

(De)Prescribing
In Nursing Home Residents

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Colofon

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voor **Milan**

mijn **zoon**

bron van het **leven**

mijn begin en mijn **toekomst**

Cover design

The cover design is inspired by ancient Persepolis, where envoys from all corners of the world offered their gifts to the king as a sign of respect and solidarity. In this contemporary interpretation, the gifts represent the abundance of medicines that modern medicine has produced. Yet, not every gift is accepted. In that subtle choice lies the essence of deprescribing: the wisdom not only to treat, but also to consciously refrain when less means more.

To me, the choice of Persepolis is more than a historical reference. As the land of my birth, Persia reminds me of a rich civilization, but for me, it also holds a quiet hope: that wisdom, recovery, and balance will not only guide healthcare, but one day also the land where my roots lie. The concept is my own and was designed by my brother.

Omslagontwerp

Het omslagontwerp is geïnspireerd op het oude Persepolis, waar afgezanten uit alle windstreken hun gaven aanboden aan de koning als teken van respect en verbondenheid. In deze eigentijdse interpretatie verbeelden de geschenken de overvloed aan geneesmiddelen die de moderne geneeskunde heeft voortgebracht. Toch wordt niet elk geschenk aanvaard. In die subtiele keuze ligt de essentie van deprescribing: de wijsheid om niet alleen te behandelen, maar ook bewust af te zien, wanneer minder meer betekent. De keuze voor Persepolis is voor mij meer dan een historische verwijzing. Als land van mijn geboorte herinnert Perzië aan een rijke beschaving, maar draagt het voor mij ook een stille hoop in zich: dat wijsheid, herstel en evenwicht niet alleen richting geven aan de zorg, maar ooit ook aan het land waar mijn wortels liggen. Het concept is van mijn hand en werd vormgegeven door mijn broer.

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"True knowledge leads to right action, and right action contributes to the healing of man and soul."

Inspired by Ibn Sina (Avicenna), Persian physician and philosopher, one of the greatest physicians in history and founder of classical medicine.

"Ware kennis leidt tot juist handelen, en juist handelen draagt bij aan genezing van mens en ziel."

Geïnspireerd op Ibn Sina (Avicenna), Perzisch arts en filosoof, een van de grootste artsen uit de geschiedenis en grondlegger van de klassieke geneeskunde.

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CHAPTER 1

General Introduction

Polypharmacy and Deprescribing in Nursing Homes

Case: A Daily Journey in a Nursing Home

Mrs. Jansen, an 84 years old nursing home resident, sits quietly in her room, her medication organizer filled with colorful pills. Every morning, a nurse hands her a cup containing twelve tablets and capsules. Mrs. Jansen sighs as her frail hands tremble while swallowing each one, grimacing at the bitter taste. Over the years, these medications have accumulated to address her various conditions, including hypertension, type 2 diabetes, osteoarthritis, insomnia, and mild depression. Recently, however, she has begun experiencing persistent dizziness, fatigue, and occasional confusion. Concerned, her family consults her Elderly Care Specialist (ECS), who notices prescriptions that might no longer be necessary or could be causing adverse drug reactions.

Recognizing the need for **deprescribing**—the careful reduction or discontinuation of unnecessary medications—ECS faces a dilemma whether to stop or continue.

Increasing Vulnerability and Multimorbidity

We face a global demographic shift characterized by a rapidly growing proportion of older adults. The World Health Organization (WHO) estimates that by 2050, one in five individuals will be over the age of 60, a substantial increase from one in nine today.¹

These demographic changes will of course affect nursing home care. Multimorbidity—defined as the presence of two or more chronic conditions—is highly prevalent among nursing home residents, who often experience cognitive impairment, reduced mobility, and limited life expectancy^{2,3,4}, which often necessitates management through extensive pharmacotherapy and polypharmacy.

Polypharmacy, commonly defined as the concurrent use of five or more medications, including both chronic and short-term prescriptions, is highly prevalent among elderly populations, particularly in institutional care settings such as nursing homes.⁵ Approximately 44% of older adults (≥65 years) in the Netherlands receive five or more chronic medications.^{6,7} In nursing home residents aged 65 and older in Europe, about 49.8% are affected by polypharmacy, while 24.3% are on extreme drug regimens, i.e., hyper-polypharmacy, defined as the use of 10 or more medications.^{8,9} Polypharmacy is particularly common among prefrail and frail individuals in nursing homes, who are more likely than robust older adults to be on multiple medications.⁹

Medication use can be beneficial but may also lead to serious adverse events. Polypharmacy has been associated with numerous negative clinical outcomes, including increased risk of falls, delirium, renal failure, and unplanned hospitalization.^{10,11,12} Dutch studies show that a significant proportion of emergency admissions in older adults are medication-related and

potentially preventable. The medication safety study estimated that between 2008 and 2013 in the Netherlands, the number of medication-related hospital admissions among individuals aged 65 and older increased from approximately 39,000 to 49,000. Around 47–50% of these admissions were considered potentially preventable. This rise in absolute numbers is partly explained by an overall increase in acute hospital admissions, while the risk per patient remained largely unchanged.¹³ These findings highlight the significant impact of medication-related issues on hospitalizations in the elderly and underscore the importance of targeted interventions to improve medication safety. Inappropriate prescribing (IP)—including mis-prescribing, overprescribing, and under-prescribing—is also common and contributes to patient burden.^{14,15}

The prevalence of potentially inappropriate medications (PIMs), drugs for which the potential risks outweigh the expected clinical benefits in older adults, particularly in situations where safer or more effective alternatives are available¹⁶, in elderly populations varies widely, with studies reporting rates between 11.5% and 62.5%.¹⁷ These large differences can be attributed to variations in the definitions used (e.g., Beers Criteria, STOPP/START), the settings studied (community-dwelling versus nursing home or hospital populations), patient characteristics (age, frailty, comorbidities), and differences in healthcare systems and prescribing practices across countries.¹⁷

The Risks of Polypharmacy: Drug–Drug and Drug–Disease Interactions

In older adults, age-related changes in pharmacokinetics (e.g., reduced renal and hepatic clearance) and pharmacodynamics (e.g., increased sensitivity to drugs) further exacerbate risks of adverse drug reactions. Additionally, drug–drug interactions can lead to enhanced toxicity or reduced therapeutic effects, while drug–disease interactions—where medications adversely affect coexisting conditions—can complicate disease management. For example, NSAIDs prescribed for osteoarthritis induced pain may worsen heart failure or impair kidney function.

Polypharmacy may also contribute to "prescribing cascades," where side effects of medications are misinterpreted as new illnesses, leading to further prescriptions.^{11,18,19,20} Prescribing cascades can lead to further side effects, loss of independence, and poor treatment adherence, ultimately affecting patients' quality of life. Such cascades often go unrecognized, resulting in inappropriate treatment and extra inappropriate medication, adverse events, and increased healthcare costs. The psychological burden of managing multiple medications also affects adherence and quality of life in frail elderly populations.²¹ A well-known example involves proton pump inhibitors (PPIs), which can induce hypomagnesemia; instead of recognizing the PPI as the cause, clinicians may prescribe magnesium supplements, even though discontinuing the PPI (when no clear indication exists) would often resolve the problem. Similarly, anticholinesterase inhibitors used in dementia may cause urinary incontinence, which is sometimes treated with anticholinergic

drugs—a problematic combination, as these can worsen cognitive function. Another common cascade arises when calcium channel blockers lead to peripheral edema, prompting the use of diuretics despite the fact that the edema is due to vasodilation rather than fluid overload. Likewise, diuretics can increase uric acid levels, resulting in gout that is then treated with allopurinol or colchicine, and antipsychotics may cause Parkinsonian symptoms for which antiparkinsonian drugs are added. Levothyroxine initiation following amiodarone therapy due to amiodarone-induced hypothyroidism, and the prescription of antibiotics after ACE-inhibitor use, potentially in response to drug-related urinary symptoms.²⁰ Another systematic reviews have reported similar cascades, such as the use of anti-Parkinson medication following antipsychotic-induced extrapyramidal symptoms, and switching to ondansetron or granisetron after metoclopramide-induced extrapyramidal symptoms to prevent further cascades.¹⁹ Finally, NSAIDs can raise blood pressure, sometimes leading to the unnecessary initiation of antihypertensive therapy. These examples illustrate how prescribing cascades can increase medication burden and the risk of adverse effects, underscoring the importance of regularly reviewing medications and considering deprescribing when appropriate.

Another concern is the increased complexity in managing adverse effects when multiple medications are involved. Adverse drug reactions (ADRs) are frequently underreported in the elderly, in part due to non-specific symptoms such as fatigue, cognitive decline, or balance issues, which are often attributed to ageing itself.

But there are other concerns. Studies have reported that polypharmacy is associated with decreased medication adherence, increased drug costs, and poorer quality of life.^{12,17} Moreover, polypharmacy can negatively affect medication compliance and financial resources. Patients may struggle to manage complicated regimens, especially those with cognitive impairment or without sufficient caregiver support.

Polypharmacy represents a clearly unsustainable practice in modern healthcare. First, from an environmental standpoint, overprescribing and unnecessary medication use will lead to substantial CO₂ emissions both upstream (in manufacturing and distribution) and downstream (through disposal).²² Second, the economic and operational burdens are considerable: Polypharmacy is associated with higher healthcare costs (medication cost, outpatient and inpatient care) and increased risk of hospitalization and mortality among older adults.^{23,24,25} However, these associations are partly driven by the fact that older and/or sicker individuals are more likely to require multiple medications. While polypharmacy may sometimes be clinically appropriate, it inherently, as mentioned before, increases the risk of adverse outcomes due to drug–drug and drug–disease interactions. Targeting potentially inappropriate or avoidable medications for deprescribing can further help reduce these risks and associated costs. Third, it places a burden on the care process itself: medications must be prescribed, dispensed, monitored, controlled for interactions and side effects—all of which uses clinician time, introduces complexity and risk, and

increases the chances of error. For instance, medication-related harm following hospital discharge—which includes adverse drug reactions, drug–drug interactions, prescribing errors, or problems with adherence after leaving the hospital—not only degrades patient outcomes but imposes large costs on health systems (e.g., in the UK $\approx$ £396 million annually), much of which is thought preventable.^{23,24,25}

Shifting Goals in Limited Life Expectancy

In frail individuals with limited life expectancy, as found in nursing homes, the traditional goals of medical treatment—preventing long-term complications and prolonging life—are often no longer appropriate. Instead, it may be more appropriate to shift clinical focus towards improving or maintaining quality of life, alleviating symptoms, and supporting functional autonomy.^{26,27,28,29} Medications aimed at primary or secondary prevention, such as statins for hyperlipidemia or diabetes or bisphosphonates for osteoporosis, may not confer meaningful benefit within the remaining lifespan. For example, the cardiovascular benefits of statins typically require around 2–3 years to manifest³⁰, while bisphosphonates may take about 12 months to prevent a non-vertebral fracture.³¹ However, the time until benefit (TUB) is relevant when initiating treatment, but not when considering deprescribing. Conversely, these drugs may cause fatigue, gastrointestinal side effects, or increase fall risk. As a result, the balance between risk and benefit can change substantially as life expectancy shortens, and medication regimens must be re-evaluated accordingly. In practical terms, this paradigm shift implies a move away from standardized clinical targets, such as HbA1c or blood pressure thresholds, toward more individualized and comfort-oriented approaches. For instance, tight glycemic control may be deprioritized to avoid hypoglycemia, which is strongly associated with falls and cognitive impairment in the elderly.³² Similarly, antihypertensive regimens may need to be adjusted in the context of postural hypotension and fall risk.³³ This requires continuous dialogue among patients, families, and healthcare professionals. However, deprescribing requires caution, as stopping symptom-oriented antihypertensive treatment in late-stage dementia may cause dizziness or shortness of breath, suggesting some ongoing therapy may still be needed for comfort.³⁴

Many older patients are prescribed medications for asymptomatic conditions that may not cause morbidity in the short term but carry risks of adverse effects. Medications such as lipid-lowering agents, or antiplatelet therapy should be carefully evaluated in the context of life expectancy, treatment burden, and patient values. Frailty and cognitive decline may necessitate an approach focused primarily on symptom relief and comfort, rather than risk reduction over years.^{27,28,29} At the same time, it remains important in other patients, based on their individual risks and wishes, to treat risk factors like hypertension or osteoporosis adequately to reduce the risk of major events like fractures or strokes.

Need for Medication Review and Tools for Implementation

Medication review is an essential component of good prescribing practice in elderly care and aims not merely to reduce the number of medications, but to ensure that each drug has a valid indication, is dosed appropriately, and aligns with the patient's health goals and life expectancy. Several structured tools have been developed to assist in this process. Deprescribing can be guided by explicit tools, such as the STOPP/START^{35,36}, STOPP-NL, STOPP Fall, STOPP-COG, STOPP-Frail^{14,27} and ReNeWAL method which is developed for nursing homes and provide standardized recommendations for potentially inappropriate medications.³⁷ These tools are straightforward and efficient but may lack flexibility for individual patient contexts. Implicit tools, in contrast, rely on clinical judgment and patient-centered assessment, considering factors like comorbidities, life expectancy, and personal goals. Examples include the Medication Appropriateness Index (MAI) and the STRIP method. Combining both approaches can optimize deprescribing, balancing efficiency with individualized and safe care.³⁸

Engaging the patient in the decision-making process is essential, and several instruments are available to support this shared decision-making. It is important to note that evidence supporting improved patient outcomes through these tools is limited, and the quality of the studies is often suboptimal.³⁸

In the Netherlands, the WHO 6-step method for appropriate prescribing is integrated into Elderly Care Specialist training and supports medication review through a cyclical, reflective process. The approach includes re-evaluation of pharmacological goals, considering whether treatment still aligns with evolving functional status and care preferences. Interdisciplinary collaboration—particularly with pharmacists and nursing staff—is fundamental to its success.

The implementation of these tools in clinical practice has led to improved prescribing appropriateness, reduced adverse events, and even cost savings in geriatric institutions.^{39,40} Still, these frameworks are not universally adopted and remain underused in many long-term care settings. Particularly in residents with advanced dementia, deprescribing can significantly reduce medication burden and risks without compromising comfort.⁴¹

Deprescribing Dilemmas: Perspectives of Patients and Physicians

Deprescribing is often perceived as complex by both patients and physicians. Patients may be uncertain to discontinue long-standing medications due to fear of symptom recurrence or loss of therapeutic benefit, while physicians face challenges balancing guideline recommendations, clinical judgment, and individual patient preferences. The Dutch guideline³⁸ emphasizes a structured, patient-centered approach, recommending the use of both explicit tools (e.g., STOPP/START criteria) and implicit frameworks (e.g., individualized assessment and shared decision-making) to support safe and effective deprescribing.

Engagement in shared decision-making, careful monitoring, and consideration of patient goals are critical to overcoming barriers and minimizing potential harm. Mrs. Jansen's reluctance to stop her blood pressure medication, despite possible side effects, reflects this common concern. Family members, often involved in decision-making, may also be hesitant due to lack of understanding or emotional attachment to existing treatment routines.

From the physician's perspective, deprescribing requires time, confidence, and communication skills. Clinical uncertainty, fear of legal liability, and absence of deprescribing protocols contribute to inertia. Furthermore, existing tools like STOPP/START and BEERS criteria may not fully accommodate the complex profiles of nursing home residents.^{42,43,44} In this context, the developed ReNeWAL criteria³⁷ may provide a more suitable framework. Building upon STOPP/START version 2, these criteria are specifically designed for older nursing home residents with limited life expectancy, addressing frailty, multimorbidity, and shifting treatment goals toward comfort and quality of life. This makes the ReNeWAL approach potentially more applicable and clinically meaningful within long-term care settings. Although the ReNeWAL criteria aim to improve prescribing appropriateness, empirical evidence on their implementation and effectiveness remains limited. Additionally, the Dutch nursing home context differs substantially from many other European countries, in terms of care organization and the role of Elderly Care Specialist. Therefore, it is not always clear how Dutch prescribing culture and deprescribing practices compare to those in other European long-term care systems. It is also why we used the shelter database⁴⁵ to try to compare different countries in terms of differences in medication use. This database provides a wide range of data on medication and clinical characteristics of nursing home residents from several European countries.

Knowledge of patients' and carers' attitudes towards deprescribing is essential to facilitate shared decision-making. A trusting relationship and clear communication enhance willingness to consider medication changes.^{46,47,48} Elderly Care Specialist play a key role here: their training in comprehensive geriatric care equips them to assess the interplay between medical, psychological, and social domains, all of which influence prescribing decisions. Understanding the barriers and facilitators of deprescribing in nursing homes remains limited. Our study provides preliminary understanding, highlighting factors from Elderly Care Specialist perspectives, but further research is needed to clarify these influences and guide effective interventions.

Thesis Objective and Research Questions

This thesis explores the prescribing of potentially inappropriate medications (PIMs) in nursing home residents, with a focus on clinical patterns, safety, and the factors that guide rational medication use. By examining these aspects, the study aims to provide insights into how Elderly Care Specialists —professionals uniquely trained in the Netherlands to

manage complex chronic conditions in long-term care—can optimize medication use for frail older adults, balancing biomedical knowledge with person-centered care. Specifically, this thesis assessed and explored the prevalence of PIMs across European countries, examined patterns of preventive cardiovascular and osteoporosis medication prescribing in relation to resident characteristics and country, and investigated the barriers and facilitators that influence deprescribing decisions among Elderly Care Specialist.

Thesis Outline:

Chapter 2 Cross-national comparison of prescribing using STOPP-Frail criteria in nursing home residents:

Investigated the prevalence of potentially inappropriate medications (PIMs) among nursing home residents across eight countries, including differences by cognitive status and life expectancy.

Chapter 3 Analysis of cardiovascular medication use and deprescribing potential in nursing home residents:

Examined the prevalence of preventive cardiovascular medications among nursing home residents across eight countries, and explored differences by length of stay, mortality risk, cognitive impairment, and functional disability.

Chapter 4 Focus on osteoporosis medication and its clinical relevance:

Assessed the prevalence of pharmacological osteoporosis prevention (bisphosphonates, calcium, vitamin D) among nursing home residents in eight countries and its association with patient characteristics, highlighting under-treatment in high-risk residents and variability across countries.

Chapter 5 Qualitative study on Elderly Care Specialist perspectives regarding (de)prescribing:

Explored the barriers and enablers of deprescribing potentially inappropriate medications among Elderly Care Specialists in the Netherlands, emphasizing the importance of clinical experience, patient and family involvement, and interdisciplinary collaboration.

Chapter 6 General discussion, synthesis of findings, and recommendations:

Provides a comprehensive discussion of the key contributions of this thesis, synthesizing its main findings, strengths, and limitations, and outlining implications for future practice and research in improving (in)appropriate prescribing and optimizing medication use in nursing home residents.

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CHAPTER 2

Prevalence of Potentially Inappropriate Medications According to STOPP-Frail Criteria in Nursing Home Residents: The SHELTER Study

Authors

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Abstract

Objective

The aim of this study was to determine the prevalence of potentially inappropriate medications (PIMs) in nursing home (NH) residents across eight countries and investigate differences between residents with and without cognitive impairment, as well as those with and without life expectancy of six months or less.

Methods and Design

The study utilized the second edition of the STOPP-Frail criteria to operationalize PIMs in the baseline assessment of nursing home residents participating in the Services and Health for Elderly in Long TERM care (SHELTER) project. The data were collected between 2009 and 2012. The project was conducted in eight countries: Czech Republic, England, Finland, France, Germany, Italy, the Netherlands, and Israel. Cognitive impairment was measured by the cognitive performance scale (CPS). The presence of end-stage disease with a life expectancy of six months or less was recorded. The study included residents aged 60 years or older who underwent a valid medication assessment.

Results

Among the 3,832 eligible residents, 87.9% had at least one PIM. Specifically, 24.3%, 23.5%, 18.8%, and 19.3% of residents had one, two, three, and four or more PIMs, respectively. On average, each person was prescribed 2.16 PIMs. Cognitively impaired residents ($n = 1999$) had an average of 1.96 PIMs (SD 1.49) per person, while residents with a low CPS score ($n = 1783$) had an average of 2.40 PIMs (SD 1.57) per person, showing a statistically significant difference ($P < 0.001$). Similarly, NH residents with life expectancy of six months or less had an average of 1.66 PIMs (SD 1.30), whereas those without had an average of 2.17 PIMs (SD 1.55) ($p < 0.001$). The average number of PIMs varied across countries, ranging from 3.23 in Finland to 2.15 in the UK ($P < 0.001$). Anti-platelets and aspirin were the most prescribed PIMs, accounting for over 38.0% of prescriptions.

Conclusions

This study highlights the high prevalence of PIMs among nursing home residents. However, PIMs were somewhat lower in residents with cognitive impairment and life expectancy of six months or less. Efforts must continue to improve the rationale behind prescribing practices in nursing homes.

Introduction

Ageing is often accompanied by an increased prevalence of chronic diseases, leading to a higher utilization of medications.¹ A significant portion of these medications is prescribed with the intention of mitigating the risk of future adverse health events. However, as individuals approach the end of life, the appropriateness of using preventive medications becomes a subject of debate, as the potential long-term benefits may no longer outweigh the associated adverse effects.^{2,3} This may be especially true for patients with a very limited life expectancy or end stage neurodegenerative disease. Given the high probability of medication becoming inappropriate in these situations, we hypothesized that cognitive impairment and limited life expectancy should be associated with a lower prevalence of PIMs.

Among older adults residing in nursing homes, especially those with progressive disorders like dementia, life expectancy is typically limited. Across six European countries, the proportion of deaths occurring within one year of admission to long-term care facilities ranged from 32 to 63%. The average length of stay in these facilities ranged from 6 months to 2 years.⁴ Polypharmacy and hyper-polypharmacy (the use of ten or more medications) are prevalent among older nursing home residents.^{5,6} Studies have reported persistently high utilization of potentially inappropriate medications, including in nursing home patients with dementia, up until a few weeks prior to death.⁷

Explicit screening tools such as the STOPP-START and Beers criteria have been developed to aid prescribers in identifying potential inappropriate medication use in older individuals. In 2017, the STOPP-Frail criteria were introduced as an explicit screening tool specifically designed to recognize inappropriate medication use in patients with a limited life expectancy.⁸ An updated version of the STOPP-Frail criteria was published in 2020.^{9,10} These criteria were developed to assist physicians in discontinuing potentially inappropriate medications in older individuals with end-stage irreversible conditions, poor one-year survival prognosis, severe functional impairment, severe cognitive impairment, or a combination thereof, with a focus on symptom control rather than disease prevention.^{8–10}

The objective of this study was to determine the prevalence of potentially inappropriate medications (PIMs) among nursing home residents across eight countries and investigate the differences between residents with and without cognitive impairment, as well as those with and without end-stage diseases. We hypothesized that cognitive impairment and limited life expectancy would be associated with a lower prevalence of PIMs.

Methods and Materials

Study Setting and Residents

The data for this study was obtained from the Services and Health for Elderly in Long TERM care (SHELTER) project, conducted between 2009 and 2012. The project aimed to validate the interRAI instrument for long-term care facilities (interRAI-LTCF)¹¹. The interRAI-LTCF is a standardized assessment tool used to evaluate the care needs and preferences of nursing home (NH) residents, aiding in care planning. It encompasses over 350 items that capture comprehensive information on residents, including sociodemographic variables, clinical characteristics (such as physical and cognitive status, clinical diagnoses), current service utilization, and medication use. The study included 4,156 residents from 57 NHs across 8 countries (Czech Republic, England, Finland, France, Germany, Italy, the Netherlands, and Israel). NHs that routinely utilized the interRAI-LTCF were selected as study partners in each country, without random selection, aiming to represent diverse NHs.

Eligibility

Both existing residents and those *entering the home* during the 3-month enrolment period within the homes were assessed using the interRAI-LTCF. Reassessments were conducted at 6 and 12 months for residents still in the facility. For this study, the baseline assessment of each participant was utilized. The study included residents aged 60 years or older with a valid medication assessment, without any specific exclusion criteria. A valid medication assessment comprised both the medication name and the ATC code.

Ethical Approval

To conduct the study was given by the Ethics and Research Committee of Catholic University of the Sacred Heart of Rome, Italy. Ethical approval was obtained also from the Ethics Committees of the participating centers (Univerzita Karlova, Czech Republic; Universitaet Ulm, Germany; Terveystieteiden tutkimuskeskus, Finland; Assistance Publique Hopitaux De Paris, France; University of Haifa, Israel; University of Kent, United Kingdom; Vereniging Voor Christelijk Hoger Onderwijs Wetenschappelijk Onderzoek En Patientenzorg, The Netherlands) and written informed consent was obtained from all participants. All procedures performed in this study involving human participants were in accordance with the ethical approval and standards of the local ethics committees. Regarding informed consent, both opt in and opt out procedures were followed.

Determinants

Medication Use

Was recorded in the interRAI-LTCF, considering the medications taken by each resident in the three days preceding each assessment. Medication data was gathered and verified from multiple sources, including physician order sheets and medication administration records. The information collected included proprietary names, Anatomical Therapeutic

and Chemical (ATC) codes provided by the World Health Organization Collaborating Centre for Drug Statistics Methodology, formulation, dosage, frequency, and route of administration. Additionally, information was collected regarding medications taken on an “as-needed” basis.

Cognitive Impairment

Was assessed using the Cognitive Performance Scale (CPS), which evaluates decision-making capacity, memory impairment, level of consciousness, and executive function. The CPS score ranges from 0 (indicating intact cognition) to 6 (representing severe cognitive impairment).¹² The CPS has been validated in various studies.^{12,13} The CPS has comparability with the Mini Mental State Examination (MMSE) a score ≥ 2 being associated to a diagnosis of dementia or a MMSE score of ≤ 19 .¹⁴ So the CPS is used quite widely and the cut-off value of 2 or more is associated with cognitive impairment and dementia and therefore we considered 2 as the cut-off and cognitive impairment was considered present if the CPS score exceeded 2, indicating moderate or more severe cognitive impairment.

Life Expectancy

Life expectancy of six months or less according to best clinical judgment and supported by a diagnosis of end-stage disease and communicated with the patient or their family.¹⁵

Outcome

Potentially Inappropriate Medications (PIMs) According to the 2nd Edition of the STOPP-Frail Criteria

The selection and compilation of PIMs were based on the explicit criteria for PIM use in frail older adults with limited life expectancy, known as the STOPP-Frail-2 list, specifically sections B to J.^{9,10} For each section, the medications were converted to Anatomical Therapeutic and Chemical (ATC) codes, utilizing levels 3 to 5 depending on the specific criterion, in accordance with the codes provided by the World Health Organization Collaborating Centre for Drug Statistics Methodology. The ATC codes are all included and listed in Table 1. It should be noted that we did not have access to information regarding the indications for medication use or specific clinical conditions, which prevented the operationalization of section A. Section A defines PIMs in general terms, encompassing medications that residents persistently fail to take or tolerate without a clear indication or for symptoms that have already resolved (refer to Table 1). However, all SHELTER residents fulfilled the general pre-conditions, namely (i) requiring assistance with activities of daily living (ADL), (ii) having severe irreversible frailty, and (iii) being under the care of a physician who would not be surprised if the individuals died within the next 12 months.

Data Analysis

The data analysis was conducted using Statistical Package for the Social Sciences (SPSS) version 26 (SPSS Inc, Chicago, IL, USA). Prevalence was reported as frequency and percentage. Continuous variables were presented as mean with standard deviation (SD). Differences in prevalence were assessed using Chi-square tests for categorical variables and T-tests for continuous variables. Statistical significance was set at a p-value below 0.05.

Results

Of the 4156 residents included in the SHELTER study, 324 did not meet the eligibility criteria; hence, 3832 residents were included in this study. Of 324 residents not included, 96 were under 60 years, and another 228 had no valid medication registration. The average age of the residents was 84 years, ranging from 60 to 110 years, with 74% being women. On average, residents were taking 7.2 medications (SD 3.5) (Table 1; Fig. 1). Between 2.2% and 4% of the medications were prescribed as needed. Residents with moderate to severe cognitive impairment ($N = 1999$, 52.2%) used fewer medications and PIMs compared to those without. Medication use of residents with a life expectancy of less than six months was not statistically different from those with a longer life expectancy (Table 2). In addition, 80% of the residents with a life expectancy of less than six months, used one or more PIMs versus 86% in those with a longer life expectancy ($p=0.06$).

On average, residents had 2.16 PIMs (SD 1.54). Among the residents, 87.9% had at least one PIM, with 24.3%, 23.5%, 18.8%, and 19.3% having one, two, three, or four or more PIMs, respectively. The percentage of residents with one or more PIMs was 83.1% in those with cognitive impairment ($n = 1999$) compared to 89.4% in those with no or mild cognitive impairment ($n = 1783$) ($p < 0.0001$). Additionally, residents with cognitive impairment had a lower average number of PIMs: 1.96 (SD 1.49) compared to 2.40 (SD 1.57) in residents without cognitive impairment.

Similarly, residents with the shortest life expectancy (< 6 months) had a lower average number of PIMs compared to those with a longer life expectancy 1.66 (SD 1.30) versus 2.17 (SD 1.55) (Table 2).

Regarding the types of PIMs, anti-platelet drugs and antihypertensive therapies (AHT) were the most common PIMs with preventative indications, accounting for 38.5% and 35.7% of PIMs, respectively. Although these drugs were less frequently prescribed to cognitively impaired residents ($CPS > 2$) and residents with a shorter life expectancy, their prevalence still exceeded 20% in both groups. Proton pump inhibitors and antipsychotic drugs, commonly used for symptomatic purposes, were also highly prevalent at 35.7% and 20.6%, respectively. Antipsychotic drugs, however, had a higher prevalence in patients with cognitive impairment (26.6% versus 14.0%, $p < 0.05$) (Table 2; Fig. 1).

The prevalence of residents with one or more PIMs varied across countries, ranging from 93.3% in Finland to 80.4% in England (Figures. 1 and 2). In six countries, the group of residents with cognitive impairment had a larger proportion without PIMs compared

to those without cognitive impairment ($P < 0.001$). Only in Italy and the Netherlands, no significant difference was found. There were no cross-country differences in PIM prevalence between residents with longer and shorter life expectancies. Due to the low percentage of residents with limited life expectancy, between country comparison of PIM prevalence was not feasible for this item.

In Finland, residents with cognitive impairment ($CPS > 2$) had significantly higher use of the following medications compared to other countries ($P < 0.01$): anti-anginal therapy (27.0% compared to less than 5.0% in most other countries), calcium supplements (26.3% vs. less than 10% in other countries), calciferol (38% vs. less than 10% in other countries), and multivitamin supplements (43.2% vs. less than 10% in all other countries). These medications were also more frequently prescribed to residents with lower CPS scores compared to other countries. Osteoporosis medication use in Finland differed substantially from use in all other countries. Almost two thirds of the residents used at least one of these medications. This was mainly the result of a high vitamin D use (65.6%), but also calcium use was higher than in other countries (29%). Interestingly, in Finland, the use of these medications was significantly higher among residents with a life expectancy of over 6 months compared to the same group in other countries.

Discussion

This study presents data on the prevalence of inappropriate medications in European nursing home residents, based on the 2nd edition STOPP-Frail criteria. The results reveal that PIMs (Potentially Inappropriate Medications), as defined by the STOPP-Frail criteria, are present in nearly 90% of the residents within a typical European sample of nursing home residents. It is noteworthy that, on average, two out of seven prescribed medications were considered PIMs. As expected, our study found a lower prevalence of PIMs in patients with cognitive impairment compared to those with no or mild cognitive impairment, as well as in residents with a life expectancy of less than 6 months. This indicates that physicians appear to exercise more caution when prescribing medications for individuals with advanced dementia or poor prognosis. It is possible that because of the role physicians have in both (de)prescribing and estimating life expectancy, this strengthened this association. There seems to be an association between the average number of PIMs and the overall number of medications prescribed. However, it is concerning that 15.4% of nursing home residents with cognitive impairment still had four or more PIMs. Moreover, over 20% of the residents were using antihypertensive medications or platelet aggregation inhibitors, and over 10% were using lipid-lowering medication. Even in residents with a life expectancy of less than six months, the average number of PIMs remained high at 1.66.

These findings align with previous studies highlight the continued use of medications in the last years or months of life.^{16, 17.}

While this study provides valuable insights, it is important to acknowledge its limitations. Although the SHELTER study data collection took place between 2009 and 2012, the data is still relevant. More recent studies on PIM prevalence based on STOPP-Frail use

in nursing homes are in accordance with our results. Recent data shows a prevalence of PIM use between 85% and 96%^{18–21} in nursing home residents which is close to what we found (around 87%). Since other studies only look at data in 1 country at the time, we feel that our study comparing data from 8 countries and many residents adds knowledge to existing data.

Based on the ADL scale, not every resident in the SHELTER study appears to meet the STOPP-Frail criteria (as opposed to STOPP criteria).²² At the same time, it is expected that admission to a nursing home is evidence of vulnerability that will increase over time and lead to death. A recent study showed that almost 65% of patients awaiting long-term care are eligible for the application of STOPP-Frail criteria with over 90% prescribed at least one PIM. We expect that in case of people already admitted to long-term care the percentage of patients meeting STOPP-Frail criteria will be larger than the mentioned 65%. However, we realize that using these criteria on all residents in this study may overestimate the number of patients with inappropriate medication.

The low percentage of residents with a limited life expectancy in this study seems surprising but can be explained by the way this item is defined in the interRAI. While many studies only require the doctor's best clinical judgement to determine life expectancy, the interRAI also requires that 2 other conditions are met: it must be supported by a diagnosis of end-stage disease and communicated with the patient or their family. We believe that these last 2 criteria often are not met. For instance, an earlier SHELTER study showed that 86.4% of residents close to death did not receive an accurate prognosis.²³ Detailed clinical information such as blood pressure or the specific indications for drug prescriptions was not available, which may also have resulted in an overestimation of the actual number of PIMs. Additionally changes in medication use over time were not studied for individual patients during their stay in nursing homes, potentially missing any decreases in prevalence among cognitively affected residents. Due to the cross-sectional nature of our study, we could not say anything about the course of medication use, although given the including data after 3 months of admission to the nursing home, it can be assumed that the first medication review had already taken place.

We were not able to operationalize all STOPP-Frail criteria specifically. Therefore, the number of PIMs may be overestimated.

Finally, the convenience sampling method used for participant selection limits the generalizability of the conclusions to the participating countries.

Strengths of this study include the use of a multinational cohort and the application of the internationally well-validated interRAI standard for monitoring. This ensured reliable and fair comparisons.¹¹ Moreover, the large sample size enabled meaningful comparisons between residents with and without PIMs.

What are the implications of this study? First, these findings raise questions regarding medication prescriptions for nursing home residents, particularly those in the end-stage of life or with end-stage dementia, where the potential health benefits over a median life expectancy of 1 to 2 years need to be carefully weighed against the risks of adverse drug events. While deprescribing appears to be feasible and relatively safe towards the

end of life²⁴, this study suggests that it is not a common practice. Clinicians often find it challenging to discontinue medications, particularly those related to coagulation. Various factors contribute to this phenomenon, as suggested in the literature.^{25,26} Some physicians believe there is sufficient evidence to justify medication prescriptions, while others are hesitant to change medications initiated by their colleagues. Lack of education and experience in safely deprescribing, difficulty in communicating deprescribing decisions, and concerns about “giving up on the patient” and hastening death are other barriers. Additionally, clinicians may feel pressured to adhere to clinical guidelines that often lack evidence from studies involving older populations with limited life expectancies. For instance, the use of psychotropic drugs remains common in home-dwelling individuals with mild dementia, despite limited evidence of their benefit.²⁷ Patients and their relatives may also express anxiety about discontinuing medications they have been using for many years.²⁸

For nursing home residents, prescribing physicians must carefully consider the expected treatment benefits while considering the short life expectancy and the risk of side effects.²⁹

Conclusion

This study conducted as part of the SHELTER study suggests a high prevalence of PIMs among nursing home residents across countries. While PIMs were somewhat lower in residents with cognitive impairment and those with end-stage diseases, there is an ongoing need for efforts to improve rational prescribing in nursing home settings and reduce potential adverse effects.

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Author Contributions

RvM conceived the study idea; RvM, AMM and HvH operationalized the metrics in the SHELTER study; HvH and AMM performed the analyses; AMM drafted the manuscript; all authors contributed to and approved of the final version.

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Data Availability

Data are not publicly accessible due to privacy regulations. Reasonable requests for data access and material can be directed to the corresponding author.

Declarations

Ethical Approval

SHELTER was ethically approved by the representative committees from the participating countries: Services and Health for Elderly in Long TERM care | SHELTER | Project | Fact sheet | FP7 | CORDIS | European Commission (europa. eu). We confirm that all methods were carried out in accordance with relevant guidelines and regulations. We confirm that all experimental protocols were approved by a named institutional and/or licensing committees. We confirm that informed consent was obtained from all subjects and/or their legal guardian(s) in the countries where data was collected in context of this research. In some countries, opt out procedures were in place data in the context of routine care observations. Also here, residents and relatives were informed and had the possibility to object.

Consent for Publication

Not applicable.

Competing Interests

The authors declare no competing interests.

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Table 1. PIMs prevalence according to STOPP-Frail version2 in all residents, residents with vs without cognitive impairment, with longer versus shorter life expectancy*

STOPP-Frail version 2 sections	PIM (ATC code)	All (n:3832)	CPS>2 (n:1999)	CPS0-2 (n:1783)
Section B: Cardiology system	lipid- lowering therapies (C10AA, C10AB)	10.3 (396)	7.2 (143)	14.0 (250)
	Antihypertensive therapies (C03A, C03BA, C03EA, C03B, C08CA, C08GA01, C08GA02, C09BB, C09BX01, C09XA53, C09)	35.7 (1369)	28.3 (566)	44.7 (797)
	Anti-anginal therapy (nitrates, nicorandil, ranolazine), (C01DA, C01DX16, C01EB18)	8.1 (312)	6.4 (127)	10.2 (181)
Section C: Coagulation system	Anti-platelets (B01AC) And Aspirin (N02BA01, A01AD05)	38.5 (1475)	35.3 (706)	42.0 (757)
Section D: Central nervous system	Neuroleptic- antipsychotics (N05A)	20.6 (790)	26.6 (532)	14.0 (250)
	memantine (N06DX01)	4.4 (170)	6.1 (121)	2.7 (49)
Section E: Gastrointestinal system	proton pump inhibitors (A02BC)	35.7 (1368)	31.7 (634)	40.4 (720)
	H2 receptor antagonist (A02BA)	1.7 (64)	1.2 (2.4)	2.1 (38)
Section F: Respiratory system	theophylline (R03D)	2.2 (84)	1.8 (36)	2.5 (45)
	leukotriene antagonist (R03DC)	0.3 (10)	0.2 (4)	0.3 (6)
Section G: Musculoskeletal system	calcium_supplements (A12AX)	8.5 (324)	8.2 (163)	9.0 (161)
	Vitamin D (ergocalifero and calciferol) (A11CC01, A11CC, M05BB03, M05BB04, M05BB05, M05BB06, M05BB07, M05BB08, M05BX53)	8.1 (309)	7.6 (152)	8.7 (157)
	Anti-resorptive/bone anabolic drugs for osteoporosis (bisphosphonates, strontium, teriparatide, denosumab), (M05B)	4.5 (172)	3.1 (62)	6.1 (109)
	Long-term oral nonsteroidal anti-inflammatory drugs (M01A)	3.6 (138)	2.1 (42)	5.4 (96)
	Long-term oral corticosteroids (H02)	3.5 (134)	3.0 (59)	4.2 (74)
Section H: Urogenital system	Drugs for benign prostatic hyperplasia (5-alpha reductase inhibitors (G04CA, G04CB)and alpha-blockers (C02CA, C02LE)	3.3 (126)	2.9 (58)	3.8 (68)
	Drugs for overactive bladder (muscarinic antagonists and mirabegron (A04AD01, G04BD12)	0.1 (4)	0.1 (2)	0.1 (2)
Section I: Endocrine system	Anti-diabetic drugs (A10AD , A10B)	10.7 (411)	9.3 (185)	12.4 (221)
Section J: Miscellaneous	Multivitamin combination supplements (A11)	10.6 (407)	9.9 (198)	11.6 (207)
	Folic acid (B03BB, B03AD, B03AE01, B03AE02, L01BA, V04CX02)	5.8 (221)	5.9 (118)	5.5 (98)

Ns = not significant ($P>0.05$)

CPS= Cognitive Performance Scale

*Life expectancy less than 6 months with documented end stage disease and discussed with resident and/or relatives

P value CPS>2 vs CPS)-2	Life expectancy <6 months (n:120)	Life expectancy >6 months (n:3698)	P value Life expectancy <6 months vs >6 months
<0.01	5.8 (7)	10.5 (388)	ns
<0.01	20.8 (25)	36.3 (1341)	<0.01
<0.01	3.3 (4)	8.2 (305)	ns
<0.01	20.8 (25)	39.0 (1444)	<0.01
<0.01	20.8 (25)	20.6 (763)	ns
<0.01	0.8 (1)	4.5 (167)	ns
<0.01	42.5 (51)	35.4 (1308)	ns
<0.05	3.3 (4)	1.6 (59)	ns
ns	5.0 (6)	2.1 (78)	ns
ns	0.0 (0)	0.3 (10)	
ns	2.5 (3)	8.6 (309)	<0.05
ns	3.3 (4)	8.1 (299)	ns
<0.01	3.3 (4)	4.5 (168)	ns
<0.01	4.2 (5)	3.6 (133)	ns
<0.05	7.5 (9)	3.4 (125)	ns
ns	2.5 (3)	3.3 (123)	ns
ns	0.0 (0)	0.1 (4)	ns
<0.01	10.8 (13)	10.7 (397)	ns
ns	3.3 (4)	10.7 (396)	<0.01
ns	5.8 (7)	5.8 (214)	ns

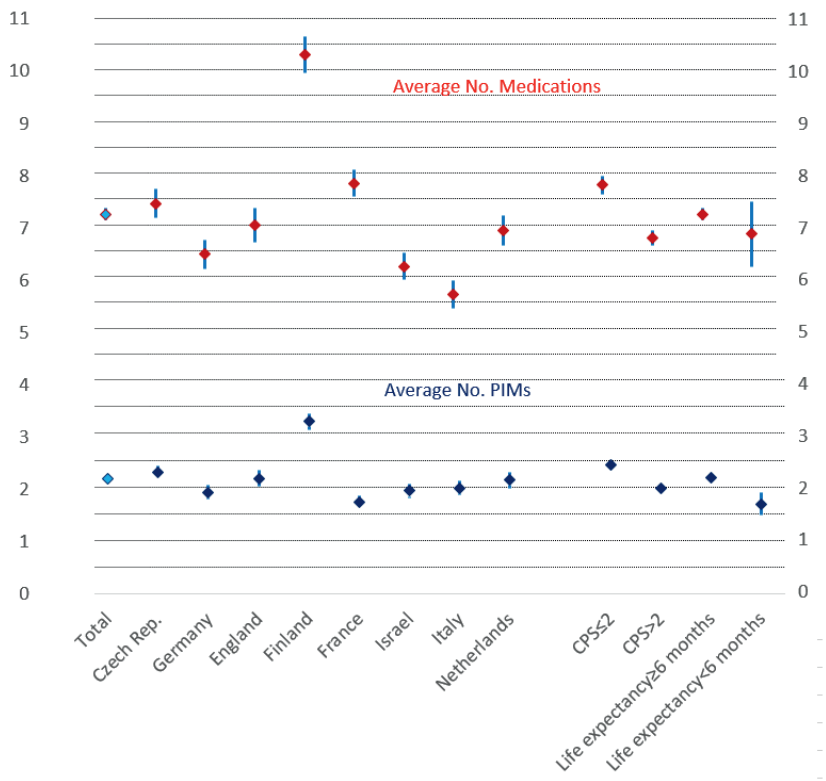
Table 2. Mean number of all medication vs PIMs in all residents, residents with vs without cognitive impairment, residents with lower and longer life expectancy*

	Total Sample (N=3832)	Cognitive impairment Moderate-severe (CPS>2, n=1999) No-mild (CPS≤2, n=1783)	Life expectancy* <6 month (n=120) ≥6 month (n=3698)
Mean no of drugs used (SD)	7.20 (3.50)	6.75 (3.33) 7.77 (3.61) P<0.001	6.81 (3.49) 7.20 (3.50) Ns
Mean no of PIMs (SD)	2.16 (1.54)	1.97 (1.50) 2.4 (1.57) P<0.001	1.66 (1.31) 2.17 (1.55) P<0.001

CPS=Cognitive Performance Scale

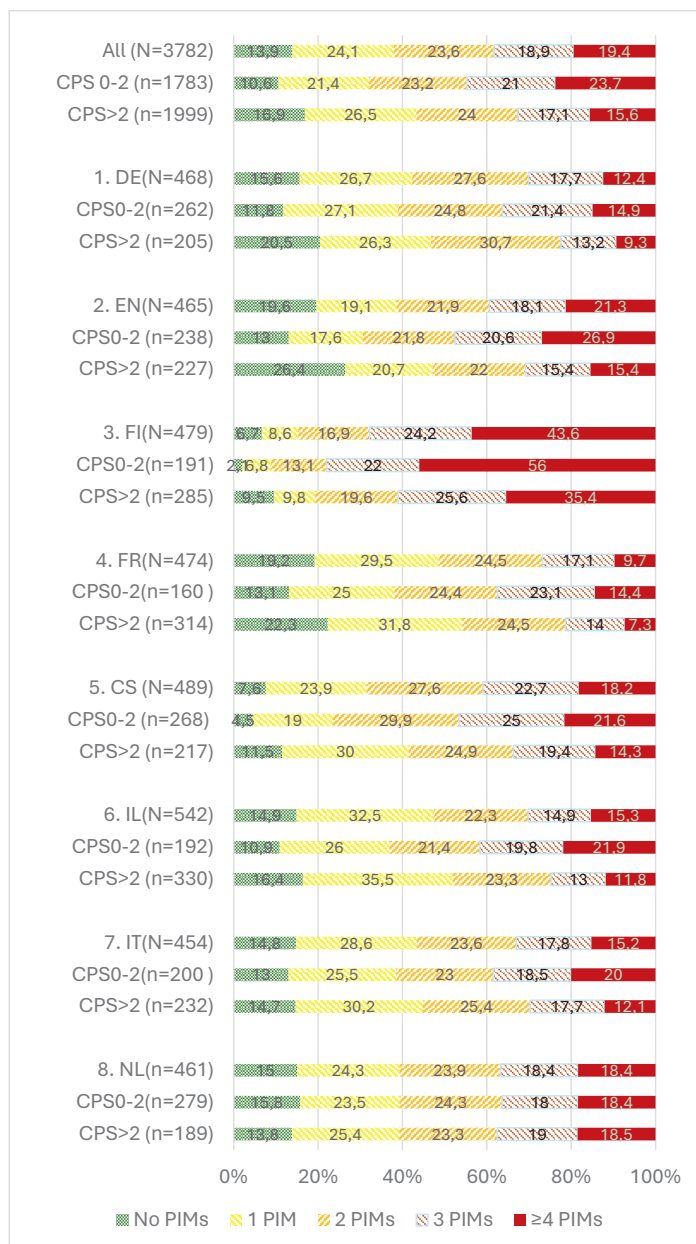
*Life expectancy less than 6 months with documented end stage disease and discussed with resident and/or relatives

Figure 1. Average number of PIMs (upper panel) and number of drugs (lower panel) across countries with 95% Confidence Intervals, level of cognitive impairment (CPS) and life expectancy*.



CPS= Cognitive Performance Scale, > 2 reflects moderate to severe impairment

*Life expectancy less than 6 months with documented end stage disease and discussed with resident and/or relatives

Figure 2. PIMs prevalence in residents with and without cognitive impairment across countries

CPS= Cognitive Performance Scale > 2 indicates moderate to severe impairment

CS=Czech Republic, DE=Germany, EN=England, FI=Finland, FR=France, IL=Israel, IT=Italy, NL=the Netherlands

* $P < 0.0001$ (comparison between high and low CPS on percentage of PIMs)



CHAPTER 3

Prevalence of Preventive Cardiovascular Medication Use in Nursing Home Residents. Room for Deprescribing? The Shelter Study

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Abstract

Introduction: In nursing home (NH) residents with a very short life expectancy, the benefits of preventive cardiovascular medication maintenance are questionable.

Objective: To assess the prevalence of 4 classes of preventive cardiovascular medication (PCM) in NH residents, and to explore differences of prevalence across length of stay, mortality risk, cognitive impairment, functional disability, and across countries.

Methods: A 12-month prospective cohort study was conducted in 57 NHs in 8 countries (Czech Republic, England, Finland, France, Germany, Italy, The Netherlands, and Israel). We assessed the prevalence at first measurement of 4 classes of PCM: oral anticoagulants (OAC), platelet aggregation inhibitor (PAI), antihypertensive (AHT), and lipid-modifying agent (LMA), in older (60+ years) residents with valid medication assessments. The PCM prevalence was compared across the length of stay (short <60 days, mid, long >12 months), health instability as defined by Changes in Health, End-Stage Disease, Signs, and Symptoms Scale (CHESS) > 3, cognitive impairment by Cognitive Performance Scale (CPS) > 2, and functional disability was measured using the Activities of Daily Living Hierarchy Scale (ADLH) ≥5.

Results: Of the 3759 eligible residents, 2175 (57.9%) used at least 1 PCM. The prevalence of the 4 groups of PCM: OAC, PAI, AHT and LMA were 5.6%, 34.9%, 35.7%, and 10.4%, respectively. PCM use was lower in long stay residents versus mid-stay: 56.0% vs. 62.7%, in cognitively impaired residents (47.1% vs. 67%), in residents with a high mortality risk (47.4% vs. 58.6%), and in residents with a high ADLH score (48.6% vs 64.0%).

Conclusion: Although the prevalence of PCM use was lower in long-stay, cognitively impaired residents, persons with a high mortality risk, and residents with more functional disabilities, there seems to be room for deprescribing.

Introduction

In nursing home (NH) residents with a poor prognosis, the advantages of preventive cardiovascular medication (PCM) maintenance are vague and controversial.

People are now living longer than before. This demographic transition has been accompanied by an increase in prevalence of chronic diseases and multimorbidity. Older people with multimorbidity frequently use 5 or more medications (polypharmacy). A large part of this polypharmacy is formed by PCM. Studies on which current guidelines for cardiovascular prevention are based seldom include multimorbid frail elderly with polypharmacy and a limited life expectancy. Polypharmacy, however, is associated with increased risks of drug-drug and drug-disease interactions and thereby with adverse effects; for example, falls, bleeds, electrolyte disturbances, cognitive deficits,¹ and mortality.² Especially in the frail elderly, medication with a theoretical use or clear indication in the past can become inappropriate in later life. Medication can be defined as inappropriate when potential risks outweigh potential benefits. This is the case when the risk of side effects is strongly increased (for instance due to changed pharmacokinetics or pharmacodynamics), but also when the chance of potential benefits are very low or perhaps no longer wanted (eg, the use of cardiovascular preventive medication in end-stage dementia).³ Optimizing medication through targeted deprescribing: The process of withdrawal of an inappropriate medication, supervised by a health care professional with the goal of managing polypharmacy and improving outcomes, is a vital part of managing chronic conditions, avoiding adverse effects, and improving patient-centered outcomes.^{4,5}

Given the changed balance between harms and benefits of medicines at the end of life, one would expect that, especially in NH residents, the ratio of preventive therapy would decrease in proportion to symptomatic treatment⁶ as residents get more cognitively impaired or life expectancy decreases to months instead of years. Based on discussions in literature and media on the risks and benefits of different classes of PCM, it can be expected that physicians tend to stop some drugs (eg, statins) easier than others (eg, vitamin K antagonists, platelet aggregation inhibitors PAIs.). Because there may be cross-cultural differences, we also expect differences in (de)prescribing between countries.

Therefore, we conducted a study to assess the prevalence of 4 classes of preventive PCM in NH residents, and to explore differences of prevalence across length of stay, health instability, cognitive impairment, and functional disabilities and across countries.

Methods and Materials

Study Setting

The study was performed with data derived from the Services and Health for Elderly in Long TERM care (SHELTER) project. The project was conducted from 2009 to 2011 and designed to validate the interRAI instrument for long-term care facilities (interRAI LTCF).⁷ The interRAI LTCF is a standardized assessment instrument designed to assess care needs and preferences of NH residents and to assist with care planning. It contains more than 350 items that comprehensively capture client characteristics, including sociodemographic variables, clinical characteristics as physical and cognitive status, clinical diagnoses, current service utilization, and medication use. This instrument has been shown to be reliable in capturing resident information, allowing databases to be created to facilitate reliable comparisons of resident characteristics across countries, languages, and cultures.^{8,9}

The study included 4156 residents from 57 NHs in 8 countries (Czech Republic, England, Finland, France, Germany, Italy, the Netherlands, and Israel). In each country, study partners identified a sample of NHs willing to participate in the study that used the inter-RAI LTCF in routine care. The sample was not selected randomly and it was not intended to be representative of all NHs in each country. Older adults residing in participating NHs at the beginning of the study and those admitted during the 3-month enrollment period after the initiation of the study were assessed using the interRAI LTCF and reassessed at 6 and 12 months if still in the facility. For this study, only the first assessment from each participant was used for analysis.

According to local regulations regarding ethics, approval for this study was obtained in all participating countries. Only residents aged 60 years or older who had been institutionalized for 1 or more days and who had valid medication assessment were included for this study. No exclusion criteria were adopted.

Outcome: PCM Use

The interRAI LTCF registers medication use in the 3 days before the assessment. Drug data were collected and verified from multiple sources, including physician order sheets and medication administration records. Information about proprietary names, Anatomical Therapeutic and Chemical (ATC) codes of the World Health Organization Collaborating Centre for Drug Statistics Methodology (www.whocc.no), formulation, dosage, frequency, and route of administration were recorded for each used medication. Information was also collected regarding medications taken on an "as-needed" basis.

For the purposes of this study, we assessed the prevalence of 4 classes of PCM based on the following ATC codes:

- (1) Oral anticoagulants (OAC: ATC codes: B01AA03 warfarin, B01AA04 phenprocoumon, B01AA07 acenocoumarol).
- (2) PAls (ATC codes: B01AC06 acetylsalicylic acid, B01AC08 carbasalate calcium, B01AC056 acetylsalicylic acid, combinations with proton pump inhibitors, N02BA01 acetylsalicylic acid); in case of inconsistency among the ATC codes with the dosage, we considered all

the registered PAIs with different ATC codes and a dose up to 100 mg as a preventive prescription.

- (3) Antihypertensive therapy (AHT diuretics, calcium channel blockers, agents acting on renin- angiotensin system.: ATC codes: C03A, C03BA, C03EA, C03B, C08CA, C08GA01 + C08GA02, C09BB ACE, C09BX01, C09BX01, C09XA53, C09).
- (4) Lipid-modifying agents (LMA: ATC codes: C10AA HMG CoA reductase inhibitors, C10AB fibrates).

Independent Variables

Length of Stay

Because SHELTER provides information on medication use only associated with the 3 assessments and no continuous prescription data, specifically for medication use on admission and in the last months of life, individual patient trajectories with regard to medication use during stay in the NH could not be followed. Therefore, the used assessments were grouped by the length of stay of the resident in the NH at the moment of assessment (<2 months: short stay (recent admission), 2-12 months: mid stay, and >12 months: long stay).

Cognitive Impairment

Cognitive impairment is captured in the interRAI LTCF by the Cognitive Performance Scale (CPS), which incorporates memory impairment, level of consciousness, and executive function into a score ranging from 0 (cognition intact) to 6 (very severe cognitive impairment).¹⁰ The CPS has been shown to be highly correlated with the Mini Mental State Examination in a number of validation studies.^{10,11,12} Cognitive disorder in our study was considered present by CPS scores higher than 2 (moderate or more severe cognitive impairment).

Health Instability

Health instability was captured using the Changes in Health, End stage disease and Signs and Symptoms (CHESS) Scale. The CHESS score is a composite measure addressing changes in health, end-stage disease, and symptoms and signs of medical problems. It is a strong predictor of mortality independent of the effects of age, sex, activities of daily living impairment, cognition, and do-not-resuscitate orders. It is also strongly associated with physician activity, complex medical procedures, and pain.¹³ It creates a 6-point scale from 0 = not at all unstable to 5 = highly unstable, with higher levels predictive of adverse outcomes, such as mortality, hospitalization, pain, caregiver stress, and poor self-rated health.

The CHESS Scale is calculated by adding sign and symptom variables up to a maximum of 2, then adding 3 other variables (change in decision making, change in ADL status, and

end-stage disease), giving a highest CHESS score of 5. Residents were classified as high if CHESS was >3 (high or very high health instability).

Functional Disability

Functional disability was measured using the Activities of Daily Living Hierarchy (ADLH) scale, embedded within the interRAI LTCF.¹⁴ This 7-point scale ranges from 0 (indicating no impairment) to 6 (indicating total dependence). For the purposes of this study, ADL disability was classified as assistance required (ADLH score of 2-4) and dependent (ADLH score ≥ 5). In this category, residents were included if ADLH ≥ 5 .

Data Analysis

The statistical analysis of the data was performed using Statistical Package for Social Sciences version 20 (SPSS Inc, Chicago, IL). Prevalence was expressed in frequency and percentage. The results on continuous variables were presented as mean $\pm$ SD. Differences in prevalence between the various functional categories were tested by the X^2 tests. A P value less than .05 was considered statistically significant. A multivariable analysis was done to study the association between the 4 independent variables and the outcome variable "one or more PCM use."

Table 1. General characteristics of our studied population

Characteristics	Mean $\pm$ SD / n (%)
Age, Mean $\pm$ SD	84.3 $\pm$ 8.2
ADL hierarchy scale 0-6 range, Mean $\pm$ SD	3.4 $\pm$ 1.9
Sex, Women, n (%)	2783(74.0)

Table 2. Total estimate prevalence of combined medications based on length of stay, CHESS, CPS score and ADLH score

Medication	All N=3759 (%)	Length of stay			Chess >3 n=97	CPS >2 n=1963	ADLH ≥ 5 n=1495
		Short n=419	Mid n=923	Long n=2420			
OAC	212 (5.6)	23 (5.5)	62 (6.7)	127 (5.2)	4 (4.1)	86 (40.6) ^c	61 (4.1) ^a
PAI	1313 (34.9)	141(33.9)	351(38.0)	821 (33.9)	27 (27.8)	630 (48.3) ^c	476(31.8) ^a
AHT	1343 (35.7)	162 (38.9)	342 (37.1)	839 (34.7)	27(27.8) ^a	555 (41.5) ^c	399(26.7) ^c
LMA	390 (10.4)	55 (13.2)	94 (10.2)	241 (10.0)	6 (6.2)	141 (36.3) ^c	108 (7.2) ^c
1 or more	2175(57.9)	242 (58.2)	579 (62.7)	1354(56.0) ^a	46 (47.4) ^a	993 (45.9) ^c	727(48.6) ^c

N differs per subcategory due to missing, ^a: $p < 0.05$, ^b: $p < 0.01$, ^c: $p < 0.001$

Results

In total, 3759 cases fulfilled the inclusion criteria (mean age 84.3 ± 8.2 years, 74.0% women). Most patients (64%) lived in the NH for more than 1 year (short stay: 11%, mid stay: 25%). Residents' general characteristics are presented in Table 1. From these cases, 57.9% received PCM, with AHT (35.7%) and PAI (34.9%) being the most commonly used agents, followed by LMA (10.4%) and OAC (5.6%) (Table 2).

Although residents with mid stay had statistically significantly more prescribed PCMs (62.7%) compared with short-stay residents (58.2) or long-stay residents (56.0%), absolute differences were small. Within the separate medication groups, no significant differences based on length of stay were found.

Cognitive impairment (CPS score >2) was found in 1357 residents (36%) and was related to lower use of all 4 PCM groups ($P < .001$). Total PCM use decreased from 67.5% (CPS score 0) to 40.3% (worst CPS score 6), a relative reduction (RR) of 40%. Also, the prevalence of most medication groups was lower with worse cognition (AHT from 48.7% to 20.6% RR 58%; PAI from 38.3% to 26.7% RR 30%; LMA from 15.5% to 4.3% RR 72%; and OAC use from 6.7% to 4.0% RR 40%) (Figure 1).

Only 97 (2.6%) of the residents had a CHES score of more than 3. In these residents, AHT use (27.8%, 27 cases) was lower ($P < .05$) compared with the other residents. Also, any PCM was approximately 10% lower among these persons (47.4% 46 cases.) (Table 2).

The ADLH score was significantly related to the prevalence of overall PCM use: the higher the score, the lower the prevalence (Table 2, Figure 2). Use of 1 or more cardiovascular medications ranged from 72.2% (independent ADLH score 0) to 40.9% (maximum dependence, ADLH score 6), a RR of 43%. The prevalence of all medication groups dropped in persons with worse functional abilities (AHT from 54.2% to 19.3% RR 64%; PAI from 36.8% to 28.4% RR 23%; LMA from 17.6% to 4.8% RR 73%; and OAC use from 7.1% to 4.1% RR 42%). AHT was significantly lower with higher CHES scores, other categories did not reach significance (Figure 3).

In a multivariate logistic regression analysis the level of cognitive impairment (CPS) and daily functioning (ADLH) remained significant determinants explaining less CVD medications (Odds ratio CPS=.88 95%CI (.85-.92), odds ratio ADLH=.89 95%CI (.85-.93).

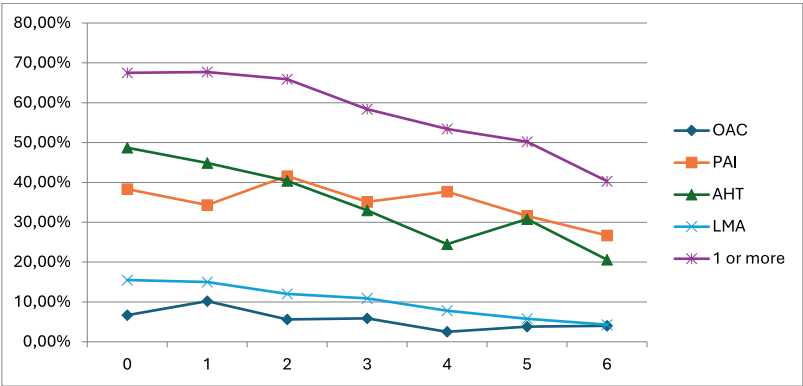


Figure 1. PCM prevalence in residents with CPS score 0 (intact) to 6 (very severe impairment).
Test for trend χ^2 : OAC <0.0001, PAI <0.0001, AHT <0.0001, LMA <0.0001, 1 or more <.0001

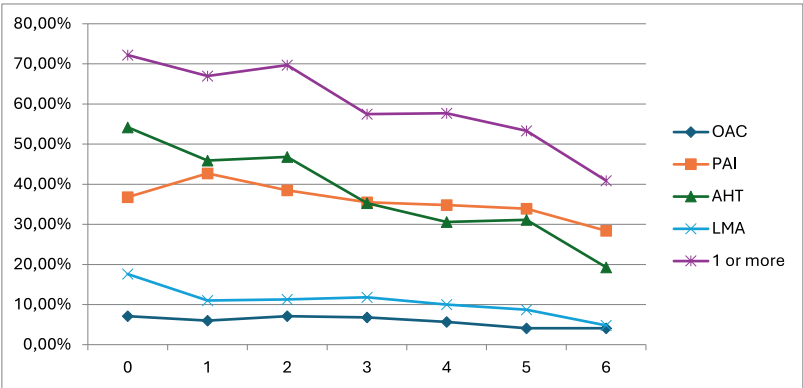


Figure 2. PCM prevalence in residents with ADLH score 0 (independent) to 6 (totally dependent).
Test for trend χ^2 : OAC = 0.054, PAI = 0.003, AHT < .0001, LMA < .0001, 1 or more <.0001

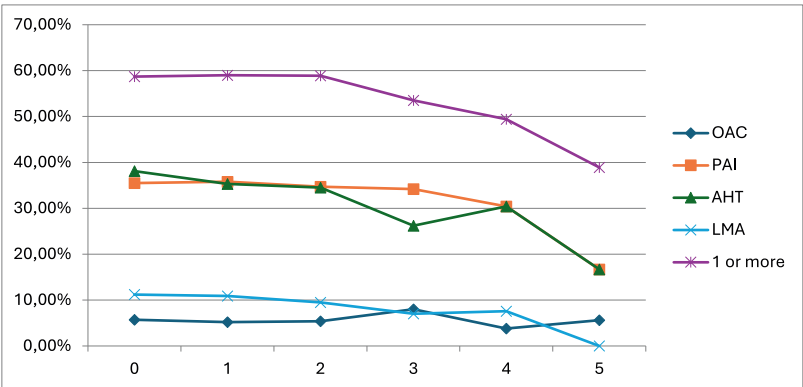


Figure 3. PCM prevalence in residents with CHES score 0 (no health instability) to 5 (very high health instability).
Test for trend χ^2 : OAC = 0.708, PAI = 0.568, AHT = 0.006, LMA = 0.232, 1 or more = 0.180

Prevalence Across Countries

The overall prevalence of 1 or more PCMs varied in European counties between 54.6% (Finland) and 69.5% (Czech Republic). PCM prevalence in Israel was remarkably lower (40.8%). There was a consistent prescribing pattern across the countries, with PAI and AHT prescribed most, and OAC prescribed least ($P < .001$) (Figure 4).

The influence of length of stay in most countries is difficult to determine due to the limited number of residents in the “short-stay” category in most countries. Absolute differences between medium and long stay were minimal in most countries (Table 3). With the exception of Italy (-10.0%) and Israel (-9.8%), the change in PCM prevalence varied between +2.9% and -3.2%.

Variation between countries in PCM use in NHs was limited, varying roughly between 55.0% and 65.0%, Israel being the exception with a total prevalence of 40.8%.

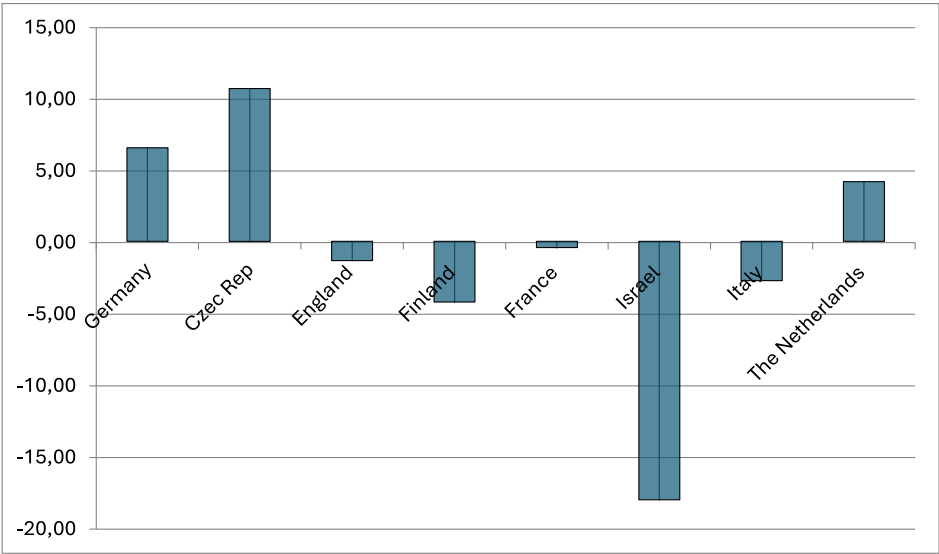


Figure 4. Percent differences across countries in the prevalence of 1 or more PCMs against the total sample

Table 3. Prevalence of PCM in short, mid, and long stay NH residents, between residents with high mortality risk, with cognitive impairment, with severe functional disabilities across 8 countries

Medication, n(%)		All	Length of stay			Chess>3	CPS>2	ADLH>=5
			Short	Mid	Long			
Germany n=464	OAC	13 (2.8) ^c	0 (0.0)	6 (4.6)	7 (2.2)	0 (0.0)	6 (46.2)	3 (2.7)
	PAI	163 (35.1) ^c	2 (6.7)	49 (37.7)	112 (34.8)	1 (20.0)	61(37.7) ^a	33 (29.2)
	AHT	233 (50.2) ^c	3 (25.0)	74 (56.9)	156 (48.4)	0 (0.0)	87 (37.5) ^b	44 (38.9) ^b
	LMA	30 (6.5) ^c	0 (0.0)	8 (6.2)	22 (6.8)	1 (20.0)	8 (26.7) ^a	6 (5.3)
	1or more	300 (64.7) ^c	4 (33.3)	89 (68.5)	207 (64.3)	1 (20.0) ^a	118 (39.5) ^b	63 (55.8) ^a
Czech Rep n=486	OAC	15 (3.1) ^c	4 (2.2)	5 (2.9)	6 (4.5)	2 (7.4)	5 (33.3)	4 (2.0)
	PAI	228 (46.9) ^c	82 (45.8)	78 (44.8)	68 (51.1)	7 (25.9)	88 (38.6) ^a	76 (38.2) ^a
	AHT	210 (43.2) ^c	80 (44.7)	71 (40.8)	59 (44.4)	11 (40.7)	74 (35.4) ^c	73 (36.7) ^a
	LMA	37 (7.6) ^c	25 (14.0)	8 (4.6)	8 (4.3) ^c	1 (3.7)	9 (24.3) ^a	6 (3.0) ^a
	1or more	338 (69.5) ^c	124 (69.3)	120 (69.0)	94 (70.7)	16 (59.3)	128 (38.0) ^c	116 (58.3) ^c
England n=463	OAC	10 (2.2) ^c	0 (0.0)	5 (3.8)	5 (1.8)	0 (0.0)	2 (20.0)	6 (2.1)
	PAI	166 (35.9) ^c	12 (21.4)	51 (39.2)	103 (37.2)	6 (31.6)	79 (47.0)	104 (36.9)
	AHT	132 (28.5) ^c	18 (32.1)	30 (23.1)	84 (30.3)	2 (10.5)	52 (39.4) ^a	69 (24.5)
	LMA	80 (17.3) ^c	11 (19.6)	25 (19.2)	44 (15.9)	2 (10.5)	29 (36.3) ^a	44 (15.6)
	1or more	266 (57.5) ^c	26 (46.4)	79 (60.8)	161 (58.1)	8 (42.1)	118 (44.4) ^a	160 (56.7)
Finland n=476	OAC	43 (9.0) ^c	2 (16.7)	3 (8.1)	38 (8.9)	0 (0.0)	19 (44.2) ^a	7 (5.5)
	PAI	159 (33.4) ^c	5 (41.7)	10 (27.0)	144 (33.7)	3 (75.0)	92 (57.9)	35 (27.3)
	AHT	115 (24.2) ^c	5 (41.7)	11 (29.7)	99 (23.2)	1 (25.0)	57 (49.6) ^a	19 (14.8) ^b
	LMA	49 (10.3) ^c	3 (25.0)	5 (13.5)	41 (9.6)	1 (25.0)	20 (40.8) ^b	6 (4.7) ^a
	1or more	260 (54.6) ^c	9 (75.0)	19 (51.4)	232 (54.3)	3 (75.0)	138 (53.1) ^b	50 (39.1) ^c

Medication, n(%)		All	Length of stay			Chess>3	CPS>2	ADLH>=5
			Short	Mid	Long			
France n=469	Group1	26 (5.5) ^c	2 (13.3)	5 (4.7)	19 (5.5)	1 (8.3)	17 (65.4)	15 (6.8)
	PAI	124 (26.4) ^c	2 (13.3)	30 (28.3)	92 (26.4)	3 (25.0)	71 (57.3) ^a	56 (25.5)
	AHT	181 (38.6) ^c	10 (66.7)	37 (34.9)	134 (38.5)	6 (50.0)	91 (50.3) ^c	57 (25.9) ^c
	LMA	36 (7.7) ^c	1 (6.7)	11 (10.4)	24 (6.9)	0 (0.0)	12 (33.3) ^c	6 (2.7) ^c
	1or more	274 (58.4) ^c	11 (73.3)	64 (60.4)	199 (57.2)	7 (58.3)	157 (57.3) ^c	109 (49.5) ^c
Israel n=527	OAC	18 (3.4) ^c	3 (9.1)	6 (5.7)	9 (2.3) ^a	0 (0.0)	6 (33.3) ^b	8 (3.0)
	PAI	182 (34.5) ^c	13 (39.4)	38 (36.2)	131 (33.7)	0 (0.0)	91 (51.4) ^c	80 (29.9) ^a
	AHT	168 (31.9) ^c	11 (33.3)	36 (34.3)	121 (31.1)	1 (50.0)	85 (50.9) ^c	69 (25.7) ^b
	LMA	75 (14.2) ^c	4 (12.1)	19 (18.1)	52 (13.4)	0 (0.0)	35 (47.3) ^b	26 (9.7) ^a
	1or more	215 (40.8) ^c	13 (39.4)	51 (48.6)	151 (38.8)	1 (50.0)	110 (51.6) ^c	89 (33.2) ^c
Italy n=417	OAC	16 (3.8) ^c	0 (0.0)	6 (5.3)	10 (3.6)	0 (0.0)	5 (31.3)	5 (2.8)
	PAI	131(31.4) ^c	6 (20.7)	48 (42.5)	77 (28.0) ^b	1 (14.3)	73 (57.5)	52 (29.)
	AHT	148 (35.5) ^c	6 (20.7)	43 (38.1)	99 (36.0)	1 (14.3)	61 (41.8) ^c	44 (25.0) ^c
	LMA	19 (4.6) ^c	1 (3.4)	3 (2.7)	15 (5.5)	0 (0.0)	6 (33.3)	3 (1.7) ^a
	1or more	234 (56.1) ^c	10 (34.5)	74 (65.5)	150 (54.5) ^b	2 (28.6)	109 (47.8) ^b	79 (44.9) ^c
The Netherland n=457	OAC	71 (15.5) ^c	12 (15.0)	26 (20.3)	33 (13.3)	1 (4.8)	26 (36.6)	13 (11.9)
	PAI	160(35.0) ^c	19 (23.8)	47 (36.7)	94 (37.8)	6 (28.6)	75 (46.9)	40 (36.7)
	AHT	156 (34.1) ^c	29 (36.3)	40 (31.3)	87 (34.9)	5 (23.8)	48 (30.8) ^b	24 (22.0) ^b
	LMA	64 (14.0) ^c	10 (12.5)	15 (11.7)	39 (15.7)	1 (4.8)	22 (34.4)	11 (10.1)
	1or more	288 (63.0) ^c	45 (56.3)	83 (64.8)	160 (64.3)	8 (38.1) ^a	115 (39.9)	61 (56.0)

N differs per subcategory due to missing, ^a: $p < 0.05$, ^b: $p < 0.01$, ^c: $p < 0.001$

Discussion

The prescription of PCMs in NHs at the end of life (and especially in end-stage dementia) is often inappropriate due to the changed balance between expected health gain during a life expectancy of 1 to 2 years versus risk of adverse drug events.^{14-19.}

In this study, approximately 57.9 % of the NH patients used 1 or more PCMs. There were some differences between countries, but even in the country with the lowest prevalence (Israel), still approximately 40% was found. Length of stay seemed hardly related to prevalence of PCM use. Although statistical significance was found between length of stay periods, the absolute changes between groups were very small. We did find lower PCM use in patients with more severe cognitive impairment, more health instability, and dependent in ADL functioning, so physicians seem to stop some PCMs in case of clinical deterioration. Despite this drop in prescribing, total PCM prevalence did not decrease below 40%. This is in line with many studies that found a continuing use of preventive medication in the last years or even the last months of life.^{20-22.}

The impact of clinical impairment on medication use in this study was estimated reliably in relation to cognitive impairment and disability. Results with regard to health instability were less reliable given the limited number of residents with a high CHESS score. The RR of medication related to clinical impairment (cognition and ADL) was largest for LMA and AHT. RRs of approximately 60% to 70% were found for these medication groups compared with reductions <30% for PAI and OAC. The reduction for OAC cannot be attributed to the replacement of OAC by the new oral anticoagulants since these were not in widespread use in nursing homes in the period 2009-2011. Because the major indications for PAIs (prevention of stroke and myocardial infarction) have relatively large numbers needed to treat (NNT) (ranging from 50 to >300 depending on the indication), it is surprising that even in the most frail NH patients, PAI treatment is continued whereas LMAs with comparable NNT are often discontinued.^{23,24.} The small percentage of LMA users (10.4%) at measurement is surprising knowing that LMA use is much higher in community-dwelling elderly.^{24.} There has been a lot of discussion regarding safety and benefits of and compliance with statins in elderly patients. Perhaps LMAs are the first drugs to be stopped by physicians when patients are admitted to the NH and for those in whom LMA therapy is continued, also the first to be stopped during admission. The prevalence of OAC users is within the expected range given that atrial fibrillation, being the primary indication for OAC use in the elderly, has a prevalence of approximately 5% to 15% in elderly patients.^{25.} The figures indicate that physicians are reluctant to discontinue OAC in NH patients despite the preventive nature of the medication in combination with a low life expectancy. We cannot draw firm conclusions concerning differences between countries with regard to the impact of CHESS, CPS, or ADLH scores on the prescription of individual medication groups, due to the sometimes small numbers for individual medication groups.

In the last few years, more focus has been put on the need to weigh potential harms and benefits of CVRM in frail elderly patients. Once appropriate medication may become inappropriate when frailty increases and life expectancy decreases. This requires a careful

examination of medication use, therapeutic goals, expected life expectancy, patient preferences and balancing potential benefits and harms. Stopping all preventive medication in all nursing home residents regardless of life expectancy or other considerations can be considered inappropriate but it may become appropriate when functionality declines and life expectancy becomes very limited (eg less than 1 year). Recently a delphi consensus survey of an expert panel comprising academic geriatricians, clinical pharmacologists, palliative care physicians, old age psychiatrists, general practitioners and clinical pharmacists advised on stopping most CVRM in the frail patients with limited life expectancy.²⁶ Deprescribing seems to be feasible and relatively safe at the end of life.²⁷⁻³²

Despite the emerging evidence on the potential of deprescribing in reducing patient harms, this study also suggests that deprescribing is not yet routine practice. Clinicians seem to find it difficult to stop medications, especially those working on coagulation. Several explanations for this phenomenon have been suggested in the literature.^{33,34} Some physicians believe there is appropriate evidence for prescribing the medications. Other physicians are reluctant to change orders for medications started by specialists or feel they lack the education and experience to taper off or stop medications. Still other physicians voice concerns that patients will feel the physician is “giving up on them” or “leading them to quicker deaths.” In addition, clinicians feel pressured to prescribe according to clinical guidelines but recognize that such guidelines are rarely based on evidence from studies in older populations and rarely address modifying clinical targets with advancing age or care goals. But, also, patient beliefs and attitudes may, or those of their caregivers, hinder the deprescribing of potential inappropriate medication.³⁵

Strengths and Limitations

Some limitations to this work need to be acknowledged. The cross-sectional nature of the study does not allow for statements about causality between lower prevalence and a worsening clinical status. We did not monitor changes in medication use within individual patients during the stay in the NH. The acute indications for the PCM are not part of the discussion or the results. These can be considered as a limitation.

In addition, the participants in some countries may not be representative of the NH population in these countries and therefore the conclusion cannot be generalized to the whole country.

The ATC coding was not consistent in all countries; therefore, we recoded some ATC codes based on their dosage; for example, in Israel, PAs were recorded with several ATC codes. Strengths of this study include the large cohort and the comprehensiveness of factors that could be explored as covariates. interRAI data allowed for comparable information to be collected from NH populations in multiple European countries.⁷ The sample size was large enough to allow exploration of use of some of all medication therapies, providing richer data than a comparison of any or no drug therapy. Despite the convenience sample, the similarity trends were seen across countries, which may reflect a typical NH population in these countries.

Conclusion

Although the prevalence of PCM use was lower in cognitively impaired residents, persons with a high mortality risk, and residents with more functional disabilities, there still remains room for deprescribing.

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CHAPTER 4

Pharmacological Management of Osteoporosis in Nursing Home Residents: The SHELTER Study

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Abstract

Objective: To prevent osteoporotic fractures in nursing home residents a combination of bisphosphonates, calcium and vitamin D is recommended. This study assessed the prevalence of pharmacological osteoporosis prevention in nursing home residents from eight countries and assessed its association with patient characteristics.

Design: Cross-sectional analyses of the SHELTER study data. We assessed the overall prevalence of osteoporosis medication (OM) use (vitamin D, calcium and bisphosphonates) in residents stratified for falls and fractures over last 30 days, health instability with high mortality risk, cognitive impairment, and dependence in walking. Setting and Participants: Nursing home residents in the Czech Republic, England, Finland, France, Germany, Italy, The Netherlands and Israel.

Results: Of 3832 eligible residents, vitamin D, calcium and bisphosphonates were used by 16.2%, 10.4%, and 4.5% respectively. All 3 classes of OM together were used by 1.5% of all residents. Of residents with a recent fracture, 9.5% used a bisphosphonate (2.7% all 3 OMs). In patients with recent falls, 20.8% used vitamin D and 15.3% calcium. In residents with severe cognitive impairment, 15.5% used vitamin D and 9.3% used calcium. Of the bisphosphonate users, 33.7% also used both vitamin D and calcium, 25.8% used only calcium in addition and 17.4% only vitamin D in addition. The use of any OM varied widely across countries, from 66.8% in Finland to 3.0% in Israel.

Conclusions and Implications: We found substantial pharmacological under-treatment of prevention of osteoporosis in residents with recent falls, fractures and dependence in walking. Only two-thirds of bisphosphonate users also took a vitamin D–calcium combination, despite guideline recommendations. On the other hand, possible over-treatment was found in residents with high mortality risk in whom preventive pharmacotherapy might not have still been appropriate. The prevalence of pharmacological prevention of osteoporosis differed substantially between countries. Efforts are needed to improve pharmacotherapy in residents.

Introduction

The prevalence of osteoporosis is estimated at 75 million in United States, Europe and Japan¹ and this is about 13.5% to 24.2% in nursing home residents in United States.² About two thirds of people with osteoporosis are women. With increasing life expectancy, the prevalence of osteoporosis increases.³ The main problem of osteoporosis is the increased risk of fractures. Osteoporotic fractures can have serious consequences such as chronic pain, reduced quality of life, increased dependence on others, depression, anxiety and alterations in self-esteem and increased mortality.^{4–8}

It was estimated that roughly one third of all fractures in older persons can be attributed to osteoporosis. For women this percentage was considerably higher (36%) than for men (21%). In particular, hip fractures and vertebral fractures in women over the age of 50 can be attributed to osteoporosis in more than 50% of cases.⁹ Approximately 3.5 million new osteoporotic fractures occur annually in the EU. In 2010 alone, the economic burden of osteoporotic fractures was estimated at €37 billion. The number of deaths due to osteoporotic fractures in 2010 was estimated at 24 per 100,000 EU inhabitants aged 50 years and older.¹⁰ Given these figures, it seems logical to focus on secondary and tertiary prevention of osteoporotic fractures. Pharmacological treatment of osteoporosis is a cornerstone of prevention. Since nursing home (NH) residents have a strongly increased risk of fractures due to the combination of a high risk of falling and osteoporosis, optimal treatment of osteoporosis is crucial in this population.

There is a general consensus that osteoporosis treatment can be effective in preventing osteoporotic fractures. Most guidelines therefore advise treatment of osteoporosis with a combination of bisphosphonates, calcium and vitamin D. European guidelines even advise that all older adults should be supplemented with vitamin D throughout the whole year.¹¹ On the other hand, there is discussion concerning the appropriateness of preventive medication in the final stages of life. It can be questioned if benefits of osteoporotic treatment in the last years of life outweigh the possible adverse drug events? The initiation of therapy may not lead to a reduced fracture risk if expected life expectancy is shorter than expected time until benefit of medication. The intake of medication can be difficult (especially bisphosphonates). Also the risk of adverse drug reactions may increase in multimorbid patients with polypharmacy. It is therefore often suggested that osteoporosis treatment may be inappropriate in older nursing home residents with a limited life expectancy (e.g. severe dementia, end-stage organ failure, medically unstable).¹² It is unclear how often osteoporosis treatment is provided in nursing homes, which medication are prescribed, and if differences exist between countries. Therefore, we assessed the prevalence of osteoporosis treatment in nursing home residents across seven European countries and Israel. Furthermore, we assessed the influence of patient characteristics on the prevalence of osteoporosis treatment.

Methods and Materials

Study Setting and Residents

The study was performed with data derived from the Services and Health for Elderly in Long TERM care (SHELTER) project. This project was conducted from 2009 to 2011 and designed to validate the interRAI instrument for long-term care facilities (interRAI LTCF).¹³ The InterRAI LTCF is a standardized assessment instrument designed to assess care needs and preferences of NH residents and to assist with care planning. It contains over 350 items that comprehensively capture client characteristics, including sociodemographic variables, clinical characteristics as physical and cognitive status, clinical diagnoses, current service utilization, and medication use. The study included 4156 residents from 57 NHs in 8 countries (Czech Republic, England, Finland, France, Germany, Italy, the Netherlands and Israel). In each country, study partners identified a sample of nursing homes that used the interRAI-LTCF in routine care.

The sample was not selected randomly and was not intended to be representative of all nursing homes in each country. Older adults residing in participating nursing homes at the beginning of the study and those admitted during the 3-month enrolment period after the initiation of the study were assessed using the InterRAI LTCF and reassessed at 6 and 12 months if still in the facility. For this study, only the first assessment from each participant was used for analysis.

We included residents aged 60 years or older who had been institutionalized for one or more days and who had a valid medication assessment. A valid medication assessment comprised presence of name, dose and ATC code. No exclusion criteria were adopted. Approval for this study was obtained in all participating countries, according to local regulations regarding ethics.

Outcome: Osteoporosis Medication Use

The interRAI LTCF registers medication use in the 3 days before the assessment. Drug data were collected and verified from multiple sources, including physician order sheets and medication administration records. Information about proprietary names, Anatomical Therapeutic and Chemical (ATC) codes of the World Health Organization Collaborating Centre for Drug Statistics Methodology (www.whocc.no), formulation, dosage, frequency, and route of administration were recorded for each used medication. Information was also collected regarding medications taken on an “as-needed” basis. Osteoporosis medication use was defined as the presence of the following drugs:

- Vitamin D and analogues (ATC code: A11CC, M05BB03, M05BB04, M05BB05, M05BB06, M05BB07, M05BB08, M05BX53)
- Calcium (ATC code: A12AA Calcium, combinations with vitamin D and/or other drugs) (M05BB01, M05BB02, M05BB04, M05BB05, M05BB08)
- Bisphosphonates (ATC code M05BA, M05BB,)

- Strontium ranelate (ATC code M05BX03, M05BX53)
- Denosumab (M05BX04)
- SERMs (G03XC)
- Teriparatide (H05AA02)

Independent Variables

Recent falls: Any falls over last 30 days.

Recent fractures: Any fractures over last 30 days

Health instability: Captured using the Changes in Health, End-stage disease and Signs and Symptoms (CHESS) Scale.¹⁴ The CHESS score is a composite measure addressing changes in health, end-stage disease, and symptoms and signs of medical problems. It is a strong predictor of mortality independent of the effects of age, sex, activities of daily living impairment, cognition, and do-not-resuscitate orders. It is also strongly associated with physician activity, complex medical procedures, and pain.¹⁴ It creates a 6- point scale from 0 = not at all unstable to 5 = highly unstable, with higher levels predictive of adverse outcomes such as mortality, hospitalization, pain, caregiver stress, and poor self-rated health. The CHESS Scale is calculated by adding sign and symptom variables up to a maximum of 2, then adding three other variables (change in decision making, change in ADL status, and end-stage disease), giving a highest CHESS score of 5. Residents were classified as high if CHESS>3(high or very high health instability).

Cognitive impairment: Assessed in the interRAI LTCF by the Cognitive Performance Scale (CPS), which incorporates memory impairment, level of consciousness, and executive function into a score ranging from 0 (cognition intact) to 6 (very severe cognitive impairment)¹⁵. The CPS has been shown to be highly correlated with the Mini Mental State Examination (MMSE) in a number of validation studies^{15–17}. Cognitive disorder in our study was considered present by CPS scores higher than 2 (moderate or more severe cognitive impairment).

Dependence in walking: Determined on the basis of the amount of support needed: Independent, 1. Set up help only, 2. Supervision, 3. Limited Assistance, 4. Extensive Assistance, 5. Maximal Assistance, 6. Total Dependence.

Data Analysis

The statistical analysis of the data was performed using Statistical Package for Social Sciences version 20 (SPSS Inc, Chicago, IL, USA). Prevalence was expressed in frequency and percentage. The results on continuous variables were presented as mean with standard deviation (SD). Differences in prevalence between the various functional categories were tested by the Chi-square tests. A p-value less than 0.05 was considered statistically significant.

Results

In total 3832 cases of 4156 cases fulfilled the inclusion criteria (mean age 84.2 ± 8.2 years, 73.9% women). Of these cases, 19.5% used at least 1 of the OM. The prevalence of vitamin D, calcium and bisphosphonates was 16.2%, 10.4 %, and 4.5 % respectively (Table 1 and Fig. 1). Six residents (0.2%) were registered with denosumab or zero Teriparatide. The use of strontium ranelate and SERMs was not studied further in detail because of their very low prevalence.

Osteoporosis Medication (OM) Use

Recent falls or fractures were associated with an increased prevalence of all OM medication groups compared to no falls or fractures. Residents with recent falls more often used vitamin D and calcium than non-fallers (20.8% vs. 15% and 15.3% vs. 9.2%), but not more bisphosphonates. Also, In residents with recent fractures Calcium, vitamin D and bisphosphonates were more often used than in residents without a recent fracture, but in this group with a high probability of osteoporosis, bisphosphonates were only used in 9.5% of the residents (compared to 4.3% in the non-fracture group). In residents with walking dependency, we found less use of calcium and bisphosphonates than independent walkers. A high health instability with elevated mortality risk was not associated with less use of OM. Cognitive impairment (CPS score >2) was associated with lower use of all OM. Of the 177 residents using bisphosphonates, only 33.7% also used both vitamin D and calcium. Only vitamin D or only calcium were used in 17.4% and 33.7% in bisphosphonate users.

Prevalence Across Countries

Results indicate differences between countries in the use of OM. In Italy, Israel, Germany and the Czech Republic, less than 10% of nursing homes residents used vitamin D and calcium. In the Netherlands, France and the UK these drugs were used between 10-18%. OM use in Finland differed substantially from OM use in all other countries. Almost two thirds of the residents used at least one OM. This was mainly the result of a high vitamin D use (65.6%), but also calcium use was higher than in other countries (29%). Vitamin D or calcium use in Israel was very low (0.2% and 0.6%). Less than 10% of nursing home residents used a bisphosphonate with an exception for the residents from the UK where 10.5% used a bisphosphonate (Table 2 and Fig. 2).

Discussion

The study findings indicate that prevalence of osteoporosis treatment was low amongst nursing home residents. Despite guideline recommendations to prescribe vitamin D and calcium as prevention to all older nursing home residents, only a minority received these in our study. Substantial variations were observed in preventive osteoporosis medications between the countries. Finnish residents were an exception with substantial higher use of vitamin D. Also regarding secondary prevention (residents with a recent fracture) the prevalence of vitamin D or calcium treatment was low. Surprising was the low prevalence of bisphosphonate use in the group of residents with recent fractures. Since the SHELTER database does not register a diagnosis osteoporosis, we used fractures as a proxy. In general, the probability of the presence of osteoporosis is very high in frail older nursing home patients, especially in those with a recent fracture. Less than 10% of patients with a recent fracture used a bisphosphonate. These figures suggest that in European nursing homes undertreatment of osteoporosis and fracture risk is highly prevalent. The undertreatment was also found in the United States Nursing Home residents who were at high risk of fracture.² Based on the availability of European guidelines during the data studied period, it is not to be expected that the found variations between countries can be attributed to differences in local guidelines.¹⁸ Bisphosphonates, calcium and vitamin D are widely available in Europe and have relatively low costs, so availability or costs are not expected to drive the found under-prescribing or differences between countries. The second line medications such as teriparatide and denosumab are more expensive and this may mean that a small proportion of patients who were intolerant or irresponsive to bisphosphonates have not had the optimal osteoporosis therapy.

Although the drugs such as denosumab are only in use in the EU and the USA after 2010 and this may be the reason that the negligible number of registrations in shelter database for tertiary prevention agents for osteoporosis can be found.

Clinical guidelines recommend standard prescription of vitamin D and calcium in all nursing home residents.¹¹ The prevalence of osteoporosis in aged nursing home residents is considered to be high.¹

Table 1. Prevalence of osteoporosis medications stratified for persons with recent fall, recent fractures, CHESS, CPS and walking dependency

Medication	Recent Falls		Recent Fractures		Health instability by CHESS			Cognitive impairment by CPS		Walking	
	Total n=3832 (%)	None n=3077 %	Any n=745 %	None n=3685 %	Any n=147 %	0-3 n=3585 %	>3 Very instable n=97 %	0-2 n=1783 %	>2 impaired n=1999 %	Independent n=1040 %	dependent n=2788 %
All 3 OM medication	58(1.5)	1.4	2.1	1.5	2.7	1.5	3.1	2.0 ^c	1.1 ^c	2.1	1.3
any use of OM meds	746(19.5)	18.4 ^b	24.0 ^b	19.0 ^a	33.3 ^a	19.7	13.4	22.2 ^a	17.6 ^a	21.0	19.1
Vitamin D	622(16.2)	15.0	20.8 ^a	15.8	25.9 ^b	16.3	10.3	17.4	15.5	16.5	16.1
Calcium	397(10.4)	9.2	15.3 ^a	10.1	17.0 ^b	10.7	5.2	11.8 ^c	9.3 ^c	12.1 ^c	9.7 ^c
Bisphosphonate	(172(4.5)	4.4	4.8	4.3	9.5 ^b	4.5	6.2	6.1 ^a	3.1 ^a	6.3 ^b	3.8 ^b

^aP<.001, ^bP<.01, ^cP<.05

Differences in N depend on item missings

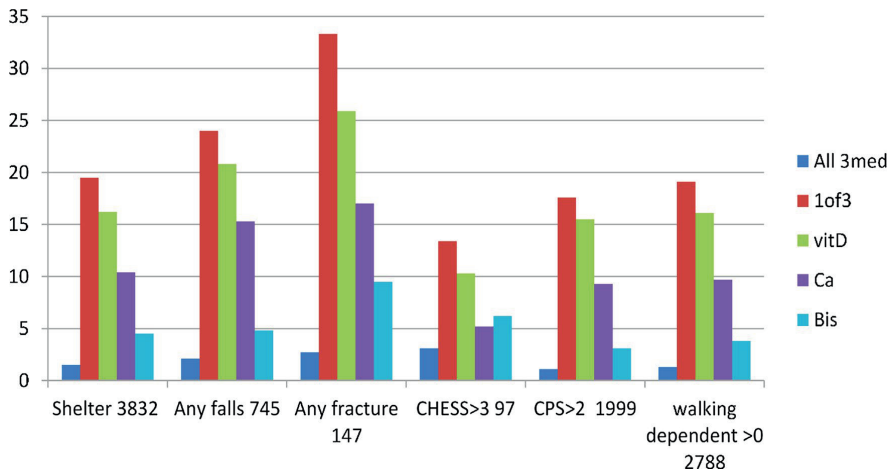


Figure 1. Percentage of osteoporosis medications use, stratified for persons with recent fall, fractures, CHESS, CPS and walking dependency

vitD = Vitamin D Ca = Calcium Bis = Bisphosphonate CHESS = Changes in Health, End-Stage Disease, Signs, and Symptoms Scale CPS = Cognitive Performance Scale

X-axis = variables in term of number (n) Y-axis = %

Table 2. Prevalence of osteoporosis medication across the countries in percentages

Country (3832)	All 3 medications classes	Any use	Vitamin D	Calcium	Bisphosphonate
CZE (n=489)	1.2	9.0	6.3	7.6	1.4
GER (n=468)	0	8.3	4.3	3	2.6
UK (n=465)	3.2	22.8	17.8	10.1	10.5
Fin (n=479)	2.3	66.8	65.6	29	3.8
Fr (n=474)	1.3	14.1	11.8	12.4	3.2
Isr (n=542)	0	3.0	0.2	0.6	2.2
It (n=454)	1.5	13.2	9	7.5	5.7
Nl (n=461)	2.8	21.3	16.5	13.9	7.2

Therefore, one would expect a high use of medication used for prevention or treatment of osteoporosis or osteoporotic fractures. While up to two thirds of the Finnish residents received vitamin D, Israeli residents were found at the lower end of the group. It may not be a coincidence that the geographical most northern and southern country in our study demonstrated these extremes. Exposure to sunlight (and thus vitamin D production) differs largely between these two countries. One may expect that in the geographically most northern areas, where people have least exposure to the sun, the official recommendations to use vitamin D supplements year

around, have had a good penetration. In countries like Israel, with a high amount of sun hours, older people often cover large parts of their bodies and therefore the vitamin-D formation in the skin may remain uninitiated.

Guidelines also recommend that bisphosphonates are accompanied with the prescription of both vitamin D and calcium.¹¹ Surprisingly this was observed in only one third of the bisphosphonate users. This may be rational if all these residents for instance use enough calcium and vitamin D containing products, but this seems unlikely. Also only half of these residents used vitamin D.

Physicians may have various reasons not to prescribe OM to patients for primary prevention of falls or fractures: The time needed to benefit is mostly longer than the remaining life expectancy, the number needed to treat to prevent a fracture is high, medication management adds up to the treatment burden and is accompanied with potential adverse effects. Also, shared decision making may lead to deviation from the guideline. One potential reason for underuse of bisphosphonates may be previous history of using bisphosphonates or denosumab. In nursing home residents, the use of bisphosphonates may further be hampered by a higher prevalence of contraindications (e.g. severe renal impairment), practical problems (e.g. swallowing difficulties, needs to be swallowed in sitting position). Also fear for an increased risk of adverse drug reactions (e.g. upper gastrointestinal adverse reactions, musculoskeletal pain) may prevent physicians to prescribe especially bisphosphonates since nursing home residents may already experience similar complaints due to existing multimorbidity.

So, in nursing homes, the prescribing physician considers the expected benefit of treatment and take into consideration short life expectancy and risk of polypharmacy and side-effects in nursing home residents. This often leads to a different approach than mentioned in guidelines, as these guidelines are not based on nursing home residents but a broader population where benefit of treatment will outweigh the risk of side effects and polypharmacy.

If physicians take expected survival and medical condition into account when prescribing preventive medication, one may expect lower prescription figures in residents with moderate and severe cognitive impairment, advanced dementia or high health instability. Our study only partially confirms this expectation. The use of preventive OM was significantly lower in residents with severe cognitive impairment compared to other residents but not in residents with high health instability. Even though prescription figures were lower in these subgroups, there still remains room for further deprescribing.

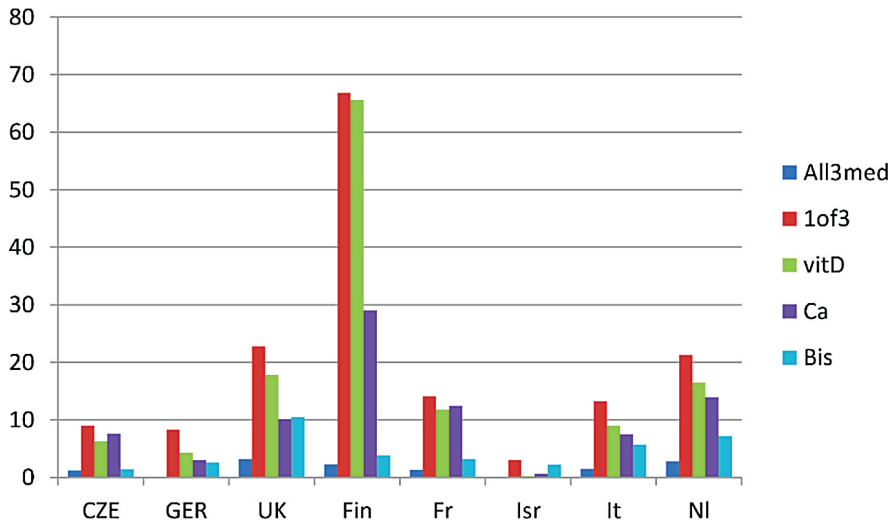


Figure 2. Percentage of the osteoporosis medication prevalence across the countries

CZ = Czech Republic GER = Germany UK = United Kingdom Fin = Finland Fr = France Isr = Israel It = Italy NL = Netherlands

Y-axis = %

Strengths and Limitations

Some limitations need to be acknowledged. The cross-sectional nature of the study does not allow for statements about causality. We did not monitor changes in the medication use within individual patients during the stay in NH and, so perhaps the prevalence may have increased in high risk groups which we failed to detect. Moreover, we did not collect previous medication history and that is why we do not know how many of the residents have already previously received 3-5 years bisphosphonates. Also we have not included the osteoporosis diagnosis as variable in our study. It was not possible to distinguish the severity or type of the fractures in the database. However, in general, osteoporosis treatment is not dependent on these characteristics but on the assumption that osteoporosis is one of the variables accountable for the fracture.

We acknowledge that a limitation of this study is that the analyzed data dates from several years ago. However due to the nature of prescribing in nursing homes de data would still be representative. In addition, the participants in some countries may not be representative of the nursing home population in these countries because of convenience sampling and therefore the conclusions cannot be generalized to the participating countries without proper comparisons.

Strengths of this study include the large cohort and the comprehensiveness of factors that could be explored as covariates. InterRAI data allowed for comparable information to be collected from NH populations in multiple European countries.¹³ The sample size was large enough to allow exploration of not only comparing any versus no drug therapy, but also comparison of specific combinations of osteoporosis medication. Despite the convenience

sample, the similar trends were seen across countries, which may reflect a typical nursing home population in these countries.

Conclusion and Implication

We found substantial pharmacological under treatment of prevention of osteoporosis in residents with recent falls, fractures and the walking's dependency. Only two third of bisphosphonate users had vitamin D–calcium combination, despite guideline recommendations. On the other hand also possible overtreatment was found in residents with high mortality risk in whom preventive pharmacotherapy may not be appropriate anymore. The prevalence of pharmacological prevention of osteoporosis differed substantially between countries. Efforts are needed to improve pharmacotherapy in residents.

Contributors

Alireza Malek Makan, Hein van Hout and Rob van Marum contributed to the conception, design, and execution of the study, and to the interpretation of the results.

Graziano Onder, Henriëtte van der Roest, Harriet Finne-Soveri, Eva Topinkova, Michael Denking, and Jacob Gindin contributed to the interpretation of the results.

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Ethical Approval

SHELTER was ethically approved by the representative committees from the participating countries.

Provenance and Peer Review

This article was not commissioned and was externally peer reviewed.

Research Data (Data Sharing and Collaboration)

There are no linked research data sets for this paper. Data will be made available on request. Ethical Statement: SHELTER was ethically approved by the representative committees from the participating countries.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

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CHAPTER 5

Barriers and Enablers of Elderly Care Specialists towards Deprescribing Practices in the Nursing Homes: A Focus Group Study

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Abstract

Introduction

Polypharmacy increases as patients age. It is associated with a decline in quality of life and an increased risk of potentially inappropriate medications (PIMs). These are highly prevalent among long-term care residents in European countries. The potential benefits of deprescribing, as the process of withdrawing PIMs are widespread, including improvements in both health and quality of life for patients. An overview of the barriers and enablers of deprescribing is still lacking in national research or policy discussions involving a larger group of Elderly Care specialist (ECS), who aim to maintain or improve the quality of life of elderly and chronically ill patients in the Netherlands. In this study, we explored the barriers and enablers of deprescribing among ECSs.

Methods

A focus group study was conducted with two groups comprising a total of 11 ECSs. A theme list was prepared to guide the interviews. The audio recordings were transcribed verbatim by one and verified independently by another researcher. Analysis of the reports was carried out through thematic coding using Atlas.TI, performed independently by two researchers. After each step of the coding they were compared, verified and, if necessary, adjusted after consultation.

Results

ECSs mentioned that gaining clinical experience and knowledge contributed to a positive attitude towards deprescribing. It is crucial to involve patients and their families and have support from care managers through official policy. Obstacles for deprescribing comprised lack of a medical history, the fear of the negative consequences of reducing medication, the lack of clinical guidelines regarding deprescribing, and the believe that a particular medication can be effective. The factor related to patient and family has a direct positive or negative impact on deprescribing if there is or is not cooperation.

Conclusion

Deprescribing in nursing home residents remains a challenge. The ECSs are both positive about and aware of its importance. At the same time the collaboration between all parties, including doctor and patient/family and other disciplines such as management and pharmacists and paramedics, was mentioned as a key working method in this regard.

Keywords Deprescribing, Barriers and enablers, Nursing homes Introduction

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Introduction

Polypharmacy has more than doubled between 1999 and 2014.¹ Polypharmacy is common among the elderly population because of the development of multimorbidity. Although polypharmacy may be indicated and leading to health improvement, it may also result in negative effects. Polypharmacy has been defined as the use of five or more medications, which is not necessarily inappropriate, “problematic polypharmacy” refers to the use of multiple medications that may not be clinically indicated, have unclear benefit, or pose more risks than benefits. Polypharmacy is associated with a decline of quality of life, serious side effects, increased mortality and high costs.^{2,3} The Benefit-Risk-Balance (BRB) of medications decreases especially for “the very old, with comorbidity, dementia, frailty and limited life-expectancy” (VOCODFLEX)⁴, a description that fits the nursing home residents.⁴ Polypharmacy increases the risk of potentially inappropriate medications (PIMs).⁵ Deprescribing, the process of withdrawing inappropriate medication, supervised by a healthcare professional⁶ may therefore improve patient outcomes and can also lead to cost benefits to the health care system.^{7–11}

Several studies have identified barriers to deprescribing reported by healthcare providers, such as a lack of evidence that discontinuation of medication would be more beneficial than continuation, uncertainty and fear of negative consequences (such as potential conflict), reluctance of patients and family members, and lack of time or support for deprescribing.^{12–16} These studies have examined enablers and barriers to deprescribing in general, while such factors may differ for different drug classes, and for type of patients. Furthermore, most studies focused on clinicians’ perspectives.

The majority of nursing home residents are in the last phase of life. In this phase, the intention of treatment should be more focused on symptom therapy than on prevention.^{17–20} Nevertheless, the prevalence of polypharmacy (>5 medications) in the nursing home remains high: 30.3% to 94%.^{21–23} More than 18% of the residents in Dutch nursing homes used 4 or more inappropriate medications according to the STOPP-Frail criteria version2. In some European countries this percentage is even higher.²⁴ So it can be noted that deprescribing practice in nursing homes is not optimal. In the Netherlands, medical care for nursing home residents is provided by Elderly Care Specialists (ECS), a medical professional trained to deliver medical care to frail elderly.

Deprescribing attitudes, practices and approaches of geriatricians, general practitioners and community pharmacists across Europe have already been investigated.²⁵ However, no qualitative research has yet been conducted into such factors among the ECSs, so it is not known whether comparable barriers and enablers factors in comparison with other studies involving other care providers are present regarding deprescribing. In this study, we explored the barriers and enablers of deprescribing among the ECSs.

Methods

Study Design, Recruitment and Setting

A focus group study was executed with two groups of in total 11 ECSs. A theme list was used to guide the interviews.

Focus groups were chosen to stimulate discussion and reveal shared and divergent perspectives among Elderly Care Specialist (ECS) regarding deprescribing. This interactive dynamic, as introduced in Kitzinger J, 1995 (PMC2550365) was considered particularly appropriate to explore shared and divergent professional experiences, organizational culture, and peer influences.

A purposive sampling technique was used to recruit participants. The first group consisted of ECSs who also supervise ECSs in training and who work in the nursing homes and were recruited from various regions in the Netherlands. The second focus group worked in the same organization and were colleagues. The moderator had no prior relationship with participants.

The participants were drawn from diverse regions of the Netherlands and various educational institutions, representing a broad spectrum of ages, levels of experience, and patient populations. Consequently, these groups can be considered highly representative of ECSs in the Netherlands. ECSs are a distinct medical specialty in the Netherlands. Unlike general practitioners or geriatricians, ECS are specialists trained specifically in care for long term care residents and geriatric rehabilitation. This typically takes three years of postgraduate training. In contrast to ECS, other medical specialists such as cardiologists or neurologists typically work in hospitals and are not responsible for daily care in nursing homes. As the first focus group the ECSs were approached by telephone to participate as part of a training day. The second focus group consisted of ECSs were active in the nursing homes and not associated with resident training. The sessions took 1.5 to 2 h each. The focus groups were led by a moderator.

Elderly Care specialist is a medicine doctor who tries to maintain or improve the quality of life of the elderly and chronically ill. These doctors mainly work in nursing homes in collaboration with paramedics, psychologists and nurses. The main goals are focused on the quality of life based on the wishes of the residents and their families and the informal care givers, where life expectancy plays a major role. The other medical specialists work in the hospital and not in the nursing homes.

The Medicines Act in the Netherlands regulates matters surrounding the production, trade, prescription and dispensing of medicines. The law contains regulations to encourage the safe use of medicines. Nurses are also included in this law. In addition, 'The Care and Coercion Act' regulates the rights in the event of involuntary care or involuntary admission

of people with an intellectual disability and people with a psychogeriatric condition (such as dementia).

Due to the vulnerability of the nursing home patients, one of the family members regularly acts as legal representative. For incapacitated residents, medical decisions must always be discussed with the legal representative.

Topic List

To create a topic list on existing literature on barriers to and enablers of deprescribing the Theoretical Domains Framework TDF was used.^{26, 27} We used a combination of deductive and inductive approach. Deductive by taking note of previous literature and based on this a topic list, and inductive by having an open conversation and interpreting the data openly. It began with a set of empirical observations, seeking patterns in those observations, and then theorizing about those patterns. We did not conduct a formal pilot. The topic guide was developed based on existing literature and pretested internally by the research team (including an ECS and an ECS resident and also other authors) for clarity and relevance. Using a topic list, four discussion points were debated around the barriers and enablers of stopping medication (deprescribing):

1. Which factors determine prescribing among nursing home residents?
2. What are your experiences with prescribing for nursing home residents?
3. What is your experience with stopping medication (deprescribing) in nursing home residents?
4. What do you need to promote deprescribing?

Data Collection and Data Analysis

The focus groups took place on October 9 and 17, 2019. Two focus group discussions of 90–120 min duration. The spoken language was Dutch and the sessions were audio recorded with permission. The group discussions were moderated by HvH, assisted by AMM and MM, who made notes in addition to the audio recording. The moderator is experienced with moderating focus group interviews. He had no direct relationship with the participants. No one other than researchers and participants present during the focus group.

After a short introduction, each participant was given the opportunity to respond to the topic list points. Afterwards the basic data of the participants were collected (age, gender, years of experience and main patient group). The audio recordings were verbatim transcribed by one researcher (MM) and verified by the other one (AMM). The transcript have not been returned to the participants for comments.

The group discussions were moderated by HvH, assisted by AMM and MM.

The participants were mostly experienced healthcare professionals with a medical background in elderly care. Participants came from various regions in the Netherlands, providing a broad range of perspectives. Those from first group were ECS for many years who also included the trainer for the ECS residents. They had completed training in multiple modules. Participants from the second group had many years' experience in various disciplines in elderly care, such as psychogeriatrics and rehabilitation and also supervision for GPs. Unfortunately, ethnicity data were not collected, and this limitation is now noted in the *Strengths and Limitations* section.

For practical reasons, the first group with trainers took place on a "ECS trainer exchange day" which is organized on a regular basis by the medical school for postgraduates for supervision and education of the trainers.

The second focus group worked in the same organization and were colleagues. The moderator had no prior relationship with participants.

We did not include the participants' IDs during data collection. The contributions of the group members were reasonably balanced (there were no silent or overly dominant participants). This was largely due to the experienced moderator, who maintained a balance in the number and duration of the responses.

The moderator guided the groups in such a way that all participants were invited to contribute. This was done by mixing group discussions with asking all individual members to reflect on a topic. This resulted in a reasonable balance in participation across the group. Analysis of the reports was performed by open coding, axial coding and selective coding. First, labels (codes) were attached to the text fragments. These codes indicate the main themes of the fragments. Then the codes were compared with each other and similar codes were grouped under a more generic code. Finally, the codes were grouped into main themes and sub-themes. The coding was performed by three researchers (MM, AMM, RvM) using Atlas.TI. After each step of the coding of the main themes and sub-themes, they were compared, verified and, if necessary, adjusted after consultation.

The COREQ guidelines were followed and completed and were added as an attachment to the submission.

Researcher Characteristics

AMM (male, MD) is an ECS with several years of clinical and research experience, AMM assisted the moderator and analyzed the data.

MM (male, MD) was an ECS resident, assisted the moderator and analyzed the data.

HvH (male, PhD) is psychologist and elderly care scientist, professor Caring for vulnerable older persons, and is an experienced moderator of focus groups with health professionals.

RvM (male, MD, PhD) is a geriatrician-clinical pharmacologist, professor of geriatric

pharmacotherapy with experience in qualitative research and former ECS.

Ethical Approval

The participants agreed with the audio recording in order to analysis and publication, the name of the participant and the work location were not included. Also no patient data were included. The study protocol was conducted in compliance with Dutch regulations governing qualitative research with healthcare professionals. According to the Dutch *Medical Research Involving Human Subjects Act (Wet medisch-wetenschappelijk onderzoek met mensen, WMO)*, ethical approval by a certified medical ethics committee is required only for studies that involve medical-scientific research in which participants are subjected to interventions or required to follow specific behavioral rules. As this study involved focus group interviews with healthcare professionals only, without patients or interventions, it did not fall under the scope of the WMO and therefore did not require ethical approval.

See: <https://wetten.overheid.nl>

See: <https://wetten.overheid.nl/BWBR0009408> and <https://english.ccmo.nl/investigators/legal-framework-for-medical-scienti-research/your-research-is-it-subject-to-the-wmo-or-not>.

Results

A total of 11 ECSs participated in two focus groups. In the first group, 7 ECSs participated, all of whom were involved in the training of residents. In the second focus group, 4 ECSs participated, all of whom worked in the same healthcare institution. The basic information is shown in Table 1.

Table 1. Characteristics of participants

	Focus group 1	Focus group 2
Number of participants (n)	7	4
Age: average (range) years	52 (34-63)	49 (40-56)
Years of experience: average (range)	20 (4-30)	18 (13-20)

Facilitating and Impeding Factors

Based on the data, we identified 4 main themes which could be further divided into subthemes with several enablers and barriers. These results are shown in Table 2. Quotations illustrating the factors are also shown.

For each quote it is indicated which focus group it comes from: FocusGroup1 will be FG1 and FocusGroup2 will be FG2.

This does not mean that the similar quotes were not discussed in the other group.

Theme 1: Physician-Related Factors

Attitude

In general, there was a positive attitude towards deprescribing. This was mainly driven by the fact that ECS treat frail elderly with a high risk of adverse drug reactions and limited life expectancy.

FG1: "...because I want to get rid of as much as possible (medication) because I see all the side effects, interactions and misery."

FG1 "...but there are often medications among them that I think 'are they still necessary?' So that is uh particularly there and that limited life expectancy is something that is always very difficult to estimate actually. So uh at the moment when it is very clear that you are really going to treat symptomatically or palliatively uh yes then it is always like ha, can we stop things?"

Clinical Experience

Having experience as a physician and using the knowledge and expertise as a skill is frequently mentioned as an enabling factor. The training for ECS plays a supporting role in this.

FG1 "...evidence-based is important, but I believe clinical judgment ('doctor-based') also matters, especially because evidence often doesn't apply to our specific patient group."

FG1 "...new doctors often do not (deprescribing independently), because they think the family decides. Or they are still very stuck in that part of evidence-based medicine, so that part of doctor expertise is not included."

Emotions

The fear and anxiety of being sued for deviation of clinical guidelines is a serious barrier to doctors stopping a medication, even if they are convinced they should:

FG1 "...I'm just going to say the word fear...that in worse situations you will get a complaint if you stop the medication..."

FG1 "...I was charged with two years sessions, the inspection with all kinds of investigations. It really had an influence on me (regarding deprescribing)..."

Theme 2: Medication-Related Factors

Clinical Guidelines

The availability of deprescribing rules in guidelines can be supportive when stopping medication, but if the guideline is not specific enough or has not been developed specifically for the elderly, it sometimes becomes difficult to work outside the guideline.

FG1 *"That it is simply stated in the guidelines."*

FG2 *"So whenever I deviate from guidelines, I have to go an extra step to explain..."*

FG2 *"...but today's young doctors grew up with guidelines..."*

FG1 *"It is not in the guideline if you have no staff or if the family is against it, no, then you are not allowed to give pills, that is not what the guideline says."*

FG2 *"What do you do if a guideline does not mention anything specific about the elderly?"*

FG1 *"Sometimes you also follow the specialist guideline.... if you are indeed unable to come up with your own..."*

FG2 *"Well, that's the aim anyway, with the Care and Coercion Act (a law in the Netherlands to evaluate psychotropic medications dynamically), psychotropic drugs must always be evaluated..."*

Scientific Evidence

Scientific evidence for the elderly and frail patient population is limited. There is a lack of evidence about the long-term effect of, for example, preventive medication in older and frail patients. Due to a lack of evidence, determining the benefit-risk balance (BRB) in older and frail patients is experienced as difficult, for example, knowing the Number Needed to Treat (NNT) and Number Needed to Harm (NNH) to substantiate the discontinuation of medication.

FG2 *"...they have to be based on something and there is no research..."*

FG2 *"...because evidence-based is not necessarily applicable to the current, our target group..."*

FG2 *"It often helps if you can explain with figures what percentage risk reduction you are actually working on and what the risk of bleeding is in return. So my experience is that if you can substantiate it with scientific figures, it will help you a lot (it went about anti-coagulation medication)..."*

Table 2. Facilitating and impeding factors per theme

Theme	Sub-Theme	Enabler	Barrier
1- Doctor related factors	Attitude	Positive Toward Deprescribing	Prefer to rely on evidence- that is rarely available for this population
	Clinical Experience	Experience and Training	Difficult to estimate prognosis; Disagreement with other specialists;
	Emotion	Support from the Medical Specialist as a second opinion	Reserved GP's attitude towards deprescribing; Co-treatment with a specialist with different opinions
2- Medication-related factors	Clinical Guidelines	Start-Stopp criteria integrated into EPS ; Guidelines; Are there still indications for medication?	Less optimal EPS
	Scientific Evidence Expected effect of deprescribing	Available Evidence Positive Experience with Deprescribing	No Guiding for Deprescribing Fear of adverse effect of stopping certain medications such as anticoagulation ; Interactions
	Adverse Drug Reactions		
3- System-Level and Organizational Support	Electronic prescription system (EPS)	Current Medication Change through timely-transfer medication list	Difficult to retrieve Medical Information; Extra time and Effort
	Cooperation/ teamwork		
	Availability of medical history And Role of external health care professionals	Medication review with pharmacist; complete and timely observations; input from other disciplines regarding side effects and complications Optimal staffing	lack of experience among team members Understaffing and therefore overcrowding; high turnover of the doctors, which reduces continuity
	Support from the organization and management	Well-organized medical staff and paramedics ; fresh perspective from new colleague ; Unity in policy in organization mental and legal support	

Theme	Sub-Theme	Enabler	Barrier
4- Patient-related factors	Patient preferences	Open for conversation and consultation ; Are there still indications for medication? Known life expectancy Side effect related complaints or No effect on main problem	Belief in the effect of certain medications;
	Life expectancy Role of relatives and informal care givers	Open for Discussion about Medication use	Negative attitude toward Deprescribing Impact of Family distrust
	Legal/medical policy Legislation	Patient Representative open to consultation regarding medical policy and follow-up Support of law in involuntary care and stop psychotropic drugs	Representative offers no room for consultation; Threat of disciplinary actions

EPS: *electronic prescription system*

Expected Effect of Deprescribing

Uncertainty concerning the effects of deprescribing may function as a barrier. Potential adverse effects of deprescribing were mentioned as barrier. Stopping medication may cause relapse of symptoms or increase the risk of unfavorable events like stroke or cardiac problems. Anticoagulation drugs were medication classes that were frequently mentioned as risk medication.

FG1 *"...yes, but that is very annoying because it is not, it is not comfortable to have a stroke in your last part (of life)."*

FG2 *"...but if someone is indeed chronically depressed and he has already had four (relapses), then I would absolutely not rather not touch it."*

Positive experiences with deprescribing were mentioned as facilitator. Situations where a patient improved clinically after deprescribing were mentioned as increasing self-confidence with deprescribing.

FG1 *"...someone on multiple medications for depression and it turned out there was no indication for it, after stopping the medication the patient improved and then it turned out to be mild hypothyroidism..."*

Adverse Drug Reactions

Another very relevant theme for ECS's were presence of adverse drug reactions (ADRs) or the risk of ADRs due to drug-drug and drug disease interactions. Older persons often respond differently to medication due to the changes in their body over time and they also use more medication due to comorbidities and therefore the risk of interactions is higher with more consequences.

FG2 *"If there are no side effects or if someone has no visible complaints from the statin, then I think I'll leave that as it is..."*

FG1 *"...so if, for example, the chance of side effects is much more in the foreground than possibly the benefits then it may be the case that I already decide, with well-reasoned reasoning, not to prescribe something."*

FG1 *"...it may sometimes be necessary for certain drugs to be reduced in dosage or to be exchanged for another drug or to be discontinued due to interactions..."*

Adverse drug reactions like constipation, drowsiness and increased risk of falls are frequently mentioned as reason for deprescribing.

FG1 *"...fall risk is an important factor for us to assess, whether it is related to medication use, drowsiness, general pain, or other complaints Constipation is a side effect that is often forgotten if you do not pay attention to it. That's why I actually say that we always prescribe rationally."*

Theme 3: System-Level and Organizational Support

Electronic Prescription System (EPS)

The EPS was mentioned as a possible support for deprescribing. The integration of START and STOPP criteria in the EPS was mentioned as an option to promote deprescribing. In this way, doctors can compare theory and clinic to determine whether there is still an indication for a particular medication.

FG2 *"...but when I hear that you have a supra-regional formulary in which everything is integrated and those STOPP and START criteria that you have built into it I think that's nice too."*

FG2 *"... because the (medication) indication changes over time..."*

Availability of Medical History

Complete and correct exchange of medical information between health care professionals is important for carrying out deprescribing. While ECS request information at the time of admission, the delay is due to procedural and system-level issues with external data sharing (e.g., hospital discharge summaries or GP medication lists). This exchange of information is often experienced as inadequate. This concerned both the (in)completeness of the information and the timeliness of the exchange. For example, medical information following hospital discharge or from the GP/ family doctor often arrives many days after nursing home admission. In addition, the large volume of medical history from the GP's was also mentioned, while an up-to-date overview would be particularly helpful. Also medical information for instance concerning indications for medication, is often incomplete.

FG2 *"We do not always receive the complete GP file It sometimes does not arrive until one or two weeks following admission."*

FG1 *"...and then I say that we are going to take a critical look at what you need, but then after four or six weeks when I have the first meeting with uh. with the resident and family, I do not always have all the information..."*

FG1 *"...yes, you are faced with the vulnerable patient who makes you think "I need to know a lot more about this before you can even make decisions..."*

Cooperation/ Teamwork

Collaboration plays a major role in deprescribing among nursing home residents. For example, doctors depend on the observations and reporting of healthcare staff for deprescribing. The competence of healthcare staff in this regard was not always experienced as sufficient, which meant that, for example, symptoms or side effects could be missed. As a result, deprescribing or evaluation of deprescribing cannot be properly carried out.

FG2 *"...because then I go to the team manager and say the nurses have to report more..."*

Optimal staffing is an increasing problem in healthcare that is referred to as an enabler.

FG2 *"Guidelines are nice if you have employees who can also facilitate them, that you have no barrier, we're short on staff..."*

Especially when deprescribing psychotropic drugs, the psychologist was seen as an essential collaboration partner.

FG1 *"What I especially do when it comes to behavior is to say that the team needs to talk to each other about this problem in order to be on the same page and still involve the psychologist."*

Role of External Health Care Professionals

The role of medical specialists is experienced both positively and negatively. If there is a consensus on the medication policy, it can be very supportive.

Sometimes, patients or their families place more trust in hospital specialists who originally prescribed the medication, which can make deprescribing discussions challenging and increase the risk of disagreement or conflict. Statements made by medical specialists about the lifelong use of medication are also frequently mentioned as barriers.

FG1 *"...when you have the discussion about statins, that of course keeps coming up again and again and all cardiologists feel they have to say with great enthusiasm that they (elderly) have to use this for their patients for the rest of their lives."*

FG 1 *"Well it's your responsibility or no this patient really needs that medication."*

Using the status of medical specialist and collaborate with them can also facilitate deprescribing.

FG2 *"...then I consult a neurologist. Ask for a second opinion if the contacts with the client (patient) or representative are such that I have done my best ... and that does not provide*

a solution and then I would say yes, let me ask an expert who specializes in that field and people see are also taken seriously."

Pharmacists are mostly perceived as facilitators for deprescribing. Medication reviews performed together with a pharmacist is experienced as positive.

FG1 *"What does help is that you otherwise check with the pharmacist per department to see what, for example, psychotropic drugs are prescribed."*

Support From the Organization and Management

Care staff shortage is a well-known problem in elderly care. There is not only a shortage of healthcare staff, but also of specialists in elderly care and other disciplines such as psychologists. This results in high work pressure and a lack of time.

FG1 *"I just took over an entire department that was all a care home and that is now a nursing home, so you have a lot of work to do."*

These stand in the way of regular consultations, such as pharmacotherapeutic consultations (FTO) and medication reviews, which is actually experienced as a positive factor for deprescribing. The consultations are used by some physicians to discuss the prevalence of medication prescriptions and prescribing behavior. In addition, there is also a high turnover of general practitioners, which hinders continuity in medical care. This continuity is experienced as an important factor in being able to carry out deprescribing.

FG1 *"There are many changes in both houses (nursing home wards). So if you can manage a little, you as colleagues will not reverse all kinds of policies of others. Or you will immediately prescribe again at the first..."*

The turnover of doctors was experienced as positive, as the fresh perspective of new doctors was appreciated. At organizational level, the vision of the organization and department was mentioned as a factor that can contribute to deprescribing.

Moreover the internal agreements in an organization regarding medication policy can help doctors to work unambiguously, which was described as an enabler.

FG1 *"...also the policy in the organization regarding when do we stop taking pills, such as limited life expectancy of two years, no cholesterol inhibitor etc. gives extra support..."*

Unfortunately, there are cases that lead to a complaint and legal action. the doctors want the mental and legal support of their organization.

FG2 *"...that is an organization that supports you and the another doesn't..."*

Theme 4: Patient-Related Factors

Patient Preferences

The patients belief in medication and the status of medication can both be experienced as a barrier and facilitator.

FG2 *"...include what is desired by the client (patient) himself. Also, uh, with experience from the past, for example, with certain medications or, uh, for example, they have had side effects."*

FG2 *"Then if they really find it valuable, I try to keep as much of it the same and at another time I try to explain in a quiet moment why it is better to use something or not."*

FG1 *"...can decide for himself "I want this medicine or not." ... I have too many side effects from this, so I don't use it."*

Life Expectancy

Life expectancy is an item that is not always clear. In the case of a clearly limited life expectancy, it is more flexible for the doctor to adjust medication. For example, it is then more acceptable to stop taking statins. Although determining life expectancy is not always easy and is considered a barrier.

FG1 *"So that limited life expectancy is something that is always very difficult to estimate. So the moment it is very clear that you are really going to treat symptomatically or palliatively, then it is always like "we can stop things." And then it is always very clear, so then you stop taking cholesterol lowering and ascal and things like that..."*

FG2 *"...of course also, for example with statins, if people are admitted and they have a cardiovascular event, but they have a limited life expectancy, then I will of course consider not prescribing that."*

FG1 *"...with limited life expectancy, at least consider your goal is to combat complaints or prevent complaints."*

For most ECS's the decision to deprescribe is not determined by the type of problem causing nursing home admittance (psychogeriatric or somatic problems). In both type of residents, life expectancy is the crucial factor.

FG2 *"...you know, I think it would be looked at in the same way with a psychogeriatric patient as with a somatic patient. Absolutely what is the life expectancy, because if someone has profound dementia you have a life expectancy of less than three years."*

FG2 *"...the question is whether a patient is a psychogeriatric patient or a somatic resident has a major influence on medication prescription behavior...in principle not, because the medication you prescribe actually has more to do with somatic complaints, quality of life and life expectancy. With psychogeriatrics it is slightly different because you can work more with psychotropic drugs. So there is a change in prescribing behavior."*

Role of Relative and Informal Caregivers

Nursing home residents usually have family involved in their care and therefore also in medication use. Depending on the attitude of the family, deprescribing can be experienced as more or less difficult. Building a relation based on trust is important.

FG1 *"...you actually have to have a relationship of trust first, ... but there are also many who want to hold on to everything they had and do not have the confidence that you will act properly."*

FG2 *"...we're going to discuss all medical decisions one-on-one with the family. And it seems nice, because you can't do it with that patient and the law says that he is the representative, so discuss EVERYTHING with the family." "Because...., but that son who thinks he knows better what is good for his father than I do..."*

FG2 *"...but family sometimes finds it very difficult to actually make that decision for that person, especially if the person (medication) has always had to be used by the doctor for life. I think that as a doctor who is now the practitioner, you must clearly indicate what you think is in the interest of that person."*

FG1 *"...but then the digital world doesn't always help. Because family can of course wander around and see that you should or should not prescribe a certain medicine for heart failure... then you will have a nice discussion..."*

Discussion

In this study, we explored the barriers and enablers to deprescribing experienced by elderly care specialists (ECS) who work in nursing homes. In general, ECS are supportive of deprescribing, especially for frail elderly patients, due to concerns about adverse drug reactions and lack of efficacy in patients with limited life expectancy. Studies with other healthcare professionals, such as GPs, pharmacists, and geriatricians, reveal similar points of view. Some GPs hesitate to initiate deprescribing conversations, concerned that patients may feel neglected.^{28–31} Others struggle with discussing limited life expectancy or identifying adverse drug effects due to polypharmacy. In contrast, ECS do not mention concerns that patients might feel abandoned or feel uncomfortable discussing life expectancy.

Decisions to deprescribe are often based on clinical experience. Recently trained physicians tend to adhere more strictly to clinical guidelines, despite the fact that these guidelines are often too general and do not align well with elderly care and there is limited scientific evidence to support deprescribing in frail patients. Fear of legal repercussions when deviating from these guidelines was a major barrier, even when deprescribing is regarded as appropriate. This lack of evidence and guidelines in nursing home residents is a significant barrier to deprescribing among the doctors working in the nursing homes.^{28–30.}

In accordance with other studies, ECS were hesitant to deprescribe high-risk medications such as anticoagulants and psychotropics due to possible adverse effects.^{28.} However, their confidence grows following positive outcomes from deprescribing efforts and the presence of guidelines like STOPP/START criteria. Effective deprescribing requires collaboration with other healthcare professionals. Deprescribing was experienced as difficult if another medical specialist is involved in the medication prescription.^{31.} Medical specialists may prescribe based on their professional guidelines which are not always appropriate for the nursing home setting.

Family involvement is an important element in deprescribing in nursing home residents. Many nursing home residents have cognitive problems^{32.}, which affect their decision-making capacity. Family often steps in as a proxy for the residents' medical decision making. In some cases, deprescribing may be complicated by the emotions and attitudes of family members, especially when family members disagree or show more faith in hospital specialists. Although family attitudes and emotions were not mentioned as barriers in earlier studies, cognitive limitations in patients were reported as deprescribing challenges for professionals in elderly care.^{28,30.} Our findings highlight the importance of involving family perspectives in deprescribing decisions.

ECS faced challenges due to time constraints, collaboration with co-workers, staff continuity, insufficient access to clinical information and limited support from electronic patient systems. These issues were reported earlier.^{31,33.} Pharmacists provide valuable support, but barriers may exist in collaboration with nurses. The competence of the nursing staff in this regard was not always experienced as sufficient, which meant that, for example, symptoms or side effects could be missed. As a result, deprescribing or evaluation of deprescribing cannot be properly carried out. Nurses can play an essential role in helping families accept deprescribing decisions, though there is disagreement on whether nurses should be involved in medication review meetings.^{31,33.} In short, compared to other studies, this study is the first qualitative exploration of deprescribing barriers/enablers from ECS perspectives in the Netherlands. The ECSs are a unique specialist group of physicians responsible for the medical care of long term care residents, who are well situated to optimize medication prescriptions. Two new themes emerged as particularly relevant, that were not described earlier in the literature: of (I) fear for legal claims (e.g., threat of disciplinary complaints) and (II) the difficulty to deal with hospital specialists as

prescribers, who were perceived to be higher in the medical hierarchy. We now highlight these as novel contributions.

This study emphasizes the importance of support from organizational-management as well as from direct colleagues (e.g. collaboration with psychologists, continuity issues).

Strengths and Limitations

The major strength of this study is that the participants were all ECSs with substantial experience with (de)prescribing in very frail older persons in nursing homes.

Peer pressure may have been present. This may mean that socially desirable answers were given, which may result in missed insights and experiences. Nevertheless, several participants shared difficult experiences including official complaints. This indicated a collegial atmosphere of trust. Unfortunately, ethnicity data were not collected, which is a limitation of this study.

Differences between the two groups might be an indication of potential differences in approaches to deprescribing, which were not identified in the results.

In the first focus group, all ECSs were trainers in various areas in the Netherlands. The geographical distribution may have influenced the findings. This also may have caused an overrepresentation of physicians who practice the latest state of the art because they work more closely with the medical residents. However, this can be a strength at the same time: It is possible that they have acquired more knowledge and/or skills, which makes barriers such as fear (reluctance to stop/change the prescribed medication) less present. Finally, no new themes emerged after the second focus group. We acknowledge the possibility that data saturation may not have been fully achieved due to the limited sample size and the lack of heterogeneity among the participants. We acknowledge the limitation of only two groups and now clearly state that saturation was considered but cannot be guaranteed.

Conclusions

Deprescribing among nursing home residents remains challenging. It is a complex and delicate process, hindered by limited evidence-based guidance and requiring the active involvement of patients, family members, and institutional support. Experienced ECSs demonstrated a positive attitude toward deprescribing and recognized its value. This attitude, identified as a newly acknowledged influencing factor, underscores the need to address training for general practitioners. To effectively promote deprescribing as a means of delivering optimal and appropriate care, it is essential to support ECS through improved digital infrastructure—such as user-friendly electronic prescribing and registration systems—and through structural, interdisciplinary collaboration. This includes coordinated efforts with patients, families, management, pharmacists, paramedics, and hospital specialists, all guided by tailored guidelines that address the specific needs of older populations.

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Author Contributions

All authors contributed to the study design. Rob van Marum contributed to the study conception. Data collection were performed by Man Chun Lee, Hein van Hout and Alireza Malek Makan. Data analysis were performed by Alireza Malek Makan and Man Chun Lee. The first draft of the manuscript was written by Alireza Malek Makan and Man Chun Lee and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Data Availability

The datasets generated and/or analyzed during the current study are not publicly available because “The full-length transcripts” are in Dutch but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The participants agreed with the audio recording in order to analysis and publication, the name of the participant and the work location were not included. Informed consent to participate was obtained from all of the participants in the study. Also no patient data were included. The study protocol was conducted in compliance with Dutch regulations governing qualitative research with healthcare professionals. These regulations state that review by a certified medical ethics committee was not required, as the study did not involve patients or invasive interventions and therefore did not require ethical approval. Dutch legislation regarding this matter is outlined on the official website: Your research: Is it subject to the WMO or not? | Investigators | The Central Committee on Research Involving Human Subjects Our study also adhered to the Declaration of Helsinki.

Consent for Publication

Not applicable.

Competing Interests

The authors declare no competing interests.

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CHAPTER 6

General Discussion

General Discussion

Increased life expectancy has led to a higher burden of age-related morbidity, posing significant challenges for healthcare systems.^{1,2} Among older adults, multimorbidity frequently results in polypharmacy, commonly defined as the use of five or more medications.³ In response to the lack of age-specific prescribing guidance, several approaches to optimize medication use have emerged, with the term “deprescribing” first appearing in 2003.⁴ Polypharmacy is highly prevalent among nursing home residents and is associated with adverse clinical outcomes.⁵ Medication review provides a structured approach to optimize pharmacotherapy by identifying and addressing drug-related problems.⁶

Building on these insights, we conducted a series of studies investigating medication use in frail elderly nursing home residents across multiple European countries, encompassing diverse clinical characteristics. Medications were systematically evaluated for appropriateness, and the attitudes and perspectives of Elderly Care Specialists (ECS) in the Netherlands regarding (de)prescribing practices were examined. Integrating these perspectives provided a comprehensive understanding of medication practices and challenges, leading to the identification of several key findings. Specifically, this thesis assessed the following objectives:

- To estimate the prevalence of potentially inappropriate medications (PIMs) in nursing home residents across eight European countries according to STOPP-Frail criteria, and variation by cognitive status and life expectancy.
- To estimate the prevalence of four classes of preventive cardiovascular medications (oral anticoagulants, platelet aggregation inhibitors, antihypertensives, and lipid-modifying agents) in nursing home residents across eight European countries, and variation by length of stay, mortality risk, cognitive status, functional disability, and country.
- To estimate the prevalence of pharmacological osteoporosis prevention in nursing home residents across eight European countries, and its relationship with patient characteristics.
- To explore the barriers and enablers of deprescribing among Elderly Care Specialists (ECSs) in the Netherlands.

Building on these study objectives, the following sections integrate quantitative findings with patient-centered reflections and European context, providing insight into both prevalence and clinical implications of medication use in older nursing home residents.

Reflection on Findings: Comparison with Recent European Data

Our findings demonstrate a high prevalence of potentially inappropriate medications (PIMs) among nursing home residents: nearly 90% received at least one PIM^{7,8,9, chapter2}, and two out of every seven medications were classified as inappropriate according to STOPP-Frail criteria.^{chapter2} This aligns with broader European evidence indicating persistently elevated PIM prevalence. A recent systematic review of nursing home residents across Europe reported PIM prevalence ranging between 67.8% and 87.7%, depending on criteria used (e.g., STOPP/START) and care setting, underscoring widespread inappropriate prescribing in institutionalized older adults. Another European cross-sectional analysis found PIM prevalence as high as 56.0% among older adults in long-term care settings, with notable inter-country variability, highlighting that PIMs remain a substantial concern beyond our cohort.¹⁰

Residents with cognitive impairment or limited life expectancy continued to receive PIMs, including a subgroup prescribed four or more PIMs and an average of 1.66 PIMs among those with life expectancy under six months.^{7,11, chapter2} Similar European evidence suggests that while cognitive impairment may slightly modify prescribing patterns, inappropriate prescriptions remain common across cognitive strata and care contexts, emphasizing ongoing challenges in deprescribing practice.¹⁰

In the Netherlands, the prevalence of residents with at least one PIM was high but comparable between cognitively impaired and non-impaired residents, unlike in most other countries where cognitively impaired residents were less likely to receive PIMs. Overall PIM use in the Netherlands was lower than for example in Finland, which showed markedly higher use of anti-anginal therapy, calcium, vitamin D, multivitamins, and osteoporosis medications. Preventive and symptomatic PIMs, such as antiplatelets, antihypertensives, proton pump inhibitors, and antipsychotics, were commonly prescribed in the Netherlands, but the patterns reflected lower or similar prevalence compared to the other countries included in the study.

Although use of preventive cardiovascular medications (PCM) was slightly lower in certain subgroups, overall prevalence remained relatively high. Long-stay residents (>12 months) had a slightly lower prevalence than mid-stay residents (2–12 months), with 56.0% versus 62.7%. Cognitively impaired residents received these medications less frequently than those without cognitive impairment (47.1% vs. 67.0%). Slightly lower use was also observed among residents with high mortality risk (47.4% vs. 58.6%) and those with high scores (≥ 5) on the Activities of Daily Living Hierarchy Scale (ADLH) (48.6% vs. 64.0%), indicating that preventive cardiovascular medications remained widely used even in higher-risk groups.

In the Netherlands, 57.9% of nursing home residents received at least one preventive cardiovascular medication (PCM), most commonly antihypertensives (35.7%) and platelet

aggregation inhibitors (34.9%), with use patterns generally consistent with other countries. Similar to international trends, PCM use decreased markedly with worsening cognitive impairment and higher dependence in daily living (ADLH), while length of stay had minimal impact. Compared to other countries, overall PCM prevalence in the Netherlands was relatively moderate, with reduction in Anti-Hypertensives, platelet aggregation inhibitors, lipid-modifying agents, and oral anticoagulants among residents with severe cognitive or functional impairment closely mirroring patterns observed elsewhere.

Beyond PIMs, our data revealed substantial undertreatment of osteoporosis care: fewer than 10% of residents with recent fractures received bisphosphonates, and only about one-third were co-prescribed vitamin D and calcium.^{12,13,chapter4} European research corroborates this therapeutic gap, indicating that secondary fracture prevention remains sub-optimally implemented in older adults, particularly in high-risk populations.¹⁴

In the Netherlands, 19.5% of nursing home residents used at least one osteoporosis medication (OM), with 10–18% using vitamin D or calcium and 4.5% using bisphosphonates. Use was lower in residents with cognitive impairment or walking dependency and higher after falls or fractures. Compared internationally, OM use in the Netherlands was moderate—higher than in Italy, Israel, Germany, and the Czech Republic (<10%), but much lower than in Finland (≈66%), while bisphosphonate use was lower than in the UK (10.5%).

ECs in Dutch nursing homes generally support deprescribing, especially for frail residents with limited life expectancy, due to concerns about adverse drug reactions and limited treatment benefit. Major barriers include limited evidence, non-tailored clinical guidelines, and fear of legal repercussions when deviating from existing guidance—a novel and significant concern.^{15,16,17} Deprescribing is further complicated by the need to collaborate with hospital specialists and involve families in the care of cognitively impaired residents, though both are considered essential.^{15–19} Additional organizational barriers—such as time constraints, insufficient electronic support, and suboptimal interdisciplinary collaboration—also hinder implementation.^{18,19}

Taken together, these findings highlight a dual challenge in medication management among nursing home residents, a population largely characterized by frailty: (1) persistent overprescribing of inappropriate medications despite tools like STOPP-Frail and systematic screening, and (2) underuse of indicated preventive osteoporosis treatment. These patterns reflect both prescribing inertia and the complexity of deprescribing in frail older adults.

Patient-Centered Reflection on PIMs and Cardiovascular Medication

The high prevalence of PIMs underscores a critical patient-centered concern. Receiving PIMs increases risks of adverse drug events and hospitalizations and may negatively affect quality of life.^{20,21} For residents with cognitive impairment or limited life expectancy, the

potential benefit of certain medications is often minimal, meaning that these drugs are unlikely to contribute meaningfully to their well-being. Some residents continue to receive four or more PIMs, among those with life expectancy six months or less, suggesting that decisions are sometimes driven more by routine than by individual care needs.²²

A patient-centered approach requires systematic medication review with attention to care goals and comfort, actively involving residents and families in decision-making.²⁰ Evidence from European studies showing substantial variability in PIM prevalence across countries and care settings highlights opportunities to share best practices and optimize care processes in favor of patients.²¹

Preventive cardiovascular medication remains common, even among residents with limited life expectancy or cognitive impairment, which may be potentially inappropriate in some cases.^{23,24, chapter3}. Deprescribing should be prognosis-driven and individualized, considering life expectancy, time to benefit, health goals, frailty, and preferences. In residents with limited life expectancy, the potential harms of long-term preventive treatments, such as hypotension, falls, or adverse drug interactions, often outweigh delayed benefits, emphasizing careful evaluation of statins, antihypertensives, and platelet aggregation inhibitors.²³⁻²⁶

European and Dutch guidelines recommend that preventive pharmacotherapy decisions should integrate cardiovascular risk, frailty, life expectancy, and patient preferences rather than rely solely on age-based criteria.^{27,28} For secondary prevention in residents with established atherosclerotic cardiovascular disease, therapy remains indicated, but intensity and tolerability should be carefully considered in frail populations. Non-pharmacological interventions remain foundational and can influence deprescribing decisions.²⁹

Patient-Centered Reflection on Osteoporosis Management

As it has been mentioned, our findings indicate substantial undertreatment of osteoporosis among nursing home residents: <10% of residents with recent fractures received bisphosphonates, and only one-third were co-prescribed vitamin D and calcium.^{12,13, chapter4}. Guidelines recommend calcium intake of 1000–1200 mg/day and vitamin D 800 IU/day, preferably alongside pharmacological therapy when indicated.^{30,31} Bisphosphonates are first-line for secondary fracture prevention, given their efficacy in reducing vertebral and non-vertebral fractures.³²

European studies show that residential older adults often fail to achieve adequate calcium and vitamin D intake, and bisphosphonate use remains low even after fragility fractures.¹⁴ Patient-centered osteoporosis care requires individualized assessment of fracture risk, nutritional status, comorbidities, and life expectancy, alongside shared decision-making with residents or proxies.^{30,32} Structured medication review tools can support deprescribing decisions, but individualized judgment considering frailty, patient preferences, and family involvement is essential.^{8,24,33}

The Netherlands versus Europe

Overall, the findings indicate that nursing home residents in the Netherlands tend to receive somewhat fewer potentially inappropriate medications and cardiovascular medications compared with residents in several other European countries, particularly Finland, suggesting a lower level of potential overtreatment. In contrast, the use of osteoporosis medications appears to be broadly comparable to that observed in the UK, France, and Italy, indicating that potential undertreatment in this area is similar across these countries. This pattern likely reflects characteristics of the Dutch long-term care system, which emphasizes multidisciplinary care teams, structured medication reviews, and a cautious approach to initiating or continuing preventive and chronic medications in frail older adults.^{chapters 2,3,4.} In contrast, countries such as Finland exhibit substantially higher use of preventive agents, including vitamin D, calcium, anti-anginal therapy, and osteoporosis medications, reflecting differences in prescribing culture, national guidelines, and healthcare organization. Nevertheless, across all countries, cognitive impairment, functional dependency, and limited life expectancy consistently correlate with reduced medication use, underscoring a shared clinical principle of tailoring pharmacotherapy to residents' frailty and prognosis. Taken together, these observations suggest that Dutch nursing homes adopt a moderately conservative and individualized prescribing approach relative to the broader European context, balancing preventive care with patient-centered risk assessment.

Taken together, these insights emphasize the importance of understanding both patient and clinician perspectives to guide safe, effective, and resident-centered deprescribing practices.

Patient-Centered Perspectives on Deprescribing Barriers and Enablers

Successful deprescribing depends on residents' attitudes, understanding, and involvement, complementing ECS-identified barriers and enablers. Surveys indicate older adults are often willing to deprescribe if supported by their General Practitioner (GP); trust, satisfaction, and clear communication strongly influence willingness.^{34-36.} Barriers include fear of stopping medications, preference for maintaining current treatments, healthcare system complexity, and clinician discouragement. Enablers include patient autonomy, safety concerns, education, and high-quality relationships with providers.^{34,37,38,39.}

Frail residents face challenges such as limited consultation time, inaccessible terminology, and insufficient information, while enablers include gradual deprescribing, multidisciplinary collaboration, and negotiated approaches.^{40-42.} Family involvement, particularly for cognitively impaired residents, plays an important role in determining care quality and health-related outcomes.^{34,37,39,40.} Proactive strategies providing rationales, preparing patients and close relatives, and ensuring follow-up are essential for effective, patient-centered deprescribing.^{36,43.}

System-level interventions include:

- Structured, tailored guidelines for frail residents^{33,44}.
- Enhanced interprofessional collaboration^{45,46}.
- Structured family engagement policies⁴⁷.
- Upgraded electronic systems for medication tracking⁴⁵.

These strategies ensure deprescribing is safe, coordinated, and aligned with resident-centered goals.

Understanding the barriers and enablers from both patient and clinician perspectives underscores the need for rational prescribing and structured deprescribing frameworks to optimize medication use safely and effectively.

Rational Prescribing

Rational prescribing is a systematic, evidence-based approach to selecting and using medications that aims to optimize clinical outcomes, minimize harm, respect patient preferences, and avoid unnecessary or inappropriate use. It involves verifying the diagnosis, setting clear therapeutic goals, selecting the most appropriate drug and dosage, and continually monitoring effectiveness and safety. In rational prescribing, the prescriber considers the best available evidence, the patient's individual circumstances—including comorbidities and preferences—and cost-effectiveness to ensure that each prescription is necessary, appropriate, and beneficial.^{48,49}

Deprescribing

Deprescribing is a recognized strategy to optimize pharmacotherapy in older adults with polypharmacy, multimorbidity, or frailty. Its main goal is to reduce potentially inappropriate medications (PIMs), thereby lowering risks of adverse drug events, falls, hospitalizations, and diminished quality of life.^{5,22,50,51,52,53,54} Systematic, stepwise deprescribing can safely decrease medication burden while maintaining or improving cognitive and physical outcomes.^{22,50,51,52,53,54} Careful planning and shared decision-making are essential to minimize withdrawal effects or symptom recurrence.^{26,54} While deprescribing has been shown to improve the appropriateness of medication regimens, evidence from numerous studies indicates that its impact on patient-centered outcomes, such as quality of life, functional status, or cognitive performance, is generally modest or inconsistent.^{22,50,51,52,53,54} Systematic deprescribing interventions, including pharmacist-led or multidisciplinary approaches, effectively reduce the number of potentially inappropriate medications and medication burden. However, these reductions do not consistently translate into measurable improvements in patient-reported or clinical outcomes. This highlights the complexity of deprescribing in older adults, suggesting that while it is a valuable strategy for

optimizing pharmacotherapy, additional supportive measures or tailored approaches may be necessary to achieve meaningful benefits for patients' overall well-being. Recent European and Dutch studies confirm that deprescribing is feasible and generally safe in older adults. The LeMON trial in the Netherlands showed that pharmacist-led, deprescribing-focused medication reviews increased deprescribing proposals and improved collaboration with general practitioners, although actual withdrawal of cardiovascular and antidiabetic medications was not statistically significant.⁵¹ Systematic reviews in community-dwelling older adults indicate that deprescribing interventions moderately reduce PIMs and total medication burden, potentially improving safety and aligning therapy with individual priorities of care.^{52,53} Primary care studies applying explicit deprescribing criteria show that while general practitioners often agree with recommendations, real-world withdrawal rates may be lower.⁵³ The OMED2 program in the Netherlands is evaluating deprescribing of blood glucose-lowering medications, further exploring safety, feasibility, and practical implementation in older adults with type 2 diabetes.⁵⁵ Successful deprescribing requires multidisciplinary collaboration: physicians provide clinical judgment, pharmacists contribute expertise in pharmacokinetics and interactions, and nurses monitor for withdrawal effects, adverse events, or symptom recurrence.^{56,57} Patient- and family-centered shared decision-making ensures that deprescribing aligns with individual goals, preferences, and life expectancy. Tools such as the Beers Criteria, STOPP/START, and the Medication Appropriateness Index (MAI) help identify PIMs while allowing clinical discretion, recognizing that some medications may retain clinical value.⁵⁸⁻⁶⁰ Structured protocols and condition-specific guidelines further support systematic, evidence-based deprescribing.^{22,57,58} Despite robust evidence and available tools, deprescribing in nursing homes remains underutilized and inconsistently implemented.⁶¹ Barriers include clinician time constraints, high workload, lack of training or confidence, fear of withdrawal effects, therapeutic inertia, fragmented communication, and challenges in aligning resident or family expectations.^{62-71,chapter5,15-19} Strategies to enhance implementation involve embedding deprescribing into routine workflows, allocating dedicated time for medication review, fostering interprofessional collaboration, providing clinician training, and ensuring policy and organizational support.^{5,63,65,67,72}

A culture of patient-centered medication management, with active involvement of residents and families, is central to aligning care decisions with individual goals. Evidence from nursing home-specific deprescribing trials illustrates both the potential and limitations of these interventions.⁷³ Demonstrated in a cluster randomized controlled trial that structured interventions can significantly reduce the use of inappropriate medications among nursing home residents. Similarly, the DANTON study⁷⁴ and the RETREAT-FRAIL trial⁷⁵ showed that targeted deprescribing of antihypertensive and other medications is feasible and can lower medication burden, with some reduction in treatment intensity. However, consistent with broader literature, these interventions often have limited impact on patient-centered outcomes, such as quality of life, functional status, or cognitive performance. Notably, it has been examined the effects of deprescribing antihypertensive medications on cognitive

function and found minimal changes, highlighting the complexity of translating medication optimization into measurable clinical benefits.⁷⁶

Overall, these findings suggest that while deprescribing is effective in reducing inappropriate medication use and potentially improving appropriateness of therapy, realizing meaningful benefits for residents' health and well-being requires careful planning, individualized approaches, and ongoing monitoring. The integration of deprescribing into routine care should therefore be complemented by strategies to engage residents and families, address organizational barriers, and ensure safety while considering both clinical and patient-reported outcomes.

In summary, deprescribing, PIM evaluation, and structured tools provide a framework for optimizing pharmacotherapy in older adults, particularly in nursing home residents. Translating this evidence into practice requires combining guideline knowledge with practical implementation strategies, multidisciplinary collaboration, and patient-centered approaches to achieve safe, effective, and individualized care.

Grounded on evidence-based deprescribing strategies and patient-centered decision-making, the Sextuple Aim framework provides a multidimensional perspective to evaluate medication optimization, encompassing patient outcomes, clinician experience, population health, costs, equity, and environmental sustainability.

Evaluating Deprescribing through the Expanded Sextuple Aim

Medication review and deprescribing are increasingly recognized strategies in older adult care, though evidence suggests they may have limited direct impact on individual patient outcomes, such as quality of life or cognitive function.^{5,22,50–54,73–76} Nevertheless, deprescribing may provide broader benefits that extend beyond immediate patient-centered outcomes, including improvements in healthcare efficiency, clinician experience, equity, and environmental sustainability.

To systematically evaluate these wider implications, the **Quintuple Aim** framework can be applied. Developed in 2021 by the United States Institute for Healthcare Improvement, the Quintuple Aim seeks to optimize health system performance through five interrelated goals: enhancing patient experience, improving population health, reducing healthcare costs, supporting clinician well-being, and promoting health equity.⁷⁷ Building on this framework, the recent addition of **environmental sustainability** as a sixth goal has led to the formulation of the **Sextuple Aim** (fig 1), highlighting the importance of minimizing the ecological footprint of healthcare interventions.^{78,79}



Figure 1. *Sextuple Aims*

Applying the Sextuple Aim to deprescribing allows a comprehensive assessment of its multidimensional benefits. From a patient experience perspective, deprescribing can increase satisfaction and engagement by reducing unnecessary or potentially harmful medications and fostering shared decision-making, while also requiring attention to potential anxiety or resistance when long-term therapies are discontinued.⁸⁰ Regarding population health, deprescribing can lower adverse drug events, hospitalizations, and frailty-related harms among older and vulnerable adults.^{78,73–75} In terms of cost reduction, deprescribing interventions can decrease medication-related and broader healthcare expenditures, although initial implementation may require resources such as pharmacist or multidisciplinary team involvement.^{74,81}

Clinician experience is influenced as well: deprescribing promotes rational, patient-centered care and professional fulfillment, yet can increase workload and complexity, emphasizing the need for adequate training and support.⁸⁰ Health equity may benefit if structured deprescribing reduces disparities in polypharmacy, though unequal access to interventions could inadvertently worsen inequities.⁸² Deprescribing may reduce the workload of nursing staff in nursing homes by decreasing medication burden, thereby freeing up time for other care activities due to fewer administration rounds, monitoring requirements, and related tasks. This potential reduction in workload may similarly apply to physicians and pharmacists. Finally, from an environmental perspective, deprescribing reduces the production, packaging, and disposal of unnecessary medications, contributing to a smaller healthcare sector ecological footprint.^{78,79}

Overall, evaluating deprescribing through the Sextuple Aim situates medication optimization within a broader framework of health system performance. While direct patient-centered outcomes may show modest changes, the approach highlights how deprescribing can contribute meaningfully across multiple dimensions of healthcare value—including safety, efficiency, clinician well-being, equity, and environmental sustainability—demonstrating its relevance beyond immediate patient effects.^{78–83}

Toward Individualized, Safe, and High-Quality Pharmacotherapy in Nursing Homes: A Sextuple Aims Perspective

Potentially inappropriate medication use remains common in nursing homes, encompassing both overtreatment—such as continuation of preventive cardiometabolic medications in residents with limited life expectancy^{23–25}—and undertreatment, including suboptimal osteoporosis prevention.^{12,13} Deprescribing is feasible and evidence-based, yet underutilized due to clinical, organizational, and interpersonal factors, including fragmented care, multiple prescribers, insufficient electronic communication, rigid guideline adherence, and family considerations.^{25,33,44–47,63,65}

Methodological Strengths and Limitations

Strengths: This study benefits from a large, multinational cohort, enabling reliable comparisons of cross-national prescribing patterns and ensuring that residents were assessed consistently and accurately. Standardized instruments such as interRAI and STOPP-Frail^{84,85} ensured systematic and reliable assessment of medication appropriateness across diverse settings. The mixed-methods approach in this thesis integrates quantitative prevalence data with qualitative insights^{33,44}, providing a rich understanding of both the scale of potentially inappropriate medication use and contextual factors influencing deprescribing in real-world nursing home settings.

Limitations: Analyses were cross-sectional despite availability of longitudinal data in chapters 2–4, preventing conclusions on persistence of prescribing nor on incidence of deprescribing. Incomplete diagnostic and prior medication data may have led to underestimation or misclassification of PIMs. Variation in ATC coding may have affected comparability across countries. While this study provides valuable insights, several limitations should be acknowledged. First, the data were collected between 2009 and 2012, meaning that the analyzed data are relatively old. However, given the relatively stable nature of prescribing practices in nursing homes, we believe the data remain representative. This is further supported by more recent studies using the STOPP-Frail criteria, which report a prevalence of potentially inappropriate medication (PIM) use ranging from 85% to 96% among nursing home residents, consistent with the prevalence observed in our study (approximately 87%). Although more recent studies generally focus on a single country, our study includes data from a large cohort of nursing home residents across eight countries, providing a unique international perspective. Despite the age of the data, the consistency

with more recent findings supports the continued relevance of our results. Moreover, by integrating quantitative prevalence estimates with qualitative insights into clinical decision-making and organizational practices, this study offers a comprehensive and multidimensional understanding of PIM use and the barriers to deprescribing.^{chapter2, discussion.}

Future Research Directions

Future research should adopt a broad evaluation framework, such as the Sextuple Aim, to comprehensively capture outcomes beyond individual patient effects, including efficiency, clinician experience, equity, and environmental sustainability.^{78–83.} This approach ensures that deprescribing interventions are assessed across multiple dimensions, reflecting their potential impact on both residents and the healthcare system.

Future studies should:

- Evaluate the implementation, feasibility, and impact of frailty-based criteria, adapted guidelines, and deprescribing tools such as STOPP-Frail, START-STOPP, or locally adapted protocols. Research should examine how effectively these tools reduce PIMs, support clinician decision-making, and contribute to outcomes across the Sextuple Aim domains.
- Assess patient safety and clinical effectiveness, including reductions in potentially inappropriate medications, adverse drug events, falls, and hospitalizations. Studies should also prioritize alignment with residents' goals of care and quality of life, while evaluating efficiency through healthcare utilization, costs, and medication-related waste. Additionally, research should investigate timeliness of deprescribing processes, equity across resident subgroups, and environmental sustainability of reduced medication use.
- Examine educational interventions for healthcare professionals—including physicians, nurses, pharmacists, and interprofessional teams—to facilitate safe and effective deprescribing. Interventions may include interprofessional workshops, case-based learning, and simulation-based training, with evaluation of their impact on clinician knowledge, confidence, and actual deprescribing practices, as well as their contribution to broader system-level outcomes.

By integrating the Sextuple Aim into future studies, researchers can ensure that deprescribing is evaluated not only for direct patient benefits but also for its wider effects on clinicians, healthcare systems, equity, and environmental sustainability, thereby providing a comprehensive understanding of its overall value.

Practical Implications for Elderly Care Specialists

When conducting medication reviews, Elderly Care Specialists should adopt a patient-centered approach, actively involving residents and, when appropriate, their families in decisions to start, continue, or stop medications. Each medication should be carefully evaluated for potential inappropriateness, balancing risks and benefits while taking functional status and life expectancy into account. Collaborative input from nurses, pharmacists, and primary care physicians can help overcome clinical and organizational barriers and ensure a safe, comprehensive review. A stepwise deprescribing approach—prioritizing high-risk medications, planning tapering schedules, and monitoring for withdrawal or symptom recurrence—supports both patient safety and adherence to best practice. In addition, a nationally implemented Minimum Data Set (MDS) could enhance these efforts by providing standardized, reliable information on residents' health, medication use, and care needs, thereby supporting clinical decision-making and quality improvement.

Integrating these actions within the Sextuple Aim framework ensures that care balances multiple dimensions: optimizing clinical quality, enhancing patient experience, promoting population health, reducing unnecessary costs, supporting provider confidence, and ensuring equitable care for all residents. By translating insights gained during this study into concrete, patient-centered strategies, Elderly Care Specialists can navigate the complexities of prescribing and deprescribing in nursing home settings more effectively.

Future Perspective: Personalized Medication Using Systematic Data

In clinical practice, optimization of medication use in older patients can already achieve significant progress using existing data and technologies. The I-CARE4OLD project has shown that systematically collected data, such as the interRAI MDS, can be used with machine learning to generate personalized predictions of treatment outcomes.⁸⁶ This demonstrates that improving data quality, accessibility, and integration can already support personalized, predictive care, targeted medication selection, and effective deprescribing.

Although quantum computing and quantum machine learning are being explored as potential future tools to process more complex biological and clinical data⁸⁷, the current focus remains on the practical use of available data to support rational prescribing and reduce the risk of unnecessary or harmful medications.^{88,89} Decision-support systems that already use machine learning can reduce clinicians' cognitive burden without replacing clinical judgment and contribute to safer and more efficient medication practices.^{89,90}

In summary, the use of existing clinical data and machine learning, as demonstrated in I-CARE4OLD, shows that personalized and predictive medication optimization is already achievable today, while advanced technologies such as quantum computing remain a prospect for the future.

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APPENDICES

Summary

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Summary

General Overview

Among older adults, multimorbidity is common and frequently leads to polypharmacy, typically defined as the concurrent use of five or more medications. In the absence of age-specific prescribing guidelines, several strategies have emerged to improve medication use in older populations, including the concept of *deprescribing*, which was first introduced in 2003. Polypharmacy is particularly prevalent among nursing home residents and has been consistently associated with adverse clinical outcomes. In this context, medication review has been promoted as a structured and systematic approach to optimize pharmacotherapy by identifying and resolving drug-related problems.

We have built upon these insights by conducting a series of studies focusing on medication use among frail nursing home residents across multiple European countries, representing diverse healthcare systems and clinical populations. Medications were systematically assessed for (in)appropriateness, and, in addition, we explored the attitudes and perspectives of Elderly Care Specialists (ECSs) in the Netherlands regarding prescribing and deprescribing practices. By integrating quantitative epidemiological analyses with qualitative insights from clinical practice, we obtained a comprehensive understanding of current prescribing patterns, decision-making processes, and perceived challenges.

We have focused in this thesis on the prescribing of potentially inappropriate medications (PIMs) in nursing home residents, with particular attention to clinical patterns, patient safety, and contextual factors influencing rational medication use. Central to this work is the role of the Elderly Care Specialist, a physician uniquely trained in the Netherlands to manage complex chronic conditions in long-term care settings by combining biomedical expertise with person-centered care principles. Specifically, we assessed the prevalence of PIMs across European countries, examined patterns of preventive cardiovascular and osteoporosis medication prescribing in relation to resident characteristics and national context, and investigated the barriers and facilitators influencing deprescribing decisions among Elderly Care Specialists.

We have applied the SEXTUPLE framework specifically to structure the discussion of prescribing and deprescribing practices, guiding the analysis of key patterns, barriers, and facilitators from the perspective of clinicians, while the empirical studies themselves were conducted using standard quantitative and qualitative methods.

Chapter 2

Prevalence of Potentially Inappropriate Medication According to STOPP-Frail Criteria in Nursing Home Residents

We have investigated the prevalence of potentially inappropriate medications among nursing home residents in eight European countries and examined differences between residents with and without cognitive impairment, as well as between residents with and without an estimated life expectancy of six months or less.

We have used baseline data from the Services and Health for Elderly in Long TERM care (SHELTER) project, collected between 2009 and 2012, and operationalized PIMs using the second edition of the STOPP-Frail criteria. The study population consisted of residents aged 60 years and older with a valid medication assessment. Cognitive impairment was assessed using the Cognitive Performance Scale (CPS), and the presence of end-stage disease with a life expectancy of six months or less was recorded.

We have found that among 3,832 eligible residents, 87.9% were prescribed at least one PIM, with an average of 2.16 PIMs per person. Approximately one quarter of residents had one PIM, while nearly one fifth had four or more. Residents with cognitive impairment had significantly fewer PIMs on average than those without cognitive impairment, and similarly, residents with a life expectancy of six months or less used fewer PIMs than those without a limited prognosis. Nevertheless, PIM use remained high across all subgroups. Substantial variation was observed between countries, with the highest average number of PIMs in Finland and the lowest in the United Kingdom. Antiplatelet agents and aspirin were the most frequently prescribed PIMs.

We have concluded that potentially inappropriate medication use is highly prevalent among nursing home residents across Europe. Although prescribing appears to be somewhat more conservative in residents with cognitive impairment or limited life expectancy, the overall burden of PIMs remains considerable, underscoring the need for continued efforts to improve prescribing practices in nursing homes.

Chapter 3

Prevalence of Preventive Cardiovascular Medication Use In Nursing Home Residents. Room for Deprescribing?

We have evaluated the prevalence of preventive cardiovascular medication use among nursing home residents and explored differences according to length of stay, mortality risk, cognitive impairment, functional disability, and country, acknowledging that the benefits of long-term preventive therapy may be limited in residents with a short life expectancy. We have conducted a 12-month prospective cohort study in 57 nursing homes across eight European countries. Four classes of preventive cardiovascular medication were assessed

at baseline: oral anticoagulants, platelet aggregation inhibitors, antihypertensive agents, and lipid-modifying agents. The analysis included 3,759 residents aged 60 years and older with valid medication assessments. Health instability was measured using the CHESS scale, cognitive impairment using the CPS, and functional disability using the Activities of Daily Living Hierarchy Scale.

We have observed that 57.9% of residents used at least one class of preventive cardiovascular medication. Use was lower among long-stay residents compared with mid-stay residents, among residents with cognitive impairment, among those with a high mortality risk, and among residents with greater functional dependency. Despite these reductions, preventive cardiovascular medication use remained substantial even in the most vulnerable groups.

We have concluded that although prescribing of preventive cardiovascular medication appears to be partially aligned with prognosis and functional status, there remains considerable room for deprescribing, particularly when the potential benefits of continued treatment are uncertain in the context of limited life expectancy.

Chapter 4

Pharmacological Management of Osteoporosis in Nursing Home Residents

We have examined the prevalence of pharmacological osteoporosis prevention among nursing home residents in eight European countries and assessed its association with resident characteristics, including recent falls or fractures, health instability, cognitive impairment, and dependence in walking.

We have performed cross-sectional analyses using data from the SHELTER study, evaluating the use of vitamin D, calcium, and bisphosphonates, both individually and in combination, in accordance with guideline recommendations for fracture prevention.

We have found that vitamin D, calcium, and bisphosphonates were used by 16.2%, 10.4%, and 4.5% of residents, respectively, while only 1.5% received all three agents concurrently. Even among residents with recent fractures or falls, the use of bisphosphonates and combination therapy was low. Conversely, preventive osteoporosis medication was still prescribed to a proportion of residents with high mortality risk, raising concerns about potential overtreatment. Marked differences in prescribing patterns were observed between countries, ranging from very high prevalence in Finland to minimal use in Israel.

We have concluded that pharmacological prevention of osteoporosis in nursing home residents is frequently suboptimal, characterized by both underuse in high-risk residents and potential overuse in those with limited life expectancy. These findings highlight the need for more individualized and context-sensitive prescribing strategies.

Chapter 5

Barriers and Enablers of Elderly Care Specialists towards Deprescribing Practices in the Nursing Homes: A Focus Group Study

We have explored the barriers and facilitators influencing deprescribing among Elderly Care Specialists in the Netherlands, recognizing the central role of these physicians in optimizing medication use for frail older adults in long-term care.

We have conducted a qualitative focus group study involving eleven Elderly Care Specialists, using a predefined topic guide to structure discussions. Audio recordings were transcribed verbatim and analyzed through thematic coding using Atlas.ti. Coding was performed independently by two researchers and refined through iterative comparison and consensus.

We have identified that increasing clinical experience and pharmacological knowledge contributed to a more positive attitude toward deprescribing. Active involvement of patients and family members, as well as organizational support through formal policies, were considered essential enablers. Key barriers included incomplete medical histories, fear of negative consequences following medication withdrawal, the absence of clear deprescribing guidelines, and persistent beliefs regarding the effectiveness of certain medications. Cooperation—or lack thereof—between physicians, patients, families, and other healthcare professionals strongly influenced deprescribing decisions.

We have concluded that deprescribing in nursing home care remains complex and challenging. While Elderly Care Specialists recognize its importance and express a generally positive attitude, effective deprescribing requires close collaboration among physicians, patients and families, pharmacists, managers, and other disciplines within a supportive organizational framework.

Authors Contributions

Authors Contributions

Chapter 2: Prevalence of Potentially Inappropriate Medications According to STOPP-Frail Criteria in Nursing Home Residents, the SHELTER Study

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Author Contributions

Rob van Marum conceived the study idea; *Rob van Marum, Alireza Malek Makan* and *Hein van Hout* operationalized the metrics in the SHELTER study; *Hein van Hout* and *Alireza Malek Makan* performed the analyses; *Alireza Malek Makan* drafted the manuscript; all authors contributed to and approved of the final version.

Chapter 3: Prevalence of Preventive Cardiovascular Medication Use In Nursing Home Residents. Room for Deprescribing? The SHELTER Study

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Chapter 4: Pharmacological Management of Osteoporosis in Nursing Home Residents: The SHELTER Study

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Rob van Marum conceived the study idea; *Rob van Marum, Alireza Malek Makan* and *Hein van Hout* operationalized the metrics in the SHELTER study; *Hein van Hout* and *Alireza Malek Makan* performed the analyses; *Alireza Malek Makan* drafted the manuscript; all authors contributed to and approved of the final version.

Chapter 5: Barriers and Enablers of Elderly Care Specialists towards Deprescribing Practices in the Nursing Homes: a Focus Group Study

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Author Contributions

All authors contributed to the study design. Rob van Marum contributed to the study conception. Data collection were performed by *Alireza Malek Makan, Man Chun Lee and Hein van Hout*. Data analysis were performed by *Alireza Malek Makan and Man Chun Lee*. The first draft of the manuscript was written by *Alireza Malek Makan and Man Chun Lee* and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Samenvatting

Samenvatting

Algemeen Overzicht

Onder ouderen komt multimorbiditeit veel voor en dit leidt vaak tot polyfarmacie, doorgaans gedefinieerd als het gelijktijdig gebruik van vijf of meer geneesmiddelen. Bij het ontbreken van leeftijdsspecifieke voorschrijfrichtlijnen zijn verschillende strategieën ontwikkeld om het medicatiegebruik bij ouderen te verbeteren, waaronder het concept deprescribing, dat voor het eerst werd geïntroduceerd in 2003. Polyfarmacie komt in het bijzonder veel voor onder verpleeghuisbewoners en is consequent geassocieerd met ongunstige klinische uitkomsten. In deze context wordt medicatiebeoordeling gezien als een gestructureerde en systematische aanpak om farmacotherapie te optimaliseren door geneesmiddelgerelateerde problemen te identificeren en op te lossen.

Wij hebben voortgebouwd op deze inzichten door een reeks studies uit te voeren naar medicatiegebruik onder kwetsbare verpleeghuisbewoners in meerdere Europese landen, die diverse gezondheidszorgsystemen en klinische populaties vertegenwoordigen. Geneesmiddelen werden systematisch beoordeeld op (on)geschiktheid en daarnaast onderzochten wij de houding en perspectieven van specialisten ouderengeneeskunde (SO's) in Nederland met betrekking tot voorschrijven en deprescribing. Door kwantitatieve epidemiologische analyses te combineren met kwalitatieve inzichten uit de klinische praktijk, verkregen wij een uitgebreid beeld van huidige voorschrijfpatronen, besluitvormingsprocessen en ervaren uitdagingen.

In dit proefschrift hebben wij ons gericht op het voorschrijven van potentieel ongeschikte medicatie (PIMs) bij verpleeghuisbewoners, met bijzondere aandacht voor klinische patronen, patiëntveiligheid en contextuele factoren die rationeel medicatiegebruik beïnvloeden. Centraal in dit werk staat de rol van de specialist ouderengeneeskunde, een arts die uniek is opgeleid in Nederland om complexe chronische aandoeningen in langdurige zorgsettings te behandelen door biomedische expertise te combineren met persoonsgerichte zorgprincipes. Specifiek hebben wij de prevalentie van PIMs in Europese landen beoordeeld, patronen onderzocht in het voorschrijven van preventieve cardiovasculaire medicatie en osteoporosemedicatie in relatie tot bewonerskenmerken en nationale context, en de barrières en bevorderende factoren onderzocht die van invloed zijn op deprescribingbeslissingen van specialisten ouderengeneeskunde.

Wij hebben het SEXTUPLE-framework toegepast om de discussie over voorschrijf- en deprescribingpraktijken te structureren, waarbij de analyse van belangrijke patronen, barrières en bevorderende factoren vanuit het perspectief van klinici werd geleid, terwijl de empirische studies zelf werden uitgevoerd met standaard kwantitatieve en kwalitatieve methoden.

Hoofdstuk 2

Prevalentie van Potentieel Ongeschikte Medicatie Volgens de STOPP-Frail-Criteria bij Verpleeghuisbewoners

Wij hebben de prevalentie van potentieel ongeschikte medicatie onder verpleeghuisbewoners in acht Europese landen onderzocht en verschillen bestudeerd tussen bewoners met en zonder cognitieve stoornissen, evenals tussen bewoners met en zonder een geschatte levensverwachting van zes maanden of minder.

Hiervoor gebruikten wij baselinegegevens van het Services and Health for Elderly in Long TERM care (SHELTER)-project, verzameld tussen 2009 en 2012, waarbij PIMs werden geoperationaliseerd met behulp van de tweede editie van de STOPP-Frail-criteria. De studiepopulatie bestond uit bewoners van 60 jaar en ouder met een geldige medicatiebeoordeling. Cognitieve stoornissen werden beoordeeld met behulp van de Cognitive Performance Scale (CPS), en de aanwezigheid van een terminaal stadium met een levensverwachting van zes maanden of minder werd geregistreerd.

Wij vonden dat van de 3.832 geïncludeerde bewoners 87,9% ten minste één PIM voorgeschreven kreeg, met een gemiddelde van 2,16 PIMs per persoon. Ongeveer een kwart van de bewoners had één PIM, terwijl bijna een vijfde vier of meer PIMs gebruikte. Bewoners met cognitieve stoornissen hadden gemiddeld significant minder PIMs dan bewoners zonder cognitieve stoornissen, en vergelijkbaar gebruikten bewoners met een levensverwachting van zes maanden of minder minder PIMs dan bewoners zonder beperkte prognose. Desondanks bleef het gebruik van PIMs hoog in alle subgroepen. Tussen landen werden aanzienlijke verschillen waargenomen, met het hoogste gemiddelde aantal PIMs in Finland en het laagste in het Verenigd Koninkrijk. Antiplateletmiddelen en aspirine waren de meest voorgeschreven PIMs.

Wij concludeerden dat het gebruik van potentieel ongeschikte medicatie zeer prevalent is onder verpleeghuisbewoners in Europa. Hoewel het voorschrijven enigszins terughoudender lijkt bij bewoners met cognitieve stoornissen of een beperkte levensverwachting, blijft de totale belasting van PIMs aanzienlijk, wat de noodzaak onderstreept van voortdurende inspanningen om voorschrijfprijktijken in verpleeghuizen te verbeteren.

Hoofdstuk 3

Prevalentie van Preventief Cardiovasculair Medicatiegebruik bij Verpleeghuisbewoners: Ruimte voor Deprescribing?

Wij hebben de prevalentie van het gebruik van preventieve cardiovasculaire medicatie onder verpleeghuisbewoners geëvalueerd en verschillen onderzocht naar verblijfsduur, mortaliteitsrisico, cognitieve stoornissen, functionele beperkingen en land, waarbij werd

erkend dat de voordelen van langdurige preventieve therapie beperkt kunnen zijn bij bewoners met een korte levensverwachting.

Wij voerden een prospectieve cohortstudie van 12 maanden uit in 57 verpleeghuizen verspreid over acht Europese landen. Vier klassen van preventieve cardiovasculaire medicatie werden bij aanvang beoordeeld: orale anticoagulantia, trombocytenaggregatieremmers, antihypertensiva en lipidenverlagende middelen. De analyse omvatte 3.759 bewoners van 60 jaar en ouder met geldige medicatiebeoordelingen. Gezondheidsinstabiliteit werd gemeten met behulp van de CHESS-schaal, cognitieve stoornissen met de CPS en functionele beperkingen met de Activities of Daily Living Hierarchy Scale.

Wij observeerden dat 57,9% van de bewoners ten minste één klasse preventieve cardiovasculaire medicatie gebruikte. Het gebruik was lager onder langdurig verblijvende bewoners in vergelijking met bewoners met een middellange verblijfsduur, onder bewoners met cognitieve stoornissen, onder bewoners met een hoog mortaliteitsrisico en onder bewoners met grotere functionele afhankelijkheid. Ondanks deze afnames bleef het gebruik van preventieve cardiovasculaire medicatie aanzienlijk, zelfs in de meest kwetsbare groepen.

Wij concludeerden dat hoewel het voorschrijven van preventieve cardiovasculaire medicatie gedeeltelijk lijkt afgestemd op prognose en functionele status, er nog steeds aanzienlijke ruimte bestaat voor deprescribing, vooral wanneer de potentiële voordelen van voortgezette behandeling onzeker zijn in de context van een beperkte levensverwachting.

Hoofdstuk 4

Farmacologisch Management van Osteoporose bij Verpleeghuisbewoners

Wij hebben de prevalentie van farmacologische preventie van osteoporose onder verpleeghuisbewoners in acht Europese landen onderzocht en de associatie ervan met bewonerskenmerken beoordeeld, waaronder recente valincidenten of fracturen, gezondheidsinstabiliteit, cognitieve stoornissen en afhankelijkheid bij het lopen.

Wij voerden cross-sectionele analyses uit met gegevens uit de SHELTER-studie, waarbij het gebruik van vitamine D, calcium en bisfosfonaten werd geëvalueerd, zowel afzonderlijk als in combinatie, overeenkomstig richtlijnadviezen voor fractuurpreventie.

Wij vonden dat vitamine D, calcium en bisfosfonaten respectievelijk door 16,2%, 10,4% en 4,5% van de bewoners werden gebruikt, terwijl slechts 1,5% alle drie de middelen gelijktijdig ontving. Zelfs onder bewoners met recente fracturen of valincidenten was het gebruik van bisfosfonaten en combinatietherapie laag. Omgekeerd werd preventieve osteoporosemedicatie nog steeds voorgeschreven aan een deel van de bewoners met een hoog mortaliteitsrisico, wat zorgen oproept over mogelijke overbehandeling. Er werden

duidelijke verschillen in voorschrijfpatronen tussen landen waargenomen, variërend van een zeer hoge prevalentie in Finland tot minimaal gebruik in Israël.

Wij concludeerden dat farmacologische preventie van osteoporose bij verpleeghuisbewoners vaak suboptimaal is, gekenmerkt door zowel ondergebruik bij bewoners met een hoog risico als mogelijk overgebruik bij bewoners met een beperkte levensverwachting. Deze bevindingen benadrukken de noodzaak van meer geïndividualiseerde en contextgevoelige voorschrijfstrategieën.

Hoofdstuk 5

Barrières en Bevorderende Factoren voor Deprescribingpraktijken van Specialist- Ouderengeneeskunde in Verpleeghuizen: Een Focusgroepstudie

Wij hebben de barrières en bevorderende factoren onderzocht die van invloed zijn op deprescribing onder specialisten ouderengeneeskunde in Nederland, waarbij de centrale rol van deze artsen in het optimaliseren van medicatiegebruik voor kwetsbare ouderen in de langdurige zorg werd erkend.

Wij voerden een kwalitatieve focusgroepstudie uit met elf specialisten ouderengeneeskunde, waarbij een vooraf opgestelde topiclijst werd gebruikt om de discussies te structureren. Audio-opnamen werden woordelijk getranscribeerd en geanalyseerd door middel van thematische codering met behulp van Atlas.ti. De codering werd onafhankelijk uitgevoerd door twee onderzoekers en verfijnd door iteratieve vergelijking en consensus.

Wij identificeerden dat toenemende klinische ervaring en farmacologische kennis bijdroegen aan een positievere houding ten opzichte van deprescribing. Actieve betrokkenheid van patiënten en familieleden, evenals organisatorische ondersteuning door middel van formeel beleid, werden beschouwd als essentiële bevorderende factoren. Belangrijke barrières waren onvolledige medische voorgeschiedenissen, angst voor negatieve gevolgen na het staken van medicatie, het ontbreken van duidelijke deprescribingrichtlijnen en hardnekkige overtuigingen over de effectiviteit van bepaalde geneesmiddelen. Samenwerking — of het gebrek daaraan — tussen artsen, patiënten, familieleden en andere zorgprofessionals beïnvloedde deprescribingbeslissingen sterk.

Wij concludeerden dat deprescribing in de verpleeghuiszorg complex en uitdagend blijft. Hoewel specialisten ouderengeneeskunde het belang ervan erkennen en over het algemeen een positieve houding hebben, vereist effectief deprescribing nauwe samenwerking tussen artsen, patiënten en familieleden, apothekers, managers en andere disciplines binnen een ondersteunend organisatorisch kader.

Dankwoord

Dankwoord

Mijn Verhaal

Het begon op een middag tijdens mijn AIOS-schap. Martien vertelde dat een geriater die hij goed kende een lezing zou geven over farmacologie bij ouderen. Mijn eerste gedachte was: *Oké, en?* Maar voor Martien was het duidelijk: Rob (prof van Marum) was de beste. Hij zorgde ervoor dat ik een verkennend gesprek met Rob had, en de rest is geschiedenis. Een tijd na mijn opleiding gingen we verder met de eerste opzet van onze onderzoeken. Het eerste paper werd afgerond, gepubliceerd en gepresenteerd op het EuGMS-congres in Lissabon. Dat was een bijzondere reis, samen met Rob.

Maar daarna sloeg het noodlot toe. Uit het niets werd ik ernstig ziek. Ik kreeg een onbegrepen ziektebeeld met langdurige koorts, wat leidde tot een ziekenhuisopname vol onzekerheden. Ondanks uitgebreide diagnostiek bleef een duidelijke diagnose uit. Niet alleen mijn onderzoekstraject, maar mijn hele leven werd abrupt op pauze gezet.

Een spontaan herstel bleef uit en mijn revalidatie duurde eindeloos. Het was een vreemde en beangstigende tijd. Ik wist niet hoe het werkelijk met me ging. Voor iemand die altijd mondig was, was het beangstigend om mezelf niet meer goed onder woorden te kunnen brengen. Lopen werd een uitdaging, de pijn was constant en mijn toekomst leek uitzichtloos. Mijn gezin maakte zich grote zorgen, en mijn zoon Milan was zo angstig dat hij een tijdlang niet meer zijn bezorgdheid los kon laten.

Toch had ik mijn leven niet voor niets zo zorgvuldig uitgestippeld. Er was maar één optie: beter worden en doorgaan. Maand na maand deden mijn gezin en ik ons uiterste best om de moed niet te verliezen. Na een lange periode van strijd, werd het rustiger, zowel lichamelijk als mentaal. Eindelijk was er ruimte om na te denken over de toekomst: kon ik mijn werk weer oppakken? Zou ik mijn promotie traject alsnog voortzetten?

Ik besloot om stap voor stap alles weer op te bouwen, in een tempo dat haalbaar was. Mijn partner was mijn steun en motiveerde me om door te zetten. Ook mijn promotoren speelden een onmisbare rol in dit proces.

En nu is het zover. Dankzij hen, dankzij mijn doorzettingsvermogen en de onvoorwaardelijke steun van de mensen om mij heen, sta ik hier.

Mijn speciale dank is voor mijn partner, zij geloofde altijd in mijn doorzettingsvermogen waardoor ik niet eens durfde te denken aan stoppen. Zij wil niet/ nooit in spotlight gezet worden, anders was ik hier oneindig bezig om haar te bedanken!

Al sinds 2015 SO, inmiddels en na het afronden van de kaderopleiding opleiden en kaderopleiding Geriatrische Revalidatie, werkzaam op de geriatrische revalidatie van de Vivium zorggroep, locatie Flevoziekenhuis, buiten gewoon leuke werk dankzij al mijn collega's. Ook bijzonder prettig om als opleider constant bezig te zijn om de volgende generatie behandelaren op te leiden: Aios ouderengeneeskunde/ aios huisartsgeneeskunde/ PA's/ coassistenten.

Als buitengewoon staflid van het Flevoziekenhuis ben ik vroeg betrokken bij het proces

opname/ontslag/nazorg van kwetsbare patiënten samen met desbetreffende specialisten in het ziekenhuis. Daarvoor ben ik de collega's van het Flevoziekenhuis dankbaar.

Er is een bijzonder constructieve samenwerking.

De geriatrische revalidatiezorg richt zich op kwetsbare patiënten, die vaak te maken hebben met achteruitgang in meerdere functionele domeinen, multimorbiditeit en polyfarmacie. Binnen deze complexe context vormt het beoordelen en optimaliseren van medicatie een bijzonder uitdagend en boeiend proces. Medicatiegebruik wordt beïnvloed door talrijke factoren, waardoor iedere afweging maatwerk vereist.

Voor artsen vraagt dit niet alleen om gedegen farmacologische kennis, maar ook om klinische ervaring en inzicht in de individuele behoeften en doelen van de patiënt. Juist deze combinatie maakt farmacotherapie en het proces van (de)prescribing tot een fascinerend onderdeel van de geriatrische zorg. Ik ben zeer dankbaar dit bijzonder leuke proces middels dit onderzoek te mogen ervaren.

Rob (Prof van Marum)

Mijn bijzondere dank gaat uit naar mijn promotor. Ik kijk naar hem op als een uitzonderlijk wetenschapper. Zijn directe, maar menselijke benadering heeft mij geholpen gemotiveerd te blijven, juist tijdens de tegenslagen die dit traject kende.

Met grote waardering en dankbaarheid richt ik dit dankwoord aan jou. Vanaf het moment dat ik als AIOS jouw colleges mocht volgen, heb ik je bewonderd als een bijzondere wetenschapper en inspirerende docent. Jouw scherpe inzichten en directe, maar altijd menselijke manier van communiceren hebben mij gevormd en gemotiveerd om het beste uit mezelf te halen.

Tijdens mijn promotietraject heb ik niet alleen geleerd van jouw diepgaande kennis en kritische blik, maar ook van jouw vermogen om mensen op de juiste manier uit te dagen en te ondersteunen. Zelfs op momenten van tegenslag wist jij me gemotiveerd te houden, door mij niet alleen te wijzen op verbeterpunten, maar ook op wat er goed ging en waar de essentie lag. Jouw visie rondom de farmacologie bij kwetsbare ouderen is zodanig alles bevattend dat het niet alleen de patiënten verder helpt maar ook een ultieme bron van inspiraties is voor de alle artsen.

Dank je wel voor je begeleiding, je vertrouwen en de inspiratie die je mij hebt gegeven. Ik hoop dat onze wegen in de toekomst blijven kruisen. Wij zijn nota bene BROK gecertificeerd.

Hein (Prof van Hout)

Graag wil ik mijn oprechte dank uitspreken aan mijn promotor, die gedurende dit traject van grote betekenis is geweest. Zijn voortdurende vriendelijkheid, toegankelijkheid en deskundige begeleiding hebben ervoor gezorgd dat ik mij steeds gesteund voelde, ook wanneer de complexiteit van het onderzoek uitdagingen met zich meebracht.

Tijdens dit traject werd jij benoemd tot hoogleraar, een welverdiende erkenning van je

kennis, expertise en wetenschappelijke bijdragen. Jouw academische kwaliteiten kwamen ook tot uiting in de begeleiding van dit onderzoek. Met name de ondersteuning bij de complexe analyses was van grote waarde. Door ingewikkelde vraagstukken helder te duiden en steeds constructieve, inhoudelijke feedback te geven, heb jij een belangrijke bijdrage geleverd aan de kwaliteit van dit proefschrift.

De expertise en ondersteuning hebben niet alleen bijgedragen aan de succesvolle afronding van dit onderzoek, maar hebben mij ook verder gevormd als onderzoeker.

Ik kijk met veel waardering terug op onze samenwerking en hoop dat deze zich in de toekomst zal voortzetten in een intensieve wetenschappelijke samenwerking op het gebied van kwetsbaarheid, veroudering en andere vraagstukken binnen de gezondheidszorg.

De Leden van de Promotiecommissie

Het verlossende woord kwam in mei: mijn proefschrift werd goedgekeurd door de leescommissie. Graag wil ik de leden van de commissie (prof.dr. M. Smalbrugge, prof.dr. J.G. Hugtenburg, prof.dr. W.P. Achterberg, prof.dr. J. Gussekloo en dr. W. Knol) hartelijk bedanken voor de tijd, aandacht en zorgvuldigheid waarmee zij mijn proefschrift hebben beoordeeld, eveneens hun waardevolle suggesties. Ik waardeer hun bereidheid om zitting te nemen in de promotiecommissie zeer.

Prof. dr. M. Smalbrugge wil ik in het bijzonder bedanken. Het is een voorrecht geweest hem gedurende verschillende fases van mijn opleiding en carrière te ontmoeten en te mogen profiteren van zijn expertise en visie op de ouderengeneeskunde.

Martien Muller

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Mijn Paranimfen

Wat ben ik blij dat juist jullie naast mij komen staan. Dat jullie mijn paranimfen wilden zijn, voelt als een grote eer.

Shahnam ooit mijn AIOS, maar al snel veel meer dan dat. Ik kijk met plezier terug op onze leerzame en fijne tijd samen. Jouw slimme, leergierige en kritische blik, gecombineerd met jouw gevoel voor de zakelijke kant van ons vak, maakten onze samenwerking altijd bijzonder.

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Dat jullie nu aan mijn zijde staan op deze bijzondere dag betekent veel voor mij.

Dank jullie wel.

Elis

Met dit dankwoord wil ik mijn diepe waardering uitspreken voor alles wat u voor mij hebt betekend in het ontwikkelen van de taal. Dat zegt veel over uw toewijding en passie voor onderwijs.

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Aan Mijn Moeder

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Aan Mijn Zus

Jouw overtuiging dat onderzoek de mooiste manier is om te blijven verbeteren, verdiepen en optimaliseren, heeft mij altijd geïnspireerd en gestimuleerd om verder te kijken.

Je bent lief, wijs en altijd oprecht betrokken. Met jouw vertrouwen, steun en luisterend

oor heb je meer betekend dan woorden kunnen omschrijven.
Zonder jou zou mijn wereld een stuk minder mooi zijn.
Dank je wel.

Aan Mijn Zoon

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En...

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Er zijn mensen die niet voortdurend aanwezig hoeven te zijn om dichtbij te blijven. Mensen bij wie een gesprek moeiteloos wordt hervat alsof er geen maanden of jaren zijn verstreken. Mensen die mij aanvullen zonder zichzelf op de voorgrond te plaatsen, en wier aanwezigheid niet altijd zichtbaar is, maar wel altijd voelbaar.

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Publications

Publications

- 2025 **Barriers and Enablers of Elderly Care Specialists towards Deprescribing practices in the Nursing Homes: A Focus Group Study**
Eerste auteur
Gepubliceerd: BMC 2025
- 2025 **Attitude and Knowledge Toward Organ Donation among University Medical Students: A Cross-Sectional Study in Southwest Iran**
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Gepubliceerd: Experimental and Clinical Transplantation (2025) 12: 778-783
- 2023 **Prevalence of potentially inappropriate medications according to STOPP-Frail criteria in nursing home residents, the SHELTER study**
Eerste auteur
Gepubliceerd: BMC Geriatrics (2024) 24:882
<https://doi.org/10.1186/s12877-024-05450-y>
- 2021 **Pharmacological management of osteoporosis in nursing home residents: The SHELTER study**
Eerste auteur
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- 2017 **Prevalence of Preventive Cardiovascular Medication Use In Nursing Home Residents. Room for Deprescribing? The SHELTER Study**
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- 1997 - 1998 **Thesis For The Degree Of MD**
Corneal Ulcer: Infectious Etiology
University of Medical Sciences, Shiraz/ Iran
Begeleid door: Dr.M. Nedjabat: Ass. Professor
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