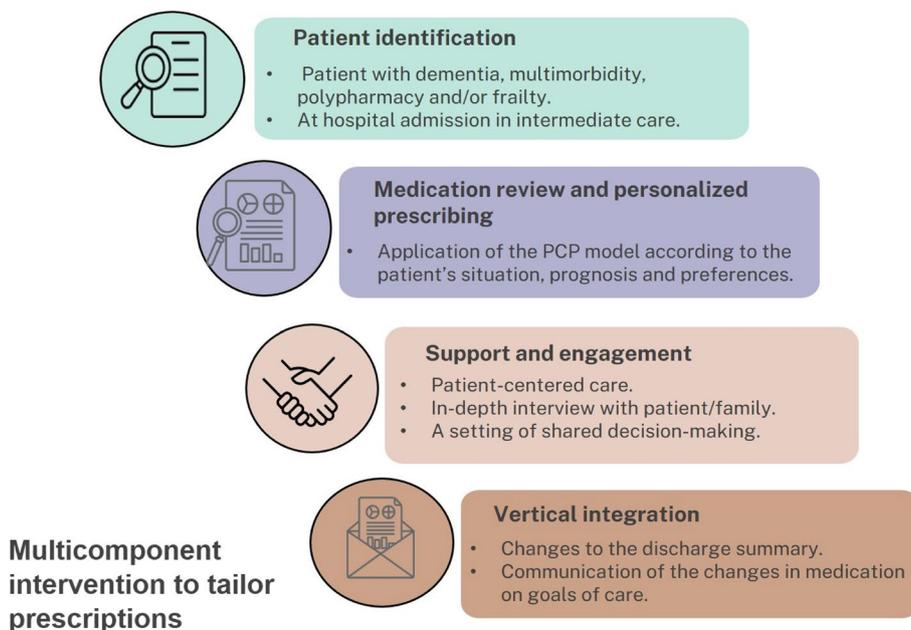


Fig. 2 Multicomponent intervention to tailor prescriptions

One of the limitations of this study is the quasi-experimental design, but a randomized design would have prevented some patients from benefiting from an intervention on medications that is known to be efficacious. Moreover, the PCP model is integrated into the clinical practice of our hospital, and random assignment to a control arm and an intervention arm might have increased the risk of contamination bias. Another limitation of this study is that, although it provides evidence for the optimization of pharmacotherapy parameters that are closely related to therapeutic adherence and side effects, other clinical outcomes, such as reduction of healthcare resource utilization (hospitalizations, use of emergency services), improvements in geriatric syndromes, quality of life and experience of the caregiver were not assessed. This suggests avenues for future research. The implementation of complex interventions in clinical practice involves cultural and contextual aspects. Nevertheless, we believe that the underlying principles of the multicomponent intervention (medication review following the PCP model, SDM with the patient and/or caregiver, discharge summary changes to ensure continuity of care, and the availability to implement pharmacological prescription upon discharge) (Fig. 2) are scalable to other settings.

We should respond to the need for personalized care, avoiding the fragmentation of care services and promoting collaboration between the different settings of care.

Conclusions

To address the challenge of providing quality care for older patients with dementia and complex care needs, the tailoring of the prescription should become a part of routine practice [23]. Identifying people with dementia who have multimorbidity and/or frailty can help clinicians know who can most benefit from MR as a standard practice routine. In our study, using the PCP model allowed IP to be detected and the prescriptions to be adjusted taking into account the patients' objectives, wishes and preferences. In our setting, making the proposal for changes in the prescription for medications in agreement with the patient/family and including it in the discharge summary along with the electronic prescription issued by the intermediate care team at discharge ensures a high rate of implementation of the proposed prescribing recommendations three months after discharge from the hospital. We believe that this four-step multicomponent intervention model is easily scalable in other intermediate care hospitals.

Abbreviations

MCG	Main care goal
SDM	Shared decision-making
IP	Inappropriate prescribing

CGA	Comprehensive geriatric assessment
MR	Medication reviews
PCP	Patient-Centered Prescription
MRCI	Medication Regimen Complexity Index
DBI	Drug Burden Index
ICH	Intermediate care hospital
BI	Barthel Index
GDS	Global Deterioration Scale
ATC	Anatomical Therapeutic Chemical Classification System
CNS	Central Nervous System
SD	Standard deviation

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12877-025-05783-2>.

Supplementary Material 1.

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Authors' contributions

All authors contributed to the conception and design of the work. Material preparation, data collection and analysis were performed by MBS, JEP, EPJ, MECD,MEF and NMB. The first draft of the manuscript was written by MBS, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data availability

The datasets generated and/or analyzed during this study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Consorci Hospitalari de Vic (Vic Hospital Consortium) on 28/09/2021, CEI (Research Ethics Committee) code number 2021175 and own code PR 306. Authors certify that the study was performed in accordance with the ethical standards as laid down in the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

No administrative permissions and/or licenses were required to access the clinical/personal patient data used in this study.

All participants (or their surrogates in cases of incapacity) provided informed consent statement, in accordance with the applicable legal regulations (Royal Decree 1090/2015 of a 4 December; European Regulation 536/2014 of 16 April; Royal Decree 41/2002 of 14 November); and they had the right to refuse participation. Afterwards, we included the patient's informed consent in their electronic health record.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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