

Original article

Polypharmacy and potentially inappropriate medications in patients requiring palliative care in hospitals and nursing homes: Evidence from a Ligurian point-prevalence multicenter study

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ABSTRACT

Objectives and background: Older adults with multimorbidity and frailty frequently require palliative care, yet prescribing practices often remain focused on primary or secondary disease prevention rather than symptom relief. Polypharmacy and potentially inappropriate medications (PIMs) may undermine quality of life and alter the benefit-to-harm ratio in this population. This study evaluated the prevalence of polypharmacy, pharmacological prescribing patterns and PIMs in hospitalized older adults requiring palliative care.

Study design: This nested study of the Italian multicenter point-prevalence study (Palliative Care 2.0) included patients aged ≥ 65 years from three metropolitan hospitals and three nursing homes in Genoa, Liguria, Italy. Needs for palliative care were assessed using the NECPAL CCOMS-ICO® tool and those categorized as 'positive' were staged I–III. Polypharmacy (≥ 5 drugs) and five PIMs were evaluated according to STOPP-Frail criteria. Data were analyzed through appropriate hypothesis tests (Mann-Whitney, Anova, chi-squared) comparing NECPAL positive and negative participants, while associations with number of PIMs were explored through regression analysis.

Results: Of 558 patients initially screened, 294 were administered the NECPAL tool, of whom 254 (45.5% of the sample screened) had PC needs (mean age 85 ± 11 years; 61% female). Polypharmacy was reported in 93.9% (276/294), with a median of 9 drugs (IQR 5). PIMs were identified in 68.2% of patients and were strongly associated with polypharmacy ($p < 0.001$), but were less common in nursing home residents compared with hospital patients ($p < 0.001$). Drug burden and the prevalence of PIMs did not decline with advancing NECPAL stage, except for increased antidiabetic use in stage III.

Conclusions: Polypharmacy and PIM use are highly prevalent in older adults who require palliative care, persisting even in advanced stages of illness. Current practice appears to fall short of both effective deprescribing and fully aligning pharmacological therapy with goals of care and overall quality of life. Systematic efforts to align pharmacotherapy with patients' care goals and clinical status are essential to minimize harm and promote quality of life in the final stages of life.

1. Introduction

Population aging is associated with multimorbidity [1,2] and frailty, which is characterized by reduced physiological reserve with increased risk of adverse health outcomes [3], including mortality, hospitalizations [4] and functional decline [5]. This is particularly evident in

Liguria, a northern Italian region with the highest median age in Europe, and older adults represent 28.5% of the population [6]. Specifically, Genoa, the largest city in the Liguria region, has the highest proportion of oldest old individuals (aged 85 years and older). [7]

Recent evidence underlined that the overall prevalence of frailty in community-dwelling older adults ranges from 11% among those who

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were 50 to 59 years of age to 51% among those who were 90 years [8,9].

Furthermore, a higher level of frailty is associated with a larger number of prescriptions. In particular, the association between frailty and polypharmacy, defined as the co-occurent presence of at least five drugs, may be complex and bidirectional: on one hand, frailty is linked to multimorbidity which can consequently lead to polypharmacy and on the other hand, there are plausible mechanisms by which drugs may affect the development of frailty, including changes in pharmacokinetic responses, especially metabolism and excretion more pronounced than with chronological age [10].

The prevalence of polypharmacy in older adults with frailty is estimated to be 59% [11] and it is highly associated with increased risk of falls, hospitalization, mortality, unpredictable worsening of the clinical trajectories of frail older patients [12].

In line with these notions, further evidence has shown that frailty prevalence was 49.7% in Italian nursing home setting and was associated with higher medication burden, meaning that the average number of drugs prescribed per resident was 7.7, and 84.8% of residents were taking five or more drugs simultaneously [13].

The progression of burdening chronic diseases and advancing disability may require the timely identification of palliative care (PC) needs, which pose decision-making challenges for the physician, resulting in unequal PC care access, especially in older non-cancer patients. Understanding the interplay between aging, frailty and PC needs is of key relevance for optimizing care objectives, improving a patient-centered approach and ensuring that care aligns with individual values and goals [14]. PC patients experience burdensome multimorbidity-related symptoms, necessitating emotional, social and spiritual support [15].

PC needs can be evaluated with specific tools, such as NECPAL CCOMS-ICO© tool (Necesidades Paliativas) [16], which was developed in Quality Observatory/WHO Collaborating Centre for Palliative Care Public Health Programs of the Catalan Institute of Oncology in Spain in 2012. Furthermore, in 2021 the NECPAL 4.0 tool [17,18] was proposed, incorporating severity stages for a prognostic assessment and notably, in a subset of highly vulnerable end-stage PC patients a high polypharmacy and overprescription pattern was commonly observed [19].

Pharmacological prescription must be aligned with the importance of symptomatic control in PC patients, fulfilling the priority to provide comfort, relief of suffering, and to balance the risk to benefit ratio in terms of life expectancy, risks of inappropriate prescriptions and adverse drug reactions. In order to align pharmacological prescription with defined care objectives, implicit and explicit deprescribing tools such as START and STOPP criteria [20], Beers Criteria [21], or Medication Appropriateness Index (MAI) [22] were developed, with the objective of avoiding unnecessary medications and simplifying or suspending drugs when risks outweighed the benefit.

In particular, STOPP-Frail criteria were specifically developed to prioritize symptom relief in PC patients, facilitating deprescribing patterns [23]. These 25 explicit criteria can be used for identifying Potentially Inappropriate Medications (PIMs), that can disproportionately augment risks of harm, drug-drug interactions, drugs-disease interaction or adverse drug effects especially in PC patients [24].

Based on this background, the present study is aimed at analyzing the pattern of pharmacological prescriptions and their inappropriateness using STOPP-Frail 2.0 criteria, with the objective of identifying PIMs in older adults with PC needs in different settings, including hospitals and nursing homes.

2. Methods

This is a nested study of the Palliative Care 2.0 point-prevalence study (under submission), including 558 consecutive patients from the main metropolitan hospitals in Genoa, Italy (IRCCS Polyclinic San Martino, Galliera Hospital and Villa Scassi Hospital) and three nursing homes (ASL 4 Chiavarese and Piccolo Cottolengo Don Orione in Genoa,

Chiossone Monte in Genoa). The study was approved by the IRB (CERA N 2024-54 12/06/2024), University of Genoa, Italy.

Patients were included if they were 65 years or older, signed an informed consent (by themselves or their caregiver/legal representative), and were admitted for more than 72 h. All patients hospitalized were admitted to internal or geriatric wards.

Based on NECPAL CCOMS-ICO© tool, the surprise question to the attending physician as an initial screening step for each patient was posed, aimed at identifying individuals who might benefit from PC according to their clinical complexity and prognosis. Analyses were performed only on patients for whom the surprise question was positive (for NECPAL CCOMS-ICO© tool details, see supplementary materials S1).

Data were collected on demographics, multimorbidity (Cumulative Illness Rating Scale – CIRS) [25], frailty (Clinical Frailty Scale – CFS) [26], PC needs (NECPAL CCOMS-ICO© tool 4.0 and with evaluation of the NECPAL stage [16,17]), dementia status (Clinical Dementia Rating Scale, CDR) [27] and polypharmacy (five or more drug per patient).

Given that this is a nested study, and the prescription pattern of the patients was not the primary focus of the Palliative Care 2.0 study, we were forced to categorize polypharmacy into 14 available classes including lipid-lowering drugs, opioids, antidiabetics, antihypertensive drugs, diuretics, pain-medicine (not opioids), proton inhibitor drugs (PPIs), corticosteroids or immunomodulatory drugs, chemotherapy, benzodiazepines (in continuous infusion or spot administration), psychoactive drugs, antibiotics and parenteral nutrition.

Medication review was performed centrally by the research team and was not part of routine clinical medication review activities at the participating sites. All data were extracted from medical records and evaluated using predefined categories and criteria established a priori. The same review framework was applied to all participants, regardless of site, in order to ensure consistency and to reduce variability related to local prescribing or medication review practices.

Pharmacological prescription was evaluated with STOPP-Frail 2.0 criteria [28] for appropriateness and for PIMs detection. Subsequently, by comparing STOPP-Frail criteria with our available PIMs categories, 5 drug-families were identified: antihypertensives, antidiabetics, PPIs, lipid lowering drugs, and psychoactive medications in patients with diagnosed dementia.

Data were stored on the REDCap platform [29] and were analyzed with RStudio software (version 2023.06.00), Jamovi software (version 2.4.28) using Mann-Whitney, Chi-squared, Fisher exact test, and Poisson regression analysis. The latter was employed in a univariate model, whose significant variables were subsequently selected for a multivariate model (with the number of PIMs as the dependent variable). Being this a point-prevalence study, a formal sample size calculation was not applicable. Statistical significance was set at two-sided α of 0.05.

3. Results

Out of 558 patients screened with the surprise question, 294 were positive and were administered the NECPAL tool. Eventually, 254 out of the original 558 patients (45.5%) required PC. Mean age was 85.0 (± 11.0) years; female sex was prevalent (61% of the sample, $n = 178$) and exhibited higher PC needs than males ($p = 0.002$).

As shown in Table 1, NECPAL-positive patients had higher multimorbidity, advanced frailty status, and advanced dementia. The bar plot in Fig. 1 graphically represents the differences between NECPAL positive patients and their negative counterparts.

The individual variables examined are represented on the x-axis. The median value of each of these variables is represented on the y-axis.

Based on NECPAL CCOMS-ICO© 4.0 stage scoring, 33 patients (13%) scored stage I, 113 (44.5%) patients scored stage II and 107 patients (42.1%) scored stage III. As the NECPAL stage increased, a progression of frailty was recorded ($p < 0.001$).

Table 1

– Clinical characteristics of the sample.

Variable	ALL (n = 294)	NECPAL + (n = 254)	NECPAL – (n = 40)	pValue (Mann-Whitney)
Age (median, IQR)	85.0 (±11.0)	85.0 (±11.0)	85.5 (±10.3)	0.57
n° of drugs (median, IQR) (n = 294)	9 (±5)	9 (±5)	9 (±3.25)	0.34
CIRS S (median, IQR) (n = 294)	1.30 (±0.64)	1.36 (±0.64)	1.04 (±0.58)	<0.001
CIRS C (median, IQR) (n = 294)	6.0 (±3.0)	7.0 (±4.0)	5.0 (±2.0)	<0.001
CFS (median, IQR) (n = 282)	7.0 (±1.0)	7.0 (±2.0)	6.0 (1.0)	<0.001
CDR (median, IQR) (n = 138)	4.0 (±1.0)	4.0 (±1.0)	3.0 (±2.0)	<0.001

Abbreviations: IQR = Interquartile Range; CIRS S = Cumulative Illness Rating Scale Severity; CIRS C = Cumulative Illness Rating Scale Comorbidity; CFS = Clinical Frailty Scale; CDR = Clinical Dementia Rating Scale.

3.1. Prescription patterns

Polypharmacy was reported in 93.9% of patients ($n = 276$) with a median number of drugs of 9.0 (±5.0). Hyper polypharmacy (>10 drugs) was reported in 37.3% of the patients.

In the hospital setting, the median number of drugs was higher (10.0 (±5.0)) than in nursing homes 8.0 (±4.0) ($p < 0.001$).

The most prescribed drug pattern included PPIs, psychoactive drugs (30.6%), diuretics (26.5%), antihypertensive drugs (24.5%), antibiotics (18%) and lipid lowering drugs (14.6%) (Table 2).

As NECPAL stage increased, no significant difference in the total number of drugs for patient was observed.

NECPAL positive patients showed a prescription pattern characterized by antihypertensives ($p = 0.02$), diuretics ($p = 0.001$), PPIs ($p < 0.001$), steroids, psychoactive drugs ($p < 0.001$), and antibiotics ($p = 0.02$). When each class of drugs was classified based on NECPAL staging score, no significant difference was observed, except for antidiabetic drugs, as shown in Table 3.

3.2. PIMs distribution

The analysis of the five categories of PIMs showed that the median number of PIMs was 1 (±2), and 68.2% of patients were subjected to at least one PIM event. In particular, 31.8% ($n = 81$) of patients did not report any PIMs, 28.7% ($n = 73$) 25.2% ($n = 64$) reported 2 PIMs, 12.6% ($n = 32$) reported 3 PIMs and 1.6% ($n = 4$) reported 4 PIMs. Patients in nursing homes had fewer PIMs events than the in-hospital counterpart ($p < 0.001$).

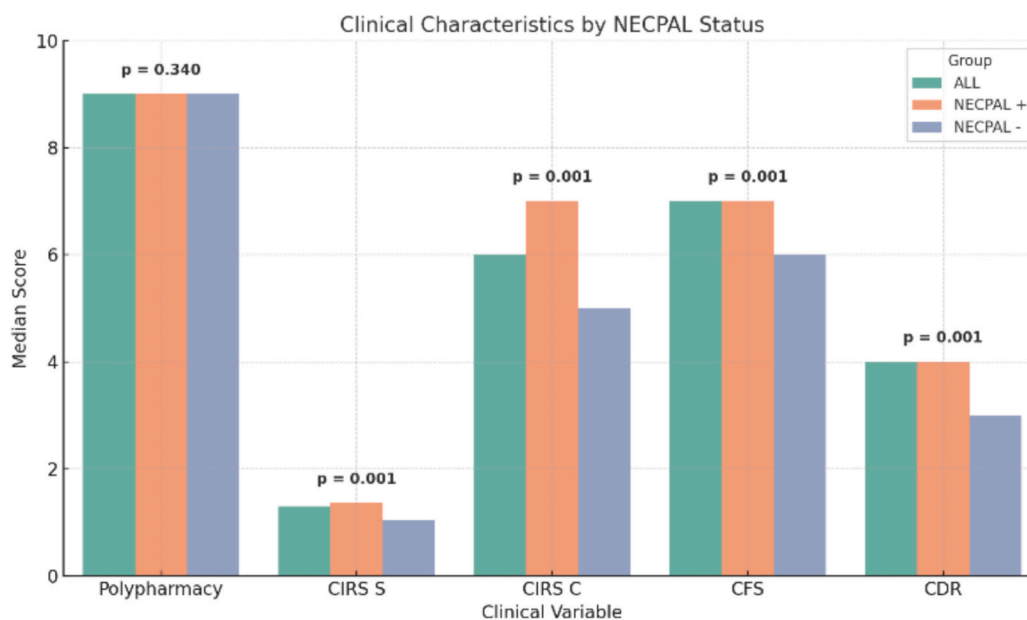
In the multivariate regression analysis (Table 4), PIMs showed a positive association with polypharmacy [IRR 1.04 (IC 95% 1.01–1.08) $p = 0.006$] and a negative association with living in nursing homes [IRR 0.43 (IC 95% 0.33–0.58), $p < 0.001$]. Due to the strong correlation with CFS ($p = 0.65$) and the small number of patients with CDR ($n = 138$), CDR variable was excluded from the multivariate analysis.

4. Discussion

This original study underscores the remarkably high prevalence of polypharmacy in PC old age patients across different care settings, including three Ligurian hospitals and two nursing homes, with a median of nine medications per patient. This older adult population requiring PC was characterized by advanced frailty and dementia and based on STOPP-Frail criteria, 68.2% of them received at least one PIM prescription. In addition, our findings demonstrated a significant positive association between polypharmacy and the presence of PIMs.

Our findings are in line with those reported by Sevilla-Sanchez et al. [30,31], that showed a disproportionately higher rate of polypharmacy (the mean number of drugs was 9.46 per patient) in older patients receiving PC in different settings such as nursing homes or hospital. Similarly, based on STOPP-Frail criteria, the authors found that 67.2% of patients received at least one (PIMs) prescription and in particular, the most common PIMs were from the alimentary tract and metabolism drugs [32]. Furthermore, a significant correlation between PIMs and polypharmacy was shown, supporting the conclusion that PIMs were associated with frailty rather than with increased mortality.

Similarly, Kirici et al. [24] evaluated the presence of polypharmacy, PIMs and related factors in older adults receiving PC. In their sample 59.2% of the patients had polypharmacy and 10.8% had

**Fig. 1. – Clinical characteristics of the sample according to NECPAL status**

Abbreviations: CIRS S = Cumulative Illness Rating Scale Severity; CIRS C = Cumulative Illness Rating Scale Comorbidity; CFS = Clinical Frailty Scale; CDR = Clinical Dementia Rating Scale.

Table 2 – PIMs distribution.

Drug	ALL (n = 294)	NECPAL + (n = 254)	NECPAL – (n = 40)	pValue (χ^2)
Antihypertensive	72 (24.5%)	68 (26.7%)	4 (10.0%)	0.02
Antidiabetics	32 (10.9%)	27 (10.6%)	5 (12.5%)	0.72
Lipid lowering drugs	43 (14.6%)	41 (16.1%)	2 (5.0%)	0.06
Diuretics	77 (26.2%)	75 (29.5%)	2 (5.0%)	0.001
Opioids	39 (13.3%)	35 (13.8%)	4 (10.0%)	0.51
Other pain drugs	18 (6.1%)	17 (6.7%)	1 (2.5%)	0.30
PPIs	153 (52%)	147 (57.9%)	6 (15%)	<0.001
Steroids	41 (13.9%)	40 (15.8%)	1 (2.5%)	0.02
Chemotherapy	10 (3.4%)	9 (3.5%)	1 (2.5%)	0.73
Continuous Benzodiazepines	2 (0.7%)	2 (0.8%)	0	0.57
Spot administration Benzodiazepines	27 (9.2%)	25 (9.8%)	2 (2.5%)	0.32
Psychoactive	90 (30.6%)	87 (34.2%)	3 (7.5%)	<0.001
Antibiotics	53 (18.0%)	51 (20.1%)	2 (2.5%)	0.02
Parenteral nutrition	14 (4.8%)	14 (5.5%)	0	0.13

Abbreviations: PPIs = Proton Pump Inhibitor.

Table 3

– Drugs distribution by NECPAL stage.

Drug	Stage 1 (n = 33)	Stage 2 (n = 113)	Stage 3 (n = 107)	pValue (χ^2 , Fisher exact test)
Antihypertensive	12	33	22	0.094
Antidiabetics*	7	7	13	0.047
Lipid lowering drugs	7	20	14	0.487
Diuretics	11	34	29	0.649
Opioids*	2	15	17	0.631
Other pain drugs	0	8	9	0.234
PPIs	20	69	57	0.446
Steroids	5	17	18	0.922
Chemotherapy*	0	6	3	0.455
Continuous Benzodiazepines*	0	1	1	1
Spot administration Benzodiazepines	3	13	9	0.772
Psychoactive	10	45	32	0.245
Antibiotics	6	23	22	0.929
Parenteral nutrition	1	6	7	0.804

Abbreviations: PPIs = Proton Pump Inhibitor.

* Where the number of drugs was small, Fisher's exact test was used.

hyperpolypharmacy. Polypharmacy was observed to increase the PIMs prescription use and the use of TIME criteria was helpful in reducing the inappropriateness of prescription patterns, in this vulnerable population.

Originally, our results showed a negative correlation between PIMs detection and living in nursing homes. Although preliminary in nature, this finding may support those reported by Lohman [33] in which nursing homes residents experienced a lower rate of PIMs compared to the hospital counterparts (40% vs 20%). This data can be attributed to the fact that hospitalized patients require acute therapy, which is often added to the chronic therapy already in place at the time of admission, potentially cumulating in a prescribing cascade and favoring iatrogenesis.

Notably, NECPAL positive patients showed a prescription pattern characterized by antihypertensives diuretics, PPIs, steroids, psychoactive drugs and antibiotics, suggesting that the prescription profile

Table 4

– Univariate and multivariate regression models with the number of PIMs as the dependent variable.

Variable	Univariate model		Multivariate model	
	IRR (IC 95%)	pValue	IRR (IC 95%)	pValue
Age	0.97 (0.96–0.98)	<0.001	0.99 (0.98–1.00)	0.605
Nursing home	0.45 (0.35–0.56)	<0.001	0.43 (0.33–0.58)	<0.001
Sex (ref. female)	0.69 (0.56–0.86)	<0.001	0.91 (0.72–1.15)	0.416
NECPAL stage (ref. stage 1)	0.87 (0.64–1.22)	0.408		
Stage 2				
Stage 3	0.79 (0.57–1.11)	0.166		
Polypharmacy	1.08 (1.05–1.11)	<0.001	1.04 (1.01–1.08)	0.006
CIRS S	1.18 (0.95–1.46)	0.131		
CIRS C	1.02 (0.98–1.06)	0.395		
CFS	0.92 (0.86–0.99)	0.022	1.01 (0.94–1.08)	0.763
CDR	0.80 (0.70–0.92)	0.002		

CIRS S = Cumulative Illness Rating Scale Severity; CIRS C = Cumulative Illness Rating Scale Comorbidity; CFS = Clinical Frailty Scale; CDR = Clinical Dementia Rating Scale; IRR = Incident Rate Ratio.

reflects the missed opportunity of both deprescription of drugs in advanced frailty and multimorbidity, and the failure in adaptation to patients care goals of symptom relief. In line with that, Lee et al. [34], in a retrospective study with a limited number of PIMs, identified them in 40.2% of older adults receiving PC, unveiling the maintenance of active treatments of underlying chronic diseases with intensive prescription of regular medications. Moreover, Jung [35] et al., in 2025, evaluated the prevalence of PIMs in older PC patients, finding 64.4% of them receiving an inappropriate medication, and demonstrated the related association with higher disability and mortality, after adjusting for frailty and polypharmacy, pointing out the key relevant role of PIMs detection in the appropriate prescription management of PC.

Based on our findings, it is worth noting that, although frailty was associated with the severity of PC needs according to NECPAL staging scoring, the number of drugs and the distribution of pharmacological prescription did not significantly differ with the worsening of NECPAL staging, with the exception of antidiabetic drugs. This last prescription pattern may hypothesize the concomitant presence of steroid therapy, which, contributing to hyperglycemia, leads to increased prescription of antidiabetics.

To the best of our knowledge, this is the first study to analyze prescribing patterns according to PC needs in frail older adults. Our findings suggest that patients who would benefit from specialized PC often continue to receive medications intended for primary or secondary prevention—drugs that are no longer necessary at this stage—thereby increasing the harm-to-benefit ratio and potentially triggering a prescription cascade.

In patients with advanced-stages diseases and higher intensity PC needs, such as NECPAL 3 stage patients in whom the median life expectancy is below 3.6 months of life [17], it is good practice to anticipate the possibility of frequent discomfort symptoms ensuring an effective adaptation of therapy to care goals, and quality of life.

Thus, the presence of polypharmacy and hyperpolypharmacy in PC patients reveals that physicians seem inattentive to deprescribing therapies in presence of advancing diseases, higher frailty and/or clinical complexity as reported by Turrillas in 2021 [17].

These Italian observations align with broader European data showing substantial polypharmacy among older adults, highlighting the unique intensity of medication use in vulnerable populations where frailty and multimorbidity are highly prevalent. Such high-intensity medication exposure in both hospitals and nursing homes underscores the importance of studying medication appropriateness and deprescribing strategies and provides context for interpreting the results of pharmacological risk assessments in regions with aging populations.

The main limitation of this study is the restricted availability of detailed prescription data for the entire sample (limited to 14 drugs

categories). This restriction forced us to group PIMs in only five groups, according to the STOPP-Frail 2.0 criteria. Moreover, because this is a nested study within a larger point-prevalence investigation aimed at assessing the epidemiological magnitude of PC needs among older Italian non-cancer patients, the depth of prescription analysis was inherently limited.

The interpretation of our findings should also consider the potential confounding influence of multimorbidity, frailty, and dementia status. These conditions frequently coexist in older adults with advanced illnesses and may both simultaneously affect prescribing. In our cohort, these factors were strongly interrelated, as shown by the substantial collinearity between CFS and CDR. This clinical profile may have diluted or masked specific associations between PC needs, polypharmacy, and PIMs.

The strengths of the study include the large sample size and the multicentric setting of a real-world cohort of very old age patients with non-cancer conditions, experiencing PC needs. Moreover, the analysis of the PC needs based on NECPAL staging scoring and the potential association with frailty, polypharmacy and PIMs detection may allow for refining the alignment of therapeutic strategies to patient's stage of life, considering the individual frailty trajectory and evolving higher intensity PC needs. Our results highlight the importance of the implementation of deprescribing strategies, tailored medication reviews, and closer collaboration between geriatricians, PC specialists, and other medical professionals. This approach could optimize treatment goals and quality of life at the end of life, minimize unnecessary medication burden, and support a shift toward care models centered on comfort, functionality, and quality of life, particularly in advanced frailty and multimorbidity.

5. Conclusions

Our findings reveal a substantial burden of both polypharmacy and inappropriate prescribing in older inpatients with PC needs, indicating a clear gap between current medication practices and the therapeutic approach required in this clinical context. Current practice appears to fall short of both effective deprescribing and fully aligning pharmacological therapy with goals of care and overall quality of life.

The persistence of PIMs in end-of-life care emphasizes the value of systematic instruments such as STOPP-Frail and NECPAL in optimizing medication management based on the individual trajectory of frailty.

Systematic efforts to align pharmacotherapy with patients' care goals and clinical status are essential to minimize harm and promote quality of life in the final stages of life. In this context, this preliminary study may serve as a guide for larger prospective studies with the objective of producing generalizable results and measuring the outcomes and impact of PIMs.

Contributors

Stefania Peruzzo contributed to study concept and design, interpretation of data, statistical analysis, and drafting of the manuscript.

Luca Tagliafico contributed to study concept and design, and interpretation of data.

Silvia Ottaviani contributed to study concept and design, and critical revision of the article.

Federica Della Rovere contributed to study concept and design, and critical revision of the article.

Carlo Marani contributed to study concept and design, and critical revision of the article.

Michela Mattioli contributed to study concept and design, and critical revision of the article.

Alessio Nencioni contributed to study concept and design, and critical revision of the article.

Fiammetta Monacelli contributed to study concept and design, and critical revision of the article.

All authors saw and approved the final version and no other person made a substantial contribution to the paper.

Ethical approval

This study was approved (CERA N 2024-54 12/06/2024) by the Institutional Review Board, University of Genoa, Italy.

Provenance and peer review

This article was not commissioned and was externally peer reviewed.

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Declaration of competing interest

The authors declare that they have no competing interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.maturitas.2026.108928>.

Data availability

There are no linked research data sets for this paper. Data will be made available on request.

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