Heliyon 9 (2023) e17079

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Pharmacist comprehensive review of fall-risk-increasing drugs and polypharmacy in elderly Spanish community patients using RStudio®

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ARTICLE INFO

Keywords:
Falls
Elderly
Polypharmacy
Inappropriate prescribing
RStudio®

ABSTRACT

Objective: The aim of this study is to identify and analyze adults aged ≥65 years living in the Canary Islands, Spain, who are prescribed medications that increase the risk of falls and are polymedicated. To do so we have made use of the electronic prescription and the RStudio®.
Method: For the detection of Fall-Risk-Increasing Drugs (FRIDs), outpatient electronic prescription dispensing data were used in two pharmacies. A total of 118,890 dispensations grouped into 15,601 treatment plans for 2,312 patients were analyzed. The FRIDs analyzed were antipsychotics (APSI), benzodiazepines (BZPN), antidepressants (DEPR), opioids (OPIO) and Z-hypnotics (ZHIP). For the development of the algorithms for the construction of tables and data screening, the statistical programming language RStudio® was used.
Results: Of the total number of patients and prescriptions analyzed, 46.6% were polymedicated and 44.3% had prescribed an FRID. 28.7% of the patients presented both factors, had a dispensation from an FRID and were polymedicated. Of the 14,278 dispensations with FRID, 49% had a benzodiazepine, 22.7% opioids, 18% antidepressants, 5.6% hypnotics, and finally 4.4% antipsychotics. At least 32% of the patients had been dispensed a benzodiazepine together with another FRID and 23% an opioid together with another FRID.
Conclusions: The method of analysis developed and applied in RStudio® allows to detect and determine in a simple and fast way polymedicated patients, as well as the number and therapeutic class of drugs in their treatment plan and identify prescriptions that can increase the risk of falls. Our results show a high number of prescriptions for benzodiazepines and opioids.

1. Introduction

The progressive aging of the population, together with the greater chronicity and complexity of pathologies among the elderly and the greater ease of access to health services and drugs, has resulted in a very significant increase in the consumption of health resources including the pharmacist. In Spain, people over 65 years of age consume approximately 30% of the drugs prescribed daily for the

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https://doi.org/10.1016/j.heliyon.2023.e17079
Received 30 August 2022; Received in revised form 26 May 2023; Accepted 7 June 2023
Available online 13 June 2023

treatment of chronic pathologies, generating 75% of pharmaceutical spending [1].

One of the consequences of the increase in life expectancy is the greater risk of incidence of falls, since these increase progressively with age [2]. Many of these falls cause injuries that increase morbidity and mortality [3,4] and are a determining factor in mobility restriction, increasing the number of complications derived from them and hospital admissions [5] and also causing subsequent cognitive impairment [6].

Most falls have a multifactorial etiology. They occur as a result of the interaction of numerous risk factors: age, sex, comorbidities, previous falls, functional dependence, polypharmacy [6–10] or the use of certain medications [11].

Several authors have studied the relationship between the use of certain drugs and falls [11–14]. These drugs include Central Nervous System (CNS) depressants, such as antidepressants, antipsychotics, opiates, anxiolytics and hypnotics, and sedatives, and drugs that act at the cardiovascular level, such as diuretics or beta-blockers, which by causing postural or orthostatic hypotension [11–16] can cause falls.

In different publications, polypharmacy is related to the risk of increased falls, which are increasingly frequent, in people over 65 years of age [17,18]. Although there is no consensus to date regarding the definition of polypharmacy in terms of the cut-off point in the number of medications administered concomitantly, the most accepted criterion is that of 5 medications used chronically [11,15, 19–22].

On the other hand, there is debate about whether polypharmacy itself is the cause of falls in older people or the use of Fall-Risk-Increasing Drugs (FRIDs), which are frequently part of a patient's medication, the cause of such falls [15,23].

The objective of this paper is to identify, based on electronic prescriptions, polymedicated patients aged ≥65 years and the medications that may involve an increased risk of falls in these patients.

Our hypothesis is that there is a large number of prescriptions for these FRIDs and, therefore, a high use of them.

In the literature we can find numerous studies showing the high prevalence of polymedication and FRIDs in the population aged ≥65 years, most of them carried out, in small groups of patients and with a manual review of treatment [6,11]. Hence, the need for a tool to quickly identify polymedicated patients with treatment plans that include this group of drugs.

Therefore, we proposed an analysis method using RStudio®, which allows us a more accurate review than the one-by-one analysis of patients and their pharmacological treatments.

2. Methods

2.1. Participants

Data from electronic prescription dispensing of outpatients from two pharmacies in the Canary Islands, Spain, have been used in order to detect FRIDs.

The identification data of the patients have been recoded, so no personal data is accessed. The project presented was approved by the Research Ethics and Animal Welfare Committee of the University of La Laguna (CEIBA2017-0255). The data correspond to the dispensations made to patients over 18 years of age, over 4 years. However, for the analysis only patients aged ≥65 years who had at least some dispensing of the selected drugs were included.

2.2. Selected drugs

From the different FRIDs, the groups of antipsychotics (APSI), benzodiazepines (BZPN), antidepressants (DEPR), opioids (OPIO) and Z-hypnotics (ZHIP) (zolpidem and zoplicone) have been selected. In order to group the FRIDs by pharmacological group, the first 4 levels of the ATC (Anatomical Therapeutic Chemical Classification) code were included: antipsychotics (N05A), benzodiazepines (M03B, N03A, N05B and N05C), antidepressants (N06A, N06C), opioids (N02A, N07B, R05D) and Z-hypnotics (N05C).

2.3. Data

Patient electronic prescriptions have been downloaded as a single table database in a MS Excel® sheet following the prescription system implemented by the Canary Health Service. The tables, one for each pharmacy, contain 23 fields with demographic, prescription, and dispensing data. To work in RStudio®, both were joined into a single file called **data**.

On the other hand, the Prescription Nomenclature (Nomenclator) of the Spanish Agency for Medicines and Health Products (AEMPS) was used, which consists of a database that includes everything related to the identification and technical information of drugs [24]. It contains the **Prescription.xml** file that collects all the data for each medication. Of all of them, the national code for the presentation of the drug and the DCSA code (dcsaCod) have been selected, which defines the drug from its active principles based on the Snomed-CT terminology (Systematized NOMenclature of MEDIcine – Clinical Terms), regardless of pharmaceutical form or dose [24]. The Nomenclator also contains the **DICTIONARY_DCSA.xml** file, which contains the codes (dcsaCod) and DCSA names (dcsaName) of the drugs. These files are in.xml format.

From the **DICTIONARY_DCSA.xml** file, all the DCSA codes and denominations were imported into an Access Database® file (Catalogue DCSA file), available in Appendix, Table A.1. The FRIDs were selected, and their ATC code and pharmacological group were added to each one.

Finally, the **data** file was updated in RStudio®, so that it now contains all the information of the electronic prescription plus the name and DCSA code associated with the national codes of the drugs dispensed, obtained from **DICTIONARY_DCSA.xml** and

Prescription.xml. In this way, a single data file is available on which to make any query about the sample.

2.4. Analysis method

For the analysis of the sample, patients aged 18 years or older were first selected, determining the total number of patients, sex and number of dispensations and treatment plans (**data** file) (Appendix, Picture 1, script 1).

To analyze the FRIDs, we proceeded to select the number of patients aged ≥65 years (**data65** file) with their treatment plans (Appendix, Picture 1, script 2). The selected active principles (included in the DCSA Catalog file), the FRIDs, were entered into the RStudio® by means of the corresponding script (Appendix, Picture 1, script 3), being called **drugs** file, of which a sample is collected in Appendix, Table A.2. From this **drugs** file, the ATC code and pharmacological group were included in the **data65** (Appendix, Picture 1, scripts 4 & 5).

In order to obtain the treatment plans for each patient and identify whether or not they are polymedicated and whether or not they have been prescribed an FRID, the number of drugs for the same treatment plan was grouped into **data65**, using script 6 (Appendix, Picture 2). In the context of electronic prescriptions, a treatment plan is understood to be one that includes all the prescriptions and dispensing for the same patient and for a certain period, while a dispensing consists of the delivery of a single medication to a certain patient. The number of different physicians who have treated and prescribed medication for the same patient is also obtained (Appendix, Picture 2, script 7).

In Appendix, Table A.3, a sample of the **data65** file is collected, in which the data for several patients can be observed applying all the scripts indicated above (Appendix, Picture 1 & 2, scripts 1–7).

To obtain the total number of dispensations and treatment plans for FRIDs, as well as the number of patients who have prescriptions for said drugs, their age at the beginning and at the end of the study, and the number of dispensations for each of them, a **data652** file was generated from **data65** file (Appendix, Picture 2, scripts 8 & 9). A sample of it is collected in Appendix, Table A.4.

A **data652** file was generated from **data65** file (Appendix, Picture 2, scripts 8 & 9) in order to obtain the total number of dispensations and treatment plans for FRIDs. We have also generated the number of patients who have prescriptions for said drugs, their age at the beginning and at the end of the study, and the number of dispensations for each of them.

Script 10 (Appendix, Picture 2) was used to obtain the sex and age range of the patients, as well as the number of physicians who attended them. Script 11 (Appendix, Picture 2) was used to obtain the number of polymedicated patients and the treatment plans for patients aged ≥65 years taking FRIDs, and script 12 (Appendix, Picture 3) was used to group the patients according to the number of dispensations.

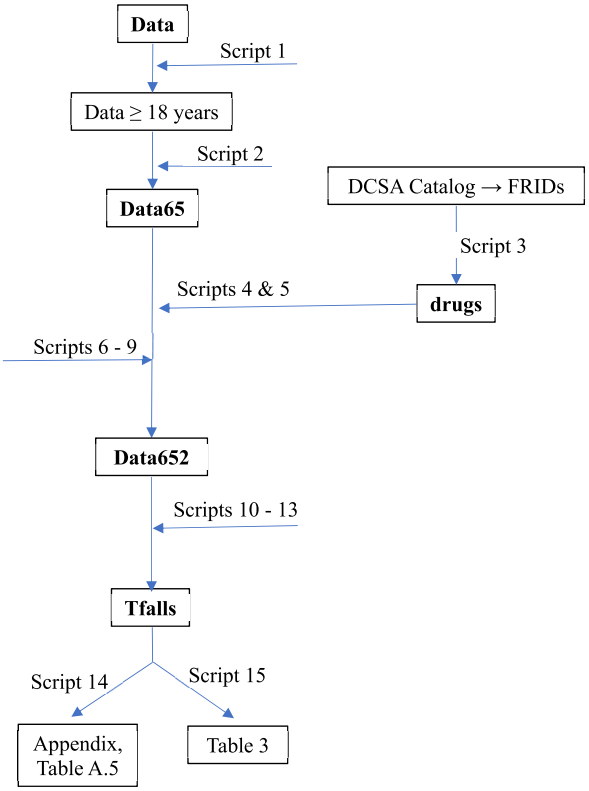

Fig. 1. Analysis method scheme.

On the other hand, from **data652** the **Tfalls** file (Appendix, Picture 3, script 13) is generated, to subsequently group by the field that identifies the patient (NUSS) and obtain the number of drugs by pharmacological group that have been dispensed to the same patient (Appendix, Picture 3, script 14). An example of this is collected in Appendix, Table A.5. Likewise, from this **Tfalls** file, the number of dispensations is obtained according to each of the ATC groups and by pharmacological groups (Appendix, Picture 3, script 15).

Fig. 1 shows the scheme of the described method. It should be noted that the method allows the use of different databases by simply carrying out the necessary conversions for their adaptation to RStudio®. From the databases of any National Health System can obtain the patient's electronic prescriptions and the medications information.

The development of the method in RStudio® has allowed us to take advantage of many of its benefits. It is functional, has an environment and a programming language that allows a statistical approach. Its calculation speed makes it possible to process and manipulate large volumes of data and, finally, it facilitates error correction and code optimisation.

3. Results

Table 1 shows the total number of patients aged 18 years or older participating in the study and the number of electronic dispensations, grouped into treatment orders, as well as the data for the aged ≥65 years, obtained from the **data** and **data65** files (Appendix, Picture 1, scripts 1 & 2). Of the 10,460 patients, 42% were men and 58% women (Appendix, Picture 1, script 1).

Of the 118,890 dispensations made to patients aged ≥65 years and who are grouped into 15,601 treatment orders, 14,278 dispensations were from FRIDs. That is, 12% of the total dispensations made to this group of patients, included in 5,672 treatment orders (36.4%) (Appendix, Picture 2, script 8). A total of 44.3% of patients aged ≥65 years have prescribed some FRID (n = 1,024), of which 65.7% were women and 34.3% men. The age of the patients is between 65 and 98 years (Appendix, Picture 2, scripts 9 & 10).

72% of these patients aged ≥65 years and with a prescription of some FRID, have been seen by a physician during the entire period under study, 18.5% have had two physicians and 9.5% they have been treated by between three and six physicians (Appendix, Picture 2, script 10).

Table 1 also shows the results of patients aged ≥65 years, polymedicated, who take FRIDs (Appendix, Pictures 1 & 2, scripts 1, 2, 8, 9, 11).

Of the patients aged ≥65 years (n = 2,312), 46.6% were polymedicated and 41% of their treatment orders contained 5 or more drugs. Of the total number of patients who have some FRID prescribed (n = 1,024), 64.7% are polymedicated and 64.2% of their treatment orders have 5 or more prescribed drugs. Finally, in the age group equal to or greater than 65 years, 28.7% of the patients and 23.3% of the treatment plans present both conditions: they have 5 or more prescribed drugs and also have FRIDs.

Table 2 groups the patients according to the FRIDs dispensed (Appendix, Picture 3, script 12). As it can be seen, around 49% of patients (n = 500) received less than 3 dispensations, but 17.5% had a high number of them, between 10 and 30, which implies that approximately half of the patients receive this medication occasionally and the other half have it chronically.

To obtain the number of patients and dispensations by pharmacological group, scripts 13–15 (Appendix, Picture 3) were used. As can be seen in Table 3, the total number of patients prescribed an FRID (1,592) differs from the number of patients participating in the study (1,024), because many of them have been prescribed more than one FRID. Table 3 also shows the number of dispensations based on each of the ATC groups, obtained from scripts 13–15 (Appendix, Picture 3).

The results collected in Table 3 show a high number of prescriptions for benzodiazepines and opioids; specifically, 49% of the 14,278 dispensations correspond to benzodiazepines and of these, 75.7% belong to the ATC N05B group (anxiolytics). Regarding opioids, 22.7% of dispensations correspond to this pharmacological group and of these, 98% correspond to the ATC N02A group (morphine, fentanyl, tramadol and its combinations, oxycodone/naloxone, buprenorphine, etc). The third most dispensed pharmacological group is that of antidepressants, with 18% of the total, practically all of which belong to the ATC N06A group. In the case of hypnotics, 5.6% of all dispensations correspond to Z-hypnotics (zolpidem or zoplicone). Both active principles are within the dispensations of the ATC N05C group together with other benzodiazepine hypnotics, therefore, 16.6% of the total dispensations correspond to the ATC N05C group, hypnotics and sedatives. Finally, in our study, the pharmacological group with the lowest number of dispensations is that of antipsychotics, which represents 4.4% of the total.

4. Discussion and implications

The use of certain drugs such as CNS depressants is one of the factors that increases the risk of falls, especially in the case of patients over 65 years of age [14,15,25–27]. However, for other authors there is not enough evidence to justify that with the deprescription of this group of drugs alone, the number of falls is reduced [28]. The detection of the prescriptions of these medications in the electronic

Table 1
Patients aged ≥65 years, polymedicated, who take FRIDs.

	Number of patients	Number of treatment orders	Number of dispensations
Total participants in the study	10,460	43,170	228,182
Age ≥65	2,312	15,601	118,890
Age ≥65 with FRIDs	1,024	5,672	14,278
Age ≥65 polymedicated	1,077	6,405	91,338
Age ≥65 polymedicated, with FRIDs	663	3,640	10,785

Table 2
Number of patients based on the number of drug dispensations that increase the risk of falls.

Dispensations	≥1 to <3	≥3 to <5	≥5 to <10	≥10 to <30	≥30 to <50	≥50 to 100	≥100 to <300
Patients (n = 1,024)	500	85	116	179	71	54	19

Table 3
Number of patients by pharmacological group and number of dispensations by pharmacological group and by ATC group.

Pharmacological Group	Patients (n = 1,592)	Dispensations (n = 14,278)	ATC Group	Dispensations by ATC Group
APSI	100	628	N05A	628
BZPN	673	7,008	M03B	29
			N03A	105
			N05B	5,302
			N05C	1,572
DEPR	325	2,599	N06A	2,597
			N06C	2
OPIO	382	3,248	N02A	3,179
			N07B	1
			R05D	68
ZHIP	112	795	N05C	795

Pharmacological groups: Antipsychotics (APSI), Benzodiazepines (BZPN), Antidepressants (DEPR), Opioids (OPIO) and Z-Hypnotics (ZHIP). ATC codes: N05A (Antipsychotics), M03B (Central-acting muscle relaxants), N03A (Antiepileptics), N05B (Anxiolytics), N05C (Hypnotics and sedatives), N06A (Antidepressants), N06C (Psycholeptics and psychoanaleptics in combination), N02A (opioids), N07B (Drugs used in addictive disorders), R05D (Cough suppressants, excluding combinations with expectorants).

prescription could avoid added health problems. Based on the databases and currently available computer programs such as RStudio®, it is possible to locate patients at risk and act accordingly.

In this study, we analyzed the dispensing of prescriptions from electronic prescriptions to a sample of outpatients, focusing on those aged 65 years or older. We found that almost half of the patients, specifically 44.3%, are prescribed some FRID and of these, 64.7% are polymedicated.

In a study by Marvin et al. [29], the authors found higher values than ours, since between 60 and 65% of hospitalized patients over 70 years of age and polymedicated who had suffered a fall had been prescribed some medication of this type, either at the time of admission or discharge from the hospital. One of the causes of the differences observed lies in the greater number of pharmacological groups studied by these authors, since in addition to CNS depressant, they analyzed other cardiovascular drugs.

On the other hand, the percentage of FRIDs with respect to the total number of medications prescribed to people over 65 years of age was 12%, very similar to that obtained by Marvin et al. [29], despite the fact that some patients were hospitalized, and others were outpatients.

These authors [29] indicate that 62% of the patients were polymedicated and of these, 92% took some FRID, which represented that 57% of the total number of patients were polymedicated and received some FRID. Our results indicate that 46.6% are polymedicated patients and of these, 61.5% are also prescribed a FRID (Table 4). Therefore, of the total number of patients aged ≥65 years, 28.7% are polymedicated patients and take a FRID (Table 1). The higher percentages obtained by these authors may be due to the greater number of drug groups taken into account in their study [29].

In several publications, the use of benzodiazepines has been associated with an increased risk of falls, by negatively affecting balance in the elderly [14,25,26,30]; To this fact we must add that the dose necessary to achieve sedation with benzodiazepines is 50% of the usual dose in a young adult [14]. In addition, a sudden increase in the dose, as well as the concomitant use with other benzodiazepines, also contribute to the increased risk of falls [25,26]. Our results show a high percentage of dispensations and therefore benzodiazepines prescriptions, specifically 49% (Table 3). These values are similar to those obtained by Milos et al. [30] in a study conducted with patients over 75 years of age, in which 24% of the prescriptions corresponded to anxiolytics and 23.1% to hypnotics and sedatives, which represents 47.1% benzodiazepines (Table 4). Finally, the work carried out by Nicieza-García et al. [31] in patients aged ≥65 years who were simultaneously taking 10 or more drugs a day, indicates that 6.3% of the sample had a benzodiazepine prescribed when they had one or more falls in the last 3 months (Table 4).

In the case of hypnotics, we find that 11% of the 1,024 patients analyzed received Z-hypnotics in 795 dispensations, which represents 5.6% of the total (Table 3). In studies that have analyzed the relationship between the use of benzodiazepines and Z-hypnotics with the risk of falls, the association between the latter with an increase in falls has been highlighted [14,32–34]. Thus, Mestres et al. [33], when analyzing the prescriptions of patients in a health and social care centres, found that 33% of them had prescribed benzodiazepines and hypnotics and of these, 20% had been with these drugs for more than four weeks. When analyzing it in detail, we observed that 13% of the patients were taking Z-hypnotics (Table 4), a result quite similar to ours, as well as that obtained by Pérez et al. [34], which is around 10%, although the latter included patients once they had prescribed the hypnotic for 28 days or more, while in our study they were counted from the moment of prescription (Table 4).

In the case of opioids, the number of dispensations found in our work is 3,248, which represents 22.7% of a total of 14,278 and specifically, 22.3% corresponds to the ATC N02A group (Table 3), values very close to those found by Milos et al. [30], 17.6% of the

total of 808 prescriptions (Table 4). In their study, Nicieza-García et al. [31] found that 5.4% of patients who suffered from recurrent falls had an opioid prescribed long-term (Table 4). One aspect to highlight is the time elapsed from the start of opioid treatment to the fall. In this sense, Söderberg et al. [35] found that of 167,257 patients who had fallen, 7,450 of them were dispensed an opioid in the 28 days prior to the fall (Table 4). Of this population, 78% were over 60 years of age. The authors noted that the greatest risk of falls occurred within the first seven days of opioid treatment. Unfortunately, in our study we were not able to determine the time elapsed between the start of opioid treatment and the possible fall, as the pharmacies did not have the patient's clinical history. With the analysis method developed in the RStudio® we can carry out an immediate search for the group of patients who have started treatment with opioids. In this way, we can identify this population and carry out a pharmaceutical intervention if necessary, such as, for example, reducing the dose of the recently started opioid in case of sedation and thus preventing a fall. Therefore, the method applied in this work allows detecting patients with pain, in recent treatment with comorbidities and/or polymedicated.

In the study carried out by Cheng et al. [36] with patients between 65 and 90 years old, 40.7% took opioids, benzodiazepines and hypnotics or combinations of them, for four weeks or more. Despite the fact that our study counts the patients from the first dispensing, we detected 11% of patients with dispensing of Z-hypnotics and 65.7% with benzodiazepines, compared to 42% and 7%, respectively, found by these authors, which could be due to the fact that in our group of patients the prescription of benzodiazepines is more common than that of Z-hypnotics. In the case of opioids, the results are 37.3% compared to 21% of these authors (Table 4).

Regarding antidepressants, both tricyclics (TCAs) and selective serotonin reuptake inhibitors (SSRIs), both included in our study,

Table 4
Patients or prescriptions with Fall-Risk-Increasing Drugs (FRIDs) analyzed.

References	Country	Patients	Results	González-Munguía's results[a]
[27] Gorgas et al. (2019)	Spain	▶Age 50–95 years ▶Emergency department with hip fracture	Patients: ▶37.5%DEPR	Patients: ▶31.7% DEPR
[29] Marvin et al. (2017)	England	▶Age ≥70 years ▶≥ 6 drugs/day ▶Medication review on admission after a fall and on discharge from hospital	Patients: ▶62% polymedicated ▶57% polymedicated & FRIDs ▶92% FRIDs/polymedicated	Patients: ▶ 46.6% polymedicated ▶ 44.3% FRIDs ▶ 28.7% polymedicated & FRIDs ▶ 64.7% FRIDs/ polymedicated ▶ 61.5% polymedicated/FRIDs
[30] Milos et al. (2014)	Sweden	▶Age ≥75 years ▶Community-dwelling and nursing home	Prescriptions: ▶47.1% BZPN ▶17.6% OPIO ▶29.4% DEPR ▶5.8% APSI	Prescriptions: ▶49.1% BZPN ▶22.7% OPIO ▶18% DEPR ▶4.4% APSI
[31] Nicieza -García et al. (2016)	Spain	▶Age ≥65 years ▶≥ 10 drugs/day ▶Hospitalized (1 or more falls during the past 3 months)	Patients: ▶6.3% BZPN ▶5.4% OPIO	Patients: ▶37.3% OPIO ▶65.7% BZPN
[33] Mestres et al. (2018)	The Netherlands	▶Age = 84.4 (±9.3) ▶Nursing homes	Patients: ▶ 33% with BZPN or ZHIP or combination of the two ▶13% ZHIP	Patients: ▶65.7% BZPN ▶11% ZHIP ▶2.3% [BZPN + ZHIP]
[34] Pérez et al. (2018)	Ireland	▶Age ≥ 65 years ▶General medicine	Patients: ▶10% ZHIP	Patients: ▶ 11% ZHIP
[35] Söderberg et al. (2013)	Sweden	▶Age: 18–90 years ▶Swedish National Inpatient Register	Patients: ▶4.5% with a fall who took OPIO 28 days earlier	Patients: ▶37.3% OPIO
[36] Cheng et al. (2020)	Norway	▶Age: 65–90 years ▶ ≥ 5 drugs/day ▶Hospitalized patients taking FRID for 4 weeks or more	Patients: ▶40.7% with one FRID and combinations of the three ▶21% OPIO ▶7% BZPN ▶42% ZHIP	Patients: ▶37.3% OPIO ▶65.7% BZPN ▶11% ZHIP ▶17% [BZPN + OPIO] ▶2.3% [BZPN + ZHIP]
[40] Veal et al. (2014)	Australia	▶Age: 60–90 years ▶Nursing home ▶Residential home	Patients: ▶38.8% OPIO ▶41.5% BZPN or ZHIP ▶48.4% [(BZPN or ZHIP) + OPIO]	Patients: ▶37.3% OPIO ▶76.7% BZPN or ZHIP ▶17% [BZPN + OPIO] ▶2.3% [BZPN + ZHIP]

[a] Data correspond to patients ≥65 years; Antipsychotics (APSI), Benzodiazepines (BZPN), Antidepressants (DEPR), Opioids (OPIO) and Z-Hypnotics (ZHIP).

have also been associated with falls [14,15,27,37–39]. Some authors even point out that with SSRIs there is a higher risk of falls than with TCAs [39]. Other authors [15] point to antidepressants as the only group of drugs associated with an increased risk of falls, according to age, sex, and the total number of medications. Gorgas et al. [27] studied the association between the use of antidepressants and hip fracture in patients between 50 and 95 years of age, observing that 37.5% of those with a hip fracture used antidepressants, compared to 12.3% of the control group (Table 4). Of the antidepressants analyzed, the risk of hip fracture was higher in the group taking SSRIs, and the number of patients taking 4 or more drugs in this group was double. On the other hand, in the case of antidepressant prescriptions, Milos et al. [30] found 29.4% compared to 18% found by us (Tables 3 and 4).

In relation to the group of antipsychotic drugs, in our study they constitute the pharmacological group with the lowest number of dispensations, 4.4%, which corresponds to 10% of the patients who take a FRID. This relationship between the use of these drugs and the increased risk of falls has been previously established by several authors [14,17], who have also confirmed that their prolonged use for more than 90 days increases the risk of falls by 81% [14,17]. With the method used by us, it is possible to identify patients who need prolonged follow-up during their treatment, as well as to evaluate other factors or medication that are frequently associated and that can increase the risk of falls.

An important aspect to highlight is the fact that many patients have prescriptions for two or more FRIDs at the same time. The analysis of the dispensations of two or more groups of FRIDs allowed us to detect patients with dispensations of several pharmacological groups concomitantly. Of the 1,024 patients analyzed aged $\geq$65 years and with FRIDs dispensed, almost 32% had some BZPN with another FRID (BZPN + OPIO: 17%; BZPN + DEPR: 9.7%; BZPN + APSI: 2, 6% and BZPN + ZHIP: 2.3%) and 23% received opioids with some other FRID (Table 4). Veal et al. [40] studied dispensing of opioids with benzodiazepines or Z-hypnotics, finding that 48.4% of patients received the association of these FRIDs (Table 4). This higher value than ours may be due to the difference between the type of patients, since the study was conducted on patients from a nursing home, who were taking opioids plus an anxiolytic or a hypnotic and who generally have a greater number of pathologies and dependency level. It should also be mentioned that in our sample of patients almost 6% had concomitant prescriptions of three FRIDs: BZPN with OPIO and DEPR.

In relation to these associations, some authors consider that the use of 2 or more FRIDs is an independent predictor of falls [15], that is, no other additional risk factor is needed. In this same sense, other authors suggest that the risk of falls is more dependent on the class of medication prescribed than on the number of drugs [11], even considering that the benefit of polypharmacy may be greater than the risk of falls. These authors conclude that the association of polypharmacy with falls may be due to the increased use of FRIDs that increase the risk of falls.

In our study, with the applied analysis method we can detect and determine polypharmacy patients in a simple and fast way, as well as the number and therapeutic class of the drugs in their treatment plan, which allows a review and approach by two different routes, both by the pharmacological group and by polypharmacy. In addition, the method developed in RStudio® allows any concept to be redefined, for example, if we establish quantitative polypharmacy as 6 drugs used chronically, it would only be necessary to make a small change in the corresponding script to obtain both the number of patients and the treatment plans. It also allows filtering by other variables such as age or gender, or any other characteristic that we need to obtain information from patients.

In this work, the prescriptions that may involve an increased risk of falls in patients equal to or older than 65 years have been identified, that is, the prevalence in our community. However, we have not been able to identify the variables or factors involved, given the impossibility of accessing the patient's clinical history, as well as selecting other groups of drugs that increase the risk of falls, nor detect those patients who have suffered falls. A additional study is necessary that includes the clinical history, as well as the family, work and social situation. In this way, a joint review of the consumption of any of the groups studied, their initial indication and the duration of treatment could be carried out. It would also allow a review of patients with a higher risk of falls who take opioids and, furthermore, to investigate whether the use of other types of non-opioid analgesics has been previously assessed.

Finally, the method applied to detect patients who have been prescribed FRIDs allows for a more accurate and rapid review of patient prescriptions, and is a great opportunity for pharmacist intervention, with the possibility of reducing the risk of falls by evaluating these groups of drugs that also increase confusion and cognitive impairment in the non-institutionalized geriatric population. In summary, at the healthcare level, it is a great tool due to the speed and flexibility it presents when obtaining information. The method has been validated on a sample of 10,460 patients.

Author contribution statement

Silvia González-Munguía; Esther Sánchez Sánchez: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Obdulia Munguía-López: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Data availability statement

The data that has been used is confidential.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e17079.

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