

ORIGINAL ARTICLE OPEN ACCESS

Use of Potentially Inappropriate Medications Identified by STOPPFrail Among Danish Care Home Residents: A Nationwide Drug Utilisation Study

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Received: 14 March 2025 | **Revised:** 11 June 2025 | **Accepted:** 21 June 2025

Funding: The authors received no specific funding for this work.

Keywords: care home residents | drug utilisation | nationwide | older people | STOPPFrail

ABSTRACT

Care home residents represent a frail population with limited life expectancy and are often prescribed multiple medications. As therapeutic goals shift in this population, certain treatments may become inappropriate. This study aims to describe potentially inappropriate medication use among Danish care home residents using the Screening Tool of Older Persons Prescriptions in Frail adults with limited life expectancy (STOPPFrail) in a nationwide cohort of all Danish care home residents admitted 2015–2023, focusing on the time around admission and the last year of life. The cohort comprised 129 635 residents (61% women, median age 84 years). Around admission, 88% used at least one STOPPFrail medication, most commonly antihypertensives (58% before, 55% after), lipid-lowering therapies (31%, 27%) and proton-pump inhibitors (30%, 30%). The rate of new use increased from 2.6/100 residents/month 2 years before admission, peaking at 9.6/100 residents/month 2 months prior. Hospital physician prescribing increased as care home admission approached, after which general practitioners prescribed most prescriptions. Over 90% used at least one STOPPFrail medication during the last year of life, with increases in proton-pump inhibitors and antipsychotics, the latter most frequently initiated in the last 4 months. These findings underscore the importance of regular assessment and targeted efforts to improve prescribing appropriateness.

1 | Background

Older people admitted to care homes represent a frail population [1]. In Denmark, the median survival after admission is approximately 26 months, reflecting a relatively limited life expectancy in this population [2]. Further, admission to care homes in Denmark is associated with increased use of medications before admission and remains at a high level [3]. This

often leads to polypharmacy, commonly defined as the concurrent use of five or more medications [4]. Polypharmacy is closely tied to underlying morbidity [5] and is associated with adverse drug events, hospitalisations, cognitive decline and increased mortality [6–8]. Due to care home residents' frailty and limited life expectancy, therapeutic goals will often differ from those of the background population, making certain medications inappropriate and emphasising the need for thoughtful

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Summary

Care home residents are often living with frailty, have limited life expectancy and use multiple medications. As therapeutic goals shift, certain medications may become inappropriate. This study examined the use of potentially inappropriate medication in Danish care home residents admitted 2015–2023. Most residents used at least one potentially inappropriate medication around care home admission, with new use peaking two months prior. These treatments were often started by hospital prescribers. In their last year of life, the majority also received at least one potentially inappropriate medication. These findings highlight the need for regular medication assessment to ensure appropriate prescribing.

prescribing [9]. Care home residents are more often prescribed inappropriate medications than community-dwelling older people [10, 11], increasing the risk of adverse drug events, hospital admissions and reduced quality of life [12–14].

The appropriateness of prescribing can be assessed using the Screening Tool of Older Persons Prescriptions in Frail adults with limited life expectancy (STOPPFrail), developed and validated in 2017 and updated in 2020 [15, 16]. STOPPFrail is an explicit list of potentially inappropriate medications for older adults living with frailty for whom the goal of care is to optimise quality of life and minimise the risk of drug-related morbidity. It is intended for individuals with limited life expectancy, operationalised as those for whom their physician would not be surprised if they died within the next 12 months and individuals requiring assistance with daily activities [15], making it particularly suitable for care home populations.

Gaining insight into the current prescribing patterns and the prevalence of potentially inappropriate medication use among care home residents is essential for developing targeted strategies and interventions to reduce their use. Currently, this information is unknown among Danish care home residents. This study aimed to examine the use of potentially inappropriate medications identified by STOPPFrail among Danish care home residents, focusing on two objectives: (1) use among all care home residents around the time of admission and (2) use specifically during the last year of life.

2 | Methods

This nationwide descriptive register-based drug utilisation study examined the use of potentially inappropriate medications identified using STOPPFrail among a cohort of all individuals admitted to a care home in Denmark between 1 January 2015 and 31 December 2023. Each individual contributed a single residency.

2.1 | Setting

In Denmark, care home residency is designated for individuals living with frailty in need of all-day care. While all Danish

citizens can apply for care home residency, the allocation of care is determined by local municipalities, independent of socio-economic status and solely based on functional capacity [17]. Although care homes in Denmark are governed by the Danish Consolidation Act on Social Services, the municipalities are responsible for their organisation [17]. As a result, there may be minor differences in the level of services provided. Within Danish care homes, a team consisting of nurses, nurse assistants and therapists facilitates the care of the residents, including personal care and administration of medication. Further, by the end of 2023, over 90% of Danish care homes had a designated physician [18]. Upon admission, residents can choose to keep their previous general practitioner (GP) or switch to the designated physician [19].

2.2 | Data Sources

The cohort was assembled, encrypted and provided by the Danish Health Data Authority and linked to data from the Danish health registers, including the Danish National Prescription Registry [20], the Danish National Patient Registry [21] and the Civil Registration System [22].

The Danish National Prescription Registry contains data on all prescriptions filled at Danish pharmacies since 1995, including prescriptions to care home residents, and was used to identify potentially inappropriate medications using STOPPFrail. Data include variables such as medication type (according to the Anatomic Therapeutic Chemical (ATC) index), dispensing date and prescriber identifier [23]. Prescribers were categorised as GPs, private specialists or hospital physicians. We linked the prescriber identifier to the Registry of Health Care Providers to identify the medical specialty of primary sector prescribers [24]. The Prescription Registry does not contain in-hospital and over-the-counter medication use.

The Danish National Patient Registry contains information on all hospital admissions and outpatient contacts since 1995, with diagnoses coded using the International Statistical Classification of Diseases, version 10 (ICD-10) [25]. It does not contain data on diagnoses from the primary care sector. Data on hospital diagnoses were used to assess comorbidity and were combined with individual-level data on medication use for certain comorbidities. Information on age, sex and vital status was obtained from the Civil Registration System.

2.3 | STOPPFrail

This study used the most recent version of STOPPFrail from 2020 [16], focusing on selected medications that were available by prescription in Denmark. We excluded calcium supplements, vitamin D, multivitamins, folic acids and nutritional supplements. Because many of these products are registered as dietary supplements and not medications, we did not have access to the necessary data [26]. In total, 17 of the 22 medication classes listed in STOPPFrail were analysed and grouped into the original organ-specific eight sections [16]. The specific STOPPFrail medications and ATC codes used in this study are available in Appendix 1.

2.4 | Ethics and Approvals

The study was registered on the repository of the University of Southern Denmark (notification number 11.277). According to Danish law, ethical approval is not required for purely registry-based studies [27]. The study was conducted in accordance with the Basic & Clinical Pharmacology & Toxicology policy for experimental and clinical studies [28].

2.5 | Analyses

2.5.1 | Characteristics

The study cohort was described in terms of resident characteristics at the time of admission for all care home residents admitted during 2015–2023 and at the time of death for those who died during 2018–2023. This description included sex, age, number of medications used (defined as medications filled during the last 4 months before admission/death, as this period reflects typical prescription durations in Denmark), number of hospitalisations during the previous year before admission/death, the Nordic Multimorbidity Index [29] and selected comorbidities. ICD-10 and ATC codes used to define comorbidities are available in Appendix 2.

2.5.2 | Use of STOPPFrail Medications Among All Care Home Residents

Several analyses were conducted to describe the use of potentially inappropriate medications identified using STOPPFrail among care home residents admitted during 2015–2023.

First, we calculated the median number of medication classes identified by STOPPFrail prescribed 4 months before and after admission.

Second, for each medication class, we calculated the proportion of residents who filled at least one prescription: (1) 4 months before admission, (2) 4 months after admission, (3) the period before but not after, (4) the period after but not before and (5) both periods. This analysis was restricted to residents surviving the entire 4 months after admission.

Third, we determined the rate of incident use of any STOPPFrail medication class as well as the individual medication classes per 100 residents per month in the 2 years before and after admission. Incident use was defined as the first filled prescription for a given medication class in at least 2 years.

Fourth, we examined the prescriber types responsible for initiating treatment (incident prescriptions) and maintaining treatment (nonincident prescriptions) overall and for STOPPFrail medications. We determined the proportion of prescriptions issued by GPs, private specialists and hospital physicians each month within the 2 years before and after care home admission.

Lastly, treatment persistence was analysed using the ‘proportion of patients covered’ approach [30]. Among care home residents who were current users of a given medication class at the time of admission, we calculated the monthly proportion of residents

still alive who had filled a prescription for the given medication class within the last 4 months. A resident was considered a current user at admission if a prescription for the given medication class was filled within the 4 months before admission. Each resident was followed until the end of the study period, death or up to a maximum of 3 years.

2.5.3 | Use of STOPPFrail Medications Specifically During the Last Year of Life

We examined the use of potentially inappropriate medications identified by STOPPFrail during the last year of life among residents who died during 2018–2023. Because the data material included individuals admitted into care homes from 2015 onwards, we restricted the analyses to the period from 2018 onwards to improve comparability in the cohort over time. We included residents regardless of their care home admission status during the entire 12 months preceding their death.

First, we calculated the prevalence proportion of any STOPPFrail medication and each specific STOPPFrail medication used during the last year of life for each study year.

Second, we calculated the median number of STOPPFrail medication classes used by each resident in 4-month intervals in a 12-month time window before death.

Lastly, we investigated the extent to which potentially inappropriate medications were discontinued or initiated in the last period of life. For each medication class, we calculated the proportion of residents who filled at least one prescription in the following periods: (1) 12 to 8 months before death, (2) 8 to 4 months before death, (3) 4 to 0 months before death, (4) the two first periods but not the last (discontinuation), (5) the last period but not the two first (initiation) and (6) all periods (continuation).

All analyses were performed using R version 4.3.3.

3 | Results

3.1 | Characteristics

The study cohort comprised 129 635 care home residents (61% women), with a median age of 84 years (interquartile range (IQR) 77–89), and the median number of medications used was 8 (IQR 5–12) (Table 1). The most common comorbidities were dementia (35%) and atrial fibrillation (25%). The median number of hospitalisations during the last year before admission was 1 (IQR 0–2).

A total of 75 464 care home residents died during 2018–2023, with a median age of 87 years (IQR 80–92). The median number of medications at the time of death was 11 (IQR 8–14).

3.2 | Use of STOPPFrail Medications Among All Care Home Residents

Residents used a median of two STOPPFrail medication classes (IQR 1–3), with 88% using at least one class in both the 4 months

TABLE 1 | Characteristics of the total cohort of Danish care home residents admitted during 2015–2023 ($n = 129\,635$) and specified for those who died between 2018 and 2023 ($n = 75\,464$).

	Care home residents admitted during 2015–2023 ($n = 129\,635$)	Care home residents who died during 2018–2023 ($n = 75\,464$)
Sex, n (%)		
Men	51 200 (39)	30 491 (40)
Women	78 435 (61)	44 973 (60)
Age at admission or death, median [IQR]	84 [77–89]	87 [80–92]
Age at admission or death, n (%)		
> 65 years	5338 (4.1)	1589 (2.1)
65–74 years	16 773 (13)	6437 (8.5)
75–89 years	76 869 (59)	40 580 (54)
≥ 90 years	30 655 (24)	26 858 (36)
Number of medications at admission or death, median [IQR]	8 [5–12]	11 [8–14]
Number of medications at admission or death, n (%)		
0	2225 (1.7)	181 (0.20)
1–4	23 118 (18)	5184 (6.9)
5–9	52 738 (41)	25 019 (33)
≥ 10	51 554 (40)	45 080 (60)
Hospitalisations during the last year prior to admission or death, median [IQR]	1 [0–2]	1 [0–2]
Hospitalisations during the last year prior to admission or death, n (%)		
0	42 000 (32)	26 770 (35)
1–2	61 072 (47)	33 806 (45)
≥ 3	26 563 (20)	14 888 (20)
Nordic Multimorbidity Index [29], median [IQR]	22 [13–32]	31 [21–41]
Comorbidity, n (%)		
COPD	30 747 (24)	20 756 (28)
Dementia	45 852 (35)	31 813 (42)
Ischemic heart disease	25 047 (19)	16 174 (21)
Heart failure	15 098 (12)	12 574 (15)
Atrial fibrillation	32 259 (25)	22 489 (30)
Stroke	28 730 (22)	19 027 (25)
Diabetes mellitus	24 480 (19)	15 543 (21)

Abbreviation: COPD, chronic obstructive pulmonary disease.

before and after care home admission (Table 2). In both periods, the most frequently used STOPPFrail medication classes were antihypertensives (58% before, 55% after), lipid-lowering therapies (31% before, 27% after) and proton-pump inhibitors (PPIs) (30% in both periods). The most frequently used medication classes in the period after but not before admission were antihypertensives (4.9%), PPIs (4.6%) and antipsychotics (4.2%) (Table S1).

The rate of new use of any STOPPFrail medication classes increased in the months leading up to admission, starting at 2.6/100 residents/month 2 years before admission and peaking at 9.6/100 residents/month 2 months prior (Figure 1). After admission, the rate declined over the following 6 to 9 months, eventually returning to levels similar to those observed before the increase. The most frequently STOPPFrail medication

TABLE 2 | The frequency of prescribed potentially inappropriate medications identified using STOPPFrail in the periods 4 months before and 4 months after care home admission ($n = 110\,050$).

	Proportion of prevalent users in the period 4 months before admission, n (%)	Proportion of prevalent users in the period 4 months after admission, n (%)
Any STOPPFrail medication class	96 718 (88)	96 437 (88)
Section B: Cardiovascular system		
Any	74 010 (67)	70 934 (64)
Lipid-lowering therapies	33 788 (31)	30 112 (27)
Antihypertensive therapies	64 232 (58)	61 061 (55)
Anti-anginal therapy	5 760 (5.2)	5 864 (5.3)
Section C: Coagulation system		
Any	35 623 (32)	33 499 (30)
Antiplatelets	19 430 (18)	18 730 (17)
Aspirin	19 083 (17)	16 613 (15)
Section D: Central nervous system		
Any	22 566 (21)	23 861 (22)
Neuroleptic antipsychotics	15 088 (14)	15 773 (14)
Memantine	9 302 (8.5)	10 688 (9.7)
Section E: Gastrointestinal system		
Any	32 906 (30)	32 643 (30)
Proton-pump inhibitors	32 864 (30)	32 604 (30)
H2 receptor antagonists	57 (0.05)	60 (0.05)
Section F: Respiratory system		
Any	477 (0.43)	427 (0.39)
Theophylline	125 (0.11)	99 (0.09)
Leukotriene antagonists	358 (0.33)	333 (0.30)
Section G: Musculoskeletal system		
Any	21 818 (20)	20 746 (19)
Anti-resorptive/bone anabolic drugs for osteoporosis	11 252 (10)	11 272 (10)
Oral NSAIDs	5 979 (5.4)	4 833 (4.4)
Oral corticosteroids	7 139 (6.5)	6 915 (6.3)
Section H: Urogenital system		
Any	11 337 (10)	10 581 (9.6)
Drugs for benign prostatic hyperplasia	6 597 (6.0)	6 197 (5.6)
Drugs for overactive bladder	5 361 (4.9)	4 949 (4.5)
Section I: Endocrine system		
Antidiabetic drugs	14 274 (13)	14 023 (13)

Abbreviation: NSAIDs, non-steroidal anti-inflammatory drugs.

classes that were initiated were largely similar before and after admission, with PPIs and antipsychotics being the most common (Tables S2 and S3).

GPs were responsible for the majority of STOPPFrail treatment initiations 2 years before care home admission (57%), followed by hospital physicians (35%) (Figure 2). As care home admission

approached, the proportion of prescriptions issued by hospital physicians increased, peaking at 56% 2 months before admission. Subsequently, this trend reversed, with GPs steadily issuing a growing proportion of prescriptions, reaching 71% 2 years after admission. Among incident STOPPFrail prescriptions issued by hospital physicians, most were issued by departments of neurology (26% and 18%, before and after care home admission), followed by internal medicine (16% and 14%). Only 9.7% and 7.3% were issued from geriatric departments (Table S4). Similar patterns were observed for initiating prescriptions across all medications, although GPs accounted for an even higher proportion. Additionally, GPs were responsible for the vast majority of prescriptions for maintaining treatment (Figure S1).

A high proportion of residents continued treatment with a STOPPFrail medication following admission, with users of anti-diabetic drugs, antiplatelets, antihypertensives and leukotriene

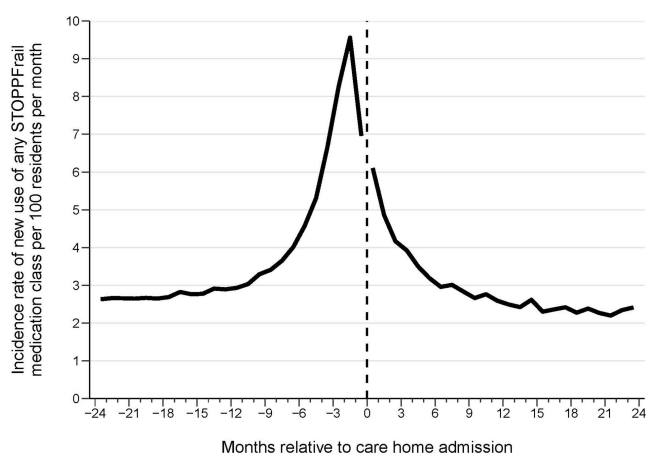


FIGURE 1 | Incidence rate of new use of any potentially inappropriate medication identified by STOPPFrail per 100 residents per month in the period 2 years before and after care home admission.

antagonists showing the highest persistence (Figure 3). In contrast, residents using oral non-steroid anti-inflammatory drugs (NSAIDs) and H2 receptor antagonists tended to discontinue therapy sooner.

3.3 | Use of STOPPFrail Medications During the Last Year of Life

Among residents who died in 2018, 94% used at least one STOPPFrail medication in the last year of life, decreasing slightly to 92% in 2023 (Table S5). From 2018 to 2023, the prevalence of low-dose aspirin use decreased from 22% to 15%, NSAID use from 9.7% to 6.1%, and the use of antipsychotics increased from 29% to 34%.

The median number of STOPPFrail medication classes remained constant at 2 (IQR 1–3) throughout the last year of life. The most prominent STOPPFrail medications during the periods 12–8 and 8–4 months before death were antihypertensives (54% and 52%, respectively), PPIs (30% and 32%) and lipid-lowering therapies (22% and 20%) (Table S6). In the period 4–0 months before death, use remained high for antihypertensives (49%) and PPIs (35%). Antipsychotics were the most frequently initiated medication class during this period (15%), making them the third most used medication class in the last 4 months of life (29%). Other frequently initiated medications included PPIs (5.9%) and oral corticosteroids (4.8%). The percentage of discontinued medication classes ranged from 0.01% for H2 receptor antagonists and theophylline to 6.5% for antihypertensives.

4 | Discussion

This nationwide study examined the use of potentially inappropriate medications, as identified by STOPPFrail, among

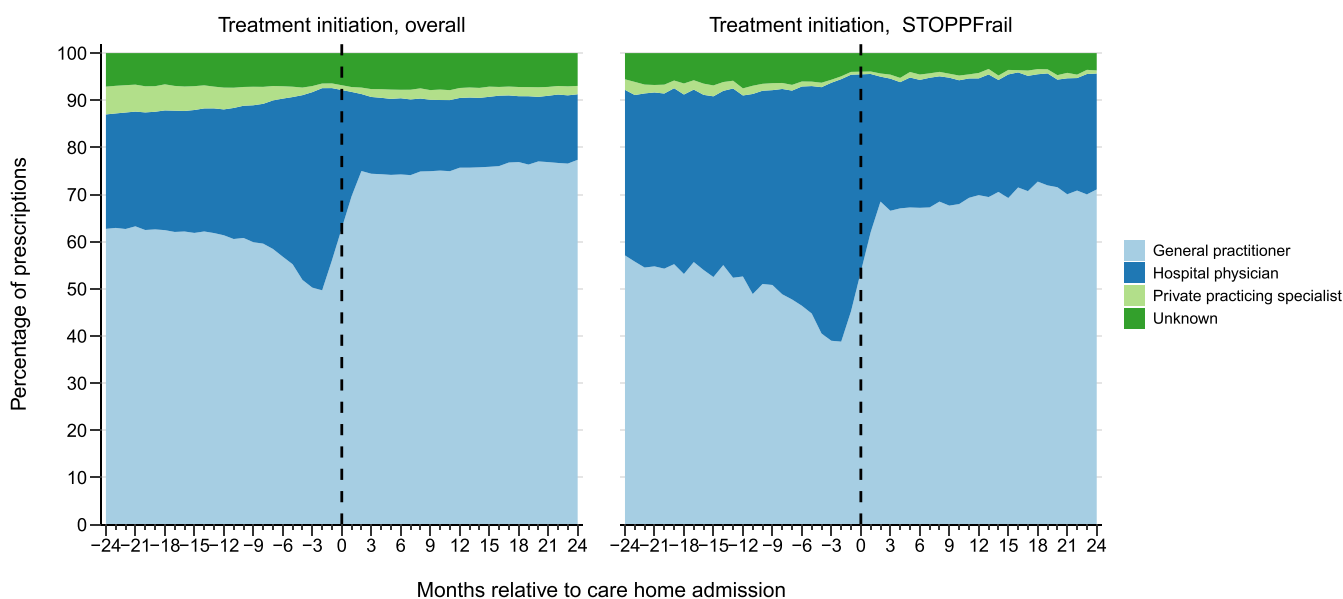


FIGURE 2 | Proportion of all prescriptions initiated (left panel) and STOPPFrail prescriptions initiated (right panel) by specialty of prescribers (general practitioners, hospital physicians, private practicing specialists and unknown) per month 2 years before and after care home admission.

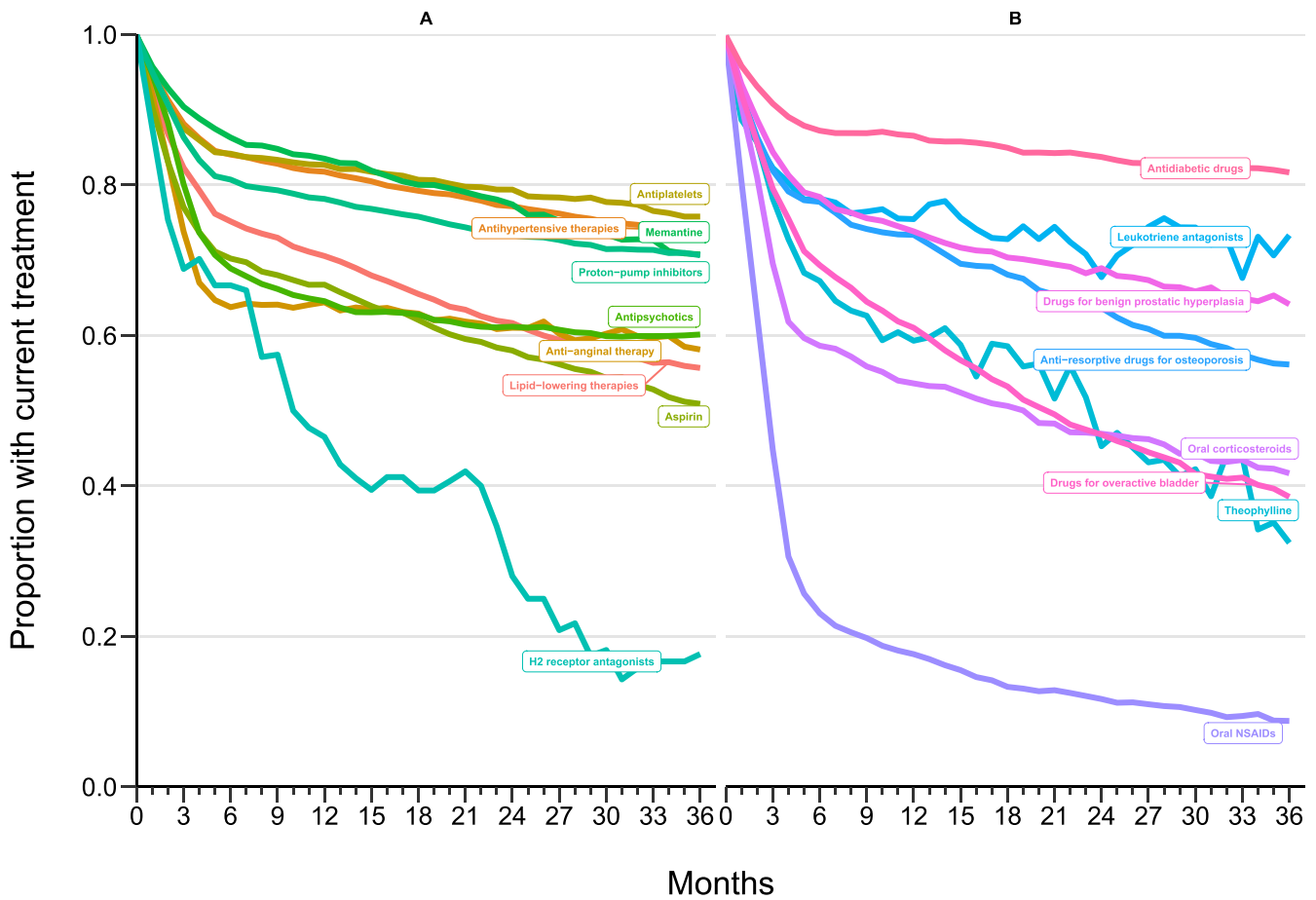


FIGURE 3 | Persistence to treatment for each potentially inappropriate medication identified using STOPPFrail among current users at care home admission in the 3 years following admission. Panel A: Lipid-lowering therapies, antihypertensive therapies, anti-anginal therapy, antiplatelets, aspirin, antipsychotics, proton-pump inhibitors and H2 receptor antagonists. Panel B: Theophylline, leukotriene antagonists, anti-resorptive/bone anabolic drugs for osteoporosis, oral non-steroidal anti-inflammatory drugs (NSAIDs), oral corticosteroids, drugs for benign prostatic hyperplasia, drugs for overactive bladder and antidiabetic drugs.

Danish care home residents. We found that most care home residents used at least one STOPPFrail medication, with antihypertensives, lipid-lowering therapies and PPIs being the most common. The rate of new use of STOPPFrail medications peaked just before care home admission and then gradually declined after admission. Hospital physicians issued a growing share of incident prescriptions as care home admission approached, after which GPs accounted for the majority. A high persistence to treatment was observed for certain STOPPFrail medications, even 3 years after care home admission. In the last year of life, at least one STOPPFrail medication was used by more than 90% of residents, with antipsychotics and PPIs being the most frequently initiated medication classes in the last 4 months of life.

The main strength of this study is the use of a unique, complete national cohort of all Danes admitted to care homes from 2015 onwards, enabling unambiguous linkage [22] with Danish nationwide health registries [20, 21] without selection bias. Some limitations should also be acknowledged. First, some of the medications investigated in the study are available over-the-counter, such as NSAIDs and PPIs, meaning that their use is possibly underreported. Further, we based our data on prescription fills, assuming that residents

receiving these medications also took them. However, Danish care home residents have their medications dispensed by care staff, requiring a physician's prescription, thereby minimising potential bias from both underreporting and non-adherence. Second, we did not examine potential drug–drug interactions. Although the high number of medications used may increase the risk of interactions, previous studies suggest that their clinical impact in this population is uncertain [31]. Third, detailed clinical information, such as blood pressure measurements, indication for prescribing and specific symptoms, was not available in our data sources, which may have resulted in an overestimation of the prevalence of potentially inappropriate medication use, as we classified medications as potentially inappropriate when this information was needed to determine their appropriateness. Additionally, we excluded all medications from the general section of STOPPFrail, which broadly defines potentially inappropriate medications as those that patients consistently fail to take or tolerate, lack a clear indication or are prescribed for already resolved symptoms [16]. This exclusion may result in some use of inappropriate medications not being addressed in this study, potentially limiting the comprehensiveness of our assessment. A general limitation of STOPPFrail and similar tools for assessing potentially inappropriate medications is that they are not intended to replace

clinical judgement in deprescribing decisions, which should prioritise goals of care, resident values and preferences [32].

The observed increase in new treatments of STOPPFrail medications around the time of care home admission aligns with the general rise in overall medication use among Danish care home residents [3]. This likely reflects a general decline in health status, more frequent hospitalisations and increased visits to GPs in this period [2]. Similar studies in other countries have also reported a high prevalence of potentially inappropriate medication use measured by STOPPFrail [33–36], with preventive medications such as antihypertensives and lipid-lowering therapies being among the most commonly prescribed [34–36]. Although we lacked information on reasons for initiation, continuation or previous attempts at discontinuation, the benefits of treatment must be carefully weighed against the risks of adverse drug events, as individuals with limited life expectancy are unlikely to benefit from preventive treatments [9], making the high prevalence of such medications particularly questionable.

We found that the majority of new STOPPFrail medications were prescribed by hospital physicians, particularly in neurological departments, whereas geriatric departments accounted for only a small proportion. This suggests that many older adults are admitted to hospital wards that may lack specific focus on frailty and limited life expectancy, increasing the risk of initiating standard treatments such as antiplatelets, statins and antihypertensives without assessing their relevance in this vulnerable population. After care home admission, these medications are often maintained by general practitioners without necessarily being reevaluated, further underscoring the importance of regular medication reviews.

Approximately 60% of residents who used antipsychotic medications upon care home admission continued to have antipsychotics prescribed 3 years after admission, and we observed an increased use around the time of admission and in the last 4 months of life. This could be concerning as antipsychotic medications carry a risk of severe side effects, particularly for residents with dementia, including an increased risk of death, hospitalisations and various other adverse effects [37–39]. Similar patterns of antipsychotic use have been observed in different countries [33, 40], highlighting the need for caution in prescribing these medications to vulnerable individuals. However, some STOPPFrail medications may be appropriate in end-of-life care. For instance, antipsychotics may be used as part of palliative care to manage symptoms like nausea or delirium [41–43], which could partially explain the observed increase in their use during the last 4 months before death.

The proportion of residents remaining on NSAIDs declined rapidly within 6 months following care home admission, which may reflect efforts to reduce long-term risks associated with these medications. However, given that NSAIDs are often used for short-term indications, this decrease may also reflect the resolution of acute pain episodes rather than a planned effort to review and discontinue potentially inappropriate treatments. In this context, opioid use may also be relevant, as opioids are often used to manage pain and may be prescribed concurrently with NSAIDs. Although opioids were not part of the present analysis, future studies could consider exploring opioid use alongside

STOPPFrail medications to better understand prescribing practices. We also observed that users of H2 receptor antagonists tended to discontinue therapy sooner. H2 receptor antagonists were withdrawn from the market during the study period [44], which may explain the low proportion of users 3 years after admission.

Our findings emphasise the importance of carefully evaluating prescribing practices for care home residents with limited life expectancy, both at initiation and discontinuation of treatments. Research indicates that residents are generally open to deprescribing, particularly when recommended by a physician [45–47], highlighting the need for implementing practical deprescribing strategies within this population. Investigating how designated physicians in care homes can facilitate deprescribing through continuous monitoring and follow-up could provide valuable insights to develop targeted strategies for reducing inappropriate medications. Further, research supports the feasibility and safety of reducing STOPPFrail medications, with no negative impact on clinical outcomes and potential cost savings [48, 49]. Moreover, a recent study demonstrated that pharmacist-led, STOPPFrail-guided deprescribing significantly reduced inappropriate medication use [50], underscoring the value of pharmacist involvement in optimising medication management in these settings.

In conclusion, our study provides a comprehensive overview of potentially inappropriate medication use according to STOPPFrail among Danish care home residents, with most residents receiving at least one STOPPFrail medication. Use of preventive medications was particularly prevalent, and a high proportion of care home residents continued to be prescribed treatment even 3 years after admission. This extensive use of potentially inappropriate medications, including the high percentage of initiation of antipsychotics in the last 4 months of life, raises concerns and underscores the importance of focusing on regular reassessment of prescribing practices and targeted deprescribing efforts of potentially inappropriate medication to improve safety and the rationale behind prescribing in this vulnerable population.

Acknowledgements

The authors have nothing to report.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data were used under license from the Danish Health Data Authority. Due to Danish data protection regulations, the authors cannot share individual-level data.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.

Appendix 1

STOPPFrail criteria version 2.

Section and medications	Original criteria	Definition based on ATC-codes in the present study
Section A: General		
A1	Any drug that the patient persistently fails to take or tolerate despite adequate education and consideration of all appropriate formulations	NA
A2	Any drug without clear clinical indication	NA
A3	Any drug for symptoms which have now resolved (e.g., pain, nausea, vertigo, pruritus)	NA
Section B: Cardiology system		
B1. Lipid-lowering therapies (statins, ezetimibe, bile acid sequestrants, fibrates, nicotinic acid, lomitapide and acipimox)		C10
B2. Antihypertensive therapies	Carefully reduce or discontinue these drugs in patients with systolic blood pressure (SBP) persistently <130 mmHg. An appropriate SBP target in frail older people is 130–160 mmHg. Before stopping, consider whether the drug is treating additional conditions (e.g., beta-blocker for rate control in atrial fibrillation, diuretics for symptomatic heart failure)	C02CA, C03A, C03B, C03D, C07, C08C, C09
B3. Anti-anginal therapy (specifically nitrates, nicorandil, ranolazine)	None of these anti-anginal drugs have been proven to reduce cardiovascular mortality or the rate of myocardial infarction. Aim to carefully reduce and discontinue these drugs in patients who have had no reported anginal symptoms in the previous 12 months AND who have no proven or objective evidence of coronary artery disease	Nicorandil: C01CD16 Nitrates: C01DA C01DA08, C01DA14, C01DA02 Ranolazine is not available on the Danish market
Section C: Coagulation system		
C1. Antiplatelets	Avoid antiplatelet agents for primary (as distinct from secondary) cardiovascular prevention (no evidence of benefit)	B01AC excl. B01AC06
C2. Aspirin for stroke prevention in atrial fibrillation	Aspirin has little or no role for stroke prevention in frail older people who are not candidates for anticoagulation therapy and may significantly increase bleeding risk	B01AC06, B01AC30
Section D: Central nervous system		
D1. Neuroleptic antipsychotics in patients with dementia	Aim to reduce dose and gradually discontinue these drugs in patients taking them for longer than 12 weeks if there are no current clinical features of behavioural and psychiatric symptoms of dementia (BPSD)	N05A
D2. Memantine	Discontinue and monitor in patients with moderate to severe dementia, unless memantine has clearly improved BPSD	N06DX01
Section E: Gastrointestinal system		
E1. Proton-pump inhibitors	Reduce dose of proton-pump inhibitors when used at full therapeutic dose \geq 8 weeks, unless persistent dyspeptic symptoms at lower maintenance dose	A02BC

(Continues)

Section and medications	Original criteria	Definition based on ATC-codes in the present study
E2. H2 receptor antagonists	Reduce dose of H2 receptor antagonists when used at full therapeutic dose for ≥ 8 weeks, unless persistent dyspeptic symptoms at lower maintenance dose	A02BA
Section F: Respiratory system		
F1. Theophylline and aminophylline	These drugs have a narrow therapeutic index, have doubtful therapeutic benefit and require monitoring of serum levels and interact with other commonly prescribed drugs putting patients at an increased risk of adverse drug events	R03DA04 Aminophylline is not available on the Danish market
F2. Leukotriene antagonists (Montelukast, Zafirlukast)	These drugs have no proven role in chronic obstructive pulmonary disease; they are indicated only in asthma	R03DC
Section G: Musculoskeletal system		
G1. Calcium supplements	Unlikely to be of any benefit in short-term unless proven, symptomatic hypocalcaemia.	Not included, as most common calcium supplement products are classified as dietary supplements [51] and data are therefore not available
G2. Vitamin D (ergocalciferol and cholecalciferol)	Lack of clear evidence to support the use of vitamin D to prevent falls and fractures, cardiovascular events, or cancers	Not included, as most common vitamin D supplement products are classified as dietary supplements [52] and data are therefore not available
G3. Anti-resorptive/bone anabolic drugs for osteoporosis (bisphosphonates, strontium, teriparatide, denosumab)		M05BA, M05BB, M05BX, H05AA02
G4. Long-term oral NSAIDs	Increased risk of side effects (e.g., peptic ulcer disease, bleeding, worsening heart failure) when taken regularly for ≥ 2 months	M01A excl. M01AX Item numbers that should not be included due to a different route of administration than oral is provided in the table below
G5. Long-term oral corticosteroids	Increased risk of major side effects (e.g., fragility fractures, proximal myopathy, peptic ulcer disease) when taken regularly for ≥ 2 months. Consider careful dose reduction and discontinuation	H02A, A07EA Item numbers that should not be included due to a different route of administration than oral is provided in the table below
Section H: Urogenital system		
H1. Drugs for benign prostatic hyperplasia (5-alpha reductase inhibitors and alpha-blockers) in catheterised male patients	No benefit with long-term urinary bladder catheterization	G04CA, G04CB
H2. Drugs for overactive bladder (muscarinic antagonists and mirabegron)	No benefit in patients with persistent, irreversible urinary incontinence unless clear history of painful detrusor hyperactivity	G04BD
Section I: Endocrine system		
I1. Antidiabetic drugs	De-intensify therapy. Avoid HbA1c targets (HbA1C $< 7.5\%$ [58 mmol/mol] associated with net harm in this population). The goal of care is to minimise symptoms related to hyperglycaemia (e.g., excessive thirst, polyuria)	A10A, A10B
Section J: Miscellaneous		
J1. Multivitamin combination supplements	Discontinue when prescribed for prophylaxis rather than treatment of hypovitaminosis	Not included, as most common multivitamin combination supplement products are classified as dietary supplements [53] and data are therefore not available

(Continues)

Section and medications	Original criteria	Definition based on ATC-codes in the present study
J2. Folic acid	Discontinue when treatment course is completed. The usual treatment duration is 1–4 months unless malabsorption, malnutrition or concomitant methotrexate use	Not included, as many folic acid products are classified at dietary supplements [54] and data are therefore not available
J3. Nutritional supplements	Discontinue when prescribed for prophylaxis rather than treatment of malnutrition	Not included, as the preparations are registered as foods for special medical purposes [55] and data are therefore not available

Items under the ATC codes M01A, H02A and A07EA that should not be included due to a different route of administration than oral44.

Item numbers under the ATC code M01A that should not be included due to a different route of administration than oral							
100504	190702	458884	525030	109725	384445	9214	1937
374890	190728	473213	534855	127748	421101	383310	1950
79263	685363	370112	534949	144836	439010	29835	1959
382925	1815	414060	595713	151486	474069	391941	29561
452284	1926	47242	140416	192053	486057		
Item numbers under the ATC code H02A that should not be included due to a different route of administration than oral							
13802	74246	434274	43186	34731	92694	453162	121274
54598	130683	465187	161091	112127	134940	488496	161117
116008	141044	489011	498190	131796	143339	530391	498464
143773	143347	533979	533912	145143	151726	571394	551572
181066	153928	590659	562056	181595	161075	685377	587583
194713	166803	685379	594325	380330	171016	685380	424525
385214	180299	685546	161125	399765	189506	92790	391522
413438	189514	93157	395792	473824	189522	102100	439954
477631	195389	115190	454378	488471	390762	127031	523273
498048	394537	129657	36431	572625	397856	152330	42093
83682	413635	153150	47663	196646	420151	159037	67283
517803	421923	178004	430305	519162	573746	29945	
Items under the ATC code A07EA that should not be included due to a different route of administration than oral							
113481	147146	165720	78949	62069	142706	430507	431410
462358	486195	513753					

Appendix 2

ICD-10 and ATC codes used to define comorbidities in Table 1. Comorbidities were defined as having at least one of the ICD-10 codes below, based on hospital diagnoses recorded in the Danish National Patient Registry at any time prior to admission/death, or a filled prescription for one of the ATC codes during the last 5 years before admission/death.

Comorbidity	ICD-10 code	ATC-code
COPD	J44.x	R03
Dementia	F00 F01 F02 F03 F1073 F1173 F1273 F1373 F1473 F1573 F1673	N06D
Ischemic heart disease	I20.x I21.x I23.x I24.x I25.x	
Heart failure	I099A I110.x I130.x I132.x I50.x	
Atrial fibrillation	I48.x	
Stroke	I60-I649	
Diabetes mellitus	E10.x-E14.x	A10 except weight loss medications, i.e., Wegovy and Saxenda

Abbreviations: ICD, International Classification of Disease; ATC, Anatomical Therapeutic Chemical.