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PHARMACOEPIDEMIOLOGY AND PRESCRIPTION

Balancing medication use in nursing home residents with life-limiting disease

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Abstract

Purpose Balancing medications that are needed and beneficial and avoiding medications that may be harmful is important to prevent drug-related problems, and improve quality of life. The aim of this study is to describe medication use, the prevalence of deprescribing of medications suitable for deprescribing, and the prevalence of new initiation of potentially inappropriate medications (PIMs) in nursing home (NH) residents with life-limiting disease in Flanders.

Methods NH residents aged ≥ 65, suffering from end stage organ failure, advanced cancer, and/or dementia ($n = 296$), were included in this cross-sectional study with retrospective analyses of medication use at the time of data collection (t2) and 3 to 6 months before (t1). The appraisal of appropriateness of medications was done using a list of medications documented as suitable for deprescribing, and STOPPFrail criteria.

Results Residents' (mean age 86 years, 74% female) mean number of chronic medications increased from 7.4 (t1) to 7.9 (t2). In 31% of those using medications suitable for deprescribing, at least one medication was actually deprescribed. In 30% at least one PIM from the group of selected PIMs was newly initiated. In the subgroup ($n = 76$) for whom deprescribing was observed, deprescribing was associated with less new initiations of PIMs ($r = -0.234$, $p = 0.042$).

Conclusion Medication use remained high at the end of life for NH residents with life-limiting disease, and deprescribing was limited. However, in the subgroup of 76 residents for whom deprescribing was observed, less new PIMs were initiated.

Keywords Polypharmacy · Risk-benefit ratio · Deprescribing · Potentially inappropriate medications

Introduction

Balancing medication use at the end of life for nursing home (NH) residents with life-limiting disease means carefully weighing the benefit-risk ratio of every added medication and every medication that was prescribed earlier in the disease trajectory of a life-limiting disease. Physicians should always keep in mind the added drug burden when initiating a new medication or increasing the dosage of a previously prescribed drug in this situation.

Balancing medication use in older adults with multimorbid conditions, such as NH residents, is challenging, particularly when life expectancy has decreased. Research has demonstrated that people with a life-limiting disease use a mean number of 7 to 11 different medications [1–3]. The prevalence of polypharmacy—or the concomitant use of five or more chronic medications with systemic effect [4]—in this population varies between 25 and 84%, and the prevalence of excessive polypharmacy (≥ 10) between 28 and 69% [1–3]. In this frail

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population with life-limiting disease, polypharmacy and inappropriate medication use have been associated with negative health-related outcomes, such as hospitalizations, falls, drug-related problems, and decreased quality of life [5, 6].

At the end of life, medications to treat life-limiting diseases are generally combined with medications for symptom relief, medications for treatment of co-morbidities, and medications for long-term prevention [3]. When death approaches, medications for symptom relief increase [7, 8]. Consequently, when previously prescribed medications are continued, drug burden and the risk of drug-related problems, such as adverse drug reactions (ADRs), and drug-drug interactions increase [9, 10]. Hence, it is crucial to carefully balance medication use in people with a life-limiting disease, such as frail older adults residing in NHs.

Moreover, according to the definition of palliative care, care goals in those with life-limiting disease should change from quantity to quality of life [11]. This should be reflected in medication use near the end of life. In this context, adequate medication use means treating symptoms which are currently undertreated, as well as preventing possible harm caused by—potentially inappropriate—medications. However, research has demonstrated that the diagnosis of a life-limiting disease has little effect on prescribing patterns, particularly for medications for long-term prevention, which use at the end of life is questionable because they lack short-term benefit [3, 12–16].

At the end of life, it is crucial to balance medications that are needed and beneficial for the patient, and avoid initiation and/or continuation of medications that may be harmful or have no short-term benefit. Carefully balancing medications may improve quality of life, and decrease, or at least not add to, the patient's drug burden and drug-related problems.

Deprescribing can be defined as "the systematic process of withdrawal of an inappropriate medication, supervised by a healthcare professional, with the goal of identifying and discontinuing drugs in instances in which existing or potential harms outweigh existing or potential benefits within the context of an individual patient's care goals, current level of functioning, life expectancy, values, and preferences" [17]. Discontinuation is used as an umbrella term for stopping or tapering medications, e.g., by deprescribing.

Generally, medications are considered inappropriate to continue, and thus suitable for deprescribing when they lack short term benefit, cause additional harm (e.g., ADRs), or when a safer alternative exists [18–20]. Recently, international clinical practice deprescribing guidelines were developed to guide clinicians in deprescribing proton pump inhibitors (PPIs), antihyperglycemics, antipsychotics, benzodiazepine receptor agonists, cholinesterase inhibitors and memantine, statins, osteoporosis medications, antihypertensives, vitamins, and minerals [21, 22].

At the same time, numerous tools were developed to identify potentially inappropriate medications (PIMs) in older adults with a normal life expectancy (e.g., Beers [23], STOPP/START [24]). Recently, Lavan et al. (2017) developed a list of criteria to identify PIMs in frail older adults with a limited life expectancy (STOPPFrail) and to guide clinicians in deprescribing these PIMs at the end of life in all healthcare settings [25]. In addition, STOPPFrail can also help clinicians to decide which medications to avoid, and thus not initiate.

The aim of this study is to describe medication use at two time points within a period of 3 to 6 months, the prevalence of actual deprescribing of medications suitable for deprescribing, and the prevalence of new initiation of PIMs according to STOPPFrail. This information is important to get more insight in the current situation and to guide future initiatives to optimize and balance medication use in NH residents with a life-limiting disease. Unbalanced medication use may foster polypharmacy, PIM use, and associated health-related outcomes, such as falls, hospitalizations, and increased risk of mortality. Moreover, the economic cost of polypharmacy and potentially inappropriate prescribing is high and could be reduced by deprescribing [26].

Methods

Study design and study population

For this cross-sectional study with retrospective analyses of medication use, NHs were eligible for inclusion if they had at least 100 beds and a mixed population of older adults with and without dementia. Forty-four NHs in Flanders, the Dutch speaking part of Belgium, were provided with study information by telephone and they received the study protocol by email. One week later they received another phone call to confirm consent with participation. Ten NHs agreed to participate (convenience sample) and a first appointment with the researcher was scheduled.

Residents were eligible for inclusion if aged ≥ 65, Dutch speaking, able to answer questions adequately according to the responsible nurse, and suffering from one of the following life-limiting diseases: end stage organ failure, advanced cancer, or dementia. Residents with an estimated life expectancy of < 1 month were excluded for ethical reasons. Residents diagnosed with dementia who were capable to adequately answer questions (Mini Mental State Examination [MMSE] ≥ 18) were interviewed themselves. Residents diagnosed with dementia for whom this was not the case were included if their informal caregiver was aged ≥ 16 and visited them at least twice a month, and this informal caregiver was questioned instead of the resident himself. Residents who were incapable to answer questions adequately due to dementia, deafness, aphasia, or other reasons and for whom no informal caregiver was available were excluded. The selection of eligible residents was done by the NH management or the

responsible head nurse. Eligible residents and/or their informal caregivers were provided with study information by the researchers and were asked to sign an informed consent form.

Procedure

Residents or their informal caregiver were interviewed using a structured questionnaire and the following validated measuring tools: KATZ-ADL [27], Mini Mental State Examination (MMSE) [28], and Minimum Data Set Mortality Risk Index (MDS-MMRI) [29]. The Katz index in activities for daily living is mandatory in Belgian NHs and facilitates the detection of functional state with scores ranging from 6 to 24. High scores are associated with high ADL dependency [27]. The MMSE is a standard screening tool for cognitive assessment in the clinical setting with scores ranging from 0 to 30 and allows comparison of performance across time and among older adults. Low scores are associated with cognitive impairment [28]. The MDS-MMRI estimates mortality risk within the next 6 months, with scores ranging from 0 to 75. High scores are associated with a high mortality risk [29].

Medication use was based on a copy of the resident's full medication chart, and was evaluated two times: (t2) at the time of data collection and (t1) retrospectively 3 to 6 months before. Sufficient time between t1 and t2 was needed to provide time to adjust prescription. All data were collected from January to March 2018.

Data handling

Medications were recorded using the brand or generic name in a data-entry program, based on the official register of medications on the market from the Belgian Centre for Pharmaceutical Information. The medication was translated into the Anatomical Therapeutic Chemical (ATC) classification (WHO ATC/DDD index). Polypharmacy was defined as the use of five or more prescribed chronic medications with systemic effects, and excessive polypharmacy as the use of ten or more. Discontinuation was defined as stopping or withdrawal of a specific ATC code between t1 and t2.

Medications considered to be potentially suitable for deprescribing were selected based on scientific evidence from clinical practice guidelines and a randomized clinical trial [21, 22, 30–34] and discussed with two experts in clinical pharmacology (TC and RVS). These medications potentially suitable for deprescribing were cross-referenced and linked to the medications at t1 and t2 (Box 1 in online supplementary file). Deprescribing was defined as stopping or lowering the dose of the selected medications between t1 and t2. A new dichotomous variable was constructed with value one if at least one of the medications considered to be suitable for deprescribing was actually deprescribed, and value zero if this was not the case.

Initiation of new medication at the end of life was defined as initiation between t1 and t2 of a specific medication that was not used at t1. Appraisal of the appropriateness of the initiated medications was determined with explicit criteria of PIM using the STOPPFrail criteria [25]. The STOPPFrail criteria were cross-referenced and linked to the medications at t1 and t2. Because the clinical information necessary to interpret their (in)appropriateness was not available in this study due to inaccessibility of the medical file, we excluded, based on expert opinions (TC and RVS), the following PIMs: antiplatelets, leukotriene antagonists, muscarinic antagonists, diabetic oral agents, ACE inhibitors, angiotensin receptor blockers, and prophylactic antibiotics. These excluded PIMs may be appropriate in certain clinical situations. The remaining 15 PIMs can be found in Table 3. A new dichotomous variable was constructed with value one if at least one PIM was initiated at t2, and value zero if this was not the case.

Data analyses

All statistical analyses were done using SPSS 24.0 (IBM Statistics Inc., Chicago, IL). Resident characteristics, medication use, deprescribing, and initiation were explored with descriptive statistics. Differences between medication use at t1 and t2 were examined with paired sample *t* tests and McNemar. Associations of the dichotomous outcomes "at least one deprescribed" and "at least one PIM initiated" with socio-demographic and other characteristics were examined using independent sample *t* tests and chi-squared test. Correlation between the number of deprescribed medications and the number of new initiated PIMs was explored with Pearson correlations. A significance level of $p < 0.05$ was set.

Ethical considerations

The study protocol was approved by the ethics committee (EC) of the Antwerp University Hospital Belgium (EC number B300201734128). The board of directors and the supervising GP of the NH signed a study agreement. Residents or their informal caregiver signed an informed consent.

Results

Study population

Overall, 482 NH residents were eligible for inclusion, of which 181 refused to participate and 5 had incomplete medication data. Consequently, 296 residents—mean age 86 years, 74% female—participated in this study; 135 were questioned themselves and for 161 the questionnaire was filled in by their

informal caregiver. Mean KATZ-ADL was 17 and mean MDS-MMRI score was 32, indicating an average 6-month mortality risk of 36%. The most prominent life-limiting disease was dementia (73%), followed by heart failure (31%), COPD and renal failure (both 11%), and advanced cancer (7%) (Table 1).

Medication use at the time of data collection (t2) and 3 to 6 months before (t1)

The mean number of chronic medications increased from 7.4 (t1) to 7.9 (t2) ($p < 0.001$). At t1, 53% had polypharmacy (5–9) and 25% excessive polypharmacy (≥ 10), compared to, respectively, 51% and 29% at t2 ($p = 0.208$) (Fig. 1).

Medication use was high at both time points for the following ATC main anatomic groups: alimentary tract and metabolism (A), blood and blood forming agents (B), cardiovascular system (C), and nervous system (N). In all these groups, the percentage of residents with new initiation exceeded the percentage with discontinuation (Fig. 2 in online supplementary file).

The most prominent therapeutic subgroups in this population were proton pump inhibitors (PPIs), multivitamin combinations, calcium, lipid-modifying agents, opioids, non-opioids, antipsychotics, anxiolytics, sedatives, antidepressants, and antidementia agents. Between t1 and t2, the prevalence of lipid-modifying agents decreased significantly (16% to 13%, $p = 0.012$). The prevalence of analgesics (opioids and non-opioids) and antipsychotics increased significantly (respectively, 47% to 58%, $p < 0.001$ and 28% to 34%, $p = 0.009$). The prevalence of discontinuation was relatively high for anxiolytics and sedatives (respectively, 23% and 13.5%), lipid-modifying agents (22%), calcium (19%), and antidementia agents (15%). For non-opioids, multivitamin combinations, and antipsychotics, the prevalence of new initiation was relatively high (respectively, 21.5%, 15%, and 13%). Lipid-modifying agents and antidementia agents were not newly initiated (Fig. 2 and Table 4 in online supplementary file).

Table 1 Characteristics of the study population

	Residents ($n = 296$)
Age mean (SD)	86.2 (6.7)
(Range)	(65–100)
Gender (%)	
Female	74.0
Male	26.0
Marital status (%)	
Widowed	66.9
Married	22.9
Other	10.2
Highest education (%)	
No education	16.2
Primary school	8.6
Low secondary	35.7
High secondary	22.1
Higher—university	14.6
Other	2.8
Informal caregiver available (%)	85.5
Informal caregiver questioned (%)	54.4
MDS-MMRI mean (SD)	32.1 (10.7)
6-month mortality risk (%)	
< 50%	78.8
≥ 50%	21.2
KATZ-ADL mean (SD)	17.1 (5.3)
Life-limiting disease[a] (%)	
Advanced cancer (%)	6.8
Heart failure (%)	31.2
COPD (%)	11.1
Renal failure (%)	10.8
Dementia (%)	72.6

[a] More than one answer possible

Deprescribing of medications potentially suitable for deprescribing

Overall, 245 residents used at least one of the medications potentially suitable for deprescribing (Box 1 in online supplementary file). For 76 of them (31%), at least one of the medications potentially suitable for deprescribing was actually deprescribed. The prevalence of deprescribing was relatively high for lipid-modifying agents (29%), benzodiazepine receptor agonists (28%), minerals (including calcium) (21%), and antipsychotics (17%) (Table 2).

No associations were found with socio-demographic or other characteristics (data not shown).

New initiation of PIMs according to STOPPFrail

At least one PIM of the group of selected PIMs according to STOPPFrail was initiated for 83 residents (30%). Thus, 70% did not start using any new PIMs. The highest prevalence of initiation was found for multivitamin combinations (15%) and neuroleptic antipsychotics (13%) (Table 3).

Initiation of at least one PIM of the group of selected PIMs was associated with a higher number of chronic medications at baseline (10 versus 7 for residents for whom no PIMs were initiated, $p < 0.001$) and with renal failure (for 16/30 or 53% of residents with renal failure at least one PIM was initiated compared to 27% in residents without renal failure, $p = 0.003$) (data not shown).

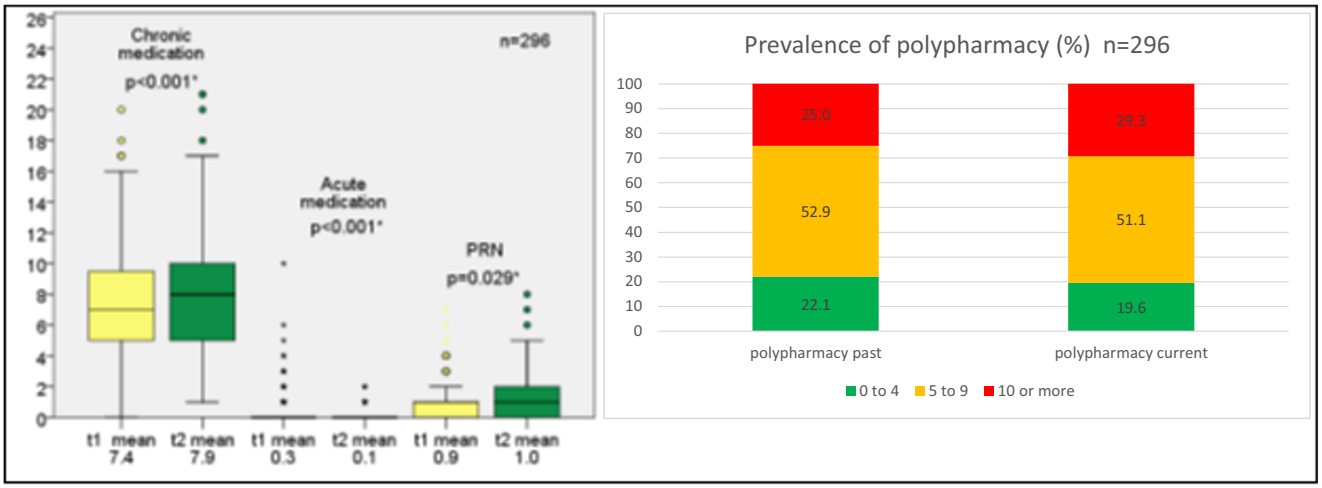

Fig. 1 Evolution of the number of chronic, acute, and pro re nata (PRN) medications between t1 (3–6 months before data collection) and t2 (at the time of data collection) and prevalence of polypharmacy

Correlation between deprescribing of medications suitable for deprescribing and new initiation of PIMs according to STOPPFrail

Changes in medication use, i.e., deprescribing of medications potentially suitable for deprescribing and/or new initiation of PIMs, were observed in 133 residents. Deprescribing was observed in 76 residents. In this subgroup of 76 residents, an increase in the number of medications potentially suitable for deprescribing that were actually deprescribed was associated with a decrease in the number of PIMs that were newly intiated ($r = -0.234$, $p = 0.042$) (data not shown).

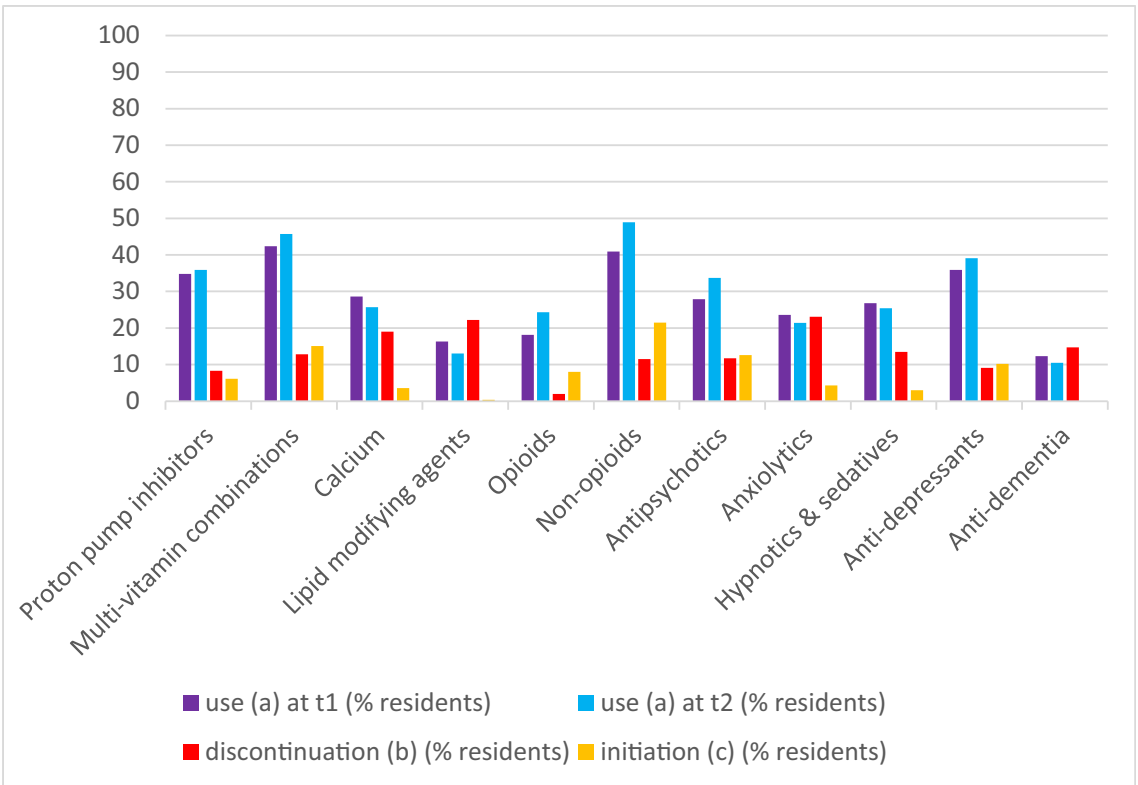

Fig. 2 Prevalence (% users) at t1 and t2, discontinuation (stopping), and initiation for the therapeutic groups that are most commonly used ($n = 296$)

Table 2 Percentage of residents for whom medications considered potentially suitable for deprescribing at t1 were actually deprescribed (stopped or tapered) at t2

Medications potentially suitable for deprescribing	Residents using these medications at t1 (%) ($n = 296$)	Residents for whom these medications were deprescribed % (n/N[a])
Proton pump inhibitors	34.8	15.6 (15/96)
Antihyperglycemics	14.5	12.5 (5/40)
Antipsychotics	27.9	16.9 (13/77)
Benzodiazepine receptor agonists	23.6	27.7 (18/65)
Cholinesterase inhibitors	10.9	13.3 (4/30)
Memantine	0.4	0.0 (0/1)
Statins (lipid-lowering agents)	16.3	28.9 (13/45)
Antihypertensives	1.4	0.0 (0/4)
Osteoporosis medications	4.7	23.1 (3/13)
Vitamins	42.4	14.5 (17/117)
Minerals	32.2	21.3 (19/89)
Deprescribing score mean (range)		0.44 (0–4)
At least one deprescribed (%)		31.1 (76/245)

[a] n/N: number of residents for whom this medication was deprescribed (= stopped or tapered) between t1 and t2 on denominator number of residents who used this medication at t1

Table 3 Prevalence of new initiation at t2 of PIMs from the group of selected PIMs of STOPPFrail

PIM initiation	$n = 296$
Number of PIMs initiated mean (range)	0.4 (0–5)
Prevalence of PIM initiation (%)	
No PIMs	69.9
1 PIM	24.6
2 PIMs	4.3
≥ 3 PIMs	1.1
STOPPFrail criteria	% (n/N[a])
Multivitamin combination supplements	15.1 (24/159)
Neuroleptic antipsychotics	12.6 (25/199)
PPIs	6.1 (11/180)
Theophylline	3.7 (9/243)
Calcium supplements	3.6 (7/197)
Gastro-intestinal antispasmodics	2.8 (7/246)
Long-term oral steroids	2.2 (6/268)
Long-term oral NSAIDs	1.5 (4/272)
5-Alpha reductase inhibitors	1.2 (3/252)
H2 receptor antagonists	1.1 (3/267)
Sex hormones (including SERMS)	0.7 (2/273)
Osteoporosis drugs	0.4 (1/263)
Lipid-modifying agents	0.4 (1/231)
Memantine	0.0 (0/275)
Antihypertensives (including alpha blockers)	0.0 (0/272)

[a] n/N: number of residents for whom this medication was initiated between t1 and t2 on denominator number of residents who were not using this medication at t1

Discussion

Main findings

During the 3- to 6-month period between first (t1) and second (t2) evaluation, mean number of chronic medications increased significantly, and the prevalence of polypharmacy and excessive polypharmacy remained high for NH residents with life-limiting disease. For one third, at least one medication potentially suitable for deprescribing was actually deprescribed. On the other hand, for one third, at least one PIM was newly initiated at the end of life. In the subgroup of 76 residents for whom deprescribing was observed, residents for whom more medications were deprescribed, had less new PIMs initiated. Most changes in medication use were observed in the group of lipid-modifying agents, multivitamin combinations, calcium and other minerals, PPIs, and medications indicated to treat diseases of the nervous system.

Strengths and limitations

The medication data used for this study were extracted from the individual's nurse administration medication chart, which is highly reliable in the NH setting in Flanders, Belgium. Consequently, data on medication use were a representation of what residents actually use, and allowed to examine changes in medication use for a sample of 296 NH residents with life-limiting disease. For the appraisal of the appropriateness of medications, international clinical practice deprescribing guidelines and validated criteria, the STOPPFrail criteria, were used.

This study has certain limitations. First, due to the absence of clinical information, we excluded PIMs for which this information is needed to interpret their (in)appropriateness. This may have led to an underestimation of PIM use in this study. However, by excluding these PIMs, we may have assessed too few disease-specific PIMs, which may had led to an overestimation of PIM use. Moreover, due to the inaccessibility of medical files, we could not determine the indications for medications considered potentially suitable for deprescribing. Thus, we can only draw cautious conclusions regarding deprescribing in this study sample. Second, we selected NH residents with a specific life-limiting disease: advanced cancer, organ failure, or dementia, which is only a small selection of life-limiting diseases. Consequently, we may have missed some residents with life-limiting disease due to other diseases.

Earlier research has demonstrated that severe dementia represents the main reason for identifying patients as being in need of palliative care [35]. Given the high prevalence of residents with dementia in our sample, we assume that this limitation is not important.

Interpretation of the findings

Consistent with earlier research in older adults with life-limiting disease [6, 8, 36], we found a significant increase in the number of chronic medications and a prevalence of polypharmacy that remained relatively high at the end of life. However, concordant with other studies in NH residents [8] and advanced cancer patients receiving palliative care [7, 37], we found that small efforts were made to engage in deprescribing of medications suitable for deprescribing. For approximately one third or 82 out of the 245 residents who used medications potentially suitable for deprescribing, at least one of these medications was actually deprescribed. On the other hand, for the other two third, medications were prescribed as before or even increased. Clearly, there is no culture of deprescribing in Flemish NHs. Apparently, a lot of—physician- and patient-related—barriers to deprescribing exist. Currently, the evidence on safety and efficacy of deprescribing is limited [38]. This is probably one of the most important barriers for physicians to engage in deprescribing and may explain the rather small efforts to engage in deprescribing [39, 40]. Interventions to support physicians in initiating deprescribing in clinical practice should take their barriers into account, because if not, these interventions are predisposed to fail.

For one third of the study population at least one PIM was newly initiated at the end of life. The relatively high prevalence of new initiation of PIMs can be explained by an unawareness of existing criteria and tools for appraisal of the appropriateness of prescribing. In Belgium, no tool exists that automatically links PIMs to the patient's medication chart and generates a systematic warning whenever a PIM is prescribed. This supports the assumption of unawareness of the prescriber.

Changes in medication use were observed in 133 residents, deprescribing in 76 residents. The finding that for those 76 people for whom medications suitable for deprescribing were actually deprescribed had less new PIMs initiated at the end of life can be interpreted as an increased attention for appropriate prescribing of medications in the context of a life-limiting disease. In these people medication use can be considered to be carefully balanced. However, this small subgroup only represented 26% of our study sample, which is most likely due to the timing of prognostication: if the negative prognosis was known before t1, deprescribing may have been initiated before t1, and no additional changes in prescribing may have been made between t1 and t2. On the other hand, prescribers may have been unaware of the impending death and have not initiated deprescribing yet. Most changes were observed in the group of lipid-modifying agents, multivitamin combinations, calcium and other minerals, PPIs, and medications to treat diseases of the nervous system. For some residents, these medications were newly initiated, and for other residents these medications were discontinued. There is no rational explanation for most of these changes. Lipid-modifying agents are one of the few therapeutic groups of medication that are generally considered to be futile at the end of life because these medications have no short-term benefit and no additional value for symptom relief. Clinical trial evidence has shown that these medications can be safely and effectively deprescribed [30]. The appropriateness of the other therapeutic groups candidate for deprescribing is still debated, although these medications are included in the recently published international clinical practice deprescribing guidelines [21, 22], aiming to increase physicians' awareness and self-efficacy of deprescribing. Given our findings on deprescribing, this raises questions regarding the dissemination of these guidelines to clinical practice.

Implications for practice, policy, and further research

Our results indicate that more attention needs to be given to balancing the benefit-risk ratio of medications and to deprescribing medications in NH residents with life-limiting disease. An urgent need occurs for deprescribing interventions in Flemish NHs. Overcoming the barriers to deprescribing is crucial for successful implementation of these deprescribing interventions. The treating GP is generally well aware of the resident's medication, particularly after years of treatment. Therefore, he/she is best fit to estimate the risk-benefit balance of medications in accordance with the changing care goals, and to coordinate a multidisciplinary medication review. Given the formerly developed relationship of trust with the resident and his family, the resident will have more confidence in medication review performed by this physician and this may increase the resident's willingness to have his medications deprescribed [41]. Furthermore, discussing care goals and treatment targets with the resident and his family is crucial to succeed in deprescribing medications. This should be included in conversations regarding wishes and preferences at the end of life.

Basic medical curricula and continuing medical education should focus on the harm of polypharmacy and PIM use, and its possible negative health-related outcomes, such as increased hospitalizations and costs, in frail older adults with life-limiting disease. Moreover, the importance of carefully balancing the benefit/risk ratio for every added medication at the time of prescribing and all other chronic medications that the resident is already using should be highlighted.

Further research should focus on reinforcing the evidence on safe and effective deprescribing of medications, on barriers and enablers to deprescribing, and on implementation of safe and effective deprescribing interventions in clinical practice.

Conclusion

Medication use remained high at the end of life for NH residents with life-limiting disease, and deprescribing was limited. However, in the subgroup of 76 residents for whom deprescribing was observed, less new PIMs were initiated. In these 76 people medication use can be considered to be carefully balanced.

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Authors' contributions Study design: Kristel Paque, Monique Elseviers, Robert Vander Stichele, Koen Pardon, Cinzia Vinkeroye, Luc Deliens, Thierry Christiaens, and Tinne Dilles.

Study protocol: Kristel Paque, Monique Elseviers, and Tinne Dilles with input from other authors.

Research: Kristel Paque, Cinzia Vinkeroye, Monique Elseviers, and Tinne Dilles.

Data analyses: Kristel Paque and Cinzia Vinkeroye.

First and other drafts: Kristel Paque wrote the first draft of this article, which was discussed at two meetings with the team of authors. Kristel Paque redrafted the article, taking the feedback and input of all co-authors into account.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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