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Optimization of Pharmacological Treatment in Institutionalized Patients in Nursing Homes in Catalonia

EMILIE ANDERSSEN NORDAHL

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Barcelona, 2024

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DOCTORAL THESIS

Department of Pharmacology, Therapeutics and Toxicology

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Supervisors: Montserrat Bosch Ferrer, Mònica Sabaté Gallego, Eladio Fernández Liz.
Tutor: Mª Antonieta Agustí Escasany.

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CERTIFY: That the present doctoral thesis, submitted by Emilie Anderssen Nordahl, with the title: " Optimization of Pharmacological Treatment in Institutionalized Patients in Nursing Homes in Catalonia" has been conducted under their supervision.

For the appropriate legal purposes, they sign this certificate in Barcelona, on September 24th, 2024.

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Report presented by Emilie Anderssen Nordahl for the doctoral degree at the Autonomous University of Barcelona.

The work " Optimization of Pharmacological Treatment in Institutionalized Patients in Nursing Homes in Catalonia" has been conducted at the Department of Pharmacology, Therapeutics, and Toxicology, of Vall d'Hebron, under the supervision of Dr. Montserrat Bosch Ferrer, Dr. Mònica Sabaté Gallego and Dr. Eladio Fernández Liz.

For the appropriate legal purposes, this certificate is signed in Barcelona, on September 24th, 2024.

Doctoral Candidate

Emilie Anderssen Nordahl

To my family and mentors, for believing in me, keeping my motivation high and for their unconditional support.

"How we treat the elderly in nursing homes is a measure of our societal values. Medical care should focus not only on prolonging life but on improving the quality of life, respecting their dignity, and addressing their unique needs and wishes." - Atul Gawande

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ACEIs Angiotensin-Converting Enzyme Inhibitors

ACP Advance Care Planning

ADR Adverse Drug Reaction

AEMPS Agencia Española de Medicamentos y Productos Sanitarios i.e., Spanish Agency of Medicines and Health Products

AGS American Geriatrics Society

AMG Adjusted Morbidity Group

ARS Anticholinergic Risk Scale

BOE Boletín Oficial del Estado, i.e., Official State Bulletin

CatSalut Catalan Health Service

CCP Complex Chronic Patient

CDSS Clinical Decision Support Systems

DBI Drug Burden Index

DDI Drug-Drug Interaction

DUR Drug Utilization Reviews

ECAP Electronical Clinical Station in Primary Care

EU European Union

GFR Glomerular filtration rate

HRP Health-Related Problems

LOSC: Health Care Management Law of Catalonia

MACA Model of Care for Advanced Chronicity

MAI Medication Appropriateness Index

MG Morbidity Groups

MRP Medication-Related Problems

NSAIDs Nonsteroidal Anti-Inflammatory Drugs

PCT Primary Care Teams

PIM Potentially Inappropriate Medications

PIP Potentially Inappropriate Prescribing

PPO Potential Prescribing Omissions

PPI Proton Pump Inhibitors

PREFASEG (PREscripción FArmacéutica SEGura, i.e., safe pharmaceutical prescription)

SISCAT Integral Public Healthcare System of Catalonia

SNRI Serotonin/Norepinephrine Reuptake Inhibitors

SSRI Selective Serotonin Reuptake Inhibitor

START Screening Tool to Alert doctors to Right i.e. appropriate indicated Treatment
STOPP Screening Tool of Older Persons Prescriptions
STOPP-Frail: Screening Tool of Older Person's Prescriptions in Frail adults with limited life expectancy
STOPP-Pal: Screening Tool of Older Person's Prescriptions in palliative care
WHO World Health Organization

The population in nursing homes is growing, which is associated with increased frailty, multimorbidity, chronic diseases, and polypharmacy. Consequently, medication-related problems (MRPs) are becoming more prevalent. Periodic pharmacological reviews, ideally conducted by a multidisciplinary team with the support of clinical decision support systems (CDSS), could help address this issue. However, such reviews are not commonly performed. The primary objective of this doctoral thesis was to describe institutionalized patients, systematically review their medication plans, and assess the impact of an intervention consisting of creating a multidisciplinary team to evaluate medication plans systematically. This was performed through two different studies. The first study was a cross-sectional analysis that described the characteristics of institutionalized patients, systematically reviewed their medication plans, and provided recommendations to identify MRPs. The second was a multicenter before-and-after study that assessed the impact of a multidisciplinary team intervention on medication review outcomes. The multidisciplinary team consisted of general practitioners, nurses, social and administrative workers from primary care, nursing home clinicians and nurses, a clinical pharmacist, and a clinical pharmacologist, who acted as the coordinator. The clinical pharmacologist actively reviewed all the prescribed medications to make recommendations, focused on the completion of absent data, drug withdrawal, verification of whether a drug was adequate, the substitution of a drug, and the addition of drugs. A total of 483 patients from five nursing homes were included, with a mean age of 86.3 years (SD 8.8), and 72% were female. All but one patient had at least one prescription, with an average of 8.22 prescribed drugs per patient (SD 3.5). On average, patients had 17.4 health-related problems (SD 5.6). The intervention resulted in recommendations for 398 patients (82.4%), with 58.5% of these patients following the recommendations given. At least one drug was discontinued in 293 patients (60.7%), with an average of 2.3 drugs withdrawn per patient (SD 1.7). Out of 1,097 recommendations made, 32.4% were followed, and the most frequently withdrawn drugs were antipsychotics, antidepressants, benzodiazepines, statins, and diuretics. In conclusion, there is a high prevalence of health-related problems and polypharmacy in nursing homes in Catalonia. The findings demonstrate the value of a multidisciplinary team, coordinated by a clinical pharmacologist, in conducting regular medication reviews with CDSS. This approach helps reduce MRPs and manage polypharmacy more effectively.

La población en residencias de ancianos está aumentando, lo que se asocia con un incremento de la fragilidad, la multimorbilidad, las enfermedades crónicas y la polifarmacia. Como resultado, los problemas relacionados con los medicamentos (PRM) son cada vez más frecuentes. Las revisiones farmacológicas periódicas, idealmente realizadas por un equipo multidisciplinario con el apoyo de sistemas de apoyo a la decisión clínica, podrían ayudar a abordar este problema. Sin embargo, estas revisiones no se realizan comúnmente. El objetivo principal de esta tesis doctoral fue describir las características de los pacientes institucionalizados, revisar sus planes de medicación y evaluar el impacto de una intervención consistente en la creación de un equipo multidisciplinario para evaluar de manera sistemática los planes de medicación. Esto se llevó a cabo a través de dos estudios multicéntricos diferentes. En el primer estudio se realizó un análisis transversal para describir las características de los pacientes institucionalizados, describir la revisión de los planes de medicación y describir las recomendaciones para identificar PRM. En el segundo estudio antes-después se evaluó el impacto de la intervención de un equipo multidisciplinario en los resultados de la revisión de la medicación. El equipo multidisciplinario estaba compuesto por médicos, enfermeros, trabajadores sociales y administrativos de atención primaria, clínicos y enfermeros de las residencias, un farmacéutico y un farmacólogo clínico, que actuaba como coordinador. El farmacólogo clínico revisaba activamente todos los medicamentos prescritos para hacer recomendaciones, centrándose en completar los datos ausentes, la retirada de un medicamento, la verificación o sustitución de un fármaco y la adición de nuevos medicamentos. Se incluyeron un total de 483 pacientes de cinco residencias de ancianos, con una edad media de 86,3 años (DE 8,8), y el 72% eran mujeres. Todos los pacientes, excepto uno, tenían al menos una prescripción, con un promedio de 8,22 medicamentos prescritos por paciente (DE 3,5). En promedio, los pacientes presentaban 17,4 problemas de salud (DE 5,6). La intervención resultó en recomendaciones para 398 pacientes (82,4%), de los cuales el 58,5% siguió las recomendaciones dadas. Al menos un medicamento fue retirado en 293 pacientes (60,7%), con un promedio de 2,3 medicamentos retirados por paciente (DE 1,7). De un total de 1.097 recomendaciones realizadas, el 32,4% fueron seguidas, y los medicamentos retirados con mayor frecuencia fueron antipsicóticos, antidepresivos, benzodiacepinas, estatinas y diuréticos. En conclusión, existe una alta prevalencia de problemas de salud y polifarmacia en las residencias de ancianos en Cataluña. Los resultados demuestran el valor de un equipo multidisciplinario, coordinado por un farmacólogo clínico, en la realización de revisiones regulares de la medicación con el apoyo de los sistemas de apoyo a la decisión clínica. Este enfoque ayuda a reducir los PRM y gestionar la polifarmacia de manera más efectiva.

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Introduction

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1.1: Overview of the population and health systems in Catalonia and Western countries

The aging population trend is a global phenomenon, particularly pronounced in developed countries. In 2022, more than one-fifth (21.1%) of the population of the European Union was aged 65 or older, and the elderly are expected to account for 31.3% in 2100 (1). This is due to multiple factors, such as improved living conditions, nutrition, advances in research, and medical care, which have increased life expectancy (2,3).

As reported by Eurostat, European countries have a life expectancy of 80.1 years. Within these countries, Spain has the highest life expectancy of 83.3 years (1). Catalonia included, faces the aging of its population, with an increase in the proportion of people over 65 years of age. In Catalonia in 2021, the life expectancy was 83.6 years (4).

Longevity correlates with the incidence of chronic diseases and multimorbidity (2,5). In recent years, the healthcare system has witnessed a significant increase in the dependency ratio of elderly people in the European Union, reaching 33% by 2022. The old-age dependency ratio is defined as the ratio of the number of people aged 65 years and over, compared to the number of people aged 15-64 years (6).

This increase means a greater number of people in nursing homes with frailty and multimorbidity. According to a systematic review and meta-analysis of population-based studies, conducted in 62 countries, frailty varies with a prevalence between 12 and 24% in people over 60 years of age in the population (7), while in people institutionalized in nursing homes the prevalence of frailty is estimated at 52.3% (8).

The concept of **frailty** has evolved from the concept of elderly people with high comorbidity, physical and mental deterioration, and short life expectancy, to a much broader concept with multiple meanings. Frailty can be defined as a progressive accumulation of deficits that places people, predominantly older people, in a situation of greater vulnerability. It is defined as a reduced capacity to withstand disease without loss of function. These phenomena are thinning, decreased physical strength, loss of energy, difficulty walking and low physical activity. It is also described as a state of vulnerability following poor resolution of homeostasis after stress and is a consequence of cumulative loss of functionality in multiple organs and systems over a lifespan (7,9–11). Frailty increases with age and is associated with increased exposure to

polypharmacy and medications with anticholinergic and sedative effects. These medications may increase the risk of adverse drug reactions (ADRs) and drug-drug interactions (DDI) (10).

Multimorbidity is also becoming a major concern due to the increased life expectancy of the population, the complexity of their health status and its relationship with increased use of health services. In addition, multiple chronic diseases are commonly associated with the use of numerous drugs, decreased function, lower quality of life and increased mortality. Generally, prescribing to patients with multimorbidity is based on disease-specific recommendations and specific clinical practice guidelines (3). However, the guidelines do not accurately reflect the situation of the elderly with multimorbidity, so new strategies are needed to manage and optimize drug prescribing in these patients (2,5).

Multimorbidity is defined as the coexistence of two or more chronic diseases in the same individual (5,11–13). These diseases include both physical and mental illnesses that can lead to disability, with complex symptoms such as chronic pain or frailty, and sensory disturbances like hearing loss or dizziness. When providing a multimorbidity-sensitive approach to care, it should be considered how these diseases and their treatments affect quality of life, individual needs, treatment preferences, health priorities, lifestyle and goals. It is important to weigh the benefits and risks of following guideline recommendations, improve quality of life by reducing treatment burden and adverse effects, and enhance the coordination of care across all services (14).

Frail patients with multiple morbidities are likely to require multiple medications to achieve optimal management of their conditions (10,15). Consequently, increased exposure to polypharmacy increases the risk of ADRs, DDI, nonadherence, decreased functional status, and multiple geriatric syndromes. Among these syndromes are cognitive impairment, including delirium and dementia, falls, urinary incontinence, and an increased risk of poor nutritional status (16–18). This has been evidenced by multiple studies reporting that outpatients taking five or more medications have an 80% increased risk of experiencing an ADR compared to patients taking fewer drugs (19,20).

Polypharmacy is defined as the simultaneous use of multiple medications and is defined as taking five or more concurrently prescribed drugs or supplements (16,19,20). This definition is controversial because polypharmacy may be appropriate for treating a patient with multiple comorbid conditions. This appropriateness is especially true for diseases such as chronic heart

failure and diabetes, which require numerous drug therapies depending on the stage of the disease (17,20).

Excessive polypharmacy is another type of polypharmacy that is defined by drug counts and generally thresholds are set at 10 or more drugs. Alternatively, polypharmacy has also been defined as taking at least one drug that is not clinically indicated. It is argued that this indication-based definition is more practical and appropriate because it is independent of the multiple medications needed to treat the several comorbidities that elderly patients are likely to have (17,21). Conceptualizing polypharmacy as a numerical threshold is not beneficial, because it does not consider that the amount of drugs varies according to the patient, and their clinical needs, and may overlook the omission of potentially beneficial drugs, which may also present risks to patient safety and wellbeing (22).

As stated in the World Health Organization (WHO), polypharmacy has increased dramatically as life expectancy increases and older people live with several chronic diseases. Polypharmacy increases the likelihood of ADRs, as well as the risk of DDI, and can make compliance difficult. If a patient requires many medications, they should be used optimally, to ensure that they produce direct benefits, with minimal side effects. The standardization of policies, procedures and protocols is essential to control polypharmacy. This applies from initial prescribing practices to regular medication reviews with technology as an aid and practical tool (23).

The **approach to patients with multimorbidity and/or frailty** should define the treatment objective considering comorbidity, measuring the burden of disease, knowing the patient's preferences, values and priorities, reviewing the benefit/risk of treatments, selecting the most appropriate treatment strategies, and agreeing on an individualized treatment plan. The intervention plan should include discussing with the patient all possible treatments (pharmacologic and nonpharmacologic), how to optimize the benefit of treatment, and drugs to avoid. Many people take preventive medications likely to offer little benefit due to reduced life expectancy from other causes. Therefore, medications and other treatments may add to the treatment burden without adding to the quality or length of life. The ability to identify individuals with reduced life expectancy could provide healthcare professionals and individuals with information that could inform decisions about initiating or continuing long-term preventive treatments (11,14,24).

The care of institutionalized persons, with the optimization and adequacy of prescriptions in this population, has become a major public health problem (25). The exact number of occupancy of nursing homes is unknown, but in Spain, there are a total of 393,581 places, with an occupancy rate of around 86%, so it is estimated that in 2022, 0.71% of the total population was institutionalized (26).

For the management of this problem, Catalonia has created its own **model of care for advanced chronicity (MACA),** which is designated for people eligible to receive care under this model. It is characterized by a case management approach with a present, important, and growing palliative care component. The palliative component does not exclude curative options but coexists with them and promotes Advance Care Planning (ACP) as an essential part of decision-making support (11,27).

A **complex chronic patient (CCP)** is considered to be one whose clinical management is perceived as particularly difficult by their referring clinicians (11,12,27). A CCP is associated with criteria related to the patient, clinical professionals, and the environment. Concerning the patient, these include multimorbidity, severe or progressive chronic single pathology, high probability of decompensation, high utilization of health services, and polypharmacy, among others. Regarding clinical professionals, there is a need for multidisciplinary management, exposure to discrepancies between different professionals, management doubts, and the benefits of an integrated care strategy. In the social sphere, adverse psychosocial situations should be highlighted. There is no specific number or set criteria that must be met to be considered a CCP, but enough criteria must be met for the referring professional to consider case management particularly difficult. CCPs and MACAs are not diseases per se, but functional labels that signal specific health needs, targeting individuals who require personalized care. They focus on improving care through specific plans, seeking optimal outcomes in effectiveness, efficiency, and patient satisfaction. The prevalence of MACA in Catalonia varies depending on the setting. In social-health centers, they constitute 70% of the patients, and in those institutionalized in nursing homes, between 30% and 70% of the patients (11,27).

The Institute for Safe Medication Practices of Catalonia estimates that 50% of medication errors and 20% of ADRs could be prevented. For this reason, various initiatives, proposals, and programs have been developed to increase safety in the use of medications. It is important to include in these models' medication reconciliation, reviews, and deprescriptions when

appropriate, and to assess adherence. According to the Catalan Health Service (CatSalut) instruction 04/2012, all patients with chronic treatment should undergo a pharmacological treatment review once a year (28).

The Scottish guidance on polypharmacy, comments that an important principle for improving patients with multiple morbidities care is to ensure minimal fragmentation of health and social services through enhanced integrated care, which can help address faulty or dysfunctional medication systems, processes and procedures. The fundamental basis for this is to use the 7-step patient-centered guide. This guide focuses on 7 questions that should be asked to assess the goal of treatment, the need for medications, effectiveness, safety, efficiency and that care is patient-centered. This process is not a single linear event, but a cyclical one, requiring repetition and periodic reviews (29).

In agreement with the Catalan model, a proactive care plan can be created, which promotes multidisciplinary work, with care teams, where the areas of leadership, reference and experience are identified to meet people's needs. Good examples of this are the initiatives of new organizational models within primary care teams (PCT), the reconfiguration of hospital and emergency services, and the functional rethinking of emergency services. For all these reasons, the 2016-2020 Health Plan of Catalonia focused on the development of models of comprehensive, integrated and person-centered care that should make it possible to provide excellent care for these patients and thus meet their needs, taking into account their preferences (11,27).

Following COVID, the latest model proposed for nursing homes in Catalonia seeks to revolutionize nursing home care, putting PCT at the center of this transformation. It aims to ensure comprehensive and quality care, facilitating coordination between the different levels of care and access to all necessary specialties and resources. It focuses on the creation of a single clinical history for each patient, proposes unifying care under a specific healthcare team, and stresses the need to reevaluate and increase the proportion of healthcare professionals, considering the additional workload this would entail for PCT (30).

Catalonia's healthcare models operate under a legal framework that governs health organizations and ensures the rational use of medicines, reflecting its commitment to a tailored and efficient healthcare system. The Health Care Management Law of Catalonia 15/1990 (LOSC), configures our health system based on a public model, centered on people-centered

care. The main characteristics of the LOSC 15/1990 are professionalized management, decentralization, and community participation. With the publication of this law, a distinction was made between the planning of health services carried out by the Department of Health, the contracting of services by CatSalut, and the provision of health services by different service providers, the most important of which is the Catalan Institute of Health, that is a public health system (31).

According to Article 83 of the Royal Legislative Decree 1/2015 published in the Official State Bulletin (BOE, Boletín Oficial del Estado), on the support structures for the rational use of medicines and health products in primary care, declare several statements as included next. Information systems on pharmacotherapy management should be established that include clinical aspects, effectiveness, safety and efficiency of the use of medicines and provide correct information and training on medicines and health products to health professionals. Develop protocols and pharmacotherapeutic guidelines that guarantee correct pharmacotherapeutic assistance to patients, especially regarding drug selection and continuity of treatment and support systems for clinical decision-making in pharmacotherapy. Establish a system for the follow-up of patient treatment that contributes to guaranteeing therapeutic compliance, as well as programs that promote the safe use of drugs. Promote coordination, teamwork, and collaboration with hospitals and specialized care services to ensure the quality of pharmaceutical services through the follow-up of treatments prescribed by the physician (32). This law gives special relevance to the Spanish pharmacovigilance system of the National Health System, with a more innovative approach that incorporates the concept of pharmacoepidemiology and risk management, as well as the guarantee of continuous monitoring of the benefit/risk balance of authorized drugs. The Spanish National Health System must guarantee to health professionals that the information, training and commercial promotion of drugs have scientific rigor, transparency and ethics in the practice of these activities as central elements of their development. Although drugs have made a decisive contribution to improving life expectancy and increasing the quality of life of citizens, they sometimes pose problems of effectiveness and safety that health professionals must be aware of (32).

1.2: Prescribing guidelines for medication reviews and tools

Medication review is defined as a detailed and critical process that seeks to evaluate and optimize the pharmacological treatment of a patient, especially those with complex chronic conditions, ensuring their agreement and participation. Its main objective is to improve the effectiveness of the medication, minimize the risks or problems associated with it, simplify the treatment regimen and increase efficiency. This procedure is regularly adapted and reviewed throughout the different phases of the patient's disease to ensure the relevance and appropriateness of the treatment to the patient's changing needs (28).

Strategies have been proposed to reduce the complexity of treatment regimens in the community and nursing homes. **Medication regimen simplification** is the process of reducing medication burden through strategies such as consolidating dosing times, standardizing administration patterns, using long-acting drugs instead of shorter-acting formulations, and switching to combination products instead of single-drug products. With all this, the best possible medication can be obtained, ensuring the appropriateness of current therapy and deprescribing when needed for simplification of treatment (33).

In people living in nursing homes, there is a particularly high risk of making prescribing errors, so a review proposes potentially feasible strategies to address prescribing errors in the elderly with multimorbidity. Methods to reduce prescribing errors include education, medication reconciliation, work environment, and prescription assessment tools, among others (34).

Medication reconciliation is a protocolized process designed to ensure continuity and safety in the management of a patient's medications during any change within the health care system. This procedure involves a careful comparison between the medications the patient was previously taking and those that have been newly prescribed due to a transfer or change in level of care. The goal is to identify, analyze, and resolve any discrepancies that arise in this process, through thorough review, evaluation, and documentation of changes, to avoid medication errors, ensure that necessary adjustments are documented and communicated, and guarantee safe medication treatment (28). Medication errors occur during the transition of patient care. The four steps to decrease mistakes are verification of all medications, both prescription and over-the-counter, that the patient is currently taking; clarification of each medication to determine its appropriateness in each case; reconciliation of the complete new medication list

with the previous medication list, with documentation of all medication changes and reasons for the changes; and communication of the updated and accurate medication list to the next care provider (34).

With all this information you can establish the **treatment adherence** of the patients, which reflects how well a patient follows the treatment recommendations agreed with his or her physician, being a crucial and dynamic component in health management where the patient plays a key role. Recently, a shift towards a more patient-centered approach has been suggested, where the patient's individual needs, values and preferences are prioritized in the decision of therapeutic options, promoting a more collaborative relationship between the patient and health professionals (28).

In vulnerable elderly and those in the end-of-life stage, decisions on treatment appropriateness should be accentuated. A very short life expectancy or a situation of severe functional or mental deterioration makes it necessary to rethink and redefine the objective of any pharmacological treatment. In this situation treatments previously considered useful can become futile, inappropriate or even harmful. In addition, elderly patients are often highly polymedicated, a condition that increases the risk of iatrogenesis and mortality. In this group, moreover, there is a high use of preventive drugs and many of the ADRs, as in the rest of the population, are preventable. Therefore, the medication review process should be rigorous and adapted to the condition of each patient (35).

To encounter polymedicated patients, appropriate deprescription is needed. **Deprescribing** has been defined as the process of identifying and discontinuing medications when potential or existing harms outweigh potential benefits within the context of an individual patient's goals, function, values, and preferences for care. Drug deprescribing has raised some ethical dilemmas, and prescribers have reported fear of negative outcomes as a barrier to deprescribing. However, studies suggest that deprescribing may be safe, feasible, well tolerated, and can generate important benefits. Research should focus on understanding the impact of deprescribing on frailty status in high-risk populations (36,37). In many cases, deprescribing is not focused on a single medication group, but on all the medication (38). In contrast to deprescription, underprescribing or **potential prescribing omissions (PPOs)** can also occur. PPOs refer to the failure to prescribe appropriate medications when there are clear and valid indications for treatment (39,40).

Taking all this into consideration, an **appropriate prescription** should be based on the clinical and functional situation of the patient, as well as on life expectancy and the therapeutic objective. This prescription should consider reasoned prescribing with benefit-risk assessment, medication review, the process of communication and information to the patient, and reconciliation in case of transition of patient care (28,29,35). Managing the transition of patient care between various healthcare settings can pose difficulties because of increased medication errors. However, ensuring thorough medication reconciliation during this transition may result in a reduction in medication-related problems (MRPs) (41).

A **MRP** is defined as an event or circumstance involving a drug treatment that can potentially interfere with a patient's health. Some MRPs are therapeutic duplications, possible DDIs, potentially inappropriate medications (PIMs) and contraindicated medications (42). There may be several reasons for a MRP such as undertreatment, inadequate monitoring of the medication taken by the patient, poor medication selection or medication dosage, therapeutic duplications, or factors related to the way the patient uses the medication. Methods to reduce and identify potential MRPs include educational interventions directed to health care professionals, comprehensive geriatric assessment, multiple drug discontinuation, clinical decision support systems (CDSS) from electronic health records targeted to certain diseases or medications, and the use of drug evaluation criteria, which often consist of prescription recommendations for various medications and/or pathologies (43).

PIMs are medications that pose an unfavorable benefit/risk ratio for older adults due to factors such as potential ADRs, DDIs, contraindicated drugs, excessive doses, duration or frequency longer than recommended, and the potential for cognitive impairment and are therefore considered **potentially inappropriate prescribing (PIP)** (10,19,29,34,44,45).

Another type of inappropriate polypharmacy would be the continuous addition of new drugs to manage other avoidable drug-related adverse events, which can create cascade prescribing (16). Evidence shows that the most powerful strategy to combat inappropriate medication use and polypharmacy is polydeprescribing. This means discontinuing as many non-life-saving medications as possible (46,47).

To evaluate the appropriate prescription of medications in the elderly, there are different tools such as the Beers, STOPP-START, PRISCUS, FORTA, ACOVE criteria, among others (39,48–51). Over time, implicit and explicit methods have been proposed to optimize medication use. Implicit methods are based on clinical judgment, evaluating each drug considering the patient's characteristics and the indication for the prescription. Some methods are Medication Appropriateness Index (MAI) or Assessing Care of Vulnerable Elders (ACOVE) (25,50,52). Explicit methods use predefined criteria based on scientific data and expert consensus to define PIM. They are a simpler and more reproducible tool for detecting inappropriate prescriptions but require constant updating. Some methods are the Beers and STOPP/START criteria (25,39,48).

Regarding the tools described, the following should be highlighted:

4. The American Geriatrics Society (AGS) **Beers Criteria**: It is an explicit list of PIMs for selected diseases or conditions. The criteria are designed for adults aged 65 years and older in all ambulatory, acute, and institutionalized care settings, except palliative care and hospice settings (48).
5. **STOPP/START** (Screening Tool of Older Persons Prescriptions (STOPP) – Screening Tool to Alert doctors to Right i.e. appropriate indicated Treatment (START): This tool describes the most common errors of treatment and omission in prescribing in older adults. It is easy to relate to the diagnosis and can be integrated into computerized prescribing systems. It is divided into chapters with criteria for withdrawing drugs (STOPP) and others for initiating drugs (START). It also includes recommendations from the NICE guideline with a direct link. The sections are gastrointestinal, cardiovascular, respiratory, nervous, endocrine, genitourinary, nutrition, musculoskeletal and eye systems. The prevalence of PIP according to the STOPP/START criteria is higher in nursing homes than in hospitals and the community (39,45).
6. **PRISCUS:** The PRISCUS list was created for the German pharmaceutical market based on expert knowledge given the lack of scientific data on the safety and efficacy of some drugs for the elderly and the difficulty in making evidence-based recommendations for the safe use of drugs in old age. Studies in several countries have shown that the use of potentially inappropriate medications, such as those on the PRISCUS list, raises the risk of ADRs. Avoidance of such drugs would presumably improve the safety of pharmacotherapy for the elderly. The PRISCUS list offers practical advice and can help physicians make individualized therapeutic decisions for their patients (49).

7. **European Union (EU)-PIM:** This is an explicit list of PIMs developed by 7 European countries, with the participation of experts who reached a consensus. The list includes 282 types of drugs, which can be grouped into 34 therapeutic groups. Some PIMs are restricted to a certain dose or duration of use, and the list suggests doses, adjustments and therapeutic alternatives. This tool makes it possible to identify and compare patterns of PIM description in the elderly (53).
8. **Medication appropriateness index (MAI):** This index is intended to assess the appropriateness of medications prescribed by a physician and to evaluate patients' self-medication practices. To properly apply the MAI, both a list of medical problems and medications are required. A 10-question scale must be completed for each active drug and frequently used drug. Each question on the scale refers to the individual patient and the drug in question. It predicts the occurrence of adverse clinical outcomes resulting in hospitalizations and emergency department visits for MRPs, and has also been shown to have criterion validity, converging with scales measuring ADRs (52,54).
9. **Drug Burden Index (DBI):** It is a pharmacological measure of a person's cumulative exposure to drugs with anticholinergic and sedative effects, which is associated with reduced functional independence and other global health outcomes in the elderly. It provides information on potential sources of drug-related functional impairment in older people. This pharmacological approach provides a useful evidence-based tool for assessing the functional effect of drug exposure in this population (55,56).

Few tools are available to assess the adequacy of treatment in frailty. A recent guide available is the **STOPP-Pal** criteria (Spanish version of the **STOPP-Frail** criteria developed by the Irish group that developed the STOPP criteria, which attempts to propose criteria for the appropriateness of treatment in patients at the end of life). It presents 27 criteria for drug withdrawal in elderly/fragile patients with the idea of improving quality of life, reducing hospitalizations and mortality (35,57).

In Catalonia, the criteria used are those established by CatSalut based on the recommendations on PIMs in the elderly (58) and the document on medication management in chronic patients (28). These documents were drawn up by consensus of a group of experts and the criteria of the drugs to be included in the list of PIMs were to be in at least 2 bibliographic databases, with an explicit recommendation or contraindication for the elderly population in the technical data sheet or with a specific alert from the Spanish Agency of Medicines and Health Products

(AEMPS). The references used were the Beers criteria, STOPP/START, the EU-PIM list, the PRISCUS list, the AEMPS information notes on medicines for human use, and anticholinergic risk scales (ARS) in older adults (28,58).

All these tools are great, but more efficient and **higher quality informatics systems** may have a greater role to play in the routine practice of optimizing pharmacotherapy for the elderly, particularly those with chronic disease, multimorbidity, and polypharmacy (34). The future of prescribing for the elderly is undoubtedly electronic as individual health records and prescription sheets move steadily from a paper format to a fully electronic format. There have been two trials called SENATOR and OPERAM that involve fully electronic deployment of STOPP / START criteria based on diagnostic and medication coding systems, along with other patient data quantifying functional and cognitive status, as well as key laboratory test results. Electronic deployment of STOPP / START criteria through the interconnection of diagnosis and medication codes within health record/prescription systems is eminently feasible (39).

The OPERAM project funded by the European Commission and the Swiss government was established based on a systematic tool to reduce inappropriate prescribing. It is one of the first computerized interventions designed to incorporate a structured medication review to review PIP and PPOs in older hospitalized patients and assess whether it reduces hospital admissions. It also recognizes the importance of identifying patient-reported clinical signs and symptoms that may be associated with PIP (59).

The SENATOR software produces a report that identifies potential risks and opportunities for improvement in the participants' current medication list. This software is designed to optimize prescriptions for elderly patients by applying the published STOPP and START criteria. It highlights DDI and drug-disease interactions and provides non-pharmacological recommendations to reduce the risk of ADRs. It is suggested that the majority of drug prescriptions for the elderly, with multimorbidity at present and in the future are not prescribed by specialized geriatricians or clinical pharmacologists (60).

A computerized **Drug Utilization Review (DUR)** is defined as a formal program to evaluate medication prescribing and patient safety. DUR reviews whether patients are receiving appropriate medications and aims to identify MRP (61). The implementation of computerized

DUR programs to monitor drug therapy appears to reduce the risk of medication errors and ADR (62).

In Catalonia, there is an **electronic clinical station** in primary care, called ECAP. This application is adopted by the Department of Health as a working tool for primary health care. It is a tool designed for the daily work of all professionals, which contains multiple applications to support decision-making and facilitate patient follow-up. A CDSS has been implemented to improve medication reconciliation and safety. These support tools are **PREFASEG** (PREscripción FArmacéutica SEGura, i.e., safe pharmaceutical prescription) and **Self-Audit** (63,64) described next:

ECAP is the computerized clinical history program used by health and social care professionals working in primary care and out-of-hospital specialized care centers when attending and visiting patients. It is a clinical and administrative management tool that is integrated with other public network information systems. On July 12, 2017, an agreement was formalized between CatSalut and the Catalan Institute of Health for the establishment of a collaboration framework. The objective of this agreement is, through the ECAP software application, to promote the technological development of the digital medical record in the field of primary and specialized care within the Integral Public Healthcare System of Catalonia (SISCAT) (65).

PREFASEG is an ECAP software that serves to prevent medication errors and ADRs by generating notifications online when a new treatment is started to warn the clinicians. The computerized medical record is accessible to all primary and specialized care professionals in Catalonia, and alerts professionals when a patient is visited by another professional and explains the medication changes made. PREFASEG addresses the following safety dimensions: safety alerts from the AEMPS, drugs not recommended for elderly patients, contraindications due to health-related problems (HRP), age or clinical variables (glomerular filtration rate (GFR) and potassium), allergies and ADRs, teratogenic drugs, teratogenicity in childbearing age, safety warnings in pediatrics, adequacy of treatment, repetitive treatments, interactions, combinations of anticholinergic drugs, treatment durations and other safety warnings (64,66).

Self-Audit is also an ECAP software accessible only to primary care professionals. It facilitates systematic medication review, as it identifies and resolves safety MRPs systematically. It generates a list of patients with active MRPs to facilitate changes or suspensions of a treatment.

The MRPs Self-Audit identifies can be therapeutic duplications, medication not recommended for advanced age, inadequate treatment durations, contraindications due to alterations in renal filtration, hyperkalemia or the patient's underlying condition, among others. This tool provides health professionals access to all their patients with medication incidents that need review and resolution (63,66).

1.3: Project justification

The care of institutionalized patients was a major challenge during the SARS-CoV-2 pandemic, with increased morbidity and mortality in nursing homes. Compared to previous years, the mortality in nursing homes was almost 10 times higher, and 71.9% of all deaths in Spain during COVID-19 occurred in nursing homes (67–70).

For this reason, the Government of Catalonia decided to transfer the management of nursing homes from the Department of Social Action and Citizenship to the Department of Health, effective April 10, 2021. Until that time, most of the public health care in nursing homes in Barcelona City and the Metropolitan Area was managed by a private group called MUTUAM, which ceased to perform these functions, and the health care management was immediately and primarily transferred to the Catalan Institute of Health. In May 2020, professionals from the Medication Area and Pharmacy Service of the Barcelona City Management were asked to collaborate with PCTs to improve care for people in nursing homes. At that time, a multidisciplinary team was created in Catalonia to carry out an intervention in nursing homes. This intervention consisted of developing an improvement plan, reviewing the validity of prescriptions and medication plans, and detecting MRPs, using the minimal criteria established by the Catalan Institute of Health. These criteria can be seen in *Annex 1: The minimal criteria established by the Catalan Institute of Health*.

Some studies already showed that the use of deprescribing tools, supported by multidisciplinary teams with physicians, reduced inappropriate polypharmacy in hospitalized older patients and helped physicians decide whether to withdraw the prescription, how to withdraw the prescription, and how to communicate the deprescription to older patients in the hospital (71).

In seeking to explore facilitators and barriers to conducting medication reviews and post-discharge follow-up in older hospitalized patients from the perspective of the healthcare

professional, the importance of a multidisciplinary team is described and theories of interprofessional collaboration emphasize the importance of facilitators. Pharmacists are seen as bringing expertise to the team and perceiving a positive contribution to the common goal of improving patient care and safety, but there is a need for greater clinical competence (72). This can be achieved with clinical pharmacologists who possess the necessary clinical expertise.

A multidisciplinary approach, integrating a team of professionals from different disciplines and specialties coming together to reach a combined decision on a complex situation, is essential for optimal care of institutionalized residents. Interprofessional teamwork allows to share experiences, clinical expertise, different disciplinary perspectives and knowledge about the institutionalized patient, to effectively address MRPs, PIMs and manage optimal individualized medication. Continuing medication should be considered an active decision that carries as much responsibility when evaluating the continuation, initiation or cessation of a treatment (44,73).

Hypothesis and Objectives

2

The **hypothesis** that was put forward before the completion of this doctoral thesis is that a multidisciplinary team reviewing medication plans, with the incorporation of a clinical pharmacologist, improves the degree of adequacy of treatments and is useful for the improvement of care in patients in nursing homes, a particularly fragile and polymedicated population.

The **general objective** of this doctoral thesis was to characterize institutionalized persons, systematically review their medication plans (describe pharmacological prescription and health-related problems) and assess the impact of an intervention consisting of the creation of a multidisciplinary team to systematically evaluate their medication plan.

To meet this objective, two studies were designed with the following objectives:

First study:

Main objective: To describe institutionalized patients and systematically review their medication plans in nursing homes in Catalonia

Secondary objectives:

- To describe the recommendations given to institutionalized patients.
- To identify MRPs by analyzing in which cases the prescribed treatments can be considered adequate and safe, inappropriate or have safer alternatives.

Second study:

Main objective: To evaluate the impact on medication plans of a multidisciplinary team intervention in nursing homes in Catalonia.

Secondary objectives:

- To analyze the medication plan before and after the intervention
- To assess whether the proposals for change had been implemented.

Methods

3

The characterization of the institutionalized patients, the review of their medication plans and the assessment of the impact of the intervention were carried out through the two studies mentioned above. The multidisciplinary team included primary care physicians, nurses, primary care social and administrative workers, physicians and nurses assigned to nursing homes, a clinical pharmacist and a clinical pharmacologist.

Study population:

The study population was the patients currently admitted to the nursing homes that were intervened. These nursing homes were those belonging to the Catalan Institute of Health in the north area of Barcelona, which is the population served by the Catalan Institute of Health corresponding to the districts of Horta, Nou Barris, Sant Andreu and the municipality of Montcada i Reixac. At the time of the intervention, there were 3,465 places in nursing homes with 100% occupancy, representing 4.4% of the total population aged ≥65 years. Finally, 5 nursing homes were included: 4 from area 3 and 1 from area 7. With this selection of nursing homes, 22.3% of those institutionalized in nursing homes were covered. All the anonymized nursing homes and their distribution can be seen in *Annex 2: Geriatric Nursing Homes in the north area of Barcelona, Spain*.

Inclusion and exclusion criteria:

The inclusion criteria was institutionalized patients with public health care coverage provided by CatSalut. The exclusion criteria were institutionalized patients with health coverage provided by other entities (MUFACE, MUGEJU, ISFAS), very short life expectancy (terminally ill or in palliative care), patients admitted to hospitals or social health centers at the time of the intervention, patients who died or were discharged within the first month of the review, and those who could not undergo the intervention due to lack of information. A formal sample size calculation was not performed because the intervention was applied to all the reviewed patients, excluding only those who met the exclusion criteria.

Data collection:

The data recorded were collected in routine clinical practice at the time of the intervention and subsequent follow-up. These anonymized data were transferred to REDCap for analysis, with the list of variables collected in REDCap (*Annex 3: REDCap Variables)*. REDCap is an electronic data capture software and workflow methodology for designing clinical trial research

and translational research databases. The privacy policies and code of conduct for the REDCap platform can be found at the following link: https://projectredcap.org/.
Prior to the analysis, a quality check was done (see *Annex 4: Quality Report*).

Statistical analysis:
Continuous variables were presented as means (standard deviation, SD) and categorical variables were presented as frequencies (percentages).
Statistical analysis was performed using R version 4.3.0.

Ethics approval:
The study was conducted according to the guidelines of the Declaration of Helsinki. The protocol was approved by both local Research Ethics Committees of Vall Hebron University Hospital (protocol code EOM(AG)067/2021(5930)) and IDIAP Jordi Gol (protocol code 22/027-P). No informed consent was necessary since the information was anonymized.

The methodology of each study is detailed in the corresponding publications attached to this doctoral thesis. However, the next section summarizes the design and methodology of each study, with the variables and results described in each article.

<u>First study:</u> Pharmacological treatments and medication-related problems in nursing homes in Catalonia: a multidisciplinary approach (74).

This is a cross-sectional study to perform a descriptive analysis of institutionalized patients and their medication. All patient data was recorded at the start of the intervention, which began on July 1, 2020 and ended on February 1, 2022.

The variables analyzed were demographic data, comorbidities, drug allergies, health-related problems according to ICD-10, pharmacological treatments according to the ATC classification system and the use of absorbents.

Comorbidities were collected according to the adjusted morbidity groups (AMG) (75,76) and PCC or MACA (11). AMG is a morbidity measure created by the Spanish Healthcare System. This tool divides patients into 31 mutually exclusive categories of six morbidity groups (MG) and five levels of complexity (A) each (75).

A descriptive analysis was made of the recommendations given, which could be to complete data on allergies or diseases, to recommend withdrawal of drugs, to change them or to adjust their use.

All drugs that were considered possible MRPs were collected. These MRPs could be due to the risk of DDI, therapeutic duplication, contraindications, drugs considered inappropriate or of doubtful efficacy.

<u>Second study:</u> The impact of a multidisciplinary team intervention on medication prescription in nursing homes in Catalonia (77)

This is a multicenter, before-after study without a control group, to assess the impact of a multidisciplinary intervention on the medication plan. The intervention started with the first review on July 1, 2020 until the last one on March 5, 2021. The first follow-up after one year started on August 2, 2021 until the last follow-up on February 28, 2022.

The variables analyzed were the number of drugs prescribed, including fixed-dose combinations, and the use of absorbents before and after the intervention, the recommendations given and followed, whether and which drugs were recommended to be withdrawn, changed or adjusted, the drugs withdrawn, the drugs added and the number of deaths.

A descriptive analysis was made of the recommendations given and followed, the drugs recommended to be withdrawn, changed, or adequate with the withdrawn drugs, the drugs added, and the number of deaths. A comparative analysis was performed before and after the intervention, with the total recommendations given and followed.

Results

4

4.1 FIRST STUDY

Pharmacological treatments and medication-related problems in nursing homes in Catalonia: a multidisciplinary approach.

Anderssen-Nordahl E, Sánchez-Arcilla Rosanas M, Bosch Ferrer M, Sabaté Gallego M, Fernández-Liz E, San-José A, Barceló-Colomer ME. Pharmacological treatments and medication-related problems in nursing homes in Catalonia: a multidisciplinary approach. Front. Pharmacol. 2024;15:1320490.

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Pharmacological treatments and medication-related problems in nursing homes in Catalonia: a multidisciplinary approach

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Background: Aging correlates with increased frailty, multi-morbidity, and chronic diseases. Furthermore, treating the aged often entails polypharmacy to achieve optimal disease management, augmenting medication-related problems (MRPs). Few guidelines and tools address the problem of polypharmacy and MRPs, mainly within the institutionalized elderly population. Routine pharmacological review is needed among institutionalized patients. This pharmacological review may improve with a multidisciplinary approach of a collaboration of multiple health professionals. This study aimed to describe institutionalized patients, systematically review their medication plans, and then give recommendations and identify MRPs.

Methods: A cross-sectional study was performed using data obtained from patients living in five nursing homes in the northern area of Barcelona, Spain. The inclusion criteria comprised institutionalized patients with public health coverage provided by the Health Department of Catalonia. A detailed description of the clinical characteristics, chronic diseases, pharmacological treatments, recommendations, incomplete data, and MRPs, such as potential drug–drug interactions, therapeutic duplications, contraindications, and drugs deemed inappropriate or of doubtful efficacy, was made. The clinical pharmacologist was the medical doctor specialist who acted as the coordinator of the multidisciplinary team and actively reviewed all the prescribed medications to make recommendations and detect MRPs.

Results: A total of 483 patients were included. Patients had a mean age of 86.3 (SD 8.8) years, and 72.0% were female individuals. All patients had at least three health-related problems, with a mean of 17.4 (SD 5.6). All patients, except one, had a minimum of one prescription, with a mean of 8.22 drugs prescribed (SD 3.5) per patient. Recommendations were made for 82.4% of the patients. Of these recommendations, verification of adequate use was made for 69.3% and withdrawal of a drug for 49.5%.

Conclusion: This study demonstrates a high prevalence of health-related problems and several prescribed drugs in nursing homes in Catalonia. Many recommendations were made, confirming the increased proportion of polypharmacy, MRPs, and the need for standardized interventions. A multidisciplinary team approach, including general practitioners, geriatric assessments, a clinical pharmacist, and a clinical pharmacologist, should address this problem.

KEYWORDS

medication review, frail elderly, nursing homes, medication therapy management, polypharmacy, potentially inappropriate medication list, primary healthcare, drug utilization

1 Introduction

Advances in research and medical care have increased life expectancy, and the aging of the population is expected to increase significantly in the coming decades (Guisado-Clavero et al., 2019; Zito et al., 2023). In 2022, more than one-fifth (21.1%) of the European Union population was aged 65 or over, and the elderly are expected to account for 31.3% by 2100 (Eurostat, 2023). Longevity correlates with the incidence of chronic disease, and 55% to 98% of elderly adults suffer from multi-morbidity (Guisado-Clavero et al., 2019). Multi-morbid and frail patients likely require multiple medications to achieve optimal disease management (Herr et al., 2015; Hilmer and Gnjidic, 2017). Increased exposure to complex drug regimens involving ≥5 drugs, known as polypharmacy, or excessive polypharmacy, as in patients treated with 10 or more medications concomitantly, raises the risk of adverse events (Stuhec et al., 2021). Polypharmacy can also affect drug safety due to potentially inappropriate medications (PIMs), adverse drug reactions (ADRs), and the risk of interactions (Burato et al., 2021; Zhang et al., 2022; Doumat et al., 2023; Reinhild Haerig et al., 2023).

A medication-related problem (MRP) is an occurrence that involves drug therapy that can potentially interfere with health outcomes. Some MRPs are therapeutic duplications, potential drug–drug interactions (DDIs), potentially inappropriate medications (PIMs), and contraindicated drugs (Troncoso-Mariño et al., 2021).

Given the impact of inappropriate prescription in elderly patients, different tools have been proposed to help optimize the use of medications in older patients, such as the Beers criteria, STOPP/START, PRISCUS, Medication Appropriateness Index, Drug Burden Index, and anticholinergic risk scale, to assess the anticholinergic load, among others (Hilmer et al., 2007; Rudolph et al., 2008; Lunghi et al., 2022; By the 2023 American Geriatrics Society Beers Criteria® Update Expert Panel, 2023; Mann et al., 2023; O'Mahony et al., 2023). According to the Catalan Health Service instruction 04/2012, all patients on chronic treatment should undergo a pharmacological review at least every year (Department of Health. Government of Catalonia, 2014).

Generally, the guidelines poorly consider the situation of the elderly with multi-morbidity (Guisado-Clavero et al., 2019; Zito et al., 2023). Furthermore, there is little information on patients in nursing homes with greater fragility and multi-morbidity, even though they present more polypharmacy, ADRs, and prevalence of interactions (Herr et al., 2015; Hilmer and Gnjidic, 2017). Some studies suggest deprescribing may be safe, feasible, well-tolerated, and beneficial for the elderly, and collaboration with clinical pharmacists can reduce polypharmacy and improve adherence to treatments (Ibrahim et al., 2021; Saeed et al., 2022). The transition of patient care between different healthcare settings can be a challenge due to elevated medication errors, but proper medication reconciliation during the transition could lead to fewer MRPs (Stuhec and Batinic, 2023).

A multidisciplinary approach, with an interprofessional collaboration, allows the sharing of clinical knowledge and different perspectives about institutionalized patients to improve their pharmacological treatments (Disalvo et al., 2020; Lunghi et al., 2022; Song et al., 2023). Data from patients with the highest multi-morbidity are essential for the provision of adequate healthcare to patients with multiple chronic conditions. This is in line with the findings of previous reviews highlighting the lack of intervention studies aimed at improving adequate polypharmacy in elderly patients (Saeed et al., 2022).

In addition, the care of institutionalized patients was a great challenge during the SARS-CoV-2 pandemic, with an increase in morbidity and mortality in nursing homes. Compared to previous years, the mortality in nursing homes was almost 10 times higher, and 71.9% of all deaths in Spain during COVID-19 were seen in nursing homes (Mas Romero et al., 2020; Ordovás et al., 2020; Rada, 2020; Arnedo-Pena et al., 2022). For this reason, a multidisciplinary team was created in Catalonia, Spain, to make a structured intervention in nursing homes. The intervention consisted of developing an improvement plan, reviewing the validity of prescriptions and medication plans, and detecting MRPs.

Therefore, the main objective of this study was to describe institutionalized patients and systematically review their medication plans in nursing homes in Catalonia. The secondary objectives were to describe the recommendations given and identify MRPs by analyzing whether the prescribed treatments can be considered adequate and safe, inappropriate, or have safer alternatives.

2 Methods

2.1 Study design and setting

The multidisciplinary intervention was a multicenter before–after study without a control group. As the first step of this intervention, a cross-sectional study was carried out to make this descriptive analysis. From a total of 48 nursing homes, the data were collected from 5 nursing homes, where the intervention was made, in the northern area of Barcelona, Spain. These 5 nursing homes were prioritized by the health administration during the intervention since it was considered that the patients in these nursing homes would benefit the most. The health administration selected these nursing homes because of their size, efficiency, and to cover the highest population

percentage. With this selection, even though it was only 5 nursing homes, the intervention covered 22.3% of the residents in the nursing homes. The study population included all patients currently admitted to a nursing home at the start of this intervention, which was initiated on 1 July 2020 and ended on 1 February 2022. The inclusion criteria comprised institutionalized patients with the public health coverage provided by the Catalan Health Service. The exclusion criteria comprised institutionalized patients with health coverage provided by other insurers, a short-term life expectancy, hospitalization during the intervention, patients who died or were discharged in the first month of the review, and those who could not be intervened due to lack of information. There was no formal sample size calculation since the descriptive analysis was done on all the reviewed patients except those who were excluded.

The multidisciplinary team included general practitioners, nurses, social and administrative workers from primary care, clinicians and nurses assigned to the nursing homes, a clinical pharmacist, and a clinical pharmacologist. The pharmacist and clinical pharmacologist acted as consultors. However, it should be pointed out that the clinical pharmacologist was the medical doctor specialist who acted as the coordinator of the multidisciplinary team and actively reviewed all the prescribed medications to make recommendations. Hence, medication reconciliation was carried out by the clinical pharmacologist at the beginning of the medication review. Medication review is an essential part of medical practice, and it is contemplated within the activities of medical professionals to ensure the rational use of medication, considering the universal health coverage in Spain (Department of Health. Government of Catalonia, 2022). The main sources of information used by the clinical pharmacologist to conduct the review and give recommendations comprised the information contained in the technical data sheets, the support tools Self-Audit and PREFASEG (PREscripción FArmacéutica SEGura) (Pons-Mesquida et al., 2021; 2022), and the list of potentially inappropriate drugs proposed by the Catalan Health Service (Department of Health. Government of Catalonia, 2014; Catalan Health Service. Department of Health, 2020).

The support tools are Self-Audit and PREFASEG (PREscripción FArmacéutica SEGura, i.e., safe pharmaceutical prescription). Self-Audit identifies and resolves safety MRPs systematically. It generates a list of patients with active MRPs to facilitate changes or suspensions of a treatment (Pons-Mesquida et al., 2022). PREFASEG generates online notifications when starting a treatment to warn clinicians of potential problems related to drug use and prevent medication errors (Pons-Mesquida et al., 2021). The computerized medical history notifies the professionals when a patient is visited by another professional and explains the medication changes made.

The criteria used to consider MRPs were those established by the Catalan Health Service from recommendations on potentially inappropriate drugs in the elderly (Catalan Health Service. Department of Health, 2020) and the document on the management of medication in chronic patients (Department of Health. Government of Catalonia, 2014). These documents were prepared by consensus of a group of experts, and the criteria of the drugs to be included in the potentially inappropriate drug list were to be in at least two bibliographic databases, with an explicit recommendation or contraindication for the elderly population in the technical sheet or with a specific alert from the Spanish Agency for Medicines and Health Products (AEMPS, Agencia Española de Medicamentos y Productos Sanitarios). The references used were the Beers criteria, STOPP/START, the EU-PIM list, the PRISCUS list, information notes on medicines for human use from AEMPS, and anticholinergic risk scales in older adults (Department of Health. Government of Catalonia, 2014; Catalan Health Service. Department of Health, 2020).

From the identified problems during the medication review, different recommendations were given. These recommendations could be to complete absent data, withdraw a drug, verify whether the use of a drug was adequate, or substitute a drug. As for the missing data, allergies or diseases could be absent. As for the withdrawal of drugs, this was recommended when MRPs were considered, such as potential DDIs, duplicated therapies, contraindicated drugs, inappropriate drugs, or drugs of doubtful efficacy. As for the adequacy of drug use, this could be due to the need to reduce the dose, a bad tolerance, to reduce anticholinergic load, or a high risk of ADRs. As for the substitution of a drug, this could be recommended due to considering other drugs as a first choice or equivalent drugs.

The study design, procedures, and reporting followed the TREND guidelines for non-randomized evaluations of behavioral and public health interventions (Des Jarlais et al., 2004) and are registered at ENCePP (Reference: EUPAS106748).

2.2 Variables and data collection

The variables analyzed were demographic data; comorbidities; drug allergies; diseases according to the International Classification of Diseases, version 10 (ICD-10); pharmacological treatments according to the Anatomical Therapeutic Chemical (ATC) classification system; and the use of absorbents. The pharmacological treatments are recorded as the number of drugs consumed. This is the number of different drugs that the residents have prescribed, including fixed-dose combinations.

A descriptive analysis was performed of the recommendations, incomplete data, and drugs recommended to verify the adequacy of use, to be substituted, or withdrawn. We defined MRPs, potential DDIs, therapeutic duplications, contraindications, and drugs deemed inappropriate or of doubtful efficacy to identify deficits in functioning and analyze whether the prescribed treatments were considered adequate.

Comorbidities were collected according to the adjusted morbidity groups (AMGs) (Monterde et al., 2016) and complex chronic patients or a model of attention to advanced chronicity (Department of Health. Government of Catalonia, 2017).

AMG is a morbidity measurement created by the Spanish Healthcare System. This tool divides patients into 31 mutually exclusive categories from six morbidity groups (MGs) and five complexity levels (A) each (Monterde et al., 2016). This grouping aims to help identify patients with greater comorbidities, polypharmacy, risk of complications, worsening of functional capacity, quality of life, and/or premature death (Department of Health. Government of Catalonia, 2017).

The morbidity groups are as follows:

- MG = 0: Healthy population.
- MG = 10: Patients with an acute disease.

- MG = 20: Patients with a pathology related to pregnancy and/or birth.
- MG = 31: Patients with one system affected by a chronic disease.
- MG = 32: Patients with two or three systems affected by a chronic disease.
- MG = 33: Patients with four or more systems affected by a chronic disease.
- MG = 40: Patients with an active neoplasm.

The level of complexity takes into account the total of each morbidity group from the entire population used for its creation and divides it into five groups according to the percentiles 40, 70, 85, and 95 (Monterde et al., 2016). When AMG was compared to the clinical risk group measurement, the results showed better performance of AMG for Primary Healthcare in Spain (Hughes et al., 2004; Monterde et al., 2019).

A patient is considered to be a complex chronic patient when their clinical management is perceived as especially difficult by their referring clinical professionals. A complex chronic patient is associated with criteria related to the patient himself, clinical professionals, and the environment. Concerning the patient, there is multi-morbidity, severe or progressive single chronic pathology, a high probability of suffering decompensation, high use of health services, and polypharmacy, among others. Regarding clinical professionals, there is the requirement for multidisciplinary management, exposure to discrepancies between different professionals, management doubts, and benefits from an integrated care strategy. As for the social sphere, it is worth noting adverse psychosocial situations. No specific criteria or number are needed, rather than their referring professional considering the case management especially difficult.

A patient is considered to be in the model of attention to advanced chronicity when characterized by a case management approach with a present, important, and growing palliative pathway. The palliative component does not exclude curative options but rather coexists with them and advances decision planning as an essential process in decision-making support (Department of Health. Government of Catalonia, 2017).

The data were collected in the usual clinical practice during the intervention, and the data source was the electronic medical record that is common in Catalonia. Then, anonymized data were entered into the Research Electronic Data Capture (REDCap) platform. A quality check was done prior to the descriptive analysis. A detailed description of the clinical characteristics, chronic diseases, and pharmacological treatments was made.

2.3 Ethics approval

The study was conducted according to the guidelines of the Declaration of Helsinki. The protocol was approved by both local Research Ethics Committees of Vall Hebron University Hospital (protocol code EOM(AG)067/2021(5930)) and IDIAP Jordi Gol (protocol code 22/027-P). No informed consent was necessary since the information was anonymized.

2.4 Statistical analysis

Continuous variables are presented as means (standard deviation, SD), and categorical variables are presented as frequencies (percentages). Statistical analysis was performed using R version 4.3.0.

3 Results

3.1 Descriptive analysis of the institutionalized patients

A total of 483 patients were included from five different nursing homes after excluding 47 patients (Figure 1).

The baseline characteristics of all the included patients are shown in Table 1. The patients had a mean age of 86.3 (SD 8.8) years, and 348 (72.0%) patients were female individuals. Complex chronic patients or patients of the model of attention to advanced chronicity were recorded in less than 2.0%, and almost 95.0% of the patients were in the morbidity group of patients, with four or more systems affected by chronic disease (MG = 33), in all nursing homes.

All patients had at least three health-related problems (HRPs), with a mean of 17.4 (SD 5.6). The most common chronic diseases were urinary incontinence, with a total of 412 patients (85.3%), followed by hypertension, with 357 patients (73.9%), and osteoarthritis, with 264 patients (54.7%), as seen in Table 2. There was a total of 8419 HRPs documented, showing that a patient normally had various HRPs registered in the superfamilies. The number and percentage of the total registered diseases divided into superfamilies are shown in Table 3. For a complete list of all HRPs divided into groups according to their ICD-10, see Supplementary Table S1. In 197 (40.8%) patients, COVID-19 was registered as an HRP.

All patients, except for 1, used a minimum of one pharmacological treatment with a mean of 8.22 drugs prescribed (SD 3.5), including fixed-dose combinations. The three most prescribed medications were omeprazole, prescribed to 274 patients (56.8%), paracetamol, prescribed to 269 patients (55.8%), and quetiapine, prescribed to 183 patients (37.9%), as seen in Table 4. For a complete list of all the pharmacological prescribed treatments divided into groups according to their ATC, see Supplementary Table S2.

3.2 Descriptive analysis of the recommendations and medication-related problems

A clinical pharmacologist made recommendations for 398 (82.4%) patients. The patients could get various recommendations. In a total of 165 (34.2%) patients, some of the data concerning their HRPs or allergies were absent. The most frequent recommendation was the verification of the adequate use of drugs for 276 (69.3%) patients. The withdrawal of at least one drug was recommended for 197 (49.5%) patients, and substitution of a drug was recommended for 39 (9.8%) patients, as seen in Figure 2.

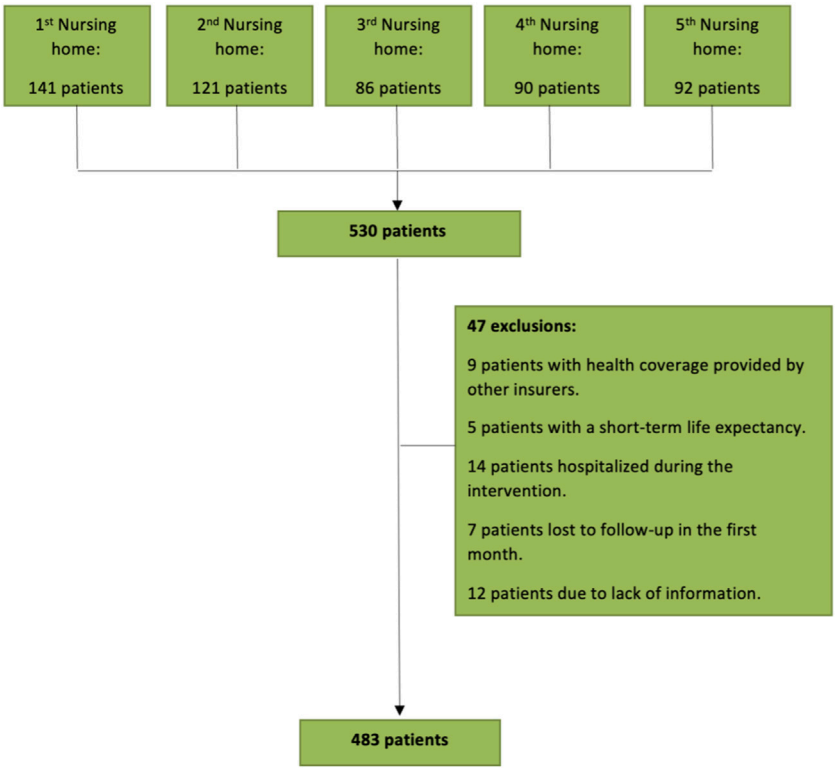

FIGURE 1
Flowchart of the study population the inclusion/exclusion procedure.

The MRPs recommended to be withdrawn were due to potential DDIs, therapeutic duplications, contraindications, and drugs deemed inappropriate or of doubtful efficacy. Combining all MRPs, there were 231 (47.8%) in total. Table 4 shows all the MRPs mentioned in the pharmacological review. There was a risk of interactions in 61 (12.6%) patients, with a total of 72 (14.9%) potential DDIs. Of all the potential DDIs, 27 of them included a selective serotonin reuptake inhibitor (SSRI) drug (37.5%), of which tramadol-SSRI was the most common, with 16 (22.2%) potential DDIs in total. Statins and calcium channel blockers were 13 (18.0%) of the potential DDIs, and a combination of different antiarrhythmics and cardiac glycosides was seen in 8 (11.1%) DDIs. Regarding the therapeutic duplications, a prevalence of vitamin D or analogs associated with calcium is seen. Contraindications were seen recurrent in metformin, NSAIDs, and haloperidol. Inappropriate drugs were mostly antipsychotics or benzodiazepines. Lastly, the drugs with doubtful efficacy were often psychostimulant and antivertiginous drugs, as can be seen in Table 5 along with the active ingredients according to their ATC classification.

4 Discussion

The main objective of this study was to describe institutionalized patients and systematically review their medication plans in nursing homes in Catalonia. The results showed a high prevalence of HRP in all patients, with a mean of 8.22 prescribed drugs per patient. This is similar to other studies in Europe (Pasina et al., 2020; Reinhild Haerig et al., 2023). More than 80% of the patients received recommendations, and for 50%, at least one drug was recommended to be withdrawn due to MRPs. These results confirm the challenge of the most fragile patients in nursing homes, with a high number of prescribed medications, raising the possibility of MRPs, PIMs, risk of ADRs, and lack of interventions to improve adequate polypharmacy. This intervention gave specific recommendations to each patient to reduce MRPs, PIMs, ADRs, and polypharmacy. This should help resolve potential MRPs and prevent medication errors.

4.1 Descriptive analysis of institutionalized patients in nursing homes

The majority of patients were female individuals (72.0%) with a mean age of 86.3 years, which is similar to other comparable European studies (San-José et al., 2014; Schneider et al., 2019; Burato et al., 2021; Troncoso-Mariño et al., 2021). This was expected since female people have a longer life expectancy (Eurostat, 2023). In a nursing home in Italy, the prevalence of female individuals was likewise elevated, being 78.3% and 74.9% of patients with and without dementia, respectively (Pasina et al., 2020).

TABLE 1 Baseline clinical characteristics of the included patients.

Baseline clinical characteristic	Total	Residency 1	Residency 2	Residency 3	Residency 4	Residency 5
Number of patients	483	129 (26.7%)	111 (22.9%)	74 (15.3%)	81 (16.7%)	88 (18.2%)
Age (years)	86.3 (8.8)	86.2 (9.8)	87.9 (8.1)	84.6 (10.2)	87.2 (7.4)	84.8 (7.6)
Sex						
Female	348 (72.0%)	100 (77.5%)	86 (77.5%)	47 (63.5%)	56 (69.1%)	59 (67.0%)
Male	135 (28.0%)	29 (22.5%)	25 (22.5%)	27 (36.5%)	25 (30.9%)	29 (33.0%)
Complex chronic patients or advanced chronicity						
Yes	6 (1.2%)	0 (0.0%)	1 (0.9%)	1 (1.4%)	1 (1.2%)	3 (3.4%)
No	2 (0.4%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	1 (1.2%)	0 (0.0%)
Not recorded	475 (98.3%)	129 (100.0%)	109 (98.2%)	73 (98.6%)	79 (97.5%)	85 (96.6%)
Recorded AMGs						
Yes	380 (78.7%)	111 (86.0%)	98 (88.3%)	42 (56.8%)	55 (67.9%)	74 (84.1%)
Exitus	86 (17.8%)	14 (10.9%)	12 (10.8%)	26 (35.1%)	24 (29.6%)	10 (11.4%)
Not recorded	17 (3.5%)	4 (3.1%)	1 (0.9%)	6 (8.1%)	2 (2.5%)	4 (4.5%)
Risk of hospitalization in %	11.5 (5.9)	12.8 (6.1)	9.7 (4.3)	9 (5.3)	11.8 (5.9)	13.1 (6.7)
Value of MG						
MG = 40	11 (2.9%)	2 (1.8%)	2 (2.0%)	1 (2.4%)	4 (7.2%)	2 (2.7%)
MG = 33	359 (94.5%)	106 (95.5%)	91 (92.9%)	40 (95.2%)	50 (91.0%)	72 (97.3%)
MG = 32	9 (2.3%)	2 (1.8%)	5 (5.1%)	1 (2.4%)	1 (1.8%)	0 (0.0%)
MG = 31	1 (0.3%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Drug allergies						
Yes	36 (7.5%)	32 (24.8%)	1 (0.9%)	2 (2.7%)	1 (1.2%)	0 (0.0%)
No	324 (67.1%)	52 (40.3%)	65 (58.6%)	70 (94.6%)	51 (63.0%)	86 (97.7%)
Not recorded	123 (25.5%)	45 (34.9%)	45 (40.5%)	2 (2.7%)	29 (35.8%)	2 (2.3%)
Number of health problems	17.4 (5.6)	17.9 (5.5)	16.6 (5.3)	15.7 (5.0)	16.2 (4.6)	20.4 (6.4)
Use of absorbents						
Yes	374 (77.4%)	98 (76.0%)	75 (67.6%)	52 (70.3%)	69 (85.2%)	80 (90.9%)
No	109 (22.6%)	31 (24.0%)	36 (32.4%)	22 (29.7%)	12 (14.8%)	8 (9.1%)
Number of drug consumption	8.22 (3.5)	8.1 (3.1)	7.7 (3.4)	8.6 (3.9)	8.2 (3.1)	8.8 (3.8)

*Numeric variables: mean (SD) and categorical variables: n (%).

The number of HRPs was also very high, with a mean of 17.4 diseases, which agrees with the AMG values and the type of patient that is mostly admitted to nursing homes. It also highlights the risks of the frailer elderly and their association with polypharmacy and increased MRPs. This does not correlate with the low percentage of complex chronic patients or model of attention to advanced chronicity described in this study. The cause of this under-registration may be due to the complexity and time needed to go through different scales and classify a patient as complex chronic or of advanced chronicity.

According to the HRPs, the proportion of dementia among the residents living in nursing homes is high. Alzheimer's or dementia was observed in 52.8% of the patients, and patients with symptoms or signs involving cognitive functions and awareness were 30.2%. These diseases are important to take into account when reviewing the medication since they are more likely to be prescribed antipsychotic drugs, leading to a higher risk of MRPs (Taxis et al., 2017; Pasina et al., 2020).

There is an excessive number of prescribed drugs in institutionalized patients in Catalonia, with a mean of 8.22 drugs, similar to nursing homes in Italy, where some regions show polypharmacy in 80.3% of the inpatients in nursing homes (Pasina et al., 2020), or Switzerland, with polypharmacy in 85.5% and a mean number of drugs of 9.4 (Schneider et al., 2019). The excessive number of prescribed drugs is consistent with other parts of the world, such as in Australia, where more than 50% of nursing

TABLE 2 Summary of the 40 most frequent chronic diseases and health-related problems.

Diseases and health-related problems	n	%
Urinary incontinence	412	85.3%
Hypertension	357	73.9%
Osteoarthritis and other arthritis	264	54.7%
Dyslipidemia	260	53.8%
Alzheimer's disease or dementia	255	52.8%
Anemia	252	52.2%
Insomnia and sleep disorders	181	37.5%
Problems related to care provider dependency or life-management	166	34.4%
Functional intestinal disorders	146	30.2%
Symptoms and signs involving cognitive functions and awareness	146	30.2%
Diabetes mellitus	144	29.8%
Depression	138	28.6%
Atrial fibrillation and flutter	135	28.0%
Chronic kidney disease	134	27.7%
Injury of a body region	133	27.5%
History of any surgical intervention	131	27.1%
Osteoporosis	130	26.9%
Pressure ulcer	122	25.3%
Varicose veins or other disorders of veins	122	25.3%
Skin changes or soft tissue disorders	120	24.8%
Heart failure	119	24.6%
Malignant neoplasm	117	24.2%
Pain	108	22.4%
Dependence on enabling machines and devices	104	21.5%
Age-related cataract	100	20.7%
Altered laboratory findings	100	20.7%
Vitamin D deficiency	99	20.5%
Cerebral infarction	97	20.1%
Personal history of allergy to drugs	93	19.3%
Hearing loss	90	18.6%
Dermatitis and eczema	89	18.4%
Abnormalities of gait and mobility	88	18.2%
Glaucoma	87	18.0%
Chronic obstructive pulmonary disease	87	18.0%
Hernia	85	17.6%
Fecal incontinence	85	17.6%
Overweight and obesity	83	17.2%
Fracture of femur or pelvis	80	16.6%
Hypothyroidism	73	15.1%
Infections	70	14.5%

(Continued in next column)

TABLE 2 (*Continued*) Summary of the 40 most frequent chronic diseases and health-related problems.

home residents use nine or more regular medications, leading to the proposal of a simplified medication regimen to reduce the medication burden (Bell et al., 2021).

The three most prescribed drugs were proton pump inhibitors (PPIs), analgesics, and antipsychotics or tranquilizers. This pattern is similar to the not institutionalized Spanish population (Troncoso-Mariño et al., 2021) but with a superior number of prescribed drugs (Cebrino and Portero de la Cruz, 2023). The sequence of most prescribed drugs is similar to that in other European countries, with the most frequent drugs being analgesics (paracetamol and metamizole), diuretics (torasemide), PPIs (pantoprazole), and tranquilizers (quetiapine) (Schneider et al., 2019). PPI use is only considered appropriate for current gastric or duodenal disorders or the prevention of NSAID effects (Zito et al., 2023). Therefore, most of the patients in our study do not meet the criteria for PPI use. Psychotropic use is higher in our study group than in nursing home reports from other countries, such as Australia (69.9%) and Germany (71.1%) (Taxis et al., 2017), but it is similar to that in Italy (Pasina et al., 2020). In nursing homes in Norway, after comparing the prescription of a psychotropic drug at baseline and after 6 months, there was a significant difference with an increase in prescribed antidepressants, atypical antipsychotics, anxiolytics, and sedatives/hypnotics (Callegari et al., 2021).

4.2 Descriptive analysis of the given recommendations and medication-related problems in nursing homes

A patient's clinical state changes over time, and it is necessary to review their treatment systematically. With a multidisciplinary team in nursing homes with both clinical pharmacologists and geriatricians, it is possible to carry out a comprehensive geriatric assessment, including a thorough review of the medication. The reason is that patients in nursing homes are mostly in a situation of advanced fragility and are candidates for deprescription to avoid ADRs and MRPs. With the multidisciplinary approach, recommendations were given, and MRPs were identified. The clinical decision support system in Catalonia helps improve these changes, but since only 28.0% of the alerts were accepted, discussion is needed on improving the approval rate of these warnings (Pons-Mesquida et al., 2021). PREFASEG and Self-Audit are tools used in Catalonia to detect MRPs like potential DDIs, but there are other tools, such as DDI-Predictor or Medscape, that are used by different health professionals in diverse situations (Marcath et al., 2018; Moreau et al., 2021). Prescription errors are more frequent in

TABLE 3 List of all the registered health-related problems divided in their superfamilies.

Superfamily	n	%*
(R00–R99): Symptoms, signs, and abnormal clinical and laboratory findings, not elsewhere classified	1237	14.7%
(I00–I99): Diseases of the circulatory system	1123	13.3%
(E00–E90): Endocrine, nutritional, and metabolic diseases	864	10.3%
(M00–M99): Diseases of the musculoskeletal system and connective tissue	692	8.2%
(Z00–Z99): Factors influencing the health status and contact with health services	654	7.8%
(G00–G99): Diseases of the nervous system	522	6.2%
(F00–F99): Mental and behavioral disorders	515	6.1%
(K00–K93): Diseases of the digestive system	511	6.1%
(N00–N99): Diseases of the genitourinary system	348	4.1%
(H00–H59): Diseases of the eye and adnexa	293	3.5%
(L00–L99): Diseases of the skin and subcutaneous tissue	289	3.4%
(D50–D89): Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	267	3.2%
(S00–T98): Injury, poisoning, and certain other consequences of external causes	256	3.0%
(U00–U99): Codes for special purposes: COVID-19	197	2.3%
(J00–J99): Diseases of the respiratory system	188	2.2%
(C00–D48): Neoplasms	150	1.8%
Interventions	131	1.6%
(H60–H95): Diseases of the ear and mastoid process	109	1.3%
(A00–B99): Certain infectious and parasitic diseases	61	0.7%
(V01–Y98): External causes of morbidity and mortality	12	0.1%
Total	8419	100.0%

* represents the percentage of the total registered diseases in each group.

frail older populations, and systems to detect prescription errors are needed. Interventions to optimize prescription are time-consuming and not always included in routine clinical care. Some consider that appropriately trained clinical pharmacists and communication-technology support are required (Lavan et al., 2016). A recent article also considers that the engagement of clinical pharmacists can prevent MRPs, collaborating with a multidisciplinary team and other international organizations, thereby achieving patient-centered healthcare in Europe and a positive impact (Urbańczyk et al., 2023). Transition of care with appropriate medication reconciliation could lead to fewer MRPs. Medication reconciliation is predominantly made by physicians and nurses, but it could also be provided by clinical pharmacists in some countries (Stuhec and Batinic, 2023). This underlines the importance of a multidisciplinary approach taking into account that, in Spain, clinical pharmacology is a medical specialty that can also prescribe and make medication changes.

The MRPs in this pharmacological review of drugs that were recommended to withdraw was 47.8%. The majority of potential DDIs included SSRIs, tramadol, statins, acenocoumarol, and calcium channel blockers. Some of these potential interactions have also been described by other authors, such as SSRIs (Pasina et al., 2020), statins (Lion et al., 2023), and warfarin (Neidecker et al., 2012). This is a concern since tramadol increases the potential of seizures when it is administered with SSRIs, serotonin/norepinephrine reuptake inhibitors (SNRIs), and tricyclic antidepressants, among others. They may also cause a life-threatening serotonin syndrome with these interactions (Spanish Agency for Medicines and Health Products, 2021). When statins and calcium channel blockers are administered in combination, the most important thing is to control or not exceed the recommended doses due to the increased risk of myopathy and rhabdomyolysis (Piccoliori et al., 2021). Levothyroxine and statins are drugs included in medications that can potentiate the anticoagulant effect of acenocoumarol, and the combination of different antiarrhythmics is not recommended in older patients due to the greater arrhythmogenic risk (Verhovsek et al., 2008; Neidecker et al., 2012; Iniesta-Navalón et al., 2019). This is without taking into

TABLE 4 Summary of the 40 most frequent pharmacological treatments.

Drug	n	%
Omeprazole	274	56.8%
Paracetamol	269	55.8%
Quetiapine	183	37.9%
Furosemide	144	29.8%
Acetylsalicylic acid	134	27.8%
Enalapril	109	22.6%
Lorazepam	105	21.7%
Bisoprolol	89	18.4%
Vitamin D and analogs	86	17.8%
Simvastatin	78	16.2%
Sertraline	74	15.3%
Trazodone	69	14.3%
Amlodipine	66	13.7%
Citalopram	62	12.8%
Atorvastatin	61	12.6%
Risperidone	61	12.6%
Metformin	60	12.4%
Ferrous glycine sulfate	60	12.4%
Levothyroxine sodium	60	12.4%
Calcium combinations with vitamin D and/or other drugs	54	11.2%
Mirtazapine	53	10.9%
Memantine	43	8.9%
Losartan	41	8.5%
Metamizole sodium	41	8.5%
Folic acid	40	8.3%
Apixaban	37	7.6%
Fentanyl	35	7.2%
Clopidogrel	34	7.0%
Hydrochlorothiazide	34	7.0%
Insulin glargine	31	6.4%
Acenocoumarol	31	6.4%
Gabapentin	31	6.4%
Pregabalin	29	6.0%
Donepezil	28	5.8%
Rivastigmine	28	5.8%
Latanoprost	27	5.6%
Tramadol	25	5.1%
Levodopa and decarboxylase inhibitor	25	5.1%
Lormetazepam	25	5.1%
Rivaroxaban	21	4.3%

(Continued in next column)

TABLE 4 (*Continued*) Summary of the 40 most frequent pharmacological treatments.

consideration the risk of hypotension, sedations, and, consequently, falls (Piccoliori et al., 2021).

A European study reported higher MRP rates, with the most frequent potentially severe DDIs being psychotropic drugs with additive effects on QTc prolongation, associations of angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers with potassium supplements, increasing the risk of hyperkalemia, and SSRI/SNRI with antiplatelets, increasing the risk of hemorrhage (Pasina et al., 2020). A study performed in a region in Italy showed that the three most frequent DDIs were antidepressants–anxiolytics (11.9%), SSRIs–aspirin (7.4%), and antidiabetics–β-adrenoceptor blockers (5.3%) (Burato et al., 2021).

Regarding the therapeutic duplications, excluding the prevalence of vitamin D or analogs associated with calcium, the rest was observed to be due to patients who are undergoing drug dose adjustments or changes. Both PREFASEG and Self-Audit detect therapeutic duplication, which helps explain the low percentage of duplications detected in this medication review (Pons-Mesquida et al., 2021; 2022). In a recent study done in a pediatric health system, where they designed clinical decision support to reduce therapeutic duplication with acetaminophen and ibuprofen, they saw a therapeutic duplication reduction, but it was associated with high rates of user frustration and alert fatigue (E Dawson et al., 2023).

There were drugs that were contraindicated, such as metformin and NSAIDs, due to chronic renal failure. During this intervention, the renal function was reviewed, and possible contraindications or dose adjustments were recommended according to glomerular filtration. If there was no determination during the last year, the convenience of performing an analysis was indicated (Wood et al., 2018; Writing Group for the CKD Prognosis Consortium et al., 2023). Another cross-sectional study on medication burden and inappropriate prescription risk among the elderly with advanced chronic kidney disease showed that at least one contraindicated drug was prescribed to 10.8% of all patients, and the most frequently prescribed were rilmenidine (16.5%), rosuvastatin (6.5%), alfuzosin (5.8%), and buflomedil (3.6%) (Roux-Marson et al., 2020). Antidepressants, antipsychotics, and benzodiazepines were mainly due to their anticholinergic effect and the increased risk of falls. This is similar to drugs deemed inappropriate or of doubtful efficacy; adding more prescribed drugs with anticholinergic effects increases the possibility of orthostatic hypotension and increased risk of falls (Catalan Health Service. Department of Health., 2020). This illustrates the main reasons why in frail patients, one must be even more consistent with the prior risk–benefit balance.

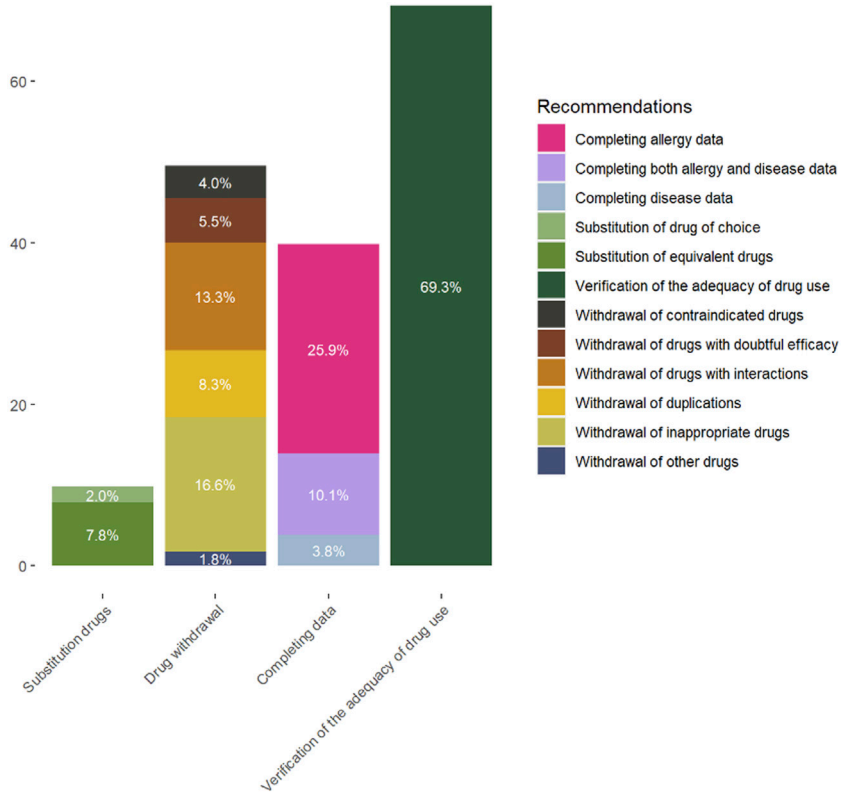

FIGURE 2
Percentages of the different recommendations subdivided.

5 Strengths and limitations

There were multiple strengths in this study. With the intervention, this study provided specific recommendations to each patient to reduce MRPs, PIMs, ADRs, and polypharmacy. The medical review was done by a medical doctor specializing in clinical pharmacology, who could change the prescriptions when needed, make an accurate medication review, and give individual recommendations. The availability of a common informatic system helped review the prescription registry and made it possible to act in a coordinated way between nursing homes and primary and hospital care. It was considered an advantage working on this project with primary care professionals, nursing homes, and medical doctors in geriatrics and clinical pharmacology, creating a multidisciplinary team with an agreed final decision.

However, there were also multiple limitations to the study. The intervention was conducted in one urban area, so the findings should be extrapolated to other regions or countries with caution. We gathered data from five different nursing homes, covering 22.3% of the population in the northern area of Barcelona, in Catalonia, so this may be representative of areas with a similar socioeconomic level. Second, the high changes in residents and the variability in the different nursing homes can make the interpretation and extrapolation of the data difficult (Ordovás et al., 2020; Rada, 2020). Third, since the intervention was carried out in routine clinical practice, some information is lacking, such as all non-pharmacological treatments, treatments not registered, or treatments not financed by the public health system, nor is there information on drug adherence. Additionally, the intervention was performed during the COVID-19 pandemic. The pandemic disrupted healthcare systems, leading to delays that influenced daily practice conditions and resulted in serious outcomes for elderly patients. This may have impacted our findings, given that the altered healthcare system complicated the clinical management of elderly populations. For instance, there was no adequate optimization of psychotropic drugs, in line with the social isolation and loneliness experienced in the pandemic, which led to depression, anxiety, cognitive decline, and exacerbation of pre-existing health conditions (Ministry of Health, Spain, 2020). To confirm these results and provide a broader international picture, similar assessment and prospective studies with a control group and out-of-the-pandemic context should be repeated in elderly people in different regions.

TABLE 5 List of all the medication-related problems mentioned in the pharmacological review.

Potential drug-drug interactions (n, %), (72, 14.9%)		Therapeutic duplications[b] (n, %), (38, 7.8%)**		Contraindications (n, %), (23, 4.7%)		Inappropriate drugs (n, %), (76, 15.7%)		Drug of doubtful efficacy (n, %), (22, 4.5%)	
Tramadol-SSRI	16 (22.2%)	Vitamin D and analogues	10 (13.1%)	Metformin	5 (21.7%)	Alprazolam	10 (13.1%)	Citicoline	6 (27.2%)
Tramadol-sertraline	8 (11.1%)	Calcium combined with vitamin D or other drugs	8 (10.5%)	Haloperidol	2 (8.7%)	Paroxetine	7 (9.2%)	Betahistine	5 (22.9%)
Tramadol-citalopram	5 (6.9%)	Levothyroxine sodium	4 (5.2%)	Citalopram	2 (8.7%)	Clonazepam	6 (7.9%)	Clebopride	2 (9.1%)
Tramadol-paroxetine	3 (4.1%)	Paracetamol	4 (5.2%)	Dabigatran etexilate	1 (4.3%)	Domperidone	5 (6.5%)	Glutamic acid hydrochloride	1 (4.5%)
Statins-calcium channel blockers	13 (18.0%)	Pregabalin	4 (5.2%)	Amiodarone	1 (4.3%)	Diazepam	5 (6.5%)	Cilostazol	1 (4.5%)
Simvastatin-amlodipine	9 (12.5%)	Quetiapine	4 (5.2%)	Hydralazine	1 (4.3%)	Digoxin	4 (5.2%)	Trimetazidine	1 (4.5%)
Simvastatin-diltiazem	3 (4.1%)	Trazodone	4 (5.2%)	Hydrochlorothiazide	1 (4.3%)	Doxazosin	4 (5.2%)	Naftidrofuryl	1 (4.5%)
Diltiazem-atorvastatin	1 (1.3%)	Omeprazole	3 (3.9%)	Spironolactone	1 (4.3%)	Metoclopramide	3 (3.9%)	Diosmin	1 (4.5%)
Acenocumarol	11 (15.3%)	Folic acid	3 (3.9%)	Enalapril	1 (4.3%)	Solifenacin	3 (3.9%)	Megestrol	1 (4.5%)
Acenocumarol-statins	6 (8.3%)	Furosemide	2 (2.6%)	Atorvastatin	1 (4.3%)	Potassium clorazepate	3 (3.9%)	Mirabegron	1 (4.5%)
Acenocumarol-levotyroxin	5 (6.9%)	Diltiazem	2 (2.6%)	Raloxifene	1 (4.3%)	Pentoxifylline	2 (2.6%)	Prunus africanae cortex	1 (4.5%)
SSRI and other drugs	11 (15.3%)	Bisoprolol	2 (2.6%)	Mirabegron	1 (4.3%)	Bisoprolol	2 (2.6%)	Levosulpiride	1 (4.5%)
Donezepil-citalopram	4 (5.5%)	Losartan	2 (2.6%)	Diclofenac	1 (4.3%)	Fesoterodine	2 (2.6%)		
Citalopram-amytriptiline	1 (1.3%)	Clobetasol	2 (2.6%)	Aceclofenac	1 (4.3%)	Hydroxyzine	2 (2.6%)		
Citalopram-domperidone	1 (1.3%)	Tramadol and paracetamol	2 (2.6%)	Dexketoprofen	1 (4.3%)	Clomethiazole	2 (2.6%)		
Citalopram-haloperidol	1 (1.3%)	Oxcarbazepine	2 (2.6%)	Alendronic acid	1 (4.3%)	Ursodeoxycholic acid	1 (1.3%)		
Citalopram-hydralazine	1 (1.3%)	Gabapentin	2 (2.6%)	Galantamine	1 (4.3%)	Liquid paraffin	1 (1.3%)		
Citalopram-sulpiride	1 (1.3%)	Levodopa and decarboxylase inhibitor	2 (2.6%)			Metformin	1 (1.3%)		
Citalopram-tapentadol	1 (1.3%)	Mirtazapine	2 (2.6%)			Hydralazine	1 (1.3%)		
Donezepil-escitalopram	1 (1.3%)	Pantoprazole	1 (1.3%)			Telmisartan and diuretics	1 (1.3%)		
Antiarrythmics and cardiac glicosides	8 (11.1%)	Vitamin B and acid folic	1 (1.3%)			Simvastatin	1 (1.3%)		
Amiodarone-beta blockers	2 (2.7%)	Hydrochlorothiazide	1 (1.3%)			Atorvastatin	1 (1.3%)		
Bisoprolol-alfuzosine	1 (1.3%)	Torasemide	1 (1.3%)			Febuxostat	1 (1.3%)		
Diltiazem-amlodipine	1 (1.3%)	Timolol and thiazides	1 (1.3%)			Trihexyphenidyl	1 (1.3%)		
Diltiazem-bisoprolol	1 (1.3%)	Captopril	1 (1.3%)			Haloperidol	1 (1.3%)		
Diltiazem-digoxin	1 (1.3%)	Enalapril	1 (1.3%)			Benzodiazepine	1 (1.3%)		
Flecainide-bisoprolol	1 (1.3%)	Fluticasone	1 (1.3%)			Bromazepam	1 (1.3%)		
Verapamil-propanolol	1 (1.3%)	Budesonide	1 (1.3%)			Loprazolam	1 (1.3%)		
Enalapril	5 (6.9%)	Timolol	1 (1.3%)			Zolpidem	1 (1.3%)		
Enalapril-potassium	3 (4.1%)	Latanoprost	1 (1.3%)			Amitriptyline	1 (1.3%)		
Enalapril-eplerenone	1 (1.3%)	Bimatoprost	1 (1.3%)			Trazodone	1 (1.3%)		
Enalapril-lithium	1 (1.3%)								
Other drugs[a]	8 (11.1%)								

n = total number of drugs with a related problem for each category in the pharmacological review.

[a]Other 8 DDIs: Simvastatin–carbamazepine (2)/amiodarone (1)/gemfibrozil (1), NSAIDs–acetylsalicylic acid (1), lamotrigine–valproic acid (1), omeprazole–cilostazol (1), and clozapine–carbamazepine (1).

[b]The therapeutic duplications are listed double since both drugs were noted. The drugs could be the same or from the same therapeutic family.

6 Conclusion

A high prevalence of health-related problems and number of prescribed drugs were observed through medication review in nursing homes. Many recommendations were made, confirming the increasing incidence of polypharmacy and the need for standardized interventions to reduce medication-related problems and the number of prescribed drugs. Specific interventions targeting nursing homes could lower the percentages of medication-related problems. Tools and clinical decision support systems help in reviewing the medication of the patients. This should be addressed with a multidisciplinary team approach, including general practitioners, geriatric assessment, a clinical pharmacist, and a clinical pharmacologist.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material; further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by the Ethics Committees of Vall Hebron University Hospital and IDIAP Jordi Gol. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and institutional requirements.

Author contributions

EA-N: writing–original draft and writing–review and editing. MS-AR: writing–review and editing. MB: writing–review and editing. MS: writing–review and editing. EF-L: writing–review and editing. AS-J: writing–review and editing. MB-C: writing–review and editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fphar.2024.1320490/full#supplementary-material

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4.2 SECOND STUDY

The impact of a multidisciplinary team intervention on medication prescription in nursing homes in Catalonia.

Anderssen-Nordahl E, Fernández-Liz E, Sabaté Gallego M, Bosch Ferrer M, Sánchez-Arcilla Rosanas M, Cervera León M, Magrinyà JM and Barceló-Colomer ME (2024) The impact of a multidisciplinary team intervention on medication prescription in nursing homes in Catalonia. Front. Pharmacol. 15:1445141. doi: 10.3389/fphar.2024.1445141

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The impact of a multidisciplinary team intervention on medication prescription in nursing homes in Catalonia

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Background: In response to the rising population of nursing home residents with frailty and multimorbidity, optimizing medication safety through drug utilization review and addressing medication-related problems (MRPs) is imperative. Clinical decision support systems help reduce medication errors and detect potential MRPs, as well as medication reviews performed by a multidisciplinary team, but these combined assessments are not commonly performed. The objective of this study was to evaluate the impact on medication plans of a multidisciplinary team intervention in nursing homes, by analyzing the medication plan before and after the intervention and assessing whether the recommendations given had been implemented.

Methods: A multicenter before-after study, involving five nursing homes, assessed the impact of a multidisciplinary team intervention, to estimate effectiveness related to the review of the prescribed medications. The follow-up period for each patient was 12 months or until death if prior, from July 2020 to February 2022, and involved 483 patients. The clinical pharmacologist coordinated the intervention and reviewed all the prescribed medications to make recommendations, focused on the completion of absent data, withdrawal of a drug, verification of whether a drug was adequate, the substitution of a drug, and the addition of drugs. Since the intervention was performed during the COVID-19 pandemic, optimization of psychotropic drugs and absorbent pads were limited.

Results: The intervention had an impact with recommendations given for 398 (82.4%) of the patients and which were followed by 58.5% of them. At least one drug was withdrawn in 293 (60.7%) of the patients, with a mean of 2.3 (SD 1.7). As for the total of 1,097 recommendations given, 355 (32.4%) were followed. From the intervention, antipsychotics, antidepressants, benzodiazepines, statins, and diuretics were the most frequently withdrawn.

Conclusion: The findings underscore the impact of targeted interventions to reduce inappropriate medications and enhance medication safety in nursing homes. The proposed recommendations given and followed show the importance of a multidisciplinary team, coordinated by a clinical pharmacologist, for a patient-centered approach to make medication reviews regularly, with the help of clinical decision support systems, to help reduce potential MRPs and polypharmacy.

KEYWORDS

drug utilization review, patient care team, frail elderly, nursing homes, potentially inappropriate medication list

1 Introduction

In recent years, the healthcare system has witnessed a marked rise in the number of nursing home residents with frailty and multimorbidity. It has therefore become essential to ensure that such individuals receive the safest and most accurate medication. Effective medication reviews with computerized drug utilization review (DUR) and the elimination of medication-related problems (MRPs) in nursing homes are crucial for optimizing patient care (Kojima, 2015; Fog et al., 2017; Osmani et al., 2023).

A computerized DUR is defined as a formal program for assessing drug prescription and patient safety. It assesses whether patients receive appropriate medication and aims to identify MRPs (Kim et al., 2021). Implementing DUR programs to monitor drug therapy seems to reduce the risk of medication errors and adverse drug reactions (ADRs) (Osmani et al., 2023). In primary healthcare in Catalonia, a clinical decision support system (CDSS) has been implemented to improve patient safety. It entails the Self Audit tool and PREFASEG (*PREscripción FArmacéutica SEGura*, i.e., safe pharmaceutical prescription) (Pons-Mesquida et al., 2021; Pons-Mesquida et al., 2022). A CDSS and its tools can help review patients' medication, and should be addressed with a multidisciplinary team approach, including a clinical pharmacologist and a clinical pharmacist (Anderssen-Nordahl et al., 2024).

An MRP is a situation involving drug therapy that can potentially interfere with health outcomes. Some MRPs include therapeutic duplications, possible drug-drug interactions (DDIs), potentially inappropriate medications (PIMs), and contraindicated drugs (Troncoso-Mariño et al., 2021). It is essential to prevent MRPs through regular medication reviews to ensure the well-being of nursing home residents.

Such individuals with frailty and multimorbidity require a personalized approach to medication management and deprescribing. This involves understanding their health priorities, assessing disease burden, evaluating treatment risks and benefits, and agreeing on an individualized treatment plan (NICE Guideline, 2016). Polypharmacy and MRPs are more prevalent in this population thus increasing the risk of ADRs and DDIs (Lavan et al., 2016). Polypharmacy is defined as the simultaneous use of five or more medications, while excessive polypharmacy refers to the use of ten or more medications (Zahlan et al., 2023). Another type of inappropriate polypharmacy is the continuous addition of new drugs to manage adverse events related to avoidable medications, which can create a prescribing cascade (Falster et al., 2021). Evidence shows that the most powerful strategy to cope with inappropriate drug use and polypharmacy is poly-deprescribing, which implies stopping as many non-lifesaving medications as possible (Campins et al., 2017; Garfinkel and Bilek, 2020). Several studies have already reported that the use of deprescribing tools, supported by multidisciplinary teams with physicians, reduced inappropriate polypharmacy in hospitalized, nursing home and primary care older patients. In addition, the tools helped physicians decide whether to withdraw the prescription, how to withdraw it, and how to communicate the deprescription to older hospitalized patients (Cooper et al., 2015; Kua et al., 2019; Duong et al., 2021; Faulkner et al., 2022; Cole et al., 2023).

A multidisciplinary approach, integrating a team of healthcare professionals from different disciplines and specialties, aimed at reaching a combined decision on a complex situation, is essential for the optimal care of nursing home residents with advanced dementia. Interprofessional teamwork allows the sharing of experience, clinical expertise, varying disciplinary perspectives, and knowledge about institutionalized patients. All of which permits the performance of an effective DUR, the management of inappropriate drugs, and the creation of optimal individualized medication. Continuing with medication should be considered an active decision that carries as much responsibility as when initiating or ceasing treatment (Disalvo et al., 2020; Cole et al., 2023; Song et al., 2023). Medication reviews in Central and Eastern European countries are also conducted by clinical pharmacists. Some studies indicate that these reviews can be beneficial for the elderly, helping to prevent MRPs and ensuring the safe and effective use of medications, particularly regarding medication adherence. However, these practices remain underdeveloped and underutilized in certain parts of Europe (Ibrahim et al., 2021; Saeed et al., 2022; Urbańczyk et al., 2023). Nonetheless, in Catalonia, there is a home healthcare program (ATDOM) at the primary care level. A study intends to conduct a pragmatic randomized clinical trial with a control group to evaluate the effectiveness of a pharmacist-led intervention. This intervention will focus on optimizing the pharmacological treatment of patients enrolled in the ATDOM program. Through prospective follow-up, the study will assess the potential of the intervention to reduce MRPs and enhance the overall quality of care for these patients (Salom-Garrigues et al., 2024). Additionally, a before-and-after intervention study in Catalonia evaluated the impact of a pharmaceutical intervention on optimizing treatment for patients with type 2 diabetes mellitus. Of the recommendations made by a pharmacist or clinical pharmacologist, 54.7% were successfully implemented (Canadell-Vilarrasa et al., 2024).

Whilst many previous studies have examined the effectiveness of medicine optimization interventions to improve appropriate polypharmacy and reduce MRPs in older people and elderly individuals residing in nursing homes, there are few registered interventions of quality (Cooper et al., 2015; Saeed et al., 2022; Sluggett et al., 2022; Cole et al., 2023). As for similar interventions in nursing homes, during the SARS-CoV-2 pandemic, there are none published to date. It is estimated that 50% of medication errors and 20% of ADRs could be avoided with proper medication reconciliation, which would contribute to improving patient safety. It is therefore crucial to review and reconcile medication, carry out deprescription when appropriate, and assess adherence. According to the Catalan Health Service instruction 04/2012, all patients with chronic treatment should undergo a pharmacological review at least once a year (Department of Health, Government of Catalonia, 2014).

The SARS-CoV-2 pandemic created a great challenge for the care of institutionalized patients. For this reason, a multidisciplinary team was created in Catalonia, Spain, to perform a structured intervention in nursing homes. The intervention consisted of reviewing medication plans, detecting MRPs, and developing an improvement strategy with proposals.

The objective of this study was to evaluate the impact on medication plans of a multidisciplinary team intervention in nursing homes, by analyzing the medication plan before and after the intervention and assessing whether the recommendations proposed had been implemented.

2 Methods

2.1 Study design and setting

A multicenter before-after study was performed, without a control group, to estimate effectiveness related to the review of the prescribed medications. From a total of 48 nursing homes in the northern area of Barcelona, Spain, data were collected from 5. These 5 nursing homes were prioritized by the health administration due to their size, for efficiency, and to cover the highest population percentage. From such a selection, even though only 5 were evaluated, the intervention covered 22.3% of the total residents in the nursing homes in the northern area of Barcelona. The study population included all patients currently admitted to a nursing home at the start of this intervention, which began in July 2020. Patient follow-up was from the beginning of the intervention until 1 year later or until death if prior, finalizing in February 2022.

The inclusion criteria encompassed institutionalized patients with public health coverage provided by the Catalan Health Service during the study period. The exclusion criteria were institutionalized patients with health coverage provided by other insurers, short-term life expectancy, hospitalization during the intervention, death or discharge in the first month of the review, and individuals who could not be intervened due to lack of information. There was no formal sample size calculation since the analysis was carried at on all the reviewed patients with the exception of those excluded.

The study design, procedures, and reporting followed the TREND guidelines for nonrandomized evaluations of behavioral and public health interventions (Des Jarlais et al., 2004) and are registered at ENCePP (Reference: EUPAS106748).

2.2 The intervention

This structured intervention was performed during the COVID-19 pandemic. It consisted of systematically evaluating the prescribed medications, and reviewing the validity of prescriptions and medication plans. With this intervention, a description of the prescribed medication before and after a year was made, and potential MRPs were detected. The MRPs registered were potential DDIs, therapeutic duplications, contraindications, and drugs deemed inappropriate or of doubtful efficacy.

The multidisciplinary team included general practitioners (GPs), nurses, social and administrative workers from primary care, clinicians and nurses assigned to the nursing homes, a clinical pharmacist, and a clinical pharmacologist. They systematically evaluated the prescribed medications to promote safe and healthy prescription (Anderssen-Nordahl et al., 2024). The clinical pharmacologist was the medical doctor specialist who coordinated the multidisciplinary team and actively reviewed all the prescribed medications to make recommendations. These recommendations were discussed with the team and the final decision was supported or not by the physician in each nursing home, who then decided how to convey this information to the patients or their representatives. The clinical pharmacologist employed around 50 min per patient thus an average of 10 patients could be reviewed daily. Intervention duration was from the first review on 1st July 2020 to the last one on the 5th March 2021. The first follow-up after a year started on 2nd August 2021 and lasted until the final follow-up on the 28th February 2022. Since the intervention took place during the pandemic, optimization of psycholeptic drugs and absorbent pads was limited.

Several recommendations arose from the issues identified during the medication review. They included the completion of absent data, withdrawal of a drug, verification of whether a drug was adequate, the substitution of a drug, and adding a drug. With respect to the data, allergies or diseases could be absent. Drug withdrawal was recommended taking into account potential MRPs. They included potential DDIs, duplicated therapies, contraindicated drugs, inappropriate drugs, or drugs of doubtful efficacy. Adequacy of drug use was related to the need for dosage reduction, bad tolerance, lowering of the anticholinergic load, or a high risk of ADRs. As for drug substitution, this could be recommended due to considering other drugs as a first choice or an equivalent. Regarding the addition of medications, it was recommended only in specific cases: vitamin B12 and folic acid or iron for anemia and deficiency, thyroid hormone for clear hypothyroidism, osteoporotic treatment for patients with fragility fractures, and proton pump inhibitors when indicated. The addition of drugs was advised only when it was evident that they were necessary.

The standard used to establish whether drugs were considered MRPs was the information contained in the technical information sheets, the support tools Self-Audit and PREFASEG (Pons-Mesquida et al., 2021; Pons-Mesquida et al., 2022), and the list of potentially inappropriate drugs and criteria proposed by the Catalan

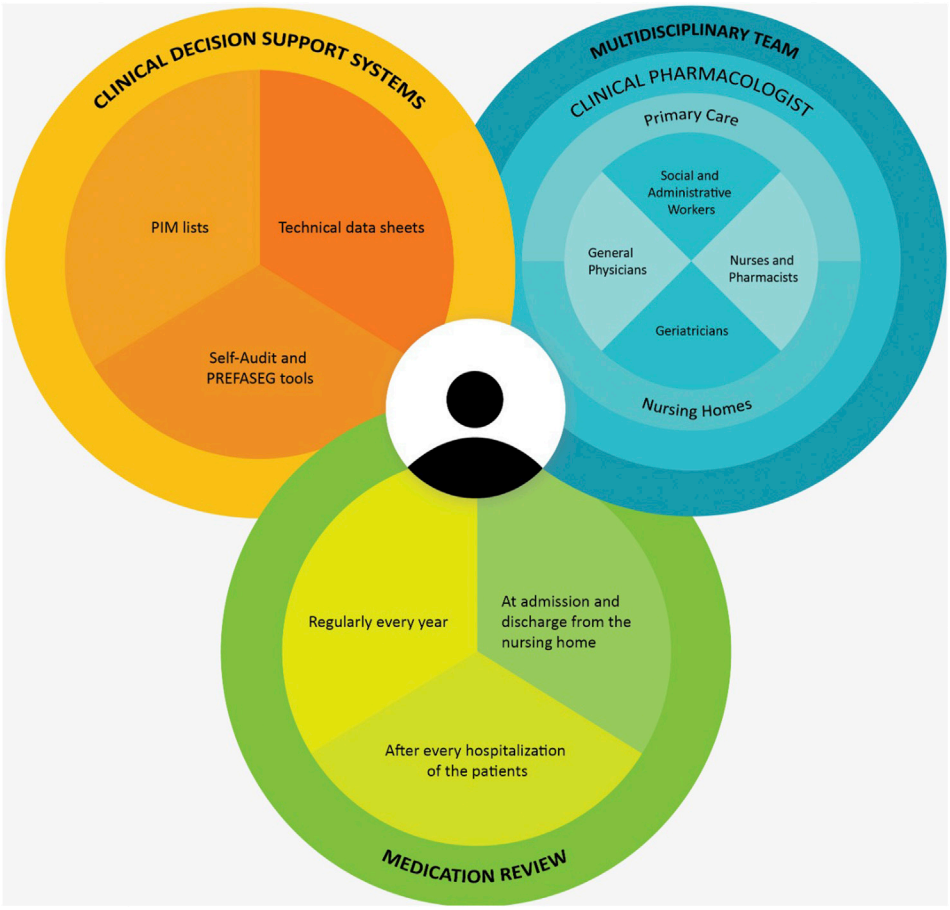

FIGURE 1
The intervention with a multidisciplinary team.

Health Service (Department of Health, Government of Catalonia, 2014; Catalan Health Service: Department of Health, 2020).

The support tools were the Self-Audit and PREFASEG. The Self Audit identifies and systematically resolves MRPs. It generates a list of patients with active MRPs so as to facilitate treatment changes or suspensions (Pons-Mesquida et al., 2022). PREFASEG generates online notifications when starting a treatment to warn clinicians of potential problems related to drug use and prevent medication errors (Pons-Mesquida et al., 2021). The computerized medical record notifies the healthcare professionals when a patient is attended by another professional and explains the medication changes made.

The criteria proposed by the Catalan Health Service on potentially inappropriate drugs in the elderly (Catalan Health Service: Department of Health, 2020) were based on documents regarding the management of medication in chronic patients (Department of Health, Government of Catalonia, 2014). Such documents were prepared by consensus from a group of experts. The criteria for the drugs to be included on the potentially inappropriate list were to appear in at least 2 bibliographic databases, with an explicit recommendation or contraindication for the elderly population in the technical sheet, or with a specific alert from the Spanish Agency for Medicines and Health Products (AEMPS, Agencia Española de Medicamentos y Productos Sanitarios). The references used were the Beers criteria, STOPP/START, the EU-PIM list, the PRISCUS list, information notes on medicines for human use from the AEMPS, and anticholinergic risk scales in older adults (Department of Health, Government of Catalonia, 2014; Catalan Health Service: Department of Health, 2020; American Geriatrics Society Beers Criteria® Update Expert Panel, 2023; Mann et al., 2023; O'Mahony et al., 2023).

The patient-centered intervention with the multidisciplinary team, medication review, and supporting tools is shown in Figure 1.

2.3 Variables and data collection

The variables analyzed were the number of prescribed medications including fixed-dose combinations and absorbent pads before and after the intervention, recommendations given, drugs recommended to be withdrawn, changed or considered adequate, drugs withdrawn or added, and the number of deaths. Medications were recorded according to the Anatomical Therapeutic Chemical (ATC) classification system.

The data were collected in usual clinical practice during the intervention, from common electronic medical records. A

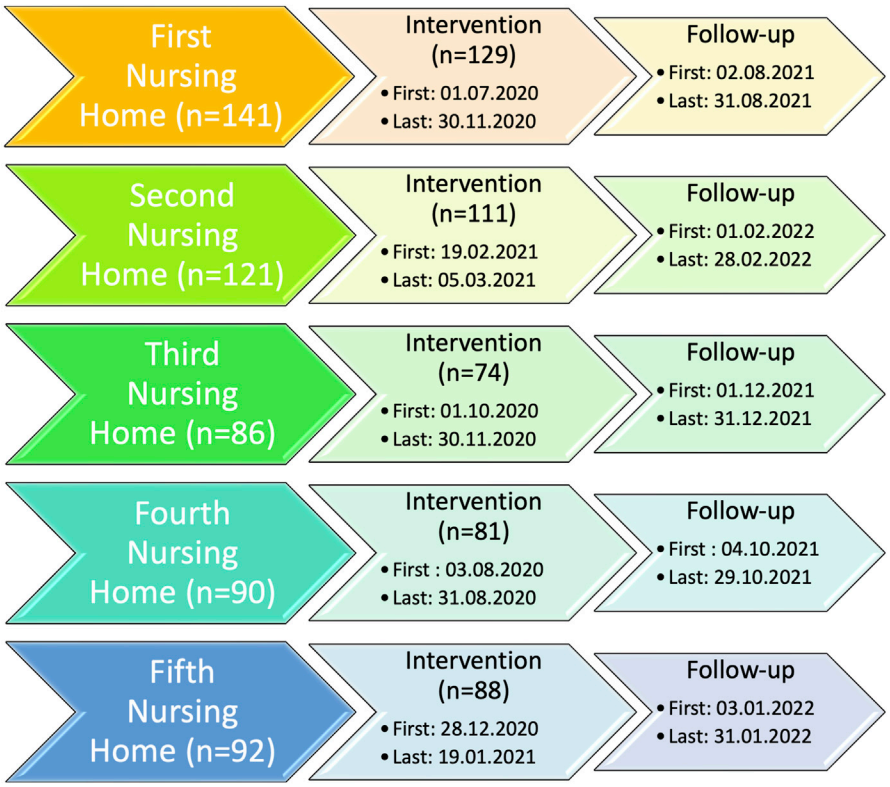

FIGURE 2
Calendar of all the patients from the intervention until follow-up divided into the five nursing homes. * All patients from the intervention were followed up.

computerized clinical history program is used by all professionals in the primary care network in Catalonia (Primary Care Clinical Station, 2024). The anonymized information was then entered into the Research Electronic Data Capture (REDCap) platform. REDCap is an electronic data capture software and workflow methodology for designing research databases for clinical trials and translational research. The privacy policies and code of conduct of REDCap platform can be consulted at the following link: https://projectredcap.org/. A quality check was carried out prior to analysis.

2.4 Ethics approval

The study was conducted according to the guidelines of the Declaration of Helsinki. The protocol was approved by both local Research Ethics Committees Vall Hebron University Hospital (protocol code EOM (AG) 067/2021 (5,930)) and IDIAP Jordi Gol (protocol code 22/027-P). No informed consent was necessary since the information was anonymized.

2.5 Statistical analysis

A descriptive analysis was performed of drugs prescribed, use of absorbent pads, recommendations given, drugs recommended to be withdrawn, changed or considered adequate, drugs withdrawn or added, and the number of deaths after a year. A comparative analysis of before and after the intervention was carried out with the total of patients, recommendations, and deaths after a year. For the analysis, continuous variables are presented as means (standard deviation, SD) and categorical variables as frequencies (percentages). Statistical analysis was performed using R version 4.3.0.

3 Results

3.1 General characteristics of the institutionalized patients

The intervention started on 1st July 2020 and ended on 28th February 2022, with the last follow-up after a year, as shown in Figure 2.

A total of 483 patients were included from 5 different nursing homes. Initially, there were 530 patients, however, due to exclusion criteria 47 were not included. These 47 exclusions were 9 patients with health coverage provided by other insurers, 5 with a short-term life expectancy, 14 hospitalized during the intervention, 7 lost to follow-up in the first month, and 12 due to lack of information.

At baseline, the mean age of the 483 patients included was 86.3 (SD 8.8) years, and 348 (72.0%) were female. The mean of the health-related problems (HRPs) was 17.4 (SD 5.6), and the mean number of prescribed medications was 8.22 (SD 3.5), including fixed-dose combinations. All the other onset clinical characteristics,

TABLE 1 Description of all the recommendations given and followed.

	Recommendations given, n	%	Recommendations followed, n	%	%*
Completing data	173	15.8	81	22.8	46.8
Allergy data	118	10.8	66	18.6	55.9
Disease data	55	5.0	15	4.2	27.3
Withdrawal of drugs	318	29.0	136	38.3	42.8
Withdrawal of inappropriate drugs	66	6.0	35	9.9	53.0
Withdrawal of drugs with interactions	53	4.8	26	7.3	49.1
Withdrawal of duplications	33	3.0	19	5.4	57.6
Withdrawal of drugs with doubtful efficacy	22	2.0	14	3.9	63.6
Withdrawal of contraindicated drugs	16	1.5	10	2.8	62.5
Witdrawal of other drugs	128	11.7	32	9.0	25.0
Substitution of drugs	45	4.1	11	3.1	24.4
Substitution of equivalent drugs	35	3.2	8	2.3	22.9
Substitution of drug of choice	10	0.9	3	0.8	30.0
Verification of the adequacy of drug use	561	51.1	127	35.8	22.6
Total	1097	100.0	355	100.0	32.4

n = number of recommendations that were given and followed.
%*, percentage of the recommendations followed compared to those given.

descriptive analysis of recommendations, incomplete data, medication recommended to verify adequacy of use, substitution, or withdrawal, and MRPs, have been previously described and commented on (Anderssen-Nordahl et al., 2024).

3.2 Impact of the intervention in nursing homes

In the 483 patients in the five nursing homes, the total number of prescribed drugs, including fixed-dose combinations, prior to the intervention and 1 year after was 3,962 and 3,893, respectively. A total of 374 (77.43%) patients used absorbent pads at the commencement of the intervention, a figure which increased to 420 (86.95%) 1 year later.

Of the 398 (82.4%) patients who received recommendations 233 (58.5%) patients followed. The recommendations given varied from 1 to 6 per patient, with a mean of 2.2 (SD 1.1). The various recommendations offered and taken up, with the total and percentage of compliance, are shown in Table 1.

A total of 318 prescribed medications were recommended to be withdrawn in 192 patients and 136 (42.8%) were removed. The five drugs most recommended in this category were omeprazole (n = 54, 17.0%), acetylsalicylic acid (n = 14, 4.4%), alprazolam (n = 11, 3.5%), simvastatin (n = 10, 3.1%), and lorazepam (n = 10, 3.1%). At follow-up, the 5 drugs that were most withdrawn were omeprazole (n = 9, 6.6%), citalopram (n = 5, 3.7%), diazepam (n = 5, 3.7%), domperidone (n = 5, 3.7%), and vitamin D and analogues (n = 5, 3.7%). All the drugs recommended to be withdrawn and those withdrawn in the pharmacological review, divided according to their ATC classification, are shown in Table 2.

Of the 45 drugs recommended to be changed in 39 patients, 11 (24.4%) were altered. The complete list of the drugs recommended to be changed and those changed during the intervention, divided according to their ATC classification, are shown in Table 3.

Finally, of the 561 drugs recommended as adequate in 276 patients, 127 (22.6%) were withdrawn. The five most frequently recommended were quetiapine (n = 56, 10.0%), acetylsalicylic acid (n = 34, 6.1%), furosemide (n = 30, 5.3%), risperidone (n = 26, 4.6%), and trazodone (n = 26, 4.6%). From this category of drugs, the five most frequently withdrawn were quetiapine (n = 10, 7.9%), risperidone (n = 10, 7.9%), acetylsalicylic acid (n = 7, 5.6%), tramadol (n = 6, 4.8%), and pregabalin (n = 5, 4.0%). All the drugs recommended to be adequate with the drugs withdrawn, are divided according to their ATC classification, are shown in Table 4.

In a total of 293 (60.7%) patients, between 1 and 9 drugs were withdrawn, with a mean of 2.3 (SD 1.7), and a total of 695 drugs. In spite of our recommendations for prescribed medications to be withdrawn, changed, or considered adequate, we could only record the withdrawn ones.

With respect to additional medication, in 276 (57.1%) patients, between 1 and 8 drugs were added, with a mean of 2.2 (SD 1.4), and a total of 626 drugs at the end of the intervention. The most frequently added drugs are shown in Table 5. A complete list of all the prescribed drugs that have been added are shown in Supplementary Table S1, and according to their ATC classification in Supplementary Table S2.

During the intervention, a total of 86 (17.8%) deaths were recorded. Of the 233 patients in whom the recommendations were adhered to there were 37 deaths (15.8%), and of the 165 patients who did not follow the recommendations there were 33 deaths (20.0%).

TABLE 2 Drugs recommended to be withdrawn with the drugs withdrawn in the pharmacological review.

Drugs recommended to withdraw				Withdrawn	
		n	%	n	%*
A- Alimentary tract and metabolism					
A02BC	Proton pump inhibitors	56	17.6	9	16.1
A02BC01	Omeprazole	54	17.0	9	16.7
A02BC02	Pantoprazole	1	0.3	0	0.0
A02BC03	Lansoprazole	1	0.3	0	0.0
A03AX13	Silicones	1	0.3	1	100.0
A03FA	Propulsives	12	3.8	9	75.0
A03FA01	Metoclopramide	3	0.9	2	66.7
A03FA03	Domperidone	6	1.9	5	83.3
A03FA06	Clebopride	3	0.9	2	66.7
A05AA02	Ursodeoxycholic acid	1	0.3	0	0.0
A09AB01	Glutamic acid hydrochloride	1	0.3	0	0.0
A10B	Blood glucose lowering drugs, excluding insulins	15	4.7	2	13.3
A10BA02	Metformin	8	2.5	1	12.5
A10BB09	Gliclazide	4	1.3	0	0.0
A10BH02	Vildagliptin	1	0.3	1	100.0
A10BH03	Saxagliptin	1	0.3	0	0.0
A10BH05	Linagliptin	1	0.3	0	0.0
A11CC	Vitamin D and analogues	8	2.5	5	62.5
A12AX	Calcium with vitamin D	1	0.3	0	0.0
A12BA	Potassium	4	1.3	4	100.0
B- Blood and blood forming organs					
B01AC	Platelet aggregation inhibitors	15	4.7	1	6.7
B01AC06	Acetylsalicylic acid	14	4.4	0	0.0
B01AC23	Cilostazol	1	0.3	1	100.0
B02AA02	Tranexamic acid	1	0.3	1	100.0
B03BA	Vitamin B12 and folic acid	3	0.9	2	66.7
B03BA01	Cyanocobalamin	3	0.9	0	0.0
B05XA13	Hydrochloric acid	1	0.3	0	0.0
C- Cardiovascular system					
C01AA05	Digoxin	5	1.6	1	20.0
C01BD01	Amiodarone	1	0.3	1	100.0
C01EB15	Trimetazidine	1	0.3	1	100.0
C02CA04	Doxazosin	4	1.3	1	25.0
C02DB02	Hydralazine	1	0.3	1	100.0
C03AA03	Hydrochlorothiazide	1	0.3	0	0.0
C03CA	Sulfonamides, plain	7	2.2	3	42.9

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TABLE 2 (*Continued*) Drugs recommended to be withdrawn with the drugs withdrawn in the pharmacological review.

Drugs recommended to withdraw				Withdrawn	
		n	%	n	%*
C03CA01	Furosemide	6	1.9	2	33.3
C03CA04	Torasemide	1	0.3	1	100.0
C03DA01	Spironolactone	1	0.3	0	0.0
C04AD03	Pentoxifylline	3	0.9	2	66.7
C05AE03	Diltiazem	1	0.3	1	100.0
C05CA03	Diosmin	1	0.3	0	0.0
C07AB12	Nebivolol	1	0.3	0	0.0
C08CA01	Amlodipine	2	0.6	1	50.0
C09AA02	Enalapril	2	0.6	2	100.0
C09CA01	Losartan	1	0.3	1	100.0
C09DA07	Telmisartan and diuretics	1	0.3	0	0.0
C09DB02	Olmesartan medoxomil and amlodipine	1	0.3	1	100.0
C10A	Lipid modifying agents	17	5.3	9	52.9
C10AA01	Simvastatin	10	3.1	3	30.0
C10AA05	Atorvastatin	5	1.6	4	80.0
C10AB04	Gemfibrozil	1	0.3	1	100.0
C10AB05	Fenofibrate	1	0.3	1	100.0
D- Dermatologicals					
D01AE16	Amorolfine	1	0.3	1	100.0
G- Genito urinary system and sex hormones					
G03AC05	Megestrol	1	0.3	1	100.0
G03XC01	Raloxifene	1	0.3	1	100.0
G04BD	Drugs for urinary frequency and incontinence	7	2.2	4	57.1
G04BD08	Solifenacin	3	0.9	1	33.3
G04BD11	Fesoterodine	2	0.6	2	100.0
G04BD12	Mirabegron	2	0.6	1	50.0
G04BX01	Magnesium hydroxide	1	0.3	0	0.0
G04CA	Alpha-adrenoreceptor antagonists	3	0.9	0	0.0
G04CA01	Alfuzosin	1	0.3	0	0.0
G04CA02	Tamsulosin	2	0.6	0	0.0
G04CX01	Prunus africanae cortex	1	0.3	0	0.0
H- Systemic hormonal preparations					
H03AA01	Levothyroxine sodium	1	0.3	0	0.0
M- Musculo-skeletal system					
M01A	Anti-inflammatory and antirheumatic, non-steroids	7	2.2	6	85.7
M01AB05	Diclofenac	4	1.3	4	100.0
M01AB16	Aceclofenac	1	0.3	1	100.0

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TABLE 2 (*Continued*) Drugs recommended to be withdrawn with the drugs withdrawn in the pharmacological review.

Drugs recommended to withdraw				Withdrawn	
		n	%	n	%*
M01AE17	Dexketoprofen	1	0.3	1	100.0
M01AE52	Naproxen and esomeprazole	1	0.3	0	0.0
M04AA	Preparations inhibiting uric acid production	3	0.9	1	33.3
M04AA01	Allopurinol	2	0.6	0	0.0
M04AA03	Febuxostat	1	0.3	1	100.0
M05B	Drugs affecting bone structure and mineralization	2	0.6	1	50.0
M05BA04	Alendronic acid	1	0.3	0	0.0
M05BX04	Denosumab	1	0.3	1	100.0
N- Nervous system					
N02A	Opioids	11	3.5	4	36.4
N02AB03	Fentanyl	1	0.3	0	0.0
N02AX02	Tramadol	8	2.5	3	37.5
N02AX06	Tapentadol	2	0.6	1	50.0
N02B	Other analgesics and antipyretics	7	2.2	6	85.7
N02BB02	Metamizole sodium	4	1.3	3	75.0
N02BE01	Paracetamol	3	0.9	3	100.0
N03A	Antiepileptics	7	2.2	3	42.9
N03AE01	Clonazepam	5	1.6	2	40.0
N03AX12	Gabapentin	2	0.6	1	50.0
N04BA02	Levodopa and decarboxylase inhibitor	1	0.3	9	900.0
N05A	Antipsychotics	9	2.8	5	55.6
N05AD01	Haloperidol	4	1.3	3	75.0
N05AH04	Quetiapine	3	0.9	0	0.0
N05AL07	Levosulpiride	1	0.3	1	100.0
N05AX08	Risperidone	1	0.3	1	100.0
N05B	Anxiolytics	30	9.4	17	56.7
N05BA	Benzodiazepine derivative anxiolytics	1	0.3	1	100.0
N05BA01	Diazepam	5	1.6	5	100.0
N05BA05	Potassium clorazepate	1	0.3	1	100.0
N05BA06	Lorazepam	10	3.1	4	40.0
N05BA12	Alprazolam	11	3.5	4	36.4
N05BB01	Hydroxyzine	2	0.6	2	100.0
N05C	Hypnotics and sedatives	10	3.1	4	40.0
N05CD06	Lormetazepam	1	0.3	0	0.0
N05CD11	Loprazolam	1	0.3	1	100.0
N05CF02	Zolpidem	1	0.3	0	0.0
N05CM02	Clomethiazole	7	2.2	3	42.9

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TABLE 2 (*Continued*) Drugs recommended to be withdrawn with the drugs withdrawn in the pharmacological review.

Drugs recommended to withdraw				Withdrawn	
		n	%	n	%*
N06A	Antidepressants	22	6.9	9	40.9
N06AA09	Amitriptyline	1	0.3	1	100.0
N06AB03	Fluoxetine	1	0.3	0	0.0
N06AB04	Citalopram	6	1.9	5	83.3
N06AB05	Paroxetine	2	0.6	0	0.0
N06AB06	Sertraline	3	0.9	1	33.3
N06AX05	Trazodone	2	0.6	1	50.0
N06AX11	Mirtazapine	6	1.9	1	16.7
N06AX16	Venlafaxine	1	0.3	0	0.0
N06BX06	Citicoline	5	1.6	4	80.0
N06D	Anti-dementia drugs	4	1.3	3	75.0
N06DA02	Donepezil	1	0.3	1	100.0
N06DA03	Rivastigmine	1	0.3	1	100.0
N06DA04	Galantamine	1	0.3	0	0.0
N06DX01	Memantine	1	0.3	1	100.0
N07CA01	Betahistine	8	2.5	4	50.0
R- Respiratory system					
R01AD05	Budesonide	1	0.3	1	100.0
S- Sensory organs					
S01EC01	Acetazolamide	1	0.3	1	100.0
S01EE01	Latanoprost	1	0.3	1	100.0
	Total active substances	103	32.4	70	68.0
	Total	318	100.0	136	42.8

n = total number of drugs recommended to withdraw, and the total number of drugs withdrawn.
%*, percentage of the drugs withdrawn compared to those recommended to be withdrawn.

4 Discussion

The objective of this study was to evaluate the impact of a multidisciplinary team intervention on medication plans in nursing homes. The results showed 1,097 recommendations were provided to 82.4% of the patients. Of these proposals, 32.4% were taken up thus considerably influencing prescribing practices and accepted by the GPs. The intervention, aimed at optimizing medication management, changed the total number of prescribed medications from 3,962 to 3,893 over 1 year. A figure influenced by the fact that drugs were not only withdrawn but also added when necessary. Although such a decrease was not significant, it should be taken into account that there was a 5.9% increase in the number of prescriptions from the Catalan Health Service centers in the period 2022 compared to 2021, and 4.12% in the period 2021 compared to 2020 (Catalan Health Service, 2024). In addition, these results are similar to other studies reporting that an integrated health intervention, performed in elderly people and nursing home residents, focusing on polypharmacy and inappropriate prescribing, proved useful in improving medication use. Nevertheless, there was no statistically significant reduction in the number of prescribed medications (Wallerstedt et al., 2014; Rankin et al., 2018; San-José et al., 2021; Spinewine et al., 2021; Saeed et al., 2022; Cole et al., 2023).

4.1 General characterization of the institutionalized patients

A marked prevalence of HRPs and number of prescribed drugs were observed throughout the medication review in all the nursing homes. The most commonly prescribed inappropriate medications were proton pump inhibitors (PPIs), analgesics, and antipsychotics/tranquilizers, with a total of 47.8% MRPs (Anderssen-Nordahl et al., 2024). Such a finding is similar to others, as commented in a 2021 review in which the most reported inappropriate

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TABLE 3 Drugs recommended to be changed with the drugs changed in the pharmacological review.

Drugs recommended to change				Changed	
		n	%	n	%*
A- Alimentary tract and metabolism					
A02BC	Proton pump inhibitors	6	13.3	1	16.7
A02BC02	Pantoprazole	3	6.7	1	33.3
A02BC03	Lansoprazole	1	2.2	0	0.0
A02BC05	Esomeprazole	2	4.4	0	0.0
A06AA01	Liquid paraffin	1	2.2	1	100.0
A10BH02	Vildagliptin	1	2.2	0	0.0
B- Blood and blood forming organs					
B01A	Antithrombotic agents	5	11.1	0	0.0
B01AE07	Dabigatran etexilate	2	4.4	0	0.0
B01AF01	Rivaroxaban	3	6.7	0	0.0
C- Cardiovascular system					
C03CA01	Furosemide	1	2.2	0	0.0
C07BA06	Timolol and thiazides	1	2.2	0	0.0
C09AA02	Enalapril	1	2.2	1	100.0
C09CA	Angiotensin II receptor blockers	6	13.3	0	0.0
C09CA02	Eprosartan	1	2.2	0	0.0
C09CA04	Irbesartan	1	2.2	0	0.0
C09CA07	Telmisartan	2	4.4	1	50.0
C09CA08	Olmesartan medoxomil	2	4.4	0	0.0
C10AA	HMG CoA reductase inhibitors	7	15.6	2	28.6
C10AA01	Simvastatin	4	8.9	1	25.0
C10AA05	Atorvastatin	2	4.4	1	50.0
C10AA08	Pitavastatin	1	2.2	0	0.0
N- Nervous system					
N02AB03	Fentanyl	1	2.2	1	100.0
N02AX02	Tramadol	1	2.2	0	0.0
N02BB02	Metamizole sodium	1	2.2	0	0.0
N03AE01	Clonazepam	2	4.4	0	0.0
N05AD01	Haloperidol	1	2.2	1	100.0
N05BA	Benzodiazepine derivatives (anxiolitics)	3	6.7	2	66.7
N05BA05	Potassium clorazepate	1	2.2	1	100.0
N05BA08	Bromazepam	1	2.2	0	0.0
N05BA12	Alprazolam	1	2.2	1	100.0
N05CD11	Loprazolam	1	2.2	0	0.0
N06AB	Selective serotonin reuptake inhibitors	6	13.3	1	16.7
N06AB04	Citalopram	1	2.2	0	0.0

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TABLE 3 (*Continued*) Drugs recommended to be changed with the drugs changed in the pharmacological review.

Drugs recommended to change				Changed	
		n	%	n	%*
N06AB05	Paroxetine	4	8.9	0	0.0
N06AB10	Escitalopram	1	2.2	1	100.0
	Total active substances	29	64.4	11	37.9
	Total	45	100.0	11	24.4

n = total number of drugs recommended to change, and the total number of drugs changed.
%*, percentage of the drugs changed compared to those recommended to be changed.

medications included psychotropic drugs, medications with anticholinergic properties, antimicrobials, nonsteroidal anti-inflammatory drugs, and PPIs (Spinewine et al., 2021). In a similar manner, it concurs with previous systematic reviews that show an overall prevalence of 43.2% PIMs, with a 49% higher prevalence estimation for European countries (Morin et al., 2016).

The elderly population often requires a greater number of medications and is more susceptible to the complexities of drug use (Ma et al., 2021). Previous studies have suggested interdisciplinary teams to target nursing homes and reduce MRPs. Despite the obvious value of medication reviews, and the recommendation of their being performed at least annually, reviews are not consistently implemented in everyday clinical settings (Kurczewska-Michalak et al., 2021). An issue that should be addressed with a multidisciplinary team approach, including a clinical pharmacologist, as has been carried out in this intervention.

4.2 Impact of the intervention on nursing homes

The number of drugs prescribed was not significantly different from the beginning to the end of the study. Nevertheless, the reduction in specific medications and the addition of others, point to a targeted and individualized approach. This is comparable to other studies, that describe enhancement by reducing polypharmacy and MRPs, without significance in the number of prescribed drugs after the intervention (San-José et al., 2021; Spinewine et al., 2021; Saeed et al., 2022; Cole et al., 2023).

A previous study with a control group, carried out with STOPP criteria to detect PIMs, reported that the discontinuation rate was significantly greater in the intervention group (39.7%) compared to the control (19.3%); OR (95% CI): 2.75 (1.22–6.24) (Dalleur et al., 2014). In addition, an intervention performed in nursing homes in Ireland, including a deprescribing plan guided by STOPPFrail, described a decrease in the number of chronic medications after 3 months in the intervention group compared to the control ($p < 0.001$), with a mean difference of 2.25 ± 0.54 (95% CI = 1.18–3.32). The intervention, however, presented no significant difference in mortality ($p = 0.22$) (Curtin et al., 2020), in a similar manner to other studies (Cooper et al., 2015; Spinewine et al., 2021). Our findings showed that 15.8% of the patients in whom the recommendations were followed died, compared to 20.0% in whom they were not. It should be noted, however, that the criteria of our recommendations are not exactly the same as those of the studies mentioned. Furthermore, some articles have described a lower risk of death (Kua et al., 2019; Sluggett et al., 2022). A retrospective cohort study in Australia examining medication reviews in nursing homes showed a 4.4% lower mortality risk (95% CI = 0.02–8.60, $p = 0.048$) over 12 months (Sluggett et al., 2022). In a systematic review and 2019 meta-analysis of randomized controlled trials in nursing homes, when a subgroup analysis was performed in the medication review, the deprescribing interventions reduced mortality by 26% (OR 0.74, 95% CI = 0.65–0.84) (Kua et al., 2019).

Our study revealed a significant impact on medication with changes, and in 58.5% of the patients who received recommendations, they were followed. Notably, antipsychotics, antidepressants, benzodiazepines, statins, and diuretics were the most frequently withdrawn drugs, indicating a concerted effort to reduce MRPs. A finding similar to other studies, such as an observational before-after intervention where the medications withdrawn included antipsychotics, antidepressants, sedatives, and diuretics (Fog et al., 2017). In a retrospective cohort study conducted in Madrid, Spain, pharmacist-led medication reviews identified an average of 4.85 (SD 3.33) MRPs per patient, with 86.73% of the proposed changes being accepted. This intervention reduced the average number of medications by 2.09 (95% CI: 1.98–2.21; $P< .001$) per patient (Peral Bolaños et al., 2024). Similarly, another retrospective observational multicentric pre-post study assessed the impact of clinical pharmacist medication reviews on the quality of pharmacotherapy in primary care psychogeriatric patients with excessive polypharmacy. The study found that clinical pharmacists proposed 374 interventions in psychopharmacotherapy, with GPs accepting 45.2% of them. This acceptance led to a 7.5% reduction in the total number of medications ($p < 0.05$) and a 21.8% reduction in the number of prescribed potentially inappropriate medications (PIMs) ($p < 0.05$), among other outcomes (Stuhec and Zorjan, 2022).

Whilst there was no specific intervention in the use of absorbent pads during this study, we observed a 9.5% increase, likewise with the optimization of psycholeptic drugs. Previous studies in patients with dementia have shown that the administration of antipsychotics increases mortality (Connors et al., 2016; Schwertner et al., 2019), and a higher risk of falls in the elderly with antipsychotic drugs, among others (Zhou et al., 2022). A recent cohort study based on electronic records in the United Kingdom demonstrated that the use of antipsychotics in patients with dementia was associated with greater risk of stroke, venous thromboembolism, myocardial infarction, heart failure, fracture, pneumonia, and acute kidney

TABLE 4 Drugs recommended as adequate with the drugs withdrawn in the pharmacological review.

Drugs recommended as adequate				Withdrawn	
		n	%	n	%*
A- Alimentary tract and metabolism					
A02BC	Proton pump inhibitors	20	3.6	2	10.0
A02BC01	Omeprazole	17	3.0	1	5.9
A02BC02	Pantoprazole	1	0.2	0	0.0
A02BC03	Esomeprazole	2	0.4	1	50.0
A03FA03	Domperidone	2	0.4	0	0.0
A05AA02	Ursodeoxycholic acid	2	0.4	1	50.0
A10A	Insulins and analogues	6	1.1	1	16.7
A10AB	Insulin fast-acting	3	0.5	1	33.3
A10AE04	Insulin glargine	3	0.5	0	0.0
A10B	Blood glucose lowering drugs, excluding insulins	10	1.8	3	30.0
A10BA02	Metformin	4	0.7	1	25.0
A10BD07	Metformin and sitagliptin	1	0.2	1	100.0
A10BH	Dipeptidyl peptidase 4 inhibitors	5	0.9	1	20.0
A11CC	Vitamin D and analogues	7	1.2	1	14.3
A11DA	Vitamin B1	1	0.2	0	0.0
A12AX	Calcium with vitamin D	2	0.4	0	0.0
A12BA	Potassium	2	0.4	1	50.0
B- Blood and blood forming organs					
B01A	Antithrombotic agents	55	9.8	12	21.8
B01AA07	Acenocoumarol	2	0.4	2	100.0
B01AB05	Enoxaparin	1	0.2	1	100.0
B01AC04	Clopidogrel	9	1.6	0	0.0
B01AC06	Acetylsalicylic acid	34	6.1	7	20.6
B01AC07	Dipyridamole	1	0.2	1	100.0
B01AC18	Triflusal	1	0.2	1	100.0
B01AE07	Dabigatran etexilate	1	0.2	0	0.0
B01AF01	Rivaroxaban	1	0.2	0	0.0
B01AF02	Apixaban	3	0.5	0	0.0
B01AF03	Edoxaban	2	0.4	0	0.0
B03AA01	Ferrous glycine sulfate	11	2.0	3	27.3
B03B	Vitamin B12 and folic acid	8	1.4	4	50.0
B03BA01	Cyanocobalamin	5	0.9	1	20.0
C- Cardiovascular system					
C01AA05	Digoxin	10	1.8	1	10.0
C01BD01	Amiodarone	2	0.4	0	0.0
C03AA03	Hydrochlorothiazide	7	1.2	4	57.1

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TABLE 4 (*Continued*) Drugs recommended as adequate with the drugs withdrawn in the pharmacological review.

Drugs recommended as adequate				Withdrawn	
		n	%	n	%*
C03CA	Sulfonamides, plain	32	5.7	3	9.4
C03CA01	Furosemide	30	5.3	3	10.0
C03CA04	Torasemide	2	0.4	0	0.0
C03DA01	Spironolactone	1	0.2	0	0.0
C04AX21	Naftidrofuryl	1	0.2	0	0.0
C05AE03	Diltiazem	1	0.2	0	0.0
C07A	Beta blocking agents	14	2.5	1	7.1
C07AA06	Timolol	1	0.2	0	0.0
C07AB07	Bisoprolol	11	2.0	1	9.1
C07AG02	Carvedilol	2	0.4	0	0.0
C07BA06	Timolol and thiazides	1	0.2	0	0.0
C08CA	Dihydropyridine derivatives	5	0.9	1	20.0
C08CA01	Amlodipine	3	0.5	0	0.0
C08CA05	Nifedipine	1	0.2	1	100.0
C08CA11	Manidipine	1	0.2	0	0.0
C09AA	ACE inhibitors, plain	7	1.2	2	28.6
C09AA01	Captopril	1	0.2	0	0.0
C09AA02	Enalapril	5	0.9	2	40.0
C09AA05	Ramipril	1	0.2	0	0.0
C09BA02	Enalapril and diuretics	2	0.4	0	0.0
C09CA01	Losartan	1	0.2	0	0.0
C10A	Lipid modifying agents	26	4.6	4	15.4
C10AA01	Simvastatin	20	3.6	2	10.0
C10AA05	Atorvastatin	5	0.9	1	20.0
C10AX09	Ezetimibe	1	0.2	1	100.0
D- Dermatologicals					
D01AE14	Ciclopirox	1	0.2	0	0.0
D06AX09	Mupirocin	1	0.2	0	0.0
D11AX10	Finasteride	1	0.2	0	0.0
G- Genito urinary system and sex hormones					
G04BD12	Mirabegron	1	0.2	1	100.0
G04CA02	Tamsulosin	2	0.4	0	0.0
H- Systemic hormonal preparations					
H02AB07	Prednisone	2	0.4	1	50.0
H02AB13	Deflazacort	1	0.2	1	100.0
H03AA01	Levothyroxine sodium	4	0.7	0	0.0

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TABLE 4 (*Continued*) Drugs recommended as adequate with the drugs withdrawn in the pharmacological review.

Drugs recommended as adequate				Withdrawn	
		n	%	n	%*
J- Antiinfective for systemic use					
J01EE04	Sulfamoxole and trimethoprim	1	0.2	1	100.0
M- Musculo-skeletal system					
M04AA01	Allopurinol	6	1.1	0	0.0
N- Nervous system					
N02A	Opioids	19	3.4	7	36.8
N02AA55	Oxycodone and naloxone	1	0.2	0	0.0
N02AB03	Fentanyl	7	1.2	1	14.3
N02AJ13	Tramadol and paracetamol	2	0.4	0	0.0
N02AX02	Tramadol	9	1.6	6	66.7
N02B	Other analgesics and antipyretics	8	1.4	6	75.0
N02BB02	Metamizole sodium	5	0.9	4	80.0
N02BE01	Paracetamol	3	0.5	2	66.7
N03A	Antiepileptics	27	4.8	7	25.9
N03AA03	Primidone	1	0.2	0	0.0
N03AE01	Clonazepam	1	0.2	0	0.0
N03AX12	Gabapentin	11	2.0	2	18.2
N03AX14	Levetiracetam	1	0.2	0	0.0
N03AX16	Pregabalin	13	2.3	5	38.5
N04AA01	Trihexyphenidyl	1	0.2	0	0.0
N04B	Dopaminergic agents	3	0.5	0	0.0
N04BA02	Levodopa and decarboxylase inhibitor	1	0.2	0	0.0
N04BC05	Pramipexole	1	0.2	0	0.0
N04BD02	Rasagiline	1	0.2	0	0.0
N05A	Antipsychotics	88	15.7	23	26.1
N05AD01	Haloperidol	2	0.4	2	100.0
N05AH03	Olanzapine	1	0.2	0	0.0
N05AH04	Quetiapine	56	10.0	10	17.9
N05AL01	Sulpiride	1	0.2	0	0.0
N05AL07	Levosulpiride	1	0.2	1	100.0
N05AN01	Lithium	1	0.2	0	0.0
N05AX08	Risperidone	26	4.6	10	38.5
N05B	Anxiolytics	25	4.5	6	24.0
N05BA05	Potassium clorazepate	1	0.2	0	0.0
N05BA06	Lorazepam	20	3.6	4	20.0
N05BA08	Bromazepam	2	0.4	1	50.0
N05BA12	Alprazolam	2	0.4	1	50.0

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TABLE 4 (*Continued*) Drugs recommended as adequate with the drugs withdrawn in the pharmacological review.

Drugs recommended as adequate				Withdrawn	
		n	%	n	%*
N05C	Hypnotics and sedatives	8	1.4	2	25.0
N05CD06	Lormetazepam	3	0.5	1	33.3
N05CF02	Zolpidem	1	0.2	1	100.0
N05CM02	Clomethiazole	4	0.7	0	0.0
N06A	Antidepressants	92	16.4	15	16.3
N06AA09	Amitriptyline	2	0.4	1	50.0
N06AB04	Citalopram	15	2.7	2	13.3
N06AB05	Paroxetine	3	0.5	1	33.3
N06AB06	Sertraline	18	3.2	2	11.1
N06AX05	Trazodone	26	4.6	3	11.5
N06AX11	Mirtazapine	19	3.4	3	15.8
N06AX16	Venlafaxine	3	0.5	0	0.0
N06AX21	Duloxetine	2	0.4	0	0.0
N06AX23	Desvenlafaxine	1	0.2	0	0.0
N06AX26	Vortioxetine	3	0.5	3	100.0
N06BX06	Citicoline	1	0.2	1	100.0
N06D	Anti-dementia drugs	6	1.1	2	33.3
N06DA02	Donepezil	2	0.4	0	0.0
N06DA03	Rivastigmine	1	0.2	1	100.0
N06DX01	Memantine	3	0.5	1	33.3
N07CA01	Betahistine	2	0.4	0	0.0
R- Respiratory system					
R01AD	Corticosteroids	7	1.2	4	57.1
R01AD05	Budesonide	6	1.1	4	66.7
R01AD09	Mometasone	1	0.2	0	0.0
R03AC	Selective beta-2-adrenoreceptor agonists	2	0.4	0	0.0
R03AC12	Salmeterol	1	0.2	0	0.0
R03AC19	Olodaterol	1	0.2	0	0.0
R03BB01	Ipratropium bromide	2	0.4	1	50.0
R06A	Antihistamines for systemic use	4	0.7	3	75.0
R06AB02	Dexchlorpheniramine	1	0.2	1	100.0
R06AE07	Cetirizine	1	0.2	1	100.0
R06AX13	Loratadine	1	0.2	0	0.0
R06AX29	Bilastine	1	0.2	1	100.0
S- Sensory organs					
S01EC01	Acetazolamide	1	0.2	0	0.0
S01ED01	Timolol	2	0.4	0	0.0

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TABLE 4 (*Continued*) Drugs recommended as adequate with the drugs withdrawn in the pharmacological review.

Drugs recommended as adequate				Withdrawn	
		n	%	n	%*
S01EE01	Latanoprost	2	0.4	0	0.0
	Total active substances	116	20.7	59	50.9
	Total	561	100.0	127	22.6

n = total number of drugs recommended to adequate, and the total number of drugs withdrawn.
%*, percentage of the drugs withdrawn compared to those recommended as adequate.

injury. Choosing the appropriate antipsychotic, determining dosage, and managing treatment duration are essential factors to prevent adverse reactions linked to its usage (Mok et al., 2024). It is also crucial to carry out specific interventions in institutionalized patients due to the considerable misuse of psycholeptic drugs. These observations could be a focal point for proposed action in future studies.

4.3 A multidisciplinary team approach

The multidisciplinary approach is a recurring theme, underscoring the importance of collaborative decision-making. Collaborative efforts within such teams play a key role and lead to optimal individualized medication management for nursing home residents (Fog et al., 2017; Disalvo et al., 2020; Song et al., 2023).

A qualitative study concerning the barriers and facilitators that affect the process of conducting medication reviews identified organizational hurdles, time constraints, and communication challenges among healthcare professionals as barriers. Key facilitators included improved communication channels, collaboration within multidisciplinary teams, and resident and family engagement in decision-making. The study provides valuable insights into the complexities of medication management in this vulnerable population (Wouters et al., 2019). All these aspects were included in our intervention considering the limitations of the lockdown period.

A systematic review investigating strategies to manage polypharmacy highlighted the importance of multifaceted interventions, including patient-centered approaches, interdisciplinary collaboration, and technology-driven solutions. It emphasized the role of education and awareness programs targeting healthcare professionals and older adults. Medication reviews, deprescribing efforts, and the integration of technology, such as clinical decision support systems, emerge as promising avenues to optimize medication regimens and enhance patient safety (Kurczewska-Michalak et al., 2021).

Findings from our study suggest that the intervention, guided by comprehensive recommendations, with different proposals, individualized improvement plans, and changes in data registration, holds promise for optimizing medication regimens in nursing homes. Our results should encourage interventions that prioritize the individual needs and preferences of the residents thus potentially improving adherence and overall health outcomes. Nevertheless, challenges and considerations should be recognized. Whilst patient quality of life in nursing homes has been described in previous reviews and interventions with control groups, differences in health-related quality of life have not been described (Cooper et al., 2015; Curtin et al., 2020; Cole et al., 2023). The logistical aspects of coordinating a multidisciplinary team, ensuring effective communication, and addressing potential conflicts in treatment plans require careful management. We believe this could be managed by incorporating a clinical pharmacologist, as shown in Figure 1, to ensure at least one annual pharmacological review in nursing homes.

5 Strengths and limitations

Our study presents multiple strengths and limitations. The intervention was carried out at the beginning of the COVID-19 pandemic and with the declaration of a state of alarm by the Spanish government (BOE-A-2020-3692, 2020). This entailed inherent difficulties, such as having appointments with patients admitted to nursing homes, which hindered the actual intervention and patient follow-up. To the best our knowledge, however, this is the first study to analyze the impact of an intervention on nursing homes in Catalonia after reviewing prescribed medications and individually giving recommendations. Data from five different nursing homes were gathered. The medical review was performed by a clinical pharmacologist, with the possibility of changing prescriptions when needed and providing individual recommendations. The availability of a common computerized data system helped review the prescription registry and made coordination possible among nursing homes, primary care, and hospital care. It was an advantage that this project included primary care professionals, nursing home staff, physicians specialized in geriatrics, clinical pharmacology, and a clinical pharmacist, thus creating a multidisciplinary team, with an agreed final decision. A project that allows us to form new proposals to improve future interventions.

With respect to limitations, the extrapolation of our findings to other regions or countries should be performed with caution since the intervention was conducted in one urban area. There was no sample size calculation since all the patients from the nursing homes, where the intervention was conducted were included. Nevertheless, as the intervention covered 22.3% of the population in the northern area of Barcelona, Catalonia, it may be representative of areas with a similar socioeconomic level. The intervention was carried out in routine clinical practice, some information therefore is lacking, such as non-pharmacological treatments, non-registered treatments, or those not financed by the public health system. Neither are there data on drug adherence as the patients' clinical records are intended for assistance and not research. The different outcomes between the nursing homes could not be reviewed since the study was not

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TABLE 5 List of the most frequently added drugs.

Drugs added			
ATC	Name	n	%
A11CC	Vitamin D and analogues	55	8.8
N02BE01	Paracetamol	39	6.2
N05AH04	Quetiapine	28	4.5
B03B	Vitamin B and folic acid	25	4.0
A02BC01	Omeprazole	22	3.5
C03CA01	Furosemide	21	3.4
B03AB	Iron trivalent, oral antianemic preparations	19	3.0
A12AX	Calcium, combinations with vitamin D and/or other drugs	18	2.9
A06AD	Osmotically acting laxatives	16	2.6
N06AX11	Mirtazapine	16	2.6
N05BA06	Lorazepam	15	2.4
N02BB02	Metamizole sodium	14	2.2
A10A	Insulins and analogs	11	1.8
B01AF	Direct factor Xa inhibitors	11	1.8
C07AB07	Bisoprolol	11	1.8
C08CA01	Amlodipine	11	1.8
N05AX08	Risperidone	11	1.8
N06AB06	Sertraline	11	1.8
N06AX05	Trazodone	11	1.8
B01AC06	Acetylsalicylic acid	10	1.6
D01A	Antifungals for topical use	10	1.6
C10AA01	Simvastatin	8	1.3
N02AB03	Fentanyl	8	1.3
C09CA01	Losartan	7	1.1
M05BA	Bisphosphonates	7	1.1
B01AC04	Clopidogrel	6	1.0
C09AA02	Enalapril	6	1.0
N02AX02	Tramadol	6	1.0
N05CD06	Lormetazepam	6	1.0
A10BA02	Metformin	5	0.8
C03AA03	Hydrochlorothiazide	5	0.8
N03AX16	Pregabalin	5	0.8
N05AD01	Haloperidol	5	0.8
R03BB01	Ipratropium bromide	5	0.8
C10AA05	Atorvastatin	4	0.6
N03AX14	Levetiracetam	4	0.6
N06AB04	Citalopram	4	0.6

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TABLE 5 (*Continued*) List of the most frequently added drugs.

Drugs added			
ATC	Name	n	%
N06DX01	Memantine	4	0.6
R06AE07	Cetirizine	4	0.6
B01AB05	Enoxaparin	3	0.5
C05AE01	Glyceryl trinitrate	3	0.5
G04CA02	Tamsulosin	3	0.5
M05BX04	Denosumab	3	0.5
N03AE01	Clonazepam	3	0.5
N05AH03	Olanzapine	3	0.5
N06AX16	Venlafaxine	3	0.5
N06DA02	Donepezil	3	0.5

n = total number of each drug added.

designed for this and it was not the main goal of the intervention. Furthermore, the correlation between drugs and death was not adjusted for age or comorbidities. Since the intervention was performed during the COVID-19 pandemic, the patients' safety was prioritized, and the complex situation meant there was no adequate optimization of psychotropic drugs. A similar study with a control group, and out of the pandemic context, should be repeated in the elderly in different regions to confirm these results.

6 Conclusion

In conclusion, many recommendations were made confirming the increasing incidence of polypharmacy and the need for standardized interventions targeting nursing homes. They could help reduce MRPs and the number of prescribed drugs, with the aim of safer drug use. The favorable outcomes of this intervention highlight the importance of collaborative healthcare models in optimizing medication practices and set a precedence for future innovations in geriatric care. A multidisciplinary team providing a patient-centered approach, interdisciplinary collaboration including a clinical pharmacologist, and technology-driven solutions, should help reduce MRPs and polypharmacy.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Ethics statement

The studies involving humans were approved by the Ethics Committees of Vall Hebron University Hospital and IDIAP Jordi Gol. The studies were conducted in accordance with the local legislation and institutional requirements. Written informed consent for participation was not required from the participants or the participants' legal guardians/next of kin in accordance with the national legislation and institutional requirements.

Author contributions

EA-N: Conceptualization, Formal Analysis, Funding acquisition, Investigation, Methodology, Project administration, Visualization, Writing–original draft, Writing–review and editing. EF-L: Supervision, Writing–original draft, Writing–review and editing. MS: Supervision, Writing–original draft, Writing–review and editing. MB: Supervision, Writing–original draft, Writing–review and editing. MS-A: Data curation, Writing–original draft, Writing–review and editing. MC: Writing–original draft, Writing–review and editing. JM: Writing–original draft, Writing–review and editing. MB-C: Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing–original draft, Writing–review and editing.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fphar.2024.1445141/full#supplementary-material

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Discussion

5

The main purpose of this thesis was to characterize institutionalized patients, systematically review their pharmacological medications and HRP, and evaluate the impact of a multidisciplinary team intervention giving recommendations on medication plans in nursing homes in Catalonia. This intervention aimed to implement a systematized medication review for the institutionalized population, conducted by a multidisciplinary team, as a fundamental strategy to ensure safe and effective use of medications in this fragile population.

The results showed a high prevalence of HRP in all patients, with a mean of 17.4 (SD 5.6), and an excessive number of medications, with a mean of 8.2 (SD 3.5) prescribed drugs per patient.

The recommendations given were divided into completing missing data, recommending withdrawal of drugs, substituting drugs, or adjusting their use appropriately The drug withdrawal was recommended when MRPs were identified. MRPs considered were potential DDIs, duplicated therapies, contraindicated drugs, inappropriate drugs, or drugs of doubtful efficacy. The addition of drugs was recommended when PPOs were identified.

The outcomes indicated that 1,097 recommendations were given to 398 (82.4%) patients. Of these, 355 recommendations were implemented in 233 (58.5%) patients, significantly impacting prescribing practices in nearly half of the patients who received interventions. The most frequently withdrawn drugs were antipsychotics, antidepressants, benzodiazepines, statins, and diuretics. The most commonly added medications were vitamin D and/or calcium supplements for patients with known osteoporosis. As for mortality, the percentage was lower in patients who followed the recommendations.

The multidisciplinary intervention, including patient-centered approaches, interdisciplinary collaboration, and technology-driven solutions, highlights the importance of collaborative decision-making to make effective medication reviews and personalized medication management in nursing homes. This could be addressed with a multidisciplinary team approach, coordinated by a clinical pharmacologist.

5.1: General characterization and descriptive analysis of institutionalized patients in nursing homes

Most patients were female (72.0%) with a mean age of 86.3 years. This was anticipated since women generally have a longer life expectancy (1), and it is consistent with other European studies. In a retrospective descriptive analysis of health insurance claims data performed in 2016 in Switzerland, the average age in nursing homes was 85.7 years, and the proportion of females was 71.9% (78). In an observational study of the geriatric population in a region of Italy, 70.4% of the nursing home residents were women, with a mean age of 84.4 years (79). In a recent descriptive study of a retrospective follow-up cohort conducted in Madrid, 71.8% of the patients were women, with a mean age of 87.3 years (80).

A marked prevalence of HRPs was observed, with a mean of 17.4 diseases across all nursing homes. This high number of HRPs aligns with the MG values, where 94.5% of the patients had an MG value of 33. This value indicates that four or more systems are affected by a chronic disease, which is reasonable given the typical profile of patients admitted to nursing homes (75,76). Conversely, it does not correlate with the low percentage of CCP or MACA reported. It was not recorded in 98.3% of the patients. The cause of this under-registration may be attributed to the complexity and time required to go through various scales and categorize a patient as either complex chronic or of advanced chronicity. This underreporting of information also made the calculation of AMG difficult.

The most common HRP was urinary incontinence in 85.3% of the patients. This is notable, as urinary incontinence is typically multifactorial, often involving multiple contributing factors, including medications. A cross-sectional study of 390 patients aged 60 years and older in Canada, seeking care for incontinence, found that 60.5% were using medications that could potentially contribute to urinary symptoms. The leading medication classes implicated were calcium channel blockers, benzodiazepines, antipsychotics, antidepressants, narcotics, ACE inhibitors, and oral estrogens (81). Although various medication groups might theoretically induce urinary incontinence based on pathophysiological mechanisms, robust evidence establishing a direct cause-effect relationship between drug usage and incontinence remains limited (82). This should be taken into account since many of these medications were prevalent among these patients, such as quetiapine in 37.9%, lorazepam in 21.7%, sertraline in 15.3%, trazodone in 14.3%, amlodipine in 13.7%, and citalopram in 12.8% of the patients.

More than 50% of the patients also had hypertension, osteoarthritis, dyslipidemia, Alzheimer's disease or other types of dementia, and anemia. Over one-third were diagnosed with insomnia and sleep disorders, and 28.6% with depression. It is also important to consider that 21.5% had dependence on enabling machines and devices, and 18.2% had abnormalities of gait and mobility. All this demonstrates the frailty and multimorbidity of institutionalized patients.

Returning to the patients with Alzheimer's or other types of dementia, who were observed in 52.8% of the cases, and patients with symptoms or signs involving cognitive functions and awareness, who were 30.2%, it is clear that the proportion of dementia among nursing home residents is high. These conditions are crucial to consider when reviewing medications, as such patients are more likely to be prescribed antipsychotic drugs, leading to a higher risk of MRPs (83,84).

The institutionalized patients in Catalonia were prescribed an average of 8.2 drugs. This number is comparable to nursing homes in Italy, where 80.3% of inpatients experience polypharmacy (84). Similarly, in Switzerland, 85.5% of nursing home residents face polypharmacy, with an average of 9.4 drugs per patient (78). In a recent intervention conducted in Madrid, an even higher average of 12.3 drugs was prescribed (80). This trend of excessive drug prescriptions is observed globally. For instance, in Australia, over 50% of nursing home residents regularly use nine or more medications, prompting the proposal of simplified medication regimens to alleviate the medication burden (33). The elderly population in particular, often requires a higher number of medications and is more vulnerable to the complexities associated with drug use (85).

The most prescribed drugs were proton pump inhibitors (PPIs), analgesics, and psychotropic drugs. This pattern is similar to the non-institutionalized Spanish population (42) but with a higher number of prescribed drugs (86). The sequence of most prescribed drugs is similar to other European countries, with the most frequent being analgesics (paracetamol and metamizole), diuretics (torasemide), PPIs (pantoprazole), and tranquilizers (quetiapine) (78).

PPI use is considered appropriate only for current gastric or duodenal disorders or for the prevention of nonsteroidal anti-inflammatory drugs (NSAIDs) effects (87). Therefore, most patients in our study do not meet the criteria for PPI use, which aligns with other studies reporting PPIs as a common PIM (88).

Analgesics are widely used in nursing homes globally, as described in a systematic review of international prescribing practices from 2018. This review shows that the percentage of residents prescribed regular analgesics from 2010 to 2015 ranged from 32% to 75.2%, including countries like Germany, Austria, Norway, and Australia (89).

Psychotropic drugs are consistently used in most countries and are a predominant PIM (88). The prevalence in our study group is higher than in nursing home reports from other countries, such as Australia (69.9%) and Germany (71.1%) (83), but similar to Italy (84). In Norwegian nursing homes, a significant increase in the prescription of psychotropic drugs, including antidepressants, atypical antipsychotics, anxiolytics, and sedatives/hypnotics, was observed after comparing baseline data with data from six months later (90).

5.2. Descriptive analysis of recommendations given and MRPs in nursing homes

A patient's clinical condition evolves, necessitating systematic reviews of their treatment. Additionally, patients in nursing homes are often in a state of advanced fragility and are candidates for deprescription to avoid ADRs and MRPs (37). Numerous recommendations were given and MRPs were identified through this intervention coordinated by a clinical pharmacologist.

The patients received various recommendations, which were categorized mainly into four groups: completing missing data, recommending withdrawal of drugs, substituting drugs, or optimizing their use accordingly. Missing data could include absent information about allergies or HRPs. Drug withdrawal was recommended when MRPs were identified, such as potential DDIs, duplicated therapies, contraindicated drugs, inappropriate drugs, or drugs of doubtful efficacy. Substitution of a drug was advised when alternative first-choice or equivalent drugs were available. Adequation in drug use was suggested to reduce doses, address poor tolerance, reduce anticholinergic load, or mitigate high risks of ADRs. As for the addition of medication, it was only recommended in specific cases, when PPOs were identified. Ultimately, the clinical pharmacologist provided 1,097 recommendations to 398 patients, of which 231 (47.8%) were related to MRPs.

Concerning MRPs, potential DDIs were frequently identified, primarily involving serotonin reuptake inhibitors (SSRIs), tramadol, statins, acenocoumarol, and calcium channel blockers. The most commonly described potential DDI was between SSRIs and tramadol. Previous

studies have also highlighted some of these interactions, including those involving SSRIs, statins, and warfarin (84,91,92). This is concerning because administering tramadol with SSRIs can increase the risk of seizures and serotonin syndrome. Similar effects can be seen with other antidepressants such as serotonin/norepinephrine reuptake inhibitors (SNRIs), and tricyclic antidepressants (93). When statins and calcium channel blockers are combined, it is crucial to monitor and not exceed the recommended doses due to the increased risk of myopathy and rhabdomyolysis (94). Levothyroxine and statins can potentiate the anticoagulant effect of acenocoumarol. Additionally, combining different antiarrhythmics in older patients is not recommended due to the increased arrhythmogenic risk (92,95,96). This does not account for the added risks of hypotension, sedation, and consequent falls (94). A European study reported higher MRP rates, with the most frequent potentially severe DDIs involving psychotropic drugs with additive effects on QTc prolongation, combinations of Angiotensin-Converting Enzyme Inhibitors (ACEIs) or Angiotensin II Receptor Blockers with potassium supplements (increasing the risk of hyperkalemia), and SSRIs/SNRIs with antiplatelets (increasing the risk of hemorrhage) (84).

Regarding therapeutic duplications, there is a notable prevalence of vitamin D or its analogs being used in combination with calcium. Other instances of therapeutic duplication were observed among patients undergoing drug dose adjustments or changes. Both PREFASEG and Self-Audit detect therapeutic duplication, which helps explain the low percentage of duplications identified in this medication review (63,64).

Contraindications were seen recurrent in metformin, NSAIDs (diclofenac, aceclofenac and dexketoprofen), haloperidol, and citalopram. Renal function was reviewed during this intervention, and possible contraindications or dose adjustments were recommended according to the GFR. This included metformin and NSAIDs due to severe chronic renal failure (GFR < 30 mL/min/1.73m2) and hyperkalemia (potassium > 5.5 mmol/L). If there was no determination in the past year, performing an analysis was recommended (97,98). A cross-sectional study analyzing prescribing data for medications that should be avoided, require dose adjustments, are ineffective, or need cautious use in patients with reduced kidney function revealed findings consistent with our study. Alendronic acid and metformin should be avoided, hydrochlorothiazide is unlikely to be effective with a GFR < 30 mL/min/1.73m2, and NSAIDs and ACEIs are likely to cause ADRs (97). A cross-sectional study on medication burden and the risk of inappropriate prescriptions among the elderly with advanced chronic kidney disease

revealed that at least one contraindicated drug was prescribed to 10.8% of patients. The most frequently prescribed contraindicated drugs included rilmenidine (16.5%), rosuvastatin (6.5%), alfuzosin (5.8%), and buflomedil (3.6%) (99). The use of antidepressants, antipsychotics, and benzodiazepines was primarily contraindicated due to their anticholinergic effects and increased risk of falls (58).

Regarding drugs considered inappropriate, many are associated with an increased risk of orthostatic hypotension, falls, and anticholinergic effects. These include benzodiazepines, antidepressants, hypnotics, and antipsychotics, which are in the PIMs and medications with anticholinergic burden lists from CatSalut. Drugs like domperidone, hydroxyzine, and antimuscarinics such as solifenacin and fesoterodine are also included in the anticholinergic burden list. Other reasons for drugs being deemed inappropriate include liquid paraffin due to the risk of aspiration and ADRs, and statins used for primary prevention (58). These examples underscore why it is crucial to carefully weigh the risk-versus-benefit considerations, especially in frail patients.

Lastly, as for the drugs of doubtful efficacy, most of them are considered inappropriate since they are given outside the approved conditions of use or are administered for a long duration, even though they are intended for short-term treatment. To highlight, there are citicoline and betahistine. Citicoline is a psychostimulant and nootropic used to treat memory and behavior alterations after an ischemic stroke or cranial trauma (100). A cross-sectional study from Spain showed that only 18.1% of the patients prescribed citicoline received it for the approved conditions (100), and the evidence from different studies considering its efficacy is unambiguous (101). As for betahistine, it is used for vertigo, even though it is only approved for Ménière's disease, and there is not enough evidence to determine whether the medication is effective or ineffective (102). For all these reasons, they are considered drugs of doubtful efficacy.

5.3: Impact of the intervention on nursing homes

The number of drugs prescribed did not change significantly from the beginning with 3962 prescribed drugs, to the end of the study with 3893 prescribed drugs. However, the reduction in specific medications and the addition of others suggest a targeted and individualized approach. This is consistent with other studies that report improvements through the reduction

of polypharmacy and MRPs, even without a significant change in the overall number of prescribed drugs after the intervention (88,103,104).

Our intervention revealed an impact on medication with 58.5% of the patients following the recommendations, which represents 32.4% of the total of recommendations followed. Considering the different types of recommendations, antipsychotics, antidepressants, benzodiazepines, statins, and diuretics were the most frequently withdrawn drugs. Despite our recommendations for prescribed medications to be withdrawn, changed, or considered adequate, when the verification of the appropriateness or substitution of a drug was recommended, we could only document whether the medication was withdrawn, which might explain why these figures are lower. However, even considering that, we believe that 32.4% represents a significant impact on the prescribed medication. This finding aligns with other studies, such as an observational before-after intervention where the withdrawn medications included antipsychotics, antidepressants, sedatives, and diuretics (105). A recent retrospective cohort study conducted in Madrid, Spain, similar to this intervention, involved pharmacist-led medication reviews. The study detected a mean of 4.85 (SD 3.33) MRPs per patient. Of the proposed changes, 86.73% were accepted, reducing the average number of medications by 2.09 (95% CI: 1.98-2.21; P<.001) per patient. These findings also support the implementation of a multidisciplinary team intervention to reduce MRPs in nursing homes (80).

Even though proper optimization of psycholeptic drugs, could not be done due to the COVID-19 pandemic, many of these drugs were withdrawn. Previous studies in patients with dementia have demonstrated that the use of antipsychotics increases mortality (106,107) and elevates the risk of falls among the elderly (108). A recent cohort study based on electronic records in the United Kingdom revealed that antipsychotic use in dementia patients is associated with a higher risk of stroke, venous thromboembolism, myocardial infarction, heart failure, fractures, pneumonia, and acute kidney injury. Selecting the appropriate antipsychotic, determining the correct dosage, and carefully managing treatment duration is crucial to prevent these adverse outcomes (109). Targeted interventions in institutionalized patients are also necessary due to the significant misuse of psycholeptic drugs in nursing homes (110–112). These findings could serve as a focal point for proposed actions in future studies.

Additional medications were recommended only when PPOs were clearly identified. Previous studies assessing the prevalence of PPOs using the START criteria have reported that at least one PPO was observed in 19.8% (95% CI: 16.1–24.0) of patients (113), 41.8% of patients (with

29.2% having one PPO and 12.6% having multiple PPOs) (45), and 13% of patients (104). This indicates variability in the prevalence and proportion of patients with PPOs. Among the most commonly prescribed medications to address PPOs were bone antiresorptive agents or vitamin D and/or calcium supplements for patients with known osteoporosis, followed by ACEi, antiplatelet therapy, anticoagulants, folic acid supplements, and appropriate beta-blockers (39,45,104,113). In our intervention, the most frequently prescribed medications were vitamin D and its analogues, either alone or in combination with calcium and/or other drugs. Other commonly prescribed medications included bisphosphonates, vitamin B and folic acid, bisoprolol, and acetylsalicylic acid.

In terms of mortality, our findings revealed that 15.8% of patients for whom the recommendations were followed passed away, compared to 20.0% of those for whom the recommendations were not followed. However, it is important to note that our criteria differ from those used in the referenced studies. For instance, an intervention in Irish nursing homes, which included a deprescribing plan guided by STOPPFrail, found no significant difference in mortality (p=0.22) (114), similar to findings from other studies (18,88). Additionally, some studies have reported a reduced risk of death. A retrospective cohort study in Australia that examined medication reviews in nursing homes demonstrated a 4.4% lower mortality risk (95% CI 0.02–8.60, p=0.048) over 12 months (115). Furthermore, a 2019 systematic review and meta-analysis of randomized controlled trials in nursing homes found that deprescribing interventions reduced mortality by 26% (OR 0.74, 95% CI 0.65–0.84) in a subgroup analysis of medication reviews (116).

5.4: A multidisciplinary team approach

Our study indicates that the intervention, based on various recommendations, personalized improvement plans, and adjustments, shows potential for improving medication regimens in nursing homes. These findings support the adoption of interventions that focus on the individual needs and preferences of residents, potentially enhancing adherence and overall health outcomes. The multidisciplinary approach consistently highlights the significance of collaborative decision-making. Team collaboration plays a key role and contributes to effective, personalized medication management for nursing home residents (44,73,105).

A systematic review has proposed interdisciplinary teams to focus on nursing homes and reduce MRPs. It highlighted the importance of multifaceted interventions, including patient-

centered approaches, interdisciplinary collaboration, and technology-driven solutions. Medication reviews, deprescribing efforts, and the use of CDSS show great potential for optimizing medication regimens and improving patient safety (117). This could be addressed with a multidisciplinary team approach, coordinated by a clinical pharmacologist, as in this intervention.

A recent article also considers that the engagement of clinical pharmacists can prevent MRPs, collaborating with a multidisciplinary team and other international organizations, thereby achieving patient-centered healthcare in Europe and a positive impact (118).

A qualitative study examining the factors influencing medication reviews identified organizational obstacles, time limitations, and communication issues among healthcare professionals as key barriers. On the other hand, enhanced communication, teamwork within multidisciplinary teams, and active involvement of residents and their families in decision-making were highlighted as important facilitators. This study offers valuable insights into the challenges of medication management within this vulnerable population (119).

However, certain challenges and considerations must be acknowledged. Although patient quality of life in nursing homes has been examined in prior reviews and interventions with control groups, variations in health-related quality of life have not been explored (18,114,120). Managing the logistical aspects of coordinating a multidisciplinary team, ensuring clear communication, and resolving potential conflicts in treatment plans demands careful attention.

5.5. Strengths and limitations

The study demonstrated several strengths and limitations. It provided personalized recommendations to address MRPs, PIMs, ADRs, and polypharmacy, with reviews conducted by a clinical pharmacologist who could modify prescriptions as needed, make an accurate medication review, and give individual recommendations. The intervention benefited from a multidisciplinary team that included primary care professionals, nursing home staff, physicians specialized in geriatrics and clinical pharmacology, and a clinical pharmacist. A shared computerized data system facilitated effective communication between nursing homes, primary care, and hospital care.

However, there were notable limitations. The study was conducted in a single urban area of northern Barcelona, which may limit the generalizability of the findings to other regions or countries. The study included five different nursing homes that covered 22.3% of the local population, which might only be representative of similar socioeconomic areas. There was no sample size calculation since all the patients from the nursing homes, where the intervention was conducted were included. Additionally, the intervention did not capture data on non-pharmacological treatments, non-registered treatments, or drug adherence, as the clinical records were used primarily for care rather than research. The study was also impacted by the COVID-19 pandemic, which disrupted healthcare delivery and patient follow-up, complicating the optimization of psychotropic medications and potentially influencing the outcomes. The declaration of a state of alarm by the Spanish government entailed inherent difficulties, such as having appointments with patients admitted to nursing homes, which hindered the actual intervention and patient follow-up. The patients' safety was prioritized, and the complex situation meant there was no adequate optimization of psychotropic drugs or absorbent pads. Furthermore, the correlation between drugs and death was not adjusted for age or comorbidities. Variability among nursing homes and the absence of a control group further limited the study's ability to provide broadly applicable conclusions. The different outcomes between the nursing homes could not be reviewed since the study was not designed for this and it was not the main goal of the intervention.

5.6: Final reflections and future proposals

The results from this project have provided information about the high prevalence of HRP and the excessive number of medications prescribed per patient, highlighting the need for interventions to optimize medication plans and systematize medication reviews in the institutionalized population. However, considering the various limitations discussed, future research with control groups conducted outside of pandemic conditions is recommended in diverse settings.

Additionally, as mentioned previously, the aim was to implement a systematized medication review for the institutionalized population, conducted by a multidisciplinary team, as a fundamental strategy to ensure the safe and effective use of medications in this fragile population.

During the development of this project, the Catalonia Health Plan 2021-2025 emphasized the need to redefine the current network of social and healthcare services to ensure that all professionals have access to comprehensive information about patient medications. It also highlighted the importance of primary care pharmacists and clinical pharmacologists in supporting medication reconciliation and conducting periodic reviews of medication plans (121). In line with this plan, a program to strengthen the professional role of primary and community care pharmacists and clinical pharmacologists was established (122). This program underscores the need for integrated and continuous therapeutic care and ensures the availability of a single, patient-centered therapeutic plan. Particularly in more complex cases, this requires reinforcing the usual care team with pharmacists and clinical pharmacologists. The involvement of these professionals in collaborative care aims to integrate and optimize prescriptions for more complex patients. As healthcare professionals with expertise in medication management, pharmacists and clinical pharmacologists promote the safe and rational use of medications, tailored to each patient's needs, to improve both quality of life and health outcomes. Since 2021, ECAP has included a specific role for pharmacists and clinical pharmacologists. This role allows them to propose the initiation, modification, or discontinuation of treatments for the prescriber’s consideration, maintain their schedule, make notes in patients' clinical records, and ensure traceability in medication review actions. However, the work platform still does not fully address all of the professionals' needs (122).

The aim is to conduct regular pharmacological reviews, coordinated by a clinical pharmacologist, with various electronic tools. To carry out this intervention regularly, it is essential to emphasize the importance of systematically recording information related to the patient’s health-related problems and the prescribed medication of the patient is correct. This allows to make recommendations regularly, and even to schedule therapeutic consultations with pharmacists and clinical pharmacologists to carry out all these interventions systematically in all nursing homes, along with periodic analyses of how the reviews are progressing and to see if measures need to be applied at any other level.

Conclusions

6

1. This study reveals a high prevalence of health-related problems, with an average of 17.4 diseases per patient and 8.2 prescribed drugs in nursing homes in Catalonia. This justifies why many recommendations were made for standardized interventions to reduce medication-related problems.
2. Most patients were female with a mean age of 86.3 years, reflecting the longer life expectancy of women and consistent with European trends.
3. Urinary incontinence was the most common health-related problem, followed by conditions like hypertension, osteoarthritis, and dementia.
4. The most prescribed medications were proton pump inhibitors, analgesics, and psychotropic drugs, mirroring prescription patterns in other European countries.
5. The recommendations given were about completing missing data, recommending withdrawal of drugs, substituting drugs, or adjusting their use appropriately, and addition of drugs.
6. The clinical pharmacologist provided 1,097 recommendations to 398 (82.4%) patients, of which 231 (47.8%) were related to MRPs, and they were followed by more than half (58.5%) of the patients.
7. Drug withdrawal was recommended when MRPs were identified. These MRPs were potential DDIs, duplicated therapies, contraindicated drugs, inappropriate drugs, or drugs of doubtful efficacy.
8. The most frequent potential drug-drug interactions primarily involved serotonin reuptake inhibitors, tramadol, statins, acenocoumarol, and calcium channel blockers.
9. A low percentage of duplications were identified in this medication review and contraindications were mainly due to chronic renal failure.
10. Most of the inappropriate drugs were associated with an increased risk of orthostatic hypotension, falls, and anticholinergic effects.
11. Drugs of doubtful efficacy were due to patients receiving medication outside the approved conditions, and most of them were considered ineffective and even unsafe.
12. The most frequently withdrawn drugs were antipsychotics, antidepressants, benzodiazepines, statins, and diuretics, and the most added medications were for patients with known osteoporosis, consistent with other studies and according to the START criteria.
13. Mortality was lower among patients who adhered to the recommendations, with 15.8% passing away compared to 20.0% of those who did not follow the recommendations.

14. An intervention with a patient-centered approach, a multidisciplinary team, and technology-driven solutions, ensures effective medication reviews and personalized medication management in nursing homes. This could be addressed with a multidisciplinary team, coordinated by a clinical pharmacologist.

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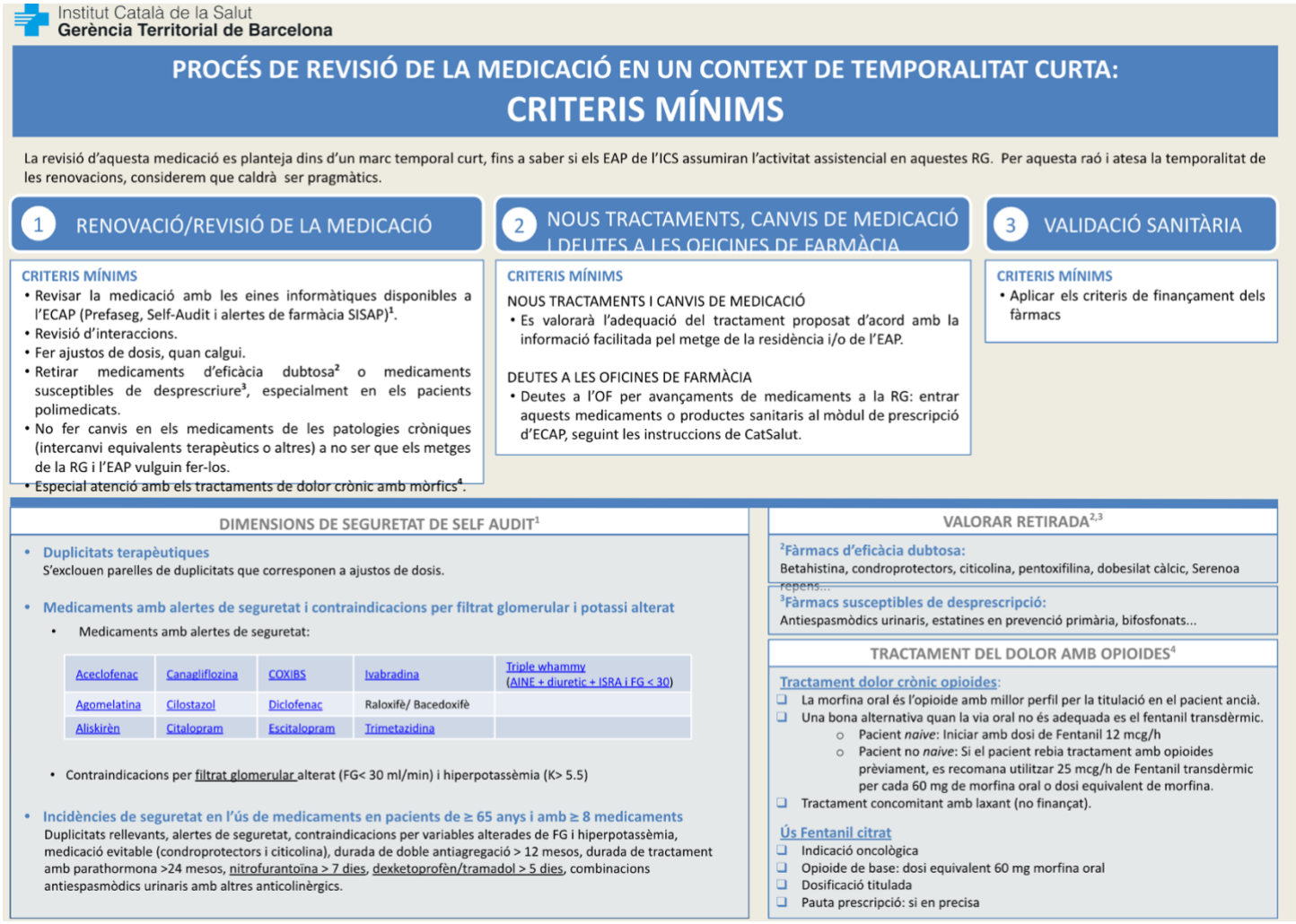
Annexes

8

Annex 1: The minimal criteria established by the Catalan Institute of Health



Institut Català de la Salut
Gerència Territorial de Barcelona

PROCÉS DE REVISIÓ DE LA MEDICACIÓ EN UN CONTEXT DE TEMPORALITAT CURTA: CRITERIS MÍNIMS

La revisió d'aquesta medicació es planteja dins d'un marc temporal curt, fins a saber si els EAP de l'ICS assumiran l'activitat assistencial en aquestes RG. Per aquesta raó i atesa la temporalitat de les renovacions, considerem que caldrà ser pragmàtics.

1 RENOVACIÓ/REVISIÓ DE LA MEDICACIÓ

CRITERIS MÍNIMS

- Revisar la medicació amb les eines informàtiques disponibles a l'ECAP (Prefaseg, Self-Audit i alertes de farmàcia SISAP)[1].
- Revisió d'interaccions.
- Fer ajustos de dosis, quan calgui.
- Retirar medicaments d'eficàcia dubtosa[2] o medicaments susceptibles de desprescriure[3], especialment en els pacients polimedicats.
- No fer canvis en els medicaments de les patologies cròniques (intercanvi equivalents terapèutics o altres) a no ser que els metges de la RG i l'EAP vulguin fer-los.
- Especial atenció amb els tractaments de dolor crònic amb mòrfics[4].

2 NOUS TRACTAMENTS, CANVIS DE MEDICACIÓ I DEUTES A LES OFICINES DE FARMÀCIA

CRITERIS MÍNIMS

NOUS TRACTAMENTS I CANVIS DE MEDICACIÓ

- Es valorarà l'adequació del tractament proposat d'acord amb la informació facilitada pel metge de la residència i/o de l'EAP.

DEUTES A LES OFICINES DE FARMÀCIA

- Deutes a l'OF per avançaments de medicaments a la RG: entrar aquests medicaments o productes sanitaris al mòdul de prescripció d'ECAP, seguint les instruccions de CatSalut.

3 VALIDACIÓ SANITÀRIA

CRITERIS MÍNIMS

- Aplicar els criteris de finançament dels fàrmacs

DIMENSIONS DE SEGURETAT DE SELF AUDIT[1]

- **Duplicitats terapèutiques**
  S'exclouen parelles de duplicitats que corresponen a ajustos de dosis.
- **Medicaments amb alertes de seguretat i contraindicacions per filtrat glomerular i potassi alterat**
  - Medicaments amb alertes de seguretat:

Aceclofenac	Canagliflozina	COXIBS	Ivabradina	Triple whammy (AINE + diuretic + ISRA i FG < 30)
Agomelatina	Cilostazol	Diclofenac	Raloxifè/ Bacedoxifè	
Aliskirèn	Citalopram	Escitalopram	Trimetazidina	

  - Contraindicacions per filtrat glomerular alterat (FG< 30 ml/min) i hiperpotassèmia (K> 5.5)
- **Incidències de seguretat en l'ús de medicaments en pacients de ≥ 65 anys i amb ≥ 8 medicaments**
  Duplicitats rellevants, alertes de seguretat, contraindicacions per variables alterades de FG i hiperpotassèmia, medicació evitable (condroprotectors i citicolina), durada de doble antiagregació > 12 mesos, durada de tractament amb parathormona >24 mesos, nitrofurantoïna > 7 dies, dexketoprofèn/tramadol > 5 dies, combinacions antiespasmòdics urinaris amb altres anticolinèrgics.

VALORAR RETIRADA[2,3]

[2]Fàrmacs d'eficàcia dubtosa:
Betahistina, condroprotectors, citicolina, pentoxifilina, dobesilat càlcic, Serenoa repens...

[3]Fàrmacs susceptibles de desprescripció:
Antiespasmòdics urinaris, estatines en prevenció primària, bifosfonats...

TRACTAMENT DEL DOLOR AMB OPIOIDES[4]

Tractament dolor crònic opioides:

- ❑ La morfina oral és l'opioide amb millor perfil per la titulació en el pacient ancià.
- ❑ Una bona alternativa quan la via oral no és adequada es el fentanil transdèrmic.
  - Pacient *naive*: Iniciar amb dosi de Fentanil 12 mcg/h
  - Pacient no *naive*: Si el pacient rebia tractament amb opioides prèviament, es recomana utilitzar 25 mcg/h de Fentanil transdèrmic per cada 60 mg de morfina oral o dosi equivalent de morfina.
- ❑ Tractament concomitant amb laxant (no finançat).

Ús Fentanil citrat

- ❑ Indicació oncològica
- ❑ Opioide de base: dosi equivalent 60 mg morfina oral
- ❑ Dosificació titulada
- ❑ Pauta prescripció: si en precisa

Annex 2: Geriatric Nursing Homes in the north area of Barcelona, Spain

In Barcelona City, the distribution of nursing homes is very uneven, as the number of residential places is much higher in the left and north areas of Barcelona. Specifically, in the north area of Barcelona (last available update from May 2020), there are 3,294 geriatric residential places and 87 more centers that care for children and adults with physical and mental disabilities.
The distribution of residential places is as follows (anonymized):

AREA	NURSING HOMES		OTHER CENTERS		TOTAL	
	CENTERS	PLACES	CENTERS	PLACES	CENTERS	PLACES
1	3	174			3	174
2	16	963			16	963
3	16	1280	1	27	17	1307
4	3	135			3	135
5	2	59	1	35	3	94
6	1	90			1	90
7	3	175			3	175
8	2	113			2	113
9	1	92			1	92
10	1	151			1	151
11	2	62	1	25	3	87
TOTAL	50	3294	3	87	53	3381

The intervention took place in 4 nursing homes of Area 3:

- 1st nursing home with 181 places
- 2nd nursing with 182 places
- 3rd nursing home with 165 places
- 4th nursing home with 109 places

The intervention also took place in Area 7 in the 5th nursing home with 98 places and in Area 8 in the 6th nursing home with 88 places.

Recogida momento 0

Número del paciente {[record_id] text}	_____ (Poner el numero del paciente (num ordre) junto con su abreviacion de residencia (RG): Por ejemplo el primero de la residencia amavir seria 1AM)
Fecha revision {[fecha_rev1] text (date_dmy Min: 2020-01-01 Max: 2022-03-01) Required}	_____
Año de nacimiento {[a_o_nacim] text (float Min: 1900 Max: 2000) Required}	_____
Edad {[age] text (float Min: 1 Max: 110) Required}	_____
Sexo {[sex] radio Required}	◯ {1} 1. Hombre ◯ {2} 2. Mujer
MACA o PCC {[macapcc] radio Required}	◯ {1} Si ◯ {2} No ◯ {3} No consta
GMA {[gma] radio Required}	◯ {1} 1. Si ◯ {2} 2. No consta
Riesgo de reingreso (%) {[gma_reingreso] text (number_1dp Min: 0.0 Max: 100.0)} {Branching logic (show if): [gma] = '1'}	_____
Valor GMA {[gma_num] text (number_1dp Min: 00.0 Max: 100.0)} {Branching logic (show if): [gma] = '1'}	_____
Alergias {[alergias1] radio}	◯ {1} SI ◯ {2} No ◯ {3} No consta
Numero de problemas de salud {[probsalud1] text (float Max: 100) Required}	_____
Problema de salud segun CIE-10 {[enf_cie1] text Required} {Branching logic (show if): [probsalud1] > 0}	_____
Problema de salud segun CIE-10 {[enf_cie2] text Required} {Branching logic (show if): [probsalud1] > 1}	_____
Problema de salud segun CIE-10 {[enf_cie3] text Required} {Branching logic (show if): [probsalud1] > 2}	_____

Problema de salud segun CIE-10
{[enf_cie4] text Required}
{Branching logic (show if): [probsalud1] > 3}
_____

Problema de salud segun CIE-10
{[enf_cie5] text Required}
{Branching logic (show if): [probsalud1] > 4}
_____

Problema de salud segun CIE-10
{[enf_cie6] text Required}
{Branching logic (show if): [probsalud1] > 5}
_____

Problema de salud segun CIE-10
{[enf_cie7] text Required}
{Branching logic (show if): [probsalud1] > 6}
_____

Problema de salud segun CIE-10
{[enf_cie8] text Required}
{Branching logic (show if): [probsalud1] > 7}
_____

Problema de salud segun CIE-10
{[enf_cie9] text Required}
{Branching logic (show if): [probsalud1] > 8}
_____

Problema de salud segun CIE-10
{[enf_cie10] text Required}
{Branching logic (show if): [probsalud1] > 9}
_____

Problema de salud segun CIE-10
{[enf_cie11] text Required}
{Branching logic (show if): [probsalud1] > 10}
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Problema de salud segun CIE-10
{[enf_cie12] text Required}
{Branching logic (show if): [probsalud1] > 11}
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Problema de salud segun CIE-10
{[enf_cie13] text Required}
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Problema de salud segun CIE-10
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{Branching logic (show if): [probsalud1] > 13}
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Problema de salud segun CIE-10
{[enf_cie15] text Required}
{Branching logic (show if): [probsalud1] > 14}
_____

Problema de salud segun CIE-10
{[enf_cie16] text Required}
{Branching logic (show if): [probsalud1] > 15}
_____

Problema de salud segun CIE-10
{[enf_cie17] text Required}
{Branching logic (show if): [probsalud1] > 16}
_____

Problema de salud segun CIE-10
{[enf_cie18] text Required}
{Branching logic (show if): [probsalud1] > 17}
_____

Problema de salud segun CIE-10
{[enf_cie19] text Required}
{Branching logic (show if): [probsalud1] > 18}
_____

Problema de salud segun CIE-10
{[enf_cie20] text Required}
{Branching logic (show if): [probsalud1] > 19}
_____

Problema de salud segun CIE-10
{[enf_cie21] text Required}
{Branching logic (show if): [probsalud1] > 20}
_____

Problema de salud segun CIE-10
{[enf_cie22] text Required}
{Branching logic (show if): [probsalud1] > 21}
_____

Problema de salud segun CIE-10
{[enf_cie23] text Required}
{Branching logic (show if): [probsalud1] > 22}
_____

Problema de salud segun CIE-10
{[enf_cie24] text Required}
{Branching logic (show if): [probsalud1] > 23}
_____

Problema de salud segun CIE-10
{[enf_cie25] text Required}
{Branching logic (show if): [probsalud1] > 24}
_____

Problema de salud segun CIE-10
{[enf_cie26] text Required}
{Branching logic (show if): [probsalud1] > 25}
_____

Problema de salud segun CIE-10
{[enf_cie27] text Required}
{Branching logic (show if): [probsalud1] > 26}
_____

Problema de salud segun CIE-10
{[enf_cie28] text Required}
{Branching logic (show if): [probsalud1] > 27}
_____

Problema de salud segun CIE-10
{[enf_cie29] text Required}
{Branching logic (show if): [probsalud1] > 28}
_____

Problema de salud segun CIE-10
{[enf_cie30] text Required}
{Branching logic (show if): [probsalud1] > 29}
_____

Problema de salud segun CIE-10
{[enf_cie31] text Required}
{Branching logic (show if): [probsalud1] > 30}
_____

Problema de salud segun CIE-10
{[enf_cie32] text Required}
{Branching logic (show if): [probsalud1] > 31}
_____

Problema de salud segun CIE-10
{[enf_cie33] text Required}
{Branching logic (show if): [probsalud1] > 32}
_____

Problema de salud segun CIE-10
{[enf_cie34] text Required}
{Branching logic (show if): [probsalud1] > 33}
_____

Problema de salud segun CIE-10
{[enf_cie35] text Required}
{Branching logic (show if): [probsalud1] > 34}
_____

Problema de salud segun CIE-10
{[enf_cie36] text Required}
{Branching logic (show if): [probsalud1] > 35}
_____

¿Ha sido intervenido?
{[iq] yesno Required}
◯ Si
◯ No

Número de problemas de salud QUIRÚRGICO
{[iqprobsalud] text (float Max: 100) Required}
{Branching logic (show if): [iq] = '1'}
_____

Problema de salud segun CIE-10PCS
{[enf_ciep1] text Required}
{Branching logic (show if): [iqprobsalud] > 0}
_____

Problema de salud segun CIE-10PCS
{[enf_ciep2] text Required}
{Branching logic (show if): [iqprobsalud] > 1}
_____

Problema de salud segun CIE-10PCS
{[enf_ciep3] text Required}
{Branching logic (show if): [iqprobsalud] > 2}
_____

Uso de Absorbentes
{[absorbentes1] yesno Required}
◯ Si
◯ No

Toma medicacion
{[medic1] yesno Required}
◯ Si
◯ No

Número de fármacos que toma
{[num_farmac] text (float Min: 1 Max: 30) Required}
{Branching logic (show if): [medic1] = '1'}
_____

fármaco con ATC
{[atc_1] text Required}
{Branching logic (show if): [num_farmac] > 0}
_____

fármaco con ATC
{[atc_2] text Required}
{Branching logic (show if): [num_farmac] > 1}
_____

fármaco con ATC
{[atc_3] text Required}
{Branching logic (show if): [num_farmac] > 2}
_____

fármaco con ATC
{[atc_4] text Required}
{Branching logic (show if): [num_farmac] > 3}
_____

fármaco con ATC
{[atc_5] text Required}
{Branching logic (show if): [num_farmac] > 4}
_____

fármaco con ATC
{[atc_6] text Required}
{Branching logic (show if): [num_farmac] > 5}
_____

fármaco con ATC
{[atc_7] text Required}
{Branching logic (show if): [num_farmac] > 6}
_____

fármaco con ATC
{[atc_8] text Required}
{Branching logic (show if): [num_farmac] > 7}
_____

fármaco con ATC
{[atc_9] text Required}
{Branching logic (show if): [num_farmac] > 8}
_____

fármaco con ATC
{[atc_10] text Required}
{Branching logic (show if): [num_farmac] > 9}
_____

fármaco con ATC
{[atc_11] text Required}
{Branching logic (show if): [num_farmac] > 10}
_____

fármaco con ATC
{[atc_12] text Required}
{Branching logic (show if): [num_farmac] > 11}
_____

fármaco con ATC
{[atc_13] text Required}
{Branching logic (show if): [num_farmac] > 12}
_____

fármaco con ATC
{[atc_14] text Required}
{Branching logic (show if): [num_farmac] > 13}
_____

fármaco con ATC
{[atc_15] text Required}
{Branching logic (show if): [num_farmac] > 14}
_____

fármaco con ATC
{[atc_16] text Required}
{Branching logic (show if): [num_farmac] > 15}
_____

fármaco con ATC
{[atc_17] text Required}
{Branching logic (show if): [num_farmac] > 16}
_____

fármaco con ATC
{[atc_18] text Required}
{Branching logic (show if): [num_farmac] > 17}
_____

fármaco con ATC
{[atc_19] text Required}
{Branching logic (show if): [num_farmac] > 18}
_____

fármaco con ATC
{[atc_20] text Required}
{Branching logic (show if): [num_farmac] > 19}
_____

fármaco con ATC
{[atc_21] text Required}
{Branching logic (show if): [num_farmac] > 20}
_____

Revisión de la medicación

Datos incompletos {[datos_incomp] radio}	◯ {1} Si ◯ {2} No ◯ {3} Algunos
Que falta ? {[datos_incomp_2] checkbox} {Branching logic (show if): [datos_incomp] = '1' or [datos_incomp] = '3'}	☐ {1} alergias ☐ {2} enfermedades
Se recomienda retirar fármacos {[recom_ret_f] yesno Required}	◯ Si ◯ No
¿Cuantos fármacos se recomienda retirar? {[num_ret_f] text (float Min: 1 Max: 30) Required} {Branching logic (show if): [recom_ret_f] = '1'}	_____
fármaco con ATC que se recomienda retirar {[f_recom_retirar1] text Required} {Branching logic (show if): [num_ret_f] > 0}	_____
Se ha retirado? {[retirada1] yesno} {Branching logic (show if): [num_ret_f] > 0}	◯ Si ◯ No
fármaco con ATC que se recomienda retirar {[f_recom_retirar2] text Required} {Branching logic (show if): [num_ret_f] > 1}	_____
Se ha retirado? {[retirada2] yesno} {Branching logic (show if): [num_ret_f] > 1}	◯ Si ◯ No
fármaco con ATC que se recomienda retirar {[f_recom_retirar3] text Required} {Branching logic (show if): [num_ret_f] > 2}	_____
Se ha retirado? {[retirada3] yesno} {Branching logic (show if): [num_ret_f] > 2}	◯ Si ◯ No
fármaco con ATC que se recomienda retirar {[f_recom_retirar4] text Required} {Branching logic (show if): [num_ret_f] > 3}	_____
Se ha retirado? {[retirada4] yesno} {Branching logic (show if): [num_ret_f] > 3}	◯ Si ◯ No
fármaco con ATC que se recomienda retirar {[f_recom_retirar5] text Required} {Branching logic (show if): [num_ret_f] > 4}	_____

Se ha retirado?
{[retirada5] yesno}
{Branching logic (show if): [num_ret_f] > 4}

◯ Si
◯ No

fármaco con ATC que se recomienda retirar
{[f_recom_retirar6] text Required}
{Branching logic (show if): [num_ret_f] > 5}

_____

Se ha retirado?
{[retirada6] yesno}
{Branching logic (show if): [num_ret_f] > 5}

◯ Si
◯ No

Se recomienda cambiar/sustituir un fármaco
{[recom_camb_sustf] yesno Required}

◯ Si
◯ No

¿Cuantos fármacos se recomienda cambiar/sustituir fármaco?
{[num_camb_sust_f] text (float Min: 1 Max: 30) Required}
{Branching logic (show if): [recom_camb_sustf] = '1'}

_____

fármaco con ATC que se recomienda cambiar/sustituir
{[f_recom_sustit1] text Required}
{Branching logic (show if): [num_camb_sust_f] > 0}

_____

Se ha cambiado/retirado?
{[cambiado_ret1] yesno}
{Branching logic (show if): [num_camb_sust_f] > 0}

◯ Si
◯ No

Por cual?
{[nuevofintrod1] text}
{Branching logic (show if): [cambiado_ret1] = '1'}

_____

fármaco con ATC que se recomienda cambiar/sustituir
{[f_recom_sustit2] text Required}
{Branching logic (show if): [num_camb_sust_f] > 1}

_____

Se ha cambiado/retirado?
{[cambiado_ret2] yesno}
{Branching logic (show if): [num_camb_sust_f] > 1}

◯ Si
◯ No

Por cual?
{[nuevofintrod2] text}
{Branching logic (show if): [cambiado_ret2] = '1'}

_____

fármaco con ATC que se recomienda cambiar/sustituir
{[f_recom_sustit3] text Required}
{Branching logic (show if): [num_camb_sust_f] > 2}

_____

Se ha cambiado/retirado?
{[cambiado_ret3] yesno}
{Branching logic (show if): [num_camb_sust_f] > 2}

◯ Si
◯ No

Por cual?
{[nuevofintrod3] text}
{Branching logic (show if): [cambiado_ret3] = '1'}

_____

Se recomienda verificar la adecuación del uso de un fármaco {[recom_adecuacionf] yesno Required}	◯ Si ◯ No
¿Cuantos fármacos se recomienda verificar su adecuación de uso? {[num_camb_adecuacionf] text (float Min: 1 Max: 30) Required} {Branching logic (show if): [recom_adecuacionf] = '1'}	_____
fármaco con ATC que se recomienda verificar/adecuar {[f_recom_adecuar_1] text Required} {Branching logic (show if): [num_camb_adecuacionf] > 0}	_____
Se ha retirado? {[retirad_verif1] yesno} {Branching logic (show if): [num_camb_adecuacionf] > 0}	◯ Si ◯ No
fármaco con ATC que se recomienda verificar/adecuar {[f_recom_adecuar_2] text Required} {Branching logic (show if): [num_camb_adecuacionf] > 1}	_____
Se ha retirado? {[retirad_verif2] yesno} {Branching logic (show if): [num_camb_adecuacionf] > 1}	◯ Si ◯ No
fármaco con ATC que se recomienda verificar/adecuar {[f_recom_adecuar_3] text Required} {Branching logic (show if): [num_camb_adecuacionf] > 2}	_____
Se ha retirado? {[retirad_verif3] yesno} {Branching logic (show if): [num_camb_adecuacionf] > 2}	◯ Si ◯ No
fármaco con ATC que se recomienda verificar/adecuar {[f_recom_adecuar_4] text Required} {Branching logic (show if): [num_camb_adecuacionf] > 3}	_____
Se ha retirado? {[retirad_verif4] yesno} {Branching logic (show if): [num_camb_adecuacionf] > 3}	◯ Si ◯ No
Riesgo de interacciones {[interacc] yesno Required}	◯ Si ◯ No
¿Cuantas interacciones hay? {[num_interacc_1] text (float Min: 1 Max: 20) Required} {Branching logic (show if): [interacc] = '1'}	_____

Poner Interaccion Fármaco-Fármaco {[num_interacc_2] text (alpha_only) Required} {Branching logic (show if): [interacc] = '1'}	_____ (por ejemplo: Paracetamol-Metamizol)
Hay duplicidades {[duplicidades] yesno Required}	◯ Si ◯ No
¿Cuantas duplicidades hay? {[num_duplicidades] text (float Min: 1 Max: 20) Required} {Branching logic (show if): [duplicidades] = '1'}	_____
fármaco con ATC duplicado {[f_duplicado_1] text Required} {Branching logic (show if): [num_duplicidades] > 0}	_____
fármaco con ATC duplicado {[f_duplicado_2] text Required} {Branching logic (show if): [num_duplicidades] > 0}	_____
fármaco con ATC duplicado {[f_duplicado_3] text Required} {Branching logic (show if): [num_duplicidades] > 1}	_____
fármaco con ATC duplicado {[f_duplicado_4] text Required} {Branching logic (show if): [num_duplicidades] > 1}	_____
fármaco con ATC duplicado {[f_duplicado_5] text Required} {Branching logic (show if): [num_duplicidades] > 2}	_____
fármaco con ATC duplicado {[f_duplicado_6] text Required} {Branching logic (show if): [num_duplicidades] > 2}	_____
Hay contraindicaciones {[contraindicaciones] yesno Required}	◯ Si ◯ No
¿Cuantas contraindicaciones hay? {[num_ci] text (float Min: 1 Max: 20) Required} {Branching logic (show if): [contraindicaciones] = '1'}	_____
fármaco con ATC contraindicado {[f_contraind1] text Required} {Branching logic (show if): [num_ci] > 0}	_____
fármaco con ATC contraindicado {[f_contraind2] text Required} {Branching logic (show if): [num_ci] > 1}	_____
fármaco con ATC contraindicado {[f_contraind3] text Required} {Branching logic (show if): [num_ci] > 2}	_____

fármaco con ATC contraindicado
{[f_contraind5] text Required}
{Branching logic (show if): [num_ci] > 3}
_____

fármaco con ATC contraindicado
{[f_contraind4] text Required}
{Branching logic (show if): [num_ci] > 4}
_____

Hay fármacos de eficacia dudosa
{[f_dudoso] yesno Required}
◯ Si
◯ No

¿Cuantos fármacos de eficacia dudosa hay?
{[num_fdudodoso] text (float Min: 1 Max: 20) Required}

{Branching logic (show if): [f_dudoso] = '1'}
_____

fármaco con ATC de eficacia dudosa
{[f_eficacdudosa_1] text Required}
{Branching logic (show if): [num_fdudodoso] > 0}
_____

fármaco con ATC de eficacia dudosa
{[f_eficacdudosa_2] text Required}
{Branching logic (show if): [num_fdudodoso] > 1}
_____

fármaco con ATC de eficacia dudosa
{[f_eficacdudosa_3] text Required}
{Branching logic (show if): [num_fdudodoso] > 2}
_____

Hay fármacos inapropiados
{[f_inaprop_2] yesno Required}
◯ Si
◯ No

¿Cuantos fármacos inapropiados hay?
{[num_finaprop_2] text (float Min: 1 Max: 20) Required}
{Branching logic (show if): [f_inaprop_2] = '1'}
_____

fármaco inapropiado con ATC
{[f_inaprop1] text Required}
{Branching logic (show if): [num_finaprop_2] > 0}
_____

fármaco inapropiado con ATC
{[f_inaprop2] text Required}
{Branching logic (show if): [num_finaprop_2] > 1}
_____

fármaco inapropiado con ATC
{[f_inaprop3] text Required}
{Branching logic (show if): [num_finaprop_2] > 2}
_____

Se realizan propuestas o recomendaciones
{[propuestas] yesno Required}
◯ Si
◯ No

¿Sobre que?
{[propuestas_2] checkbox Required}
{Branching logic (show if): [propuestas] = '1'}

- ☐ {1} Sobre completar datos de enfermedades
- ☐ {2} Sobre completar datos de alergias
- ☐ {3} Sobre retirada de fármacos
- ☐ {4} Sobre sustitución de fármacos equivalentes
- ☐ {5} Sobre sustitución al fármaco de elección
- ☐ {6} Sobre verificación de la adecuación del uso de fármacos
- ☐ {7} Sobre retirada de fármacos con interacciones
- ☐ {8} Sobre retirada de duplicidades
- ☐ {9} Sobre retirada de fármacos contraindicados
- ☐ {10} Sobre retirada de fármacos con eficacia dudosa
- ☐ {11} Sobre retirada de fármacos inapropiados

Recogida al año

Fecha revision {[fecha_rev1_v2] text (date_dmy Min: 2020-01-01 Max: 2022-03-01) Required}	_____ (poner dia 01 en todos+mes+año)
Han completado los datos de alergias {[compl_dat_incomp] radio Required}	◯ {1} Si ◯ {2} No ◯ {3} Los datos estaban completos
Alergias {[alergias1_v2] radio}	◯ {1} SI ◯ {2} No ◯ {3} No consta
Uso de Absorbentes {[absorbentes_v2] yesno Required}	◯ Si ◯ No
Toma medicacion {[medic1_v2] yesno Required} {Branching logic (show if): 1}	◯ Si ◯ No
Cambios en la medicación {[camb_medic] yesno Required}	◯ Si ◯ No
Varía los fármacos que toma {[variac_farm] yesno Required} {Branching logic (show if): 1}	◯ Si ◯ No
Número de fármacos que toma {[num_farmac_v2] text (float Min: 1 Max: 30) Required} {Branching logic (show if): [variac_farm] = '1'}	_____
Discontinuacion fármacos {[disco_farm] yesno Required}	◯ Si ◯ No
Número fármacos retirados {[num_f_retir_2] text (float Max: 30) Required}	_____
Adición de fármacos {[adic_farm_2] yesno Required}	◯ Si ◯ No
Número fármacos añadidos {[num_f_adic] text (float Max: 30) Required}	_____
fármaco con ATC que se recomienda añadir {[f_adic_1] text} {Branching logic (show if): [num_f_adic] > 0}	_____
fármaco con ATC que se recomienda añadir {[f_adic_2] text} {Branching logic (show if): [num_f_adic] > 1}	_____

fármaco con ATC que se recomienda añadir {[f_adic_3] text} {Branching logic (show if): [num_f_adic] > 2}	_____
fármaco con ATC que se recomienda añadir {[f_adic_4] text} {Branching logic (show if): [num_f_adic] > 3}	_____
fármaco con ATC que se recomienda añadir {[f_adic_5] text} {Branching logic (show if): [num_f_adic] > 4}	_____
Siguen las recomendaciones dadas {[recomend] radio Required}	◯ {1} Si ◯ {2} No ◯ {3} Algunas ◯ {4} No se dan recomendaciones
Cuales {[recomend_2] checkbox Required} {Branching logic (show if): [recomend] = '1' or [recomend] = '3'}	☐ {1} Completan datos de enfermedades ☐ {2} Completan datos de alergias ☐ {3} Retiran fármacos ☐ {4} Sustituyen fármacos por un equivalente ☐ {5} Sustiuyen fármacos por el de elección ☐ {6} Verifican adecuación del uso de un fármaco ☐ {7} Retiran fármacos con interacciones ☐ {8} Retiran duplicidades ☐ {9} Retiran fármacos contraindicados ☐ {10} Retiran fármacos de eficacia dudosa ☐ {11} Retiran fármacos inapropiados
Paciente vivo {[vivo] yesno Required}	◯ Si ◯ No
Fecha éxitus {[exitus] text (date_dmy Min: 1800-01-01 Max: 2022-12-31) Required} {Branching logic (show if): [vivo] = '0'}	_____
Comentarios {[comments] textarea}	_____ (Apuntar si habia alguna duda o cosas no claras)

INFORME DE CALIDAD

Quality Check para base de datos RedCap del estudio "Optimización del tratamiento farmacológico en pacientes institucionalizados en residencias de Cataluña".

En la siguiente tabla puede encontrar las comprobaciones que se van a realizar después de la extracción de datos y antes del análisis para garantizar la calidad de los datos y detectar posibles errores o patrones particulares que puedan afectar los resultados.

Sección	Como se ofrece los datos	Comentarios
PÉRDIDAS		
Falta registro del número del paciente	Numérico	0
Falta registro de fecha revisión 1 y al año	Numérico	0 y 0
Falta registro de año del nacimiento	Numérico	0
Falta registro de edad	Numérico	0
Falta registro de sexo	Numérico	0
Falta registro de MACA o PCC	Numérico	0
Falta registro de GMA	Numérico	0
Falta registro de alergias	Numérico	0
Falta registro de número de problemas de salud	Numérico	0
Falta registro de si ha sido intervenido	Numérico	0
Falta registro de número de IQ	Numérico	0
Falta registro de uso de absorbentes en momento 0 y al año	Numérico	0 y 0
Falta registro de si toma medicación en momento 0 y al año	Numérico	0 y 0
Falta registro de número de fármacos que toma momento 0 y al año	Numérico	0
Falta registro de datos incompletos	Numérico	0
Falta registro de si se recomienda retirar fármacos	Numérico	0
Falta registro de si se recomienda cambiar/sustituir un fármaco	Numérico	0
Falta registro de si se recomienda verificar la adecuación del uso de un fármaco	Numérico	0
Falta registro de riesgo de interacciones	Numérico	0
Falta registro de si hay duplicidades	Numérico	0

Falta registro de si hay contraindicaciones	Numérico	0
Falta registro de si hay fármacos de eficacia dudosa	Numérico	0
Falta registro de si hay fármacos inapropiados	Numérico	0
Falta registro de si se realizan propuestas o recomendaciones	Numérico	0
Falta registro de si han completado los datos de alergias	Numérico	0
Falta registro de si hay cambios en la medicación	Numérico	0
Falta registro de si varía los fármacos que toma	Numérico	0
Falta registro de si hay discontinuación de fármacos al año	Numérico	0
Falta registro de si hay adición de fármacos al año	Numérico	0
Falta registro de si siguen las recomendaciones dadas al año	Numérico	0
Falta registro de si paciente vivo	Numérico	0
CONSISTENCIA DE FECHAS		
Fecha de revisión en el momento 0, previo a la del año	Numérico	0
Fecha de revisión en el momento 0, previo a la del exitus	Numérico	0
CUENTAS GENERALES Y DISTRIBUCIONES		
Número de sujetos en los datos de origen y en la base de datos	Numérico	0
Distribución por sexo	Numérico	0
Edad	Mediana, IQR y recuentos categóricos	0
Lista de codigos diagnosticos presentes (ICD-10)	Tabla	OK
Lista de codigos diagnosticos quirurgicos presentes	Tabla	OK
Lista de codigos ATC presentes	Tabla	OK
CONSISTENCIA DE VARIABLES CATEGÓRICAS		
Sujetos con GMA = No, pero tienen apuntados riesgo de reingreso y/o valor GMA	Numérico	0
Sujetos con GMA = Si, pero NO tienen apuntados riesgo de reingreso y valor GMA	Numérico	0
Sujetos con Datos incompletos =No, pero tienen apuntados que falta alergias y/o enfermedades	Numérico	0

Sujetos con Datos incompletos = Si, pero NO tienen apuntados que falta de alergias y/o enfermedades	Numérico	0
Sujetos con Se recomienda retirar fármacos = No, pero tienen apuntados cuantos fármacos se recomienda retirar, si se ha retirado o el fármaco.	Numérico	0
Sujetos con Se recomienda retirar fármacos = Si, pero NO tienen apuntados cuantos fármacos se recomienda retirar, si se ha retirado o el fármaco.	Numérico	0
Sujetos con Se recomienda cambiar/sustituir fármacos = No, pero tienen apuntados cuantos fármacos se recomienda cambiar/sustituir, si se ha retirado o el fármaco.	Numérico	0
Sujetos con Se recomienda cambiar/sustituir fármacos = Si, pero NO tienen apuntados cuantos fármacos se recomienda cambiar/sustituir, si se ha retirado o el fármaco.	Numérico	0
Sujetos con Se recomienda verificar la adecuación del uso de fármacos = No, pero tienen apuntados cuantos fármacos se recomienda verificar la adecuación del uso, si se ha retirado o el fármaco.	Numérico	0
Sujetos con Se recomienda verificar la adecuación del uso de fármacos = Si, pero NO tienen apuntados cuantos fármacos se recomienda verificar la adecuación del uso, si se ha retirado o el fármaco.	Numérico	0
Sujetos con Riesgo de interacciones= No, pero tienen apuntado las interacciones o cuántas hay	Numérico	0
Sujetos con Riesgo de interacciones= Si, pero NO tienen apuntado las interacciones o cuántas hay	Numérico	0
Sujetos con Duplicidades= No, pero tienen apuntadas cuantas hay y/o los fármacos	Numérico	0
Sujetos con Duplicidades= SI, pero NO tienen apuntadas cuantas hay y/o los fármacos	Numérico	0
Sujetos con Contraindicaciones= No, pero tienen apuntadas cuantas hay y/o los fármacos	Numérico	0
Sujetos con Contraindicaciones= SI, pero NO tienen apuntadas cuantas hay y/o los fármacos	Numérico	0
Sujetos con fármacos de eficacia dudosa= No, pero tienen apuntadas cuantas hay y/o los fármacos	Numérico	0
Sujetos con fármacos de eficacia dudosa= SI, pero NO tienen apuntadas cuantas hay y/o los fármacos	Numérico	0
Sujetos con fármacos inapropiados= No, pero tienen apuntadas cuantas hay y/o los fármacos	Numérico	0

Sujetos con fármacos inapropiados= SI, pero NO tienen apuntadas cuantas hay y/o los fármacos	Numérico	0
Sujetos con propuestas o recomendaciones= No, pero tienen apuntadas sobre qué son las propuestas	Numérico	0
Sujetos con propuestas o recomendaciones= SI, pero NO tienen apuntadas ninguna propuesta	Numérico	0
Sujetos con Varía los fármacos que toma= No, pero tienen apuntadas el número de fármacos que toma al año	Numérico	0
Sujetos con Varía los fármacos que toma= SI, pero NO tienen apuntadas el número de fármacos que toma al año	Numérico	0
Sujetos con Discontinuación fármacos= No, pero tienen apuntadas el número de fármacos retirados al año	Numérico	0
Sujetos con Discontinuación fármacos= SI, pero NO tienen apuntadas el número de fármacos retirados al año	Numérico	0
Sujetos con Adición de fármacos= No, pero tienen apuntadas el número de fármacos añadidos al año y cual	Numérico	0
Sujetos con Adición de fármacos= SI, pero NO tienen apuntadas el número de fármacos añadidos al año y cual	Numérico	0
Sujetos con Siguen las recomendaciones dadas= No o no se dan recomendaciones, pero tienen apuntadas cuales son las recomendaciones dadas	Numérico	0
Sujetos con Siguen las recomendaciones dadas= SI o algunas, pero NO tienen apuntadas cuales son las recomendaciones dadas	Numérico	0
Sujetos con Paciente vivo= No, pero NO tienen apuntadas la fecha de exitus	Numérico	0
Sujetos con Paciente vivo= SI, pero tienen apuntadas la fecha de exitus	Numérico	0

***Todos los datos numéricos, si es igual a 0, es que es correcto. Los que no revisar de nuevo.**

Annex 5. Supplementary material from the publication of the first study

Supplementary Table S1: Complete list of all HRPs divided into groups according to their ICD-10

Superfamilies	n	%
(R00-R99): Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	1237	256.1
Unspecified urinary incontinence	412	85.3
Other symptoms and signs involving cognitive functions and awareness	146	30.2
Symptoms and signs involving emotional state	89	18.4
Abnormalities of gait and mobility	88	18.2
Fecal incontinence	85	17.6
Edema, not elsewhere classified	42	8.7
Pain, unspecified	39	8.1
Other skin changes	35	7.2
Abnormalities of breathing	29	6.0
Age-related physical debility	26	5.4
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	23	4.8
Abnormal involuntary movements	21	4.3
Other symptoms and signs involving the nervous and musculoskeletal systems	17	3.5
Elevated blood glucose level	17	3.5
Aphagia and dysphagia	16	3.3
Abnormalities of heart beat	15	3.1
Speech disturbances, not elsewhere classified	15	3.1
Other symptoms and signs involving the digestive system and abdomen	14	2.9
Nonspecific elevation of levels of transaminase and lactic acid dehydrogenase	13	2.7
Symptoms and signs concerning food and fluid intake	12	2.5
Abdominal and pelvic pain	11	2.3
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	8	1.7
Dizziness and Giddiness	7	1.4
Schizophrenia, schizotypal, delusional, and other non-mood psychotic disorders	6	1.2
Isolated proteinuria	6	1.2
Disturbances of skin sensation	5	1.0
Other lack of coordination	5	1.0
Nausea and vomiting	4	0.8
Benign and innocent cardiac murmurs	3	0.6
Abnormal blood-pressure reading, without diagnosis	3	0.6
Retention of urine	3	0.6
Other and unspecified symptoms and signs involving the genitourinary system	3	0.6

Malaise and fatigue	3	0.6
Syncope and collapse	3	0.6
Hepatomegaly and splenomegaly, not elsewhere classified	2	0.4
Anuria and oliguria	2	0.4
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	2	0.4
Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	1	0.2
Other symptoms and signs involving the circulatory and respiratory systems	1	0.2
Sexual dysfunction, unspecified	1	0.2
Convulsions, not elsewhere classified	1	0.2
Hypothermia, not associated with low environmental temperature	1	0.2
Other and unspecified abnormal findings in urine	1	0.2
Abnormal findings on diagnostic imaging of lung	1	0.2
(I00-I99): Diseases of the circulatory system	1123	232.5
Essential (Primary) Hypertension	357	73.9
Atrial fibrillation and flutter	135	28.0
Heart failure	95	19.7
Cerebral infarction	86	17.8
Other disorders of veins	59	12.2
Chronic ischemic heart disease	54	11.2
Varicose veins of lower extremities	32	6.6
Other peripheral vascular diseases	31	6.4
Nonrheumatic aortic valve disorders	26	5.4
Hypertensive heart disease with (congestive) heart failure	24	5.0
Atrioventricular and left bundle-branch block	23	4.8
Nonrheumatic mitral valve disorders	20	4.1
Acute myocardial infarction	19	3.9
Other conduction disorders	19	3.9
Angina pectoris	16	3.3
Nontraumatic intracerebral hemorrhage	11	2.3
Pulmonary embolism with mention of acute cor pulmonale	10	2.1
Occlusion and stenosis of precerebral arteries, not resulting in cerebral infarction	10	2.1
Rheumatic mitral valve diseases	9	1.9
Nonrheumatic tricuspid valve disorders	8	1.7
Complications and ill-defined descriptions of heart disease	8	1.7
Sequelae of cerebrovascular disease	7	1.4
Atherosclerosis	7	1.4
Aortic aneurysm and dissection	7	1.4
Other pulmonary heart diseases	6	1.2
Cardiomyopathy	6	1.2

Other cardiac arrhythmias	6	1.2
Other cerebrovascular diseases	6	1.2
Paroxysmal tachycardia	5	1.0
Phlebitis and thrombophlebitis	3	0.6
Other venous embolism and thrombosis	3	0.6
Other and unspecified disorders of circulatory system	3	0.6
Rheumatic aortic insufficiency	2	0.4
Other aneurysm	2	0.4
Arterial embolism and thrombosis	2	0.4
Hereditary haemorrhagic telangiectasia	2	0.4
Diseases of the circulatory system	2	0.4
Other acute ischaemic heart diseases	1	0.2
Other disorders of arteries and arterioles	1	0.2
(E00-E90): Endocrine, nutritional and metabolic diseases	864	178.9
Disorders of lipoprotein metabolism and other lipidemias	260	53.8
Diabetes mellitus	144	29.8
Vitamin D deficiency	99	20.5
Overweight and obesity	83	17.2
Hypothyroidism	59	12.2
Vitamin B deficiency, unspecified	58	12.0
Hyperuricemia	40	8.3
Other disorders of fluid, electrolyte and acid-base balance	30	6.2
Dehydration	16	3.3
Subclinical iodine-deficiency hypothyroidism	14	2.9
Thyroid nodule	14	2.9
Thyrotoxicosis [hyperthyroidism]	10	2.1
Iron deficiency	10	2.1
Mineral disorders	5	1.0
Thyroiditis	4	0.8
Hypoglycemia	3	0.6
Lactose intolerance	3	0.6
Hyperparathyroidism, unspecified	2	0.4
Malnutrition	2	0.4
Hypoparathyroidism, unspecified	1	0.2
Cushing's syndrome	1	0.2
Adrenogenital disorders	1	0.2
Endocrine disorder, unspecified	1	0.2
Wernicke's encephalopathy	1	0.2
Dietary calcium deficiency	1	0.2
Nutritional deficiency, unspecified	1	0.2
Lipodystrophy	1	0.2
(M00-M99): Diseases of the musculoskeletal system and connective tissue	692	143.3

Osteoarthritis	197	40.8
Age-Related Osteoporosis without Current Pathological Fracture	72	14.9
Other arthritis	67	13.9
Dorsalgia	66	13.7
Osteoporosis with pathological fracture	58	12.0
Other joint disorders, not elsewhere classified	48	9.9
Other soft tissue disorders, not elsewhere classified	34	7.0
Acquired deformities of fingers and toes	16	3.3
Scoliosis	16	3.3
Other disorders of synovium and tendon	14	2.9
Other disorders of bone density and structure	14	2.9
Other systemic involvement of connective tissue	13	2.7
Spondylosis	12	2.5
Idiopathic gout	9	1.9
Spinal stenosis, site unspecified	8	1.7
Other deforming dorsopathies	6	1.2
Rheumatoid arthritis with rheumatoid factor	5	1.0
Synovitis and tenosynovitis	4	0.8
Other bursopathies	4	0.8
Fibroblastic disorders	3	0.6
Other enthesopathies	3	0.6
Osteitis deformans	3	0.6
Other and unspecified arthropathy	2	0.4
Internal derangement of knee	2	0.4
Other necrotizing vasculopathies	2	0.4
Other intervertebral disc disorders	2	0.4
Disorder of bone, unspecified	2	0.4
Other disorders of cartilage	2	0.4
Other rheumatoid arthritis	1	0.2
Other crystal arthropathies	1	0.2
Other acquired deformities of limbs	1	0.2
Dentofacial anomalies	1	0.2
Other inflammatory spondylopathies	1	0.2
Soft tissue disorders related to use, overuse and pressure	1	0.2
Shoulder lesions	1	0.2
Adult osteomalacia due to malnutrition	1	0.2
(Z00-Z99): Factors influencing health status and contact with health services	654	135.4
Problems related to care provider dependency	146	30.2
Dependence on enabling machines and devices, not elsewhere classified	104	21.5
Encounter for other prophylactic measures	102	21.1
Personal history of medical treatment	97	20.1
Personal history of allergy to drugs, medicaments and biological substances	93	19.3

Presence of cardiac and vascular implants and grafts	22	4.6
Personal history of certain other diseases	21	4.3
Problems related to life-management difficulty	20	4.1
Personal history of malignant neoplasm	13	2.7
Personal risk factors, not elsewhere classified	9	1.9
Problems related to lifestyle	8	1.7
Problems related to housing and economic circumstances	3	0.6
Problems related to social environment	3	0.6
Family history of malignant neoplasm of digestive organs	2	0.4
Transplanted organ and tissue status	2	0.4
Other postprocedural states	2	0.4
Other special examinations and investigations of persons without symptoms or reported diagnosis	1	0.2
Encounter for screening for other diseases and disorders	1	0.2
Problems related to education and literacy	1	0.2
Other problems related to primary support group, including family circumstances	1	0.2
Problems related to medical facilities and other health care	1	0.2
Family history of mental and behavioural disorders	1	0.2
Presence of other devices	1	0.2
(G00-G99): Diseases of the nervous system	522	108.1
Insomnia and sleep disorders	181	37.5
Alzheimer's disease	131	27.1
Acute pain	55	11.4
Parkinson's disease	29	6.0
Epilepsy	29	6.0
Hemiplegia and hemiparesis	17	3.5
Hydrocephalus	17	3.5
Carpal tunnel syndrome	10	2.1
Polyneuropathy	9	1.9
Secondary parkinsonism	6	1.2
Dementia	5	1.0
Restless legs syndrome	4	0.8
Neuralgia	3	0.6
Mononeuropathies of lower limb	3	0.6
Myopathy	3	0.6
Parapleagia and quadriplegia	3	0.6
Myalgic encephalomyelitis/chronic fatigue syndrome	3	0.6
Other disorders of central nervous system	3	0.6
Multiple sclerosis	2	0.4
Headache	2	0.4
Cerebral palsy	2	0.4

Dyskinesia	1	0.2
Migraine	1	0.2
Stroke	1	0.2
Nerve root and plexus compressions in diseases classified elsewhere	1	0.2
Inflammatory polyneuropathy	1	0.2
(F00-F99): Mental and behavioral disorders	515	106.6
Depressive episode	138	28.6
Anxiety, dissociative, stress-related, somatoform and other nonpsychotic mental disorders (F40-F48)	130	26.9
Unspecified dementia	79	16.4
Vascular dementia	40	8.3
Nicotine	26	5.4
Delirium due to known physiological condition	21	4.3
Conduct disorder	15	3.1
Alcohol	14	2.9
Schizophrenia	13	2.7
Dysthymic disorder	7	1.4
Personality disorder	7	1.4
Bipolar affective disorder	6	1.2
Mental disorder	6	1.2
Unspecified psychosis not due to a substance or known physiological condition	4	0.8
Manic episode	2	0.4
Insomnia	2	0.4
Intellectual Disabilities	2	0.4
Delusional disorders	1	0.2
Speech and language disorder	1	0.2
Developmental disorder of scholastic skills	1	0.2
(K00-K93): Diseases of the digestive system	511	105.8
Other functional intestinal disorders	146	30.2
Hernia	85	17.6
Diseases of esophagus, stomach and duodenum	76	15.7
Disorders of gallbladder, biliary tract and pancreas	55	11.4
Diverticular disease of intestine	33	6.8
Other diseases of liver	20	4.1
Other disorders of teeth and supporting structures	15	3.1
Other diseases of intestine	15	3.1
Other noninfective gastroenteritis and colitis	12	2.5
Dental caries	8	1.7
Gingivitis and periodontal diseases	8	1.7
Irritable bowel syndrome	7	1.4
Haemorrhoids and perianal venous thrombosis	6	1.2

Paralytic ileus and intestinal obstruction without hernia	5	1.0
Other diseases of anus and rectum	3	0.6
Other diseases of digestive system	3	0.6
Stomatitis and related lesions	2	0.4
Ulcerative colitis	2	0.4
Toxic liver disease with cholestasis	2	0.4
Diseases of pulp and periapical tissues	1	0.2
Diseases of salivary glands	1	0.2
Other diseases of lip and oral mucosa	1	0.2
Crohn's disease	1	0.2
Vascular disorders of intestine	1	0.2
Fissure and fistula of anal and rectal regions	1	0.2
Fibrosis and cirrhosis of liver	1	0.2
Intestinal malabsorption	1	0.2
(N00-N99): Diseases of the genitourinary system	348	72.0
Chronic kidney disease	134	27.7
Other disorders of urinary system	71	14.7
Benign prostatic hyperplasia	60	12.4
Calculus of kidney and ureter	28	5.8
Female genital prolapse	16	3.3
Benign mammary dysplasia	7	1.4
Other disorders of breast	6	1.2
Menopausal and other perimenopausal disorders	6	1.2
Diseases of Bartholin's gland	5	1.0
Pain and other conditions associated with female genital organs and menstrual cycle	3	0.6
Other disorders of bladder	2	0.4
Inflammatory diseases of prostate	2	0.4
Noninflammatory disorders of ovary, fallopian tube and broad ligament	2	0.4
Disorders of prepuce	1	0.2
Vulvovaginal ulceration and inflammation in diseases classified elsewhere	1	0.2
Polyp of female genital tract	1	0.2
Other noninflammatory disorders of uterus, except cervix	1	0.2
Excessive, frequent and irregular menstruation	1	0.2
Postprocedural disorders of genitourinary system, not elsewhere classified	1	0.2
(H00-H59): Diseases of the eye and adnexa	293	60.7
Age-related cataract	99	20.5
Glaucoma	87	18.0
Disorders of lacrimal system	20	4.1
Other retinal disorders	19	3.9
Conjunctivitis	17	3.5
Visual disturbances	15	3.1

Visual impairment including blindness (binocular or monocular)	12	2.5
Other disorders of eyelid	5	1.0
Disorders of refraction and accommodation	4	0.8
Disorders of vitreous body	3	0.6
Retinal vascular occlusions	2	0.4
Disorders of globe	2	0.4
Other disorders of eye and adnexa	2	0.4
Corneal scars and opacities	1	0.2
Other disorders of iris and ciliary body	1	0.2
Other cataract	1	0.2
Retinal detachments and breaks	1	0.2
Retinal disorders in diseases classified elsewhere	1	0.2
Nystagmus and other irregular eye movements	1	0.2
(L00-L99): Diseases of the skin and subcutaneous tissue	289	59.8
Pressure ulcer	122	25.3
Dermatitis and eczema	89	18.4
Skin changes due to chronic exposure to nonionizing radiation	24	5.0
Diseases of the skin and subcutaneous tissue	10	2.1
Seborrheic keratosis	10	2.1
Cellulitis and acute lymphangitis	8	1.7
Other local infections of skin and subcutaneous tissue	5	1.0
Diseases of the skin and subcutaneous tissue	4	0.8
Nail disorders	4	0.8
Lichen planus	3	0.6
Cutaneous abscess, furuncle and carbuncle	2	0.4
Diseases of the skin and subcutaneous tissue	2	0.4
Erythema nodosum	1	0.2
Androgenic alopecia	1	0.2
Other follicular disorders	1	0.2
Other disorders of pigmentation	1	0.2
Hypertrophic disorders of skin	1	0.2
Vasculitis limited to skin, not elsewhere	1	0.2
(D50-D89): Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	267	55.3
Anemia, unspecified	109	22.6
Iron deficiency anemia	79	16.4
Vitamin B12 deficiency anemia	38	7.9
Folate deficiency anemia	21	4.3
Qualitative platelet defects	7	1.4
White blood count	6	1.2
Other megaloblastic anemias, not elsewhere classified	2	0.4
Acquired hemolytic anemia, unspecified	2	0.4

Thalassemia	1	0.2
Anemia in other chronic diseases classified elsewhere	1	0.2
Thrombocytosis	1	0.2
(S00-T98): Injury, poisoning and certain other consequences of external causes	256	53.0
Injury of unspecified body region	133	27.5
Fracture of femur	59	12.2
Fracture of lumbar spine and pelvis	21	4.3
Dislocation, sprain and strain of joints and ligaments of shoulder girdle	11	2.3
Intracranial injury	8	1.7
Other and unspecified injuries of head	6	1.2
Dislocation, sprain and strain of joints and ligaments of knee	3	0.6
Fracture of skull and facial bones	2	0.4
Fracture of shoulder and upper arm	2	0.4
Dislocation, sprain and strain of joints and ligaments at neck level	1	0.2
Injury of nerves and spinal cord at neck level	1	0.2
Fracture of rib(s), sternum and thoracic spine	1	0.2
Injury of muscles and tendons at shoulder and upper arm level	1	0.2
Dislocation, sprain and strain of joints and ligaments at wrist and hand level	1	0.2
Fracture of lower leg, including ankle	1	0.2
Poisoning by primarily systemic and haematological agents, not elsewhere classified	1	0.2
Toxic effect of metals	1	0.2
Exhaustion due to excessive exertion, initial encounter	1	0.2
Adult and child abuse, neglect and other maltreatment, suspected	1	0.2
Complications of procedures, not elsewhere classified	1	0.2
(U00-U99): Codes for special purposes	197	40.8
COVID-19	197	40.8
(J00-J99): Diseases of the respiratory system	188	38.9
Other chronic obstructive pulmonary disease	56	11.6
Bronchitis, not specified as acute or chronic	31	6.4
Other respiratory disorders	20	4.1
Vasomotor and allergic rhinitis	16	3.3
Asthma	13	2.7
Pneumonia, organism unspecified	9	1.9
Diseases of the respiratory system	7	1.4
Unspecified acute lower respiratory infection	6	1.2
Pneumonitis due to food and vomit	6	1.2
Pulmonary edema	5	1.0
Chronic rhinitis, nasopharyngitis and pharyngitis	4	0.8
Other interstitial pulmonary diseases	4	0.8
Acute upper respiratory infections of multiple and unspecified sites	3	0.6

Diseases of the respiratory system	3	0.6
Chronic sinusitis	2	0.4
Chronic diseases of tonsils and adenoids	1	0.2
Pneumoconiosis due to asbestos and other mineral fibers	1	0.2
Pleural effusion, not elsewhere classified	1	0.2
(C00-D48): Neoplasms	150	31.1
Malignant neoplasm	104	21.5
Benign neoplasm	38	7.9
Myelodysplastic syndromes	5	1.0
Monoclonal gammopathy	3	0.6
(H60-H95): Diseases of the ear and mastoid process	109	22.6
Other and unspecified hearing loss	90	18.6
Other disorders of ear, not elsewhere classified	11	2.3
Central perforation of tympanic membrane	4	0.8
Otitis externa	1	0.2
Other disorders of external ear	1	0.2
Disorders of external ear in diseases classified elsewhere	1	0.2
Disorders of vestibular function	1	0.2
Interventions	131	27.1
Spherophakia	29	6.0
Knee prosthesis	25	5.2
Hysterectomy	22	4.6
Cholecystectomy	20	4.1
Hip prosthesis	17	3.5
Appendectomy	11	2.3
Colostomy or ileostomy	7	1.4
(A00-B99): Certain infectious and parasitic diseases	61	12.6
Infections	61	12.6
(V01-Y98): External causes of morbidity and mortality	12	2.5
Surgical operation and other surgical procedures as the cause of abnormal reaction of the patient	4	0.8
Slipping, tripping, stumbling and falls (W00-W19)	3	0.6
Intentional self-harm by sharp object	2	0.4
Assault by other specified means	1	0.2
Other medical procedures as the cause of abnormal reaction of the patient	1	0.2
Place of occurrence of the external cause	1	0.2

Supplementary Table S2: Complete list of all the pharmacological prescribed treatments divided into groups according to their ATC

A- Alimentary tract and metabolism (n=708)			
Name	ATC	n	%
Omeprazole	A02BC01	274	56.8
Vitamin D and analogues	A11CC	86	17.8
Metformin	A10BA02	60	12.4
Calcium, combinations with vitamin D and/or other drugs	A12AX	54	11.2
Insulin glargine	A10AE04	31	6.4
Insulin aspart	A10AB05	20	4.1
Macrogol	A06AD15	16	3.3
Pantoprazole	A02BC02	14	2.9
Lactulose	A06AD11	10	2.1
Domperidone	A03FA03	8	1.7
Ispaghula (psylla seeds)	A06AC01	7	1.5
Potassium	A12BA	7	1.5
Acetylsalicylic acid	A01AD05	6	1.2
Esomeprazole	A02BC05	6	1.2
Metformin and sitagliptin	A10BD07	6	1.2
Sitagliptin	A10BH01	6	1.2
Insulin detemir	A10AE05	5	1.0
Linagliptin	A10BH05	5	1.0
Metoclopramide	A03FA01	4	0.8
Ursodeoxycholic acid	A05AA02	4	0.8
Lactitol	A06AD12	4	0.8
Betamethasone	A07EA04	4	0.8
Gliclazide	A10BB09	4	0.8
Calcium carbonate	A02AC01	3	0.6
Clebopride	A03FA06	3	0.6
Osmotically acting laxatives	A06AD	3	0.6
Rifaximin	A07AA11	3	0.6
Loperamide	A07DA03	3	0.6
Insulin lispro	A10AB04	3	0.6
Repaglinide	A10BX02	3	0.6
Vitamin B1, plain	A11DA	3	0.6
Calcium	A12AA	3	0.6
Ranitidine	A02BA02	2	0.4
Lansoprazole	A02BC03	2	0.4
Magnesium oxide	A06AD02	2	0.4
Prednisone	A07EA03	2	0.4

Insulin glulisine	A10AB06	2	0.4
Pioglitazone	A10BG03	2	0.4
Vildagliptin	A10BH02	2	0.4
Vitamin B-complex, plain	A11EA	2	0.4
Potassium hydrogencarbonate	A12BA04	2	0.4
Clotrimazole	A01AB18	1	0.2
Prednisolone, combinations	A01AC54	1	0.2
Antacids containing magnesium compounds	A02AA	1	0.2
Famotidine	A02BA03	1	0.2
Silicones	A03AX13	1	0.2
Liquid paraffin	A06AA01	1	0.2
Lactulose, combinations	A06AD61	1	0.2
Mesalazine	A07EC02	1	0.2
Glutamic acid hydrochloride	A05BA	1	0.2
Insulin (human)	A10AC01	1	0.2
Insulin degludec and insulin aspart	A10AD06	1	0.2
Insulin degludec	A10AE06	1	0.2
Metformin and vildagliptin	A10BD08	1	0.2
Metformin and saxagliptin	A10BD10	1	0.2
Saxagliptin	A10BH03	1	0.2
Dapagliflozin	A10BK01	1	0.2
Tocopherol	A11HA03	1	0.2
Calcium carbonate	A12AA04	1	0.2
Potassium citrate	A12BA02	1	0.2
Magnesium supplements, alimentary tract and metabolism	A12CC	1	0.2
Magnesium chloride	A12CC01	1	0.2
Magnesium citrate	A12CC04	1	0.2
B- Blood and blood forming organs (n=441)			
Name	ATC	n	%
Acetylsalicylic acid	B01AC06	134	27.8
Ferrous glycine sulfate	B03AA01	60	12.4
Folic acid	B03BB01	40	8.3
Apixaban	B01AF02	37	7.7
Clopidogrel	B01AC04	34	7.1
Acenocoumarol	B01AA07	31	6.4
Rivaroxaban	B01AF01	21	4.4
Cyanocobalamin	B03BA01	19	3.9
Edoxaban	B01AF03	9	1.9
Vitamin B12 and folic acid	B03B	9	1.9
Dabigatran etexilate	B01AE07	8	1.7
Ferrous sulfate	B03AD03	8	1.7
Enoxaparin	B01AB05	5	1.0

Vitamin B12 (cyanocobalamin and analogues)	B03BA	5	1.0
Warfarin	B01AA03	4	0.8
Ferrous sulfate	B03AA07	3	0.6
Triflusal	B01AC18	2	0.4
Iron trivalent, oral antianemic preparations	B03AB	2	0.4
Ferrous gluconate	B03AD05	2	0.4
Cyanocobalamin, combinations	B03BA51	2	0.4
Darbepoetin alfa	B03XA02	2	0.4
Dipyridamole	B01AC07	1	0.2
Cilostazol	B01AC23	1	0.2
Tranexamic acid	B02AA02	1	0.2
Iron, parenteral antianemic preparations	B03AC	1	0.2
C- Cardiovascular system (n=875)			
Name	ATC	n	%
Furosemide	C03CA01	144	29.9
Enalapril	C09AA02	109	22.6
Bisoprolol	C07AB07	89	18.5
Simvastatin	C10AA01	78	16.2
Amlodipine	C08CA01	66	13.7
Atorvastatin	C10AA05	61	12.7
Losartan	C09CA01	41	8.5
Hydrochlorothiazide	C03AA03	34	7.1
Glyceryl trinitrate	C05AE01	20	4.1
Digoxin	C01AA05	19	3.9
Timolol and thiazides	C07BA06	19	3.9
Carvedilol	C07AG02	16	3.3
Enalapril and diuretics	C09BA02	15	3.1
Torasemide	C03CA04	13	2.7
Spironolactone	C03DA01	13	2.7
Diltiazem	C05AE03	11	2.3
Atenolol	C07AB03	10	2.1
Losartan and diuretics	C09DA01	8	1.7
Amiodarone	C01BD01	6	1.2
Ramipril	C09AA05	6	1.2
Doxazosin	C02CA04	5	1.0
Captopril	C09AA01	5	1.0
Lisinopril	C09AA03	5	1.0
Valsartan	C09CA03	5	1.0
Telmisartan	C09CA07	5	1.0
Lisinopril and diuretics	C09BA03	4	0.8
Ezetimibe	C10AX09	4	0.8
Glyceryl trinitrate	C01DA02	3	0.6

Hydrochlorothiazide and potassium-sparing agents	C03EA01	3	0.6
Pentoxifylline	C04AD03	3	0.6
Prednisolone	C05AA04	3	0.6
Propranolol	C07AA05	3	0.6
Etilefrine	C01CA01	2	0.4
Isosorbide mononitrate	C01DA14	2	0.4
Trimetazidine	C01EB15	2	0.4
Ranolazine	C01EB18	2	0.4
Hydralazine	C02DB02	2	0.4
Indapamide	C03BA11	2	0.4
Eplerenone	C03DA04	2	0.4
Dexamethasone	C05AA09	2	0.4
Olmesartan medoxomil	C09CA08	2	0.4
Olmesartan medoxomil and amlodipine	C09DB02	2	0.4
Valsartan, amlodipine and hydrochlorothiazide	C09DX01	2	0.4
Pravastatin	C10AA03	2	0.4
Epinephrine	C01CA24	1	0.2
Propafenone	C01BC03	1	0.2
Flecainide	C01BC04	1	0.2
Ivabradine	C01EB17	1	0.2
Hydrochlorothiazide, combinations	C03AX01	1	0.2
Naftidrofuryl	C04AX21	1	0.2
Diosmin	C05CA03	1	0.2
Timolol	C07AA06	1	0.2
Nebivolol	C07AB12	1	0.2
Nifedipine	C08CA05	1	0.2
Manidipine	C08CA11	1	0.2
Lercanidipine	C08CA13	1	0.2
Verapamil	C08DA01	1	0.2
Eprosartan	C09CA02	1	0.2
Irbesartan	C09CA04	1	0.2
Valsartan and diuretics	C09DA03	1	0.2
Candesartan and diuretics	C09DA06	1	0.2
Telmisartan and diuretics	C09DA07	1	0.2
Olmesartan medoxomil and diuretics	C09DA08	1	0.2
Lovastatin	C10AA02	1	0.2
Rosuvastatin	C10AA07	1	0.2
Pitavastatin	C10AA08	1	0.2
Gemfibrozil	C10AB04	1	0.2
Fenofibrate	C10AB05	1	0.2
Colestyramine	C10AC01	1	0.2
D- Dermatologicals (n=38)			

Name	ATC	n	%
Ciclopirox	D01AE14	9	1.9
Finasteride	D11AX10	5	1.0
Budesonide	D07AC09	3	0.6
Propanol	D08AX03	3	0.6
Clindamycin	D10AF01	3	0.6
Ketoconazole	D01AC08	2	0.4
Amorolfine	D01AE16	2	0.4
Mupirocin	D06AX09	2	0.4
Clobetasol	D07AD01	2	0.4
Collagenase, combinations	D03BA52	1	0.2
Tacalcitol	D05AX04	1	0.2
Aciclovir	D06BB03	1	0.2
Methylprednisolone	D07AA01	1	0.2
Hydrocortisone	D07XA01	1	0.2
Potassium permanganate	D08AX06	1	0.2
Collagen, combinations	D11AX57	1	0.2
G- Genito urinary system and sex hormones (n=48)			
Name	ATC	n	%
Tamsulosin	G04CA02	20	4.2
Tamsulosin and dutasteride	G04CA52	9	1.9
Mirabegron	G04BD12	5	1.0
Solifenacin	G04BD08	3	0.6
Fesoterodine	G04BD11	2	0.4
Finasteride	G04CB01	2	0.4
Dutasteride	G04CB02	2	0.4
Miconazole	G01AF04	1	0.2
Megestrol	G03AC05	1	0.2
Raloxifene	G03XC01	1	0.2
Alfuzosin	G04CA01	1	0.2
Prunus africanae cortex	G04CX01	1	0.2
H- Systemic hormonal preparations (n=89)			
Name	ATC	n	%
Levothyroxine sodium	H03AA01	60	12.5
Prednisone	H02AB07	7	1.5
Deflazacort	H02AB13	3	0.6
Thiamazole	H03BB02	3	0.6
Teriparatide	H05AA02	3	0.6
Calcifediol	H05BX05	3	0.6
Methylprednisolone	H02AB04	2	0.4
Hydrocortisone	H02AB09	2	0.4
Glucagon, glucose	H04AA01	2	0.4

Pancreatic hormones	H04	2	0.4
Octreotide	H01CB02	1	0.2
Ketoconazole	H02CA03	1	0.2
J- Antiinfective for systemic use (n=9)			
Name	ATC	n	%
Sulfamoxole and trimethoprim	J01EE04	2	0.4
Azithromycin	J01FA10	2	0.4
Tobramycin	J01GB01	2	0.4
Ciprofloxacin	J01MA02	1	0.2
Fosfomycin	J01XX01	1	0.2
Fluconazole	J02AC01	1	0.2
L- Antineoplasic and inmunomodulating agents (n=24)			
Name	ATC	n	%
Letrozole	L02BG04	5	1.0
Hydroxycarbamide	L01XX05	3	0.6
Azathioprine	L04AX01	2	0.4
Cyclophosphamide	L01AA01	1	0.2
Nitrogen	L01AA	1	0.2
Anagrelide	L01XX35	1	0.2
Venetoclax	L01XX52	1	0.2
Leuprorelin	L02AE02	1	0.2
Triptorelin	L02AE04	1	0.2
Fulvestrant	L02BA03	1	0.2
Bicalutamide	L02BB03	1	0.2
Anastrozole	L02BG03	1	0.2
Exemestane	L02BG06	1	0.2
Filgrastim	L03AA02	1	0.2
Mycophenolic acid	L04AA06	1	0.2
Methotrexate	L04AX03	1	0.2
Lenalidomide	L04AX04	1	0.2
M- Musculo-skeletal system (n=57)			
Name	ATC	n	%
Allopurinol	M04AA01	18	3.7
Alendronic acid	M05BA04	14	2.9
Denosumab	M05BX04	9	1.9
Diclofenac	M01AB05	5	1.0
Baclofen	M03BX01	5	1.0
Risedronic acid	M05BA07	2	0.4
Aceclofenac	M01AB16	1	0.2
Dexketoprofen	M01AE17	1	0.2
Naproxen and esomeprazole	M01AE52	1	0.2
Febuxostat	M04AA03	1	0.2

N- Nervous system (n=1474)			
Name	ATC	n	%
Paracetamol	N02BE01	269	55.8
Quetiapine	N05AH04	183	38.0
Lorazepam	N05BA06	105	21.8
Sertraline	N06AB06	74	15.4
Trazodone	N06AX05	69	14.3
Citalopram	N06AB04	62	12.9
Risperidone	N05AX08	61	12.7
Mirtazapine	N06AX11	53	11.0
Memantine	N06DX01	43	8.9
Metamizole sodium	N02BB02	41	8.5
Fentanyl	N02AB03	35	7.3
Gabapentin	N02BF01	31	6.4
Pregabalin	N03AX16	29	6.0
Donepezil	N06DA02	28	5.8
Rivastigmine	N06DA03	28	5.8
Tramadol	N02AX02	25	5.2
Levodopa and decarboxylase inhibitor	N04BA02	25	5.2
Lormetazepam	N05CD06	25	5.2
Levetiracetam	N03AX14	21	4.4
Haloperidol	N05AD01	19	3.9
Clomethiazole	N05CM02	18	3.7
Alprazolam	N05BA12	16	3.3
Galantamine	N06DA04	16	3.3
Tramadol and paracetamol	N02AJ13	14	2.9
Paroxetine	N06AB05	13	2.7
Clonazepam	N03AE01	12	2.5
Betahistine	N07CA01	12	2.5
Venlafaxine	N06AX16	10	2.1
Diazepam	N05BA01	9	1.9
Valproic acid	N03AG01	8	1.7
Duloxetine	N06AX21	8	1.7
Citicoline	N06BX06	6	1.2
Pramipexole	N04BC05	5	1.0
Rotigotine	N04BC09	5	1.0
Aripiprazole	N05AX12	5	1.0
Potassium clorazepate	N05BA05	5	1.0
Amitriptyline	N06AA09	5	1.0
Carbamazepine	N03AF01	4	0.8
Rasagiline	N04BD02	4	0.8
Safinamide	N04BD03	4	0.8

Olanzapine	N05AH03	4	0.8
Codeine and paracetamol	N02AJ06	3	0.6
Lamotrigine	N03AX09	3	0.6
Lacosamide	N03AX18	3	0.6
Levodopa	N04BA01	3	0.6
Clozapine	N05AH02	3	0.6
Bromazepam	N05BA08	3	0.6
Escitalopram	N06AB10	3	0.6
Vortioxetine	N06AX26	3	0.6
Morphine	N02AA01	2	0.4
Tapentadol	N02AX06	2	0.4
Metamizole sodium, combinations excl. psycholeptics	N02BB52	2	0.4
Primidone	N03AA03	2	0.4
Levosulpiride	N05AL07	2	0.4
Hydroxyzine	N05BB01	2	0.4
Loprazolam	N05CD11	2	0.4
Zolpidem	N05CF02	2	0.4
Desvenlafaxine	N06AX23	2	0.4
Oxycodone and naloxone	N02AA55	1	0.2
Fentanyl	N02AB03	1	0.2
Metamizole sodium, combinations with psycholeptics	N02BB72	1	0.2
Phenytoin	N03AB02	1	0.2
Oxcarbazepine	N03AF02	1	0.2
Topiramate	N03AX11	1	0.2
Zonisamide	N03AX15	1	0.2
Perampanel	N03AX22	1	0.2
Brivaracetam	N03AX23	1	0.2
Trihexyphenidyl	N04AA01	1	0.2
Levodopa, decarboxylase inhibitor and COMT inhibitor	N04BA03	1	0.2
Entacapone	N04BX02	1	0.2
Levomepromazine	N05AA02	1	0.2
Perphenazine	N05AB03	1	0.2
Clotiapine	N05AH06	1	0.2
Sulpiride	N05AL01	1	0.2
Lithium	N05AN01	1	0.2
Benzodiazepine derivative anxiolytics	N05BA	1	0.2
Flurazepam	N05CD01	1	0.2
Midazolam	N05CD08	1	0.2
Valerianae radix	N05CM09	1	0.2
Fluoxetine	N06AB03	1	0.2
Nicotine	N07BA01	1	0.2
P- Antiparasitic products, insecticides and repellents (n=1)			

Name	ATC	n	%
Hydroxychloroquine	P01BA02	1	0.2
R- Respiratory system (n=119)			
Name	ATC	n	%
Ipratropium bromide	R03BB01	31	6.4
Tiotropium bromide	R03BB04	15	3.1
Budesonide	R01AD05	13	2.7
Salmeterol and fluticasone	R03AK06	10	2.1
Salbutamol	R03AC02	7	1.5
Salmeterol	R03AC12	7	1.5
Formoterol and budesonide	R03AK07	6	1.2
Formoterol and beclometasone	R03AK08	6	1.2
Cetirizine	R06AE07	3	0.6
Loratadine	R06AX13	3	0.6
Formoterol and fluticasone	R03AK11	2	0.4
Acetylcysteine	R05CB01	2	0.4
Ebastine	R06AX22	2	0.4
Mometasone	R01AD09	1	0.2
Formoterol	R03AC13	1	0.2
Olodaterol	R03AC19	1	0.2
Vilanterol and fluticasone furoate	R03AK10	1	0.2
Salbutamol and ipratropium bromide	R03AL02	1	0.2
Indacaterol and glycopyrronium bromide	R03AL04	1	0.2
Olodaterol and tiotropium bromide	R03AL06	1	0.2
Fluticasone furoate	R03BA09	1	0.2
Montelukast	R03DC03	1	0.2
Dexchlorpheniramine	R06AB02	1	0.2
Rupatadine	R06AX28	1	0.2
Bilastine	R06AX29	1	0.2
S- Sensory organs (n=76)			
Name	ATC	n	%
Latanoprost	S01EE01	27	5.6
Timolol	S01ED01	8	1.7
Artificial tears and other indifferent preparations	S01XA20	8	1.7
Bimatoprost	S01EE03	7	1.5
Acetazolamide	S01EC01	3	0.6
brinzolamide	S01EC04	3	0.6
brinzolamide, combinations	S01EC54	3	0.6
Timolol, combinations	S01ED51	3	0.6
Travoprost	S01EE04	3	0.6
Brimonidine	S01GA07	3	0.6
Dorzolamide	S01EC03	2	0.4

Azithromycin	S01AA26	1	0.2
Famciclovir	S01AD07	1	0.2
Carteolol	S01ED05	1	0.2
Tafluprost	S01EE05	1	0.2
Olopatadine	S01GX09	1	0.2
Fluocinolone acetonide	S02BA08	1	0.2
V- Various (n=2)			
Name	ATC	n	%
Polystyrene sulfonate	V03AE01	1	0.2
Sodium phosphate	V03AG05	1	0.2

Annex 6. Supplementary material from the publication of the second study

Supplementary Table S1: Complete list of all the added drugs

Drugs added			
ATC	**Name**	**n**	**%**
A11CC	Vitamin D and analogues	55	8.8
N02BE01	Paracetamol	39	6.2
N05AH04	Quetiapine	28	4.5
B03B	Vitamin B and folic acid	25	4.0
A02BC01	Omeprazole	22	3.5
C03CA01	Furosemide	21	3.4
B03AB	Iron trivalent, oral antianemic preparations	19	3.0
A12AX	Calcium, combinations with vitamin D and/or other drugs	18	2.9
A06AD	Osmotically acting laxatives	16	2.6
N06AX11	Mirtazapine	16	2.6
N05BA06	Lorazepam	15	2.4
N02BB02	Metamizole sodium	14	2.2
A10A	Insulins and analogs	11	1.8
B01AF	Direct factor Xa inhibitors	11	1.8
C07AB07	Bisoprolol	11	1.8
C08CA01	Amlodipine	11	1.8
N05AX08	Risperidone	11	1.8
N06AB06	Sertraline	11	1.8
N06AX05	Trazodone	11	1.8
B01AC06	Acetylsalicylic acid	10	1.6
D01A	Antifungals for topical use	10	1.6
C10AA01	Simvastatin	8	1.3
N02AB03	Fentanyl	8	1.3
C09CA01	Losartan	7	1.1
M05BA	Bisphosphonates	7	1.1
B01AC04	Clopidogrel	6	1.0
C09AA02	Enalapril	6	1.0
N02AX02	Tramadol	6	1.0
N05CD06	Lormetazepam	6	1.0
A10BA02	Metformin	5	0.8
C03AA03	Hydrochlorothiazide	5	0.8
N03AX16	Pregabalin	5	0.8
N05AD01	Haloperidol	5	0.8
R03BB01	Ipratropium bromide	5	0.8
C10AA05	Atorvastatin	4	0.6
N03AX14	Levetiracetam	4	0.6

N06AB04	Citalopram	4	0.6
N06DX01	Memantine	4	0.6
R06AE07	Cetirizine	4	0.6
B01AB05	Enoxaparin	3	0.5
C05AE01	Glyceryl trinitrate	3	0.5
G04CA02	Tamsulosin	3	0.5
M05BX04	Denosumab	3	0.5
N03AE01	Clonazepam	3	0.5
N05AH03	Olanzapine	3	0.5
N06AX16	Venlafaxine	3	0.5
N06DA02	Donepezil	3	0.5
A02AA04	Magnesium hydroxide	2	0.3
A07EA04	Betamethasone	2	0.3
A10BH01	Sitagliptin	2	0.3
C03DA01	Spironolactone	2	0.3
C04AD03	Pentoxifylline	2	0.3
C05AA06	Fluorometholone	2	0.3
C05AA09	Dexamethasone	2	0.3
D03BA52	Collagenase, combinations	2	0.3
D06AX09	Mupirocin	2	0.3
G04CA52	Tamsulosin and dutasteride	2	0.3
H02AB09	Hydrocortisone	2	0.3
M01AB05	Diclofenac	2	0.3
M04AA01	Allopurinol	2	0.3
N05CH01	Melatonin	2	0.3
N05CM02	Clomethiazole	2	0.3
N06BX06	Citicoline	2	0.3
R03AC02	Salbutamol	2	0.3
R06AX13	Loratadine	2	0.3
R06AX22	Ebastine	2	0.3
S01EE03	Bimatoprost	2	0.3
V03AE01	Polystyrene sulfonate	2	0.3
A02BC02	Pantoprazole	1	0.2
A02BC05	Esomeprazole	1	0.2
A03AA05	Trimebutine	1	0.2
A03FA03	Domperidone	1	0.2
A10BD08	Metformin and vildagliptin	1	0.2
A10BJ06	Semaglutide	1	0.2
A10BK03	Empagliflozin	1	0.2
A11EA	Vitamin B-complex, plain	1	0.2
B01AC18	Triflusal	1	0.2
C01AA05	Digoxin	1	0.2

C01CA01	Etilefrine	1	0.2
C02CA04	Doxazosin	1	0.2
C03CA04	Torasemide	1	0.2
C07AG02	Carvedilol	1	0.2
C07BA06	Timolol and thiazides	1	0.2
C09AA03	Lisinopril	1	0.2
C09CA03	Valsartan	1	0.2
C09DA03	Valsartan and diuretics	1	0.2
C09DA06	Candesartan and diuretics	1	0.2
C09DX04	Valsartan and sacubitril	1	0.2
C10AB04	Gemfibrozil	1	0.2
D07AC09	Budesonide	1	0.2
D07CC01	Betamethasone and antibiotics	1	0.2
D08AL01	Silver nitrate	1	0.2
D10AF01	Clindamycin	1	0.2
G03AC05	Megestrol	1	0.2
H02AB13	Deflazacort	1	0.2
H03AA01	Levothyroxine sodium	1	0.2
J01EE05	Sulfadimidine and trimethoprim	1	0.2
J01XC01	Fusidic acid	1	0.2
J02AB02	Ketoconazole	1	0.2
J05AB11	Valaciclovir	1	0.2
L04AX01	Azathioprine	1	0.2
L04AX03	Methotrexate	1	0.2
L04AX04	Lenalidomide	1	0.2
M03BX01	Baclofen	1	0.2
N02AA05	Oxycodone	1	0.2
N02AJ13	Tramadol and paracetamol	1	0.2
N02AX06	Tapentadol	1	0.2
N03AF01	Carbamazepine	1	0.2
N03AX11	Topiramate	1	0.2
N03AX18	Lacosamide	1	0.2
N04BA02	Levodopa and decarboxylase inhibitor	1	0.2
N05AX12	Aripiprazole	1	0.2
N05BA12	Alprazolam	1	0.2
N05CF02	Zolpidem	1	0.2
N06AB03	Fluoxetine	1	0.2
N06AX21	Duloxetine	1	0.2
N06AX23	Desvenlafaxine	1	0.2
N06AX26	Vortioxetine	1	0.2
N06DA03	Rivastigmine	1	0.2
R01AD09	Mometasone	1	0.2

R01AD58	Fluticasone, combinations	1	0.2
M01AE01	Ibuprofen	1	0.2
R03AK07	Formoterol and budesonide	1	0.2
R03AL07	Formoterol and glycopyrronium bromide	1	0.2
R03CC02	Salbutamol	1	0.2
S01EC03	Dorzolamide	1	0.2
S01ED01	Timolol	1	0.2
S01FA02	Scopolamine	1	0.2
S01GA07	Brimonidine	1	0.2
S01XA20	Artificial tears and other indifferent preparations	1	0.2
	Others	14	2.2
	TOTAL	626	100.0

Supplementary Table S2: Complete list of all the added drugs according to their ATC classification

Drugs added			
A- Alimentary tract and metabolism			
ATC	**Name**	**n**	**%**
A11CC	Vitamin D and analogues	55	9.0
A02BC01	Omeprazole	22	3.6
A12AX	Calcium, combinations with vitamin D and/or other drugs	18	2.6
A06AD	Osmotically acting laxatives	16	2.6
A10A	Insulins and analogs	11	1.8
A10BA02	Metformin	5	0.8
A02AA04	Magnesium hydroxide	2	0.3
A07EA04	Betamethasone	2	0.3
A10BH01	Sitagliptin	2	0.3
A02BC02	Pantoprazole	1	0.2
A02BC05	Esomeprazole	1	0.2
A03AA05	Trimebutine	1	0.2
A03FA03	Domperidone	1	0.2
A10BD08	Metformin and vildagliptin	1	0.2
A10BJ06	Semaglutide	1	0.2
A10BK03	Empagliflozin	1	0.2
A11EA	Vitamin B-complex, plain	1	0.2
B- Blood and blood forming organs			
ATC	**Name**	**n**	**%**
B01AC06	Acetylsalicylic acid	10	1.6
B03B	Vitamin B and folic acid	25	4.1
B03AB	Iron trivalent, oral antianemic preparations	19	2.7
B01AF	Direct factor Xa inhibitors	11	1.8
B01AC04	Clopidogrel	6	1.0
B01AB05	Enoxaparin	3	0.5
B01AC18	Triflusal	1	0.2
C- Cardiovascular system			
ATC	**Name**	**n**	**%**
C03CA01	Furosemide	21	3.4
C07AB07	Bisoprolol	11	1.8
C08CA01	Amlodipine	11	1.8
C10AA01	Simvastatin	8	1.3
C09CA01	Losartan	7	1.1
C09AA02	Enalapril	6	1.0
C03AA03	Hydrochlorothiazide	5	0.8
C10AA05	Atorvastatin	4	0.7

C05AE01	Glyceryl trinitrate	3	0.5
C03DA01	Spironolactone	2	0.3
C04AD03	Pentoxifylline	2	0.3
C05AA06	Fluorometholone	2	0.3
C05AA09	Dexamethasone	2	0.3
C01AA05	Digoxin	1	0.2
C01CA01	Etilefrine	1	0.2
C02CA04	Doxazosin	1	0.2
C03CA04	Torasemide	1	0.2
C07AG02	Carvedilol	1	0.2
C07BA06	Timolol and thiazides	1	0.2
C09AA03	Lisinopril	1	0.2
C09CA03	Valsartan	1	0.2
C09DA03	Valsartan and diuretics	1	0.2
C09DA06	Candesartan and diuretics	1	0.2
C09DX04	Valsartan and sacubitril	1	0.2
C10AB04	Gemfibrozil	1	0.2
D- Dermatologicals			
ATC	**Name**	**n**	**%**
D01A	Antifungals for topical use	10	1.6
D03BA52	Collagenase, combinations	2	0.3
D06AX09	Mupirocin	2	0.3
D07AC09	Budesonide	1	0.2
D07CC01	Betamethasone and antibiotics	1	0.2
D08AL01	Silver nitrate	1	0.2
D10AF01	Clindamycin	1	0.2
G- Genito urinary system and sex hormones			
ATC	**Name**	**n**	**%**
G04CA02	Tamsulosin	3	0.5
G04CA52	Tamsulosin and dutasteride	2	0.3
G03AC05	Megestrol	1	0.2
H- Systemic hormonal preparations			
ATC	**Name**	**n**	**%**
H02AB09	Hydrocortisone	2	0.3
H02AB13	Deflazacort	1	0.2
H03AA01	Levothyroxine sodium	1	0.2
J- Antiinfectives for systemic use			
ATC	**Name**	**n**	**%**
J01EE05	Sulfadimidine and trimethoprim	1	0.2
J01XC01	Fusidic acid	1	0.2
J02AB02	Ketoconazole	1	0.2
J05AB11	Valaciclovir	1	0.2

L- Antineoplastic and immunomodulating agents			
ATC	**Name**	**n**	**%**
L04AX01	Azathioprine	1	0.2
L04AX03	Methotrexate	1	0.2
L04AX04	Lenalidomide	1	0.2
M- Musculo-skeletal system			
ATC	**Name**	**n**	**%**
M05BA	Bisphosphonates	7	1.1
M05BX04	Denosumab	3	0.5
M01AB05	Diclofenac	2	0.3
M04AA01	Allopurinol	2	0.3
M01AE01	Ibuprofen	1	0.2
M03BX01	Baclofen	1	0.2
N- Nervous system			
ATC	**Name**	**n**	**%**
N02BE01	Paracetamol	39	6.4
N05AH04	Quetiapine	28	4.6
N06AX11	Mirtazapine	16	2.6
N05BA06	Lorazepam	15	2.5
N02BB02	Metamizole sodium	14	2.3
N05AX08	Risperidone	11	1.8
N06AB06	Sertraline	11	1.8
N06AX05	Trazodone	11	1.8
N02AB03	Fentanyl	8	1.3
N02AX02	Tramadol	6	1.0
N05CD06	Lormetazepam	6	1.0
N03AX16	Pregabalin	5	0.8
N05AD01	Haloperidol	5	0.8
N03AX14	Levetiracetam	4	0.7
N06AB04	Citalopram	4	0.7
N06DX01	Memantine	4	0.7
N03AE01	Clonazepam	3	0.5
N05AH03	Olanzapine	3	0.5
N06AX16	Venlafaxine	3	0.5
N06DA02	Donepezil	3	0.5
N05CH01	Melatonin	2	0.3
N05CM02	Clomethiazole	2	0.3
N06BX06	Citicoline	2	0.3
N02AA05	Oxycodone	1	0.2
N02AJ13	Tramadol and paracetamol	1	0.2
N02AX06	Tapentadol	1	0.2
N03AF01	Carbamazepine	1	0.2

N03AX11	Topiramate	1	0.2
N03AX18	Lacosamide	1	0.2
N04BA02	Levodopa and decarboxylase inhibitor	1	0.2
N05AX12	Aripiprazole	1	0.2
N05BA12	Alprazolam	1	0.2
N05CF02	Zolpidem	1	0.2
N06AB03	Fluoxetine	1	0.2
N06AX21	Duloxetine	1	0.2
N06AX23	Desvenlafaxine	1	0.2
N06AX26	Vortioxetine	1	0.2
N06DA03	Rivastigmine	1	0.2
R- Respiratory system			
ATC	**Name**	**n**	**%**
R03BB01	Ipratropium bromide	5	0.8
R06AE07	Cetirizine	4	0.7
R03AC02	Salbutamol	2	0.3
R06AX13	Loratadine	2	0.3
R06AX22	Ebastine	2	0.3
R01AD09	Mometasone	1	0.2
R01AD58	Fluticasone, combinations	1	0.2
R03AK07	Formoterol and budesonide	1	0.2
R03AL07	Formoterol and glycopyrronium bromide	1	0.2
R03CC02	Salbutamol	1	0.2
S- Sensory organs			
ATC	**Name**	**n**	**%**
S01EE03	Bimatoprost	2	0.3
S01EC03	Dorzolamide	1	0.2
S01ED01	Timolol	1	0.2
S01FA02	Scopolamine	1	0.2
S01GA07	Brimonidine	1	0.2
S01XA20	Artificial tears and other indifferent preparations	1	0.2
V- Various			
ATC	**Name**	**n**	**%**
V03AE01	Polystyrene sulfonate	2	0.3

Annex 7: Poster presented at the International Society for Pharmacoepidemiology (ISPE) in August 2024

PHARMACOLOGICAL TREATMENT AND MEDICATION-RELATED PROBLEMS IN NURSING HOMES IN CATALONIA: THE IMPACT OF A MULTIDISCIPLINARY TEAM INTERVENTION

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BACKGROUND

Treating the elderly often entails polypharmacy to achieve optimal disease management, augmenting medication-related problems (MRPs). Routine pharmacological review is needed among institutionalized patients and may improve with a multidisciplinary intervention.

OBJECTIVES

To describe the MRPs detected after reviewing medication plans of the institutionalized patients and the recommendations given by a multidisciplinary team in nursing homes.

METHODS

A multicenter before-after study, involving five nursing homes in Catalonia, assessed the impact of a multidisciplinary team intervention. The intervention, conducted from July 2020 to February 2022, took place during the COVID-19 pandemic, which may have affected our findings. The inclusion criteria was institutionalized patients with public health coverage provided by the Health Department of Catalonia. A patient-centered intervention was made with a multidisciplinary team, that made medication reviews with clinical decision support systems. The clinical pharmacologist acted as the team's coordinator and actively reviewed all the prescribed medications to detect MRPs and make recommendations. These recommendations entailed completing absent data, withdrawal of a drug, verification of whether a drug was adequate, and the substitution of a drug. A descriptive analysis of baseline characteristics and recommendations was performed, among others. A comparative analysis of before and after the intervention was carried out with the total of patients and recommendations.

RESULTS

A total of 483 patients were included. Their baseline clinical characteristics are shown in Table 1. Of the 398 (82.4%) patients who received recommendations 233 (48.2%) followed. The recommendations given varied from 1 to 6 per patient, with a mean of 2.2 (SD 1.1). The various recommendations offered and taken up, with the total and percentage of compliance, are shown in Table 2.

Baseline clinical characteristics	Total	Nursing home 1	Nursing home 2	Nursing home 3	Nursing home 4	Nursing home 5
Number of patients	483	129 (26.7%)	111 (22.9%)	74 (15.3%)	81 (16.7%)	88 (18.2%)
Age (years)	86.3 (8.8)	86.2 (9.8)	87.9 (8.1)	84.6 (10.2)	87.2 (7.4)	84.8 (7.6)
Sex						
Female	348 (72.0%)	100 (77.5%)	86 (77.5%)	47 (63.5%)	56 (69.1%)	59 (67.0%)
Male	135 (28.0%)	29 (22.5%)	25 (22.5%)	27 (36.5%)	25 (30.9%)	29 (33.0%)
Drug Allergies						
Yes	36 (7.5%)	32 (24.8%)	1 (0.9%)	2 (2.7%)	1 (1.2%)	0 (0.0%)
No	324 (67.1%)	52 (40.3%)	65 (58.6%)	70 (94.6%)	51 (63.0%)	86 (97.7%)
Not recorded	123 (25.5%)	45 (34.9%)	45 (40.5%)	2 (2.7%)	29 (35.8%)	2 (2.3%)
Number of health problems	17.4 (5.6)	17.9 (5.5)	16.6 (5.3)	15.7 (5.0)	16.2 (4.6)	20.4 (6.4)
Use of absorbents						
Yes	374 (77.4%)	98 (76.0%)	75 (67.6%)	52 (70.3%)	69 (85.2%)	80 (90.9%)
No	109 (22.6%)	31 (24.0%)	36 (32.4%)	22 (29.7%)	12 (14.8%)	8 (9.1%)
Number of drug consumption	8.2 (3.5)	8.1 (3.1)	7.7 (3.4)	8.6 (3.9)	8.2 (3.1)	8.8 (3.8)

Table 1: mean (SD) and n (%).

RECOMENDATIONS	Given, n	%	Followed, n	%	%*
Completing data	173	15.8	81	22.8	46.8
Allergy data	118	10.8	66	18.6	55.9
Disease data	55	5.0	15	4.2	27.3
Withdrawal of drugs	318	29.0	136	38.3	42.8
Withdrawal of inappropriate drugs	66	6.0	35	9.9	53.0
Withdrawal of drugs with interactions	53	4.8	26	7.3	49.1
Withdrawal of duplications	33	3.0	19	5.4	57.6
Withdrawal of drugs with doubtful efficacy	22	2.0	14	3.9	63.6
Withdrawal of contraindicated drugs	16	1.5	10	2.8	62.5
Witdrawal of other drugs	128	11.7	32	9.0	25.0
Substitution of drugs	45	4.1	11	3.1	24.4
Substitution of equivalent drugs	35	3.2	8	2.3	22.9
Substitution of drug of choice	10	0.9	3	0.8	30.0
Verification of the adequacy of drug use	561	51.1	127	35.8	22.6
TOTAL	1097	100.0	355	100.0	**32.4**

Table 2: n= number of recommendations that were given and followed.
%*= percentage of the recommendations followed compared to those given.

A total of 318 prescribed medications were recommended to be withdrawn in 192 patients and 136 (42.8%) were removed.

The 3 drugs most recommended to withdraw were **omeprazole** (n=54, 17.0%), **acetylsalicylic acid** (n=14, 4.4%), and **alprazolam** (n=11, 3.5%). At follow-up, the 5 most withdrawn were **omeprazole** (n=9, 6.6%), **citalopram** (n=5, 3.7%) and **diazepam** (n=5, 3.7).

Of the 45 drugs recommended to be changed in 39 patients, 11 (24.4%) drugs were altered.

Of the 561 drugs recommended to verify the adequacy in 276 patients, the drug was withdrawn in 127 (22.6%). The 3 most frequently recommended were **quetiapine** (n=56, 10.0%), **acetylsalicylic acid** (n=34, 6.1%), and **furosemide** (n=30, 5.3%). And, the 3 most frequently withdrawn were **quetiapine** (n=10, 7.9%), **risperidone** (n=10, 7.9%), and **acetylsalicylic acid** (n=7, 5.6).

Finally, in a total of 293 (60.7%) patients, between 1 to 9 drugs were withdrawn, with a mean of 2.3 (SD 1.7), and a total of 695 drugs.

CONCLUSION

The findings underscore the need for targeted interventions to reduce MRPs in nursing homes. The intervention was performed during the COVID-19 pandemic, and could have impacted our findings. The recommendations given and followed demonstrate the importance of a multidisciplinary team for a patient-centered approach with interdisciplinary collaboration including a clinical pharmacologist, and technology-driven solutions, to help reduce MRPs and polypharmacy.

Annex 8: Poster presented at the National Congress of the Spanish Society of Clinical Pharmacology (SEFC) in October 2024

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A multidisciplinary team intervention in nursing homes in Catalonia: The Role of a Clinical Pharmacologist

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Introduction: The care of institutionalized patients was a great challenge during the COVID-19 pandemic, with an increase in morbidity and mortality. In Spain, 71.9% of all COVID-19 deaths occurred in nursing homes. For this reason, a multidisciplinary team was created in Catalonia, to make a structured intervention in nursing homes.

Objective: To describe a systematized medication review implemented in institutionalized patients by a multidisciplinary team, including a clinical pharmacologist.

Methods: The main sources of information used by the clinical pharmacologist were the information contained in the summary products, support tools Self-Audit and PREFASEG, and a list of potentially inappropriate medications proposed by the Catalan Health Service.

Results: This created a patient-centered approach, to making medication reviews regularly, with the help of clinical decision support systems already mentioned, and a multidisciplinary team where the clinical pharmacologist acted as the coordinator of the team, as seen in *Figure 1*.

From the identified problems during the medication review, the recommendations entailed completing data, withdrawal of drugs, substitution of drugs, and adequacy of drugs, as seen in *Table 1*.

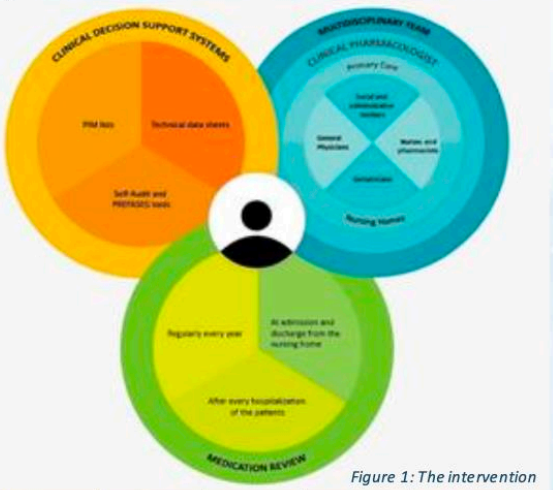

Figure 1: The intervention

Table 1: Description of all the recommendations

RECOMENDATIONS	Given, n	%	Followed, n	%	%*
Completing data	173	15.8	81	22.8	46.8
Allergy data	118	10.8	66	18.6	55.9
Disease data	55	5.0	15	4.2	27.3
Withdrawal of drugs	318	29.0	136	38.3	42.8
Withdrawal of inappropriate drugs	66	6.0	35	9.9	53.0
Withdrawal of drugs with interactions	53	4.8	26	7.3	49.1
Withdrawal of duplications	33	3.0	19	5.4	57.6
Withdrawal of drugs with doubtful efficacy	22	2.0	14	3.9	63.6
Withdrawal of contraindicated drugs	16	1.5	10	2.8	62.5
Witdrawal of other drugs	128	11.7	32	9.0	25.0
Substitution of drugs	45	4.1	11	3.1	24.4
Substitution of equivalent drugs	35	3.2	8	2.3	22.9
Substitution of drug of choice	10	0.9	3	0.8	30.0
Verification of the adequacy of drug use	561	51.1	127	35.8	22.6
TOTAL	1097	100.0	355	100.0	**32.4**

n: number of recommendations given and followed. %: percentage of the recommendations followed compared to those given*

Conclusion: The designed intervention highlights the importance of patient-centered approaches, with a multidisciplinary team, coordinated by a clinical pharmacologist, and technology-driven solutions. This will ensure proper pharmacological review in nursing homes.

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