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ORIGINAL RESEARCH ARTICLE

Use and Deprescribing of Potentially Inappropriate Medications in Frail Nursing Home Residents

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Abstract

Background The STOPPFrail criteria were developed to assist physicians in deprescribing medications among frail patients approaching end of life. We aimed to measure the prevalence of potentially inappropriate medications (PIMs) and to describe changes over time, using STOPPFrail, in frail nursing home residents (NHRs) with limited life expectancy included in a medication review trial.

Methods We conducted a post-hoc analysis of the COME-ON study, a cluster-controlled trial that evaluated the effect of a complex intervention on appropriateness of prescribing in Belgian nursing homes. We identified NHRs eligible for the application of STOPPFrail based on functional status, comorbidities, level of care and survival. PIM use was measured at baseline and at 8 months. Changes over time were compared in the control group (CG) and intervention group (IG).

Results At baseline, 308 NHRs met the STOPPFrail eligibility criteria, of whom 196 (64.1%) had one or more PIM. At 8 months, among the 218 NHRs who were alive, there was an absolute reduction in the prevalence of PIMs of 9.1% in the CG ($p < 0.05$) and 10.2% in the IG ($p < 0.05$). We found large reductions for some medications (e.g. proton pump inhibitors) but no reduction for others (e.g. calcium). The percentage of NHRs with one or more PIM discontinued without a new PIM initiated was higher in the IG than the CG but the difference was not significant (35.1% vs 23.6%, $p = 0.127$).

Conclusion Among frail NHRs with poor survival prognosis, a significant and encouraging decrease in PIM prevalence over time was observed, probably facilitated by medication reviews. The overall prevalence of PIMs remained high, however.

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Key Points

A large proportion of the frail nursing home residents had at least one potentially inappropriate medication (PIM) at baseline according to STOPPFrail criteria.

A significant and encouraging decrease in PIM prevalence over time was observed, but the overall prevalence of PIMs remained high, and no improvements were seen for some medication classes.

It is time to further educate health care providers to the identification, and possibly deprescribing, of PIMs using criteria that are best adapted to their patients.

1 Introduction

Most nursing home residents (NHRs) are exposed to a significant number of medications to treat chronic multimorbidity and symptoms [1, 2]. Along with polypharmacy, prescription of potentially inappropriate medication (PIM) often occurs [2]. Prescription of PIMs has been associated with poor outcomes such as adverse drug events (ADEs) [3, 4], hospitalizations [3, 5–10] and even death [5, 10], both in community-dwelling older adults and in NHRs.

PIMs are most often identified through the use of explicit criteria. The Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP) and Screening Tool to Alert doctors to Right Treatment (START) [11] and American Geriatrics Society (AGS) Beers criteria [12] are the most widely used explicit criteria to identify PIMs. These criteria have been validated for use in older people aged 65 years and over in general, and they may not fully apply to the nursing home (NH) population. Indeed, NHRs are frailer patients with shorter life expectancy than community-dwelling older people. In recent years, new sets that better apply to NHRs have been developed [13–15]. The STOPPFrail criteria were developed to assist physicians in deprescribing medications among frail patients approaching end of life [15]. They include 27 criteria. For less than half, there is overlap with the STOPP or Beers criteria. For example, proton-pump inhibitors (PPIs), anti-platelet drugs and lipid-lowering drugs are part of STOPPFrail. In contrast, benzodiazepines are not listed in STOPPFrail, but medications for osteoporosis, multivitamins and prophylactic antibiotics are included. A few recent studies used STOPP-Frail to describe the prevalence of PIMs in various settings [16–19]. Two observational studies were done in the NH setting and found a high prevalence of PIMs. However, the identification of PIMs in these studies was based on administrative dispensing data only. No clinical data were available, therefore limiting the applicability and validity of the measurements [19, 20].

The COME-ON (Collaborative approach to Optimise MEdication use for Older people in Nursing homes) study was a multicentre, cluster-controlled trial performed to evaluate the effect of a complex intervention on the appropriateness of medicines prescribed for older people in Belgian NHs [21–23]. The intervention included a blended learning programme, local interdisciplinary meetings and interdisciplinary case conferences. The intervention was associated with significant improvements in appropriateness of prescribing in the intervention group (IG) as compared to the control group (CG, i.e. usual care) [23]. PIMs were detected based on the STOPP/START (V2) and the AGS 2015 Beers criteria [11, 12]. The objectives of the present post-hoc analysis of the COME-ON study were (i) to measure the prevalence of PIMs at baseline, in a subset of frail NHRs with limited life expectancy, using STOPP-Frail, and (ii) among those NHRs still alive at mid-study follow-up, to describe changes of PIMs over time in both the CG and IG.

2 Methods

2.1 COME-ON Trial

The protocol of the COME-ON study has been published elsewhere [21]. Residents were eligible to participate if they were aged 65 and older, under the care of a participating general practitioner (GP), not in revalidation or short stay and not receiving palliative care at the time of informed consent. In total, 54 NHs (24 intervention; 30 control) and 1804 NHRs participated. Data collection was performed by the healthcare professionals (HCPs) involved in the care of each resident through a web application at baseline, mid-study (month 8) and end of study (month 15) [21].

2.2 Study Population

According to the authors of STOPPFrail, patients eligible for the application of the STOPPFrail criteria must meet the following conditions: (i) end-stage irreversible pathology, (ii) poor one-year survival prognosis, (iii) severe functional impairment and/or severe cognitive impairment, and (iv) symptom control is the priority rather than prevention of disease progression [15]. Using the data available in the COME-ON database on level of care, functional status, comorbidities, and occurrence of death during the study, the research team reached the following consensus on the NHRs who would be eligible for the application of STOPPFrail: (a) palliative care at baseline data collection; or (b) Cumulative Illness Rating Scale for Geriatrics (CIRS-G) score ≥ 4 (i.e. extremely severe) for at least one of the systems [24] and Katz category of dependency of C (full physical dependency, no dementia), Cd (full dependency and dementia) or D (diagnosis of dementia established by a neurologist, geriatrician or psychiatrist); or (c) CIRS-G score ≥ 3 (i.e. severe) for at least one of the systems, and a Katz category of C, Cd or D, and death over the study period.

For the evaluation of the prevalence of PIMs at baseline, we selected all NHRs who had complete baseline data (i.e. demographic, clinical, medical and medication data recorded by HCPs) and who met the STOPPFrail eligibility criteria listed above (referred to as 'baseline sample'). For measuring the evolution of PIM prevalence over time, we selected NHRs from the baseline sample who were still alive at mid-study (month 8; referred to as the 'follow-up sample'). This

timeframe (mid-study, month 8) was chosen to prevent a too-large proportion of missing data due to death if we had used end of study data (month 15).

2.3 Identification of Potentially Inappropriate Medications (PIMs) using STOPPFrail

From the 27 STOPPFrail criteria, six were excluded because of missing clinical information and ten were clarified or adapted based on discussions within the research team (see Supplementary Table S1 in the electronic supplementary material [ESM]). Similar to previous work [25], we developed a code in R software to identify STOPPFrail events from the research database. The data used included the medication, dosage and duration of use (e.g. for E1 *PPI at full therapeutic dosage for ≥ 8 weeks*), laboratory values (for I1 *antidiabetic agents, stringent glycaemic control is unnecessary*, we used HbA1c values), and clinical data (e.g. for C1 *anti-platelet agents used for primary cardiovascular prevention*). A pilot test was conducted on a subsample of 30 NHRs to check the code and edit when needed, before applying it to the whole database. The data used and coding rules are available in Supplementary Table S1 (see ESM).

The identification of PIMs was performed on the baseline and follow-up samples. When comparing baseline and follow-up data in the follow-up sample, PIM discontinuation was defined as stopping (i.e. complete cessation) of a PIM between baseline and follow-up, and PIM initiation as starting a new PIM that was not used at baseline.

2.4 Ethical Considerations

The COME-ON study was approved by the Ethics Committee of UZ Leuven (reference number s57145, ML11035) and performed in accordance with the Declaration of Helsinki and its later amendments. All NHRs or residents' representatives provided written informed consent.

2.5 Analysis

Descriptive methods were used to describe the characteristics of the study population and the use and evolution of PIMs over time. Continuous variables were described by their median (and interquartile ranges). Categorical variables were described by their frequencies (and percentages). Baseline and follow-up data in NHRs were compared using paired tests. A Wilcoxon signed-rank test was used for continuous variables and a McNemar's chi-squared test for categorical variables. The Pearson's chi-squared test was used to compare rates of PIM discontinuation and initiation between the control and intervention groups. All statistical analyses were performed using R software (version 3.3.3) [26]. A p value < 0.05 was considered statistically significant.

3 Results

Out of the 1804 NHRs included in the COME-ON study, 1507 (83.5%) had complete baseline data, of which 306 (20.3%) met STOPPFrail eligibility criteria according to our selection process. Their characteristics are presented in Table 1. Median age was 87 years, 97 (31.8%) had entered palliative care between informed consent and baseline data collection, 233 (76.1%) were fully dependent and/or had dementia and 192 (62.7%) died over the full study period (i.e. 15 months). As expected, STOPPFrail-eligible NHRs had more comorbidities and poorer functional status than the other NHRs. In contrast, both groups were similar with regard to age, sex, number of medications, recent fall or hospitalization.

At baseline, 365 (13.6%) of 2689 medications used in the 306 NHRs were potentially inappropriate (Table 2). These PIMs were identified in 196 (64.1%) of 306 NHRs. The median number of PIMs per NHR was 1 (IQR 0–2, range 0–7). The three most frequently encountered PIMs were (i) proton pump inhibitors (PPIs) at full dosage ≥ 8 weeks (E1, 18%), (ii) calcium supplementation (G1, 16.3%) and (iii) anti-platelet therapy for primary cardiovascular prevention (C1, 15.7%). Detailed data on PIMs at baseline are provided in Table 2.

At 8-month follow-up, 218 NHRs were still alive and had complete medication data available (Fig. 1). Two-thirds ($n = 146$, 67.0%) had at least one PIM at baseline. The prevalence of PIMs significantly decreased at follow-up to 57.3% (absolute reduction of 9.1% in CG and 10.2% in IG; $p < 0.05$ in both groups). Among the ten most frequent PIMs at baseline, the use of PPIs, anti-platelet agents for primary CV prevention and lipid lowering drugs (LLDs) significantly decreased between baseline and follow-up. The decrease was statistically significant for PPIs and LLDs in the IG only, and for anti-platelet agents in the CG only. The use of calcium supplementation did not decrease over time in either group. Detailed data are presented in Table 3.

Overall, PIM discontinuation among NHRs with at least one PIM at baseline occurred more frequently in the IG compared with the CG (45.9% vs 25.0%; $p = 0.008$) but PIM initiation also occurred more frequently in the IG (17.6% vs 7.3%; $p = 0.021$). The percentage of NHRs with at least one PIM discontinued without PIM initiated was higher in the IG but the difference was not statistically significant (35.1% vs 23.6%, $p = 0.127$).

Table 1 Characteristics of the study population at baseline

Study population	Included (i.e. eligible for application of STOPPFrail at baseline)	Excluded (i.e. not eligible for application of STOPPFrail at baseline)
Patients, *n* (%)	306 (20.3)	1201 (79.7)
Age in years, median [IQR]	87 [83;92]	87 [82;91]
Age, in years, *n* (%)		
< 80	56 (18.5)	233 (19.5)
80–90	150 (49.5)	604 (50.6)
> 90	97 (32.0)	356 (29.8)
Female gender, *n* (%)	214 (69.9)	865 (72.0)
Number of medications, median [IQR]	9 [6;12]	9 [6;12]
Number of medications, *n* (%)		
< 5	31 (14.8)	141 (11.7)
5–9	68 (32.5)	396 (33.0)
≥ 10	110 (52.6)	664 (55.3)
CIRS-G score, median [IQR]	12 [9; 16.75]	9 [5;13]
Common diagnoses[a], *n* (%)		
Dementia	238 (78.5)	643 (52.2)
Chronic kidney disease	82 (27.9)	337 (27.9)
Heart failure	89 (29.5)	259 (21.1)
Chronic lung disease (COPD)	39 (12.9)	139 (11.8)
Mobility data, *n* (%)		
Bedridden	41 (13.4)	11 (0.9)
Wheelchair	183 (59.8)	394 (32.8)
Mobile with help	48 (15.7)	482 (40.1)
Mobile, no support needed	34 (11.1)	314 (26.1)
Katz score, median [IQR]	21 [19; 23]	16 [12;19]
Dependency category (Katz scale)[b], *n* (%)		
O	2 (0.7)	143 (11.9)
A	2 (0.7)	198 (16.5)
B	12 (3.9)	405 (33.7)
C	57 (18.6)	133 (11.1)
Cd	222 (72.5)	296 (24.6)
D	11 (3.6)	26 (2.2)
Palliative care at baseline, *n* (%)	97 (31.8)	0 (0)
Life expectancy < 5 years, estimated by GP, *n* (%)	192 (71.9)	288 (29.9)
Fall(s) in the previous 3 months, *n* (%)	73 (24.2)	277 (23.1)
Hospitalization in the previous 3 months, *n* (%)	35 (11.4)	115 (9.6)
Death during the study period (15 months), *n* (%)	192 (62.7)	166 (13.8)

CIRS-G Cumulative Illness Rating Scale for Geriatrics, *COPD* chronic obstructive pulmonary disease, *GP* general practitioner, *IQR* interquartile range

[a]Most common diagnoses from the diagnoses considered in the STOPPFrail criteria

[b]Category O (cognitively fit and physically independent); category A (minor physical dependency, not dementia OR dementia and physically independent); category B (major physical dependency, not dementia OR dementia and minor physical dependency); category C (full physical dependency, not dementia); category Cd (full dependency and dementia); category D (diagnosis of dementia established by a neurologist, geriatrician or psychiatrist)

Table 2 Potentially inappropriate medications at baseline according to STOPPFrail (baseline sample, $N = 306$)

Overall prevalence (306 NHRs, 2689 prescriptions)	
Medications identified as PIM, n (%)	365 (13.6)
PIM per NHR, median [IQR; range]	1 [0–2; 0–7]
NHR with ≥ 1 PIM, *n* (%)	196 (64.1)
NHR with 1 PIM, *n* (%)	102 (33.3)
NHR with 2 PIMs, *n* (%)	47 (15.4)
NHR with ≥ 3 PIMs, *n* (%)	47 (15.4)
Prevalence per STOPPFrail criterion, *n* (%)	
E1. PPI, long-term high dose	55 (18.0)
G1. Calcium supplementation	50 (16.3)
C1. Anti-platelet agent for primary CV prevention	48 (15.7)
J1. Multi-vitamin combination supplements	39 (12.7)
I1. Antidiabetic agent and stringent glycaemic control	27 (8.8)
B1. Lipid lowering therapy	35 (11.4)
D1. Neuroleptic antipsychotic for > 12 weeks without BPSD	23 (7.5)
J3. Prophylactic antibiotic	16 (5.2)
E3. Regular daily prescription of GI antispasmodic	13 (4.2)
G5. Long-term oral steroid	11 (3.6)
E2. H2 receptor antagonist, long-term high dose	8 (2.6)
G4. Long-term NSAID	7 (2.3)
G2. Anti-resorptive/bone anabolic drug for osteoporosis	7 (2.3)
I2. ACE inhibitor for diabetes	3 (1.0)
I4. Systemic oestrogens for menopausal symptoms	1 (0.3)
I3. Angiotensin receptor blocker for diabetes	1 (0.3)
G3. SORM for osteoporosis	0 (0.0)
F2. Leukotriene antagonist for COPD	0 (0.0)
F1. Theophylline	0 (0.0)
D2. Memantine for moderate/severe dementia	0 (0.0)
B2. α-blocker for hypertension	0 (0.0)

ACE angiotensin converting enzyme, *BPSD* behavioural and psychological symptoms of dementia, *COPD* chronic obstructive pulmonary disease, *CV* cardiovascular, *GI* gastrointestinal, *NHR* nursing home resident, *NSAID* non-steroidal anti-inflammatory drug, *PIM* potentially inappropriate medication, *PPI* proton pump inhibitor, *SORM* selective oestrogen receptor modulator

4 Discussion

The present study shows that, in a subgroup of frail NHRs, PIM use identified using the STOPPFrail criteria is highly prevalent. Almost two-thirds of NHRs received at least one PIM, and one out of seven medications was identified as a PIM. Interestingly, PIM prevalence significantly decreased over time, and the data suggest the medication review process implemented in the COME-ON trial enables more PIM discontinuation. This is, to the best of our knowledge, one of the first experimental studies to describe PIMs in a multicentric sample of NHRs with an explicit set of criteria specifically designed for such a frail older population with a poor 1-year survival prognosis.

A few recent observational studies evaluated the prevalence of PIMs using STOPPFrail, and two were conducted in the NH setting [16–20]. The most prevalent classes of PIMs involved were similar to the classes found in the present study. Yet, overall prevalence of PIMs was higher than in the present study (> 80% compared with 64% in the present study), and prevalence of PIMs for specific classes of drugs such as PPIs, multivitamins, neuroleptic drugs and statins was twice as high in other studies compared with the present study. There are several possible explanations. First, we may have been more specific in our PIM detection, as we considered in our evaluations data on diagnoses, dosages and duration of treatment, while three studies only used administrative data with ATC codes [17, 19, 20]. Second, NHs and GPs included in the COME-ON study voluntarily applied to participate. They had some interest in medication review. Deprescribing may have occurred before the study started. Third, the study populations in the respective papers differed and our process for selecting NHRs was more restrictive than in other studies.

Very recently, Curtin et al. [27] performed a randomized controlled trial in two acute hospitals in Ireland. Although the setting differed, they were able to demonstrate that STOPPFrail-guided deprescribing significantly reduced polypharmacy and even medication costs. A direct comparison with the results from the present study is not possible, however, as the authors did not report prevalence of STOPPFrail medication before and after the intervention.

An overall 10% absolute decrease in prevalence of PIMs was observed over an 8-month period. This result is encouraging as it indicates that deprescribing is considered and partially implemented in practice. This contrasts with data from a population study in Belgian older adults showing that the prevalence of PIM increased toward death, even though deprescribing occurred more frequently in NHRs [17]. Similarly, deprescribing rates achieved in the present study were higher than in other studies. Deprescribing (i.e. cessation) of at least one PIM without PIM initiation occurred in one-fourth to one-third of NHRs. In another study on 296 NHRs from Flanders (Belgium), deprescribing (defined as cessation or decrease in dosage) was observed in 31% of NHRs but new PIMs were initiated in 30% of NHRs [19]. The higher prevalence of PIM discontinuation in the intervention group suggests that the medication review process implemented in the COME-ON study contributed to this favourable effect, even though this would require confirmation in a new prospective controlled trial.

Deprescribing occurred mainly for those medications also considered as PIMs by the STOPP or Beers criteria (i.e. PPIs, aspirin, and LLDs). In contrast, deprescribing of calcium, multivitamins and antidiabetic agents was (almost)

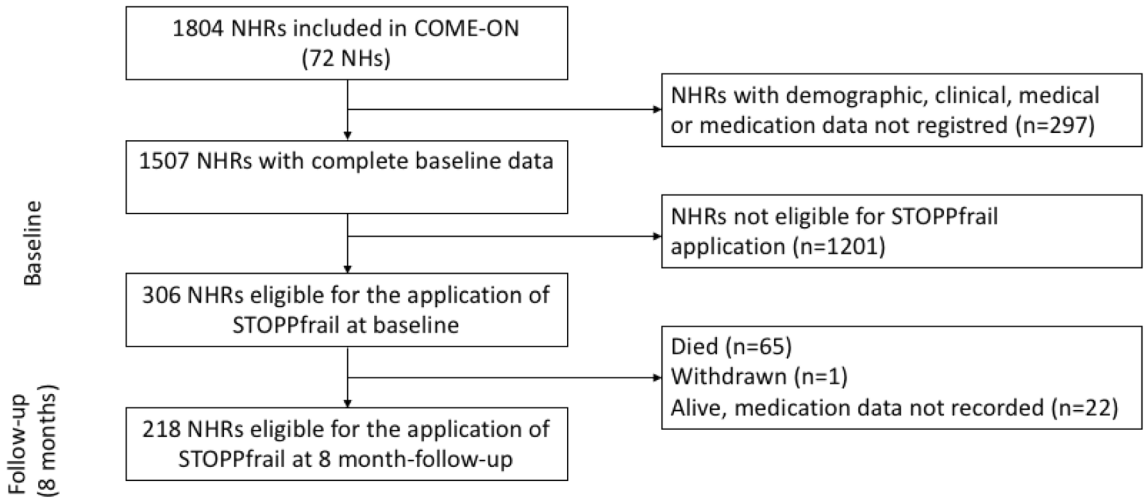

Fig. 1 Study flow chart. *NH* nursing homes, *NHRs* nursing home residents

not observed. More than half of the STOPPFrail criteria are not listed as PIMs by the STOPP and Beers criteria (e.g. calcium, multivitamins, antidiabetic agents, prophylactic antibiotics). Calcium or bisphosphonates, listed in STOPPFrail, are even part of the START criteria. Over the last decade, there have been a lot of efforts worldwide to educate physicians and pharmacists towards appropriate prescribing in older people, and the STOPP/START or Beers criteria were widely used to support this education. In the COME-ON study, the HCPs from the intervention group were trained in an implicit medication review approach. They were also trained in using an explicit list of PIMs to facilitate the identification of PIMs, and this list came from the STOPP-START/Beers but not from the STOPPFrail criteria, the latter being published after the COME-ON study started. One set of explicit criteria does not fit all older patients. Our data suggest that it is now time to educate HCPs on the use of other tools that are more specific or better adapted to the NH setting. This would contribute to better individualized approaches to identifying and deprescribing of PIMs.

Our study has several limitations. First, the identification of STOPPFrail-eligible patients was performed retrospectively using a combination of clinical and functional data. The selection may have been too restrictive. A prospective identification would have been preferred, but was not foreseen. Second, we did not ask a senior clinician to review each case and assess whether PIMs were actually appropriate for each individual patient. Even in this case, the clinician may have missed contextual information to confirm PIMs. Moreover, our identification of PIMs went beyond identification of ATC codes, as it also considered dosages, duration and clinical data. This makes our evaluations more specific than in previous studies [17, 19, 20]. Third, the analysis was made on a subsample of NHRs and statistical analysis did not account for missing data and multi-level effects. Definite conclusions on the effect of the intervention on STOPPFrail events can therefore not be drawn. Finally, we used a measure to detect PIM (i.e. STOPPFrail) that was published after the COME-ON trial started. These criteria were therefore unknown to prescribers, but the implicit nature of the medication review process enabled the identification of inappropriate medications beyond an existing explicit list.

5 Conclusion

A large proportion of the frail NHRs with poor survival prognosis had at least one PIM at baseline according to STOPPFrail. A significant decrease in PIM prevalence was observed over time, even though the overall prevalence of PIMs remained high, above 50%. It is time to further educate HCPs to the identification, and possibly deprescribing, of PIMs using criteria that are best adapted to their patients. Future research should evaluate the effect of using STOPP-Frail or other NH-specific lists of PIMs on outcomes that matter to patients [28].

Table 3 PIMs at baseline and follow-up according to STOPPFrail (follow-up sample, $N=218$)

	Total ($N=218$)			Control group ($n=110$)			Intervention group ($n=108$)		
	Baseline (1935 prescriptions)	follow-up (1786 prescriptions)	*p* value	Baseline (1014 prescriptions)	Follow-up (928 prescriptions)	*p* value	Baseline (921 prescriptions)	Follow-up (858 prescriptions)	*p* value
PIM prevalence									
Prescriptions identified as PIM, *n* (%)	258 (13.3)	217 (12.2)	0.280	126 (12.4)	112 (12.1)	0.811	132 (14.3)	105 (12.2)	0.194
PIM per NHR, median [IQR]	1 [0–2]	1 [0–2]	<0.001	1 [0–2]	1 [0–2]	0.103	1 [0–2]	1 [0–2]	<0.001
NHR with ≥ 1 PIM, *n* (%)	146 (67.0)	125 (57.3)	<0.001	72 (65.5)	62 (56.4)	0.004	74 (68.5)	63 (58.3)	0.008
NHR with 1 PIM, *n* (%)	76 (34.9)	65 (29.8)		39 (35.5)	33 (30.0)		37 (34.3)	32 (29.6)	
NHR with 2 PIMs, *n* (%)	39 (17.9)	34 (15.6)		19 (17.3)	13 (11.8)		20 (18.5)	21 (19.4)	
NHR with ≥ 3 PIMs, *n* (%)	31 (14.2)	26 (11.9)		14 (12.7)	16 (14.5)		17 (15.7)	10 (9.3)	
Prevalence per criterion (for the 10 most frequent PIMs at baseline), *n* (%)									
E1. PPIs, long-term high dose	41 (18.8)	30 (13.8)	0.012	21 (19.1)	19 (17.3)	0.480	20 (18.5)	11 (10.2)	0.007
G1. Calcium supplementation	40 (18.3)	40 (18.3)	0.999	16 (14.5)	16 (14.5)	0.999	24 (22.2)	24 (22.2)	0.999
C1. Anti-platelet agents for primary CV prevention	37 (17.0)	25 (11.5)	0.005	27 (24.5)	20 (18.2)	0.035	10 (9.3)	5 (4.6)	0.059
B1. Lipid-lowering therapies	28 (12.8)	18 (8.3)	0.004	13 (11.8)	9 (8.2)	0.103	15 (13.9)	9 (8.3)	0.014
J1. Multi-vitamin combination supplements	24 (11.0)	23 (10.6)	0.655	10 (9.1)	12 (10.9)	0.157	14 (13.0)	11 (10.2)	0.083
I1. Antidiabetic agents and stringent glycaemic control	19 (8.7)	23 (10.6)	0.206	8 (7.3)	7 (6.4)	0.317	11 (10.2)	16 (14.8)	0.096
D1. Neuroleptic antipsychotics for > 12 weeks without BPSD	17 (7.8)	15 (6.9)	0.317	7 (6.4)	5 (4.5)	0.157	10 (9.3)	10 (9.3)	0.999
J3. Prophylactic antibiotics	13 (6.0)	9 (4.1)	0.103	7 (6.4)	6 (5.5)	0.317	6 (5.6)	3 (2.8)	0.180
E3. Regular daily prescription of GI antispasmodics	9 (4.1)	7 (3.2)	0.317	4 (3.6)	4 (3.6)	0.999	5 (4.6)	3 (2.8)	0.157
G5. Long-term oral steroids	8 (3.7)	8 (3.7)	0.999	4 (3.6)	4 (3.6)	0.999	4 (3.7)	4 (3.7)	0.999

BPSD behavioural and psychological symptoms of dementia, *CV* cardiovascular, *GI* gastrointestinal, *NHR* nursing home resident, *PPIs* proton pump inhibitors

Declarations

Author contributions AF, AS, JBB and PA designed the study. AF, AS, PA, JBB, OD and SH analysed the data. AF, PA, OD, AS, VF and JBB wrote the manuscript. All authors contributed to and approved the final version of the manuscript.

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