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Prescribing potentially inappropriate medications for the elderly according to Beers Criteria: systematic review

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Abstract *The study aimed to perform a systematic review to identify and evaluate the prevalence of potentially inappropriate medicines (PIM) prescriptions for the elderly, according to Beers Criteria, in hospitalized elderly individuals aged 65 years or older. Five databases consulted: VHL; Cochrane Library; CINAHL; MEDLINE and Web of Science. Nineteen articles identified, selected based on eligibility criteria. The mean age was 78.2 years and the most used criterion for the identification of PIM for the elderly was Beers 2015 (57.9%). A total of 221,879 elderly received a prescription for PIM, the mean prevalence was 65.0%, for the gastrointestinal system (15.3%) and proton-pump inhibitors (27.7%) highlighted as the main class of medicine prescribed. It concluded that the Beers Criteria have made it possible to identify the high prevalence in the prescription of PIM. The results of this review may help in the decision making of health professionals, to avoid the administration of PIM and to propose best practices to ensure the safety of the elderly hospitalized.*

Key words *Inappropriate Prescribing, Potentially Inappropriate Medication List, Aged*

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Introduction

Drug therapy-related iatrogenic therapy has pointed out by experts in the area of the elderly healthy as a public health problem. Inadequate polypharmacy is usually prescribed in the presence of complex health problems that require treatment with a higher consumption of medicines[1,2]. Patients taking many medications are more likely to have potentially inappropriate prescriptions, contributing to make them more vulnerable to undesirable situations related to pharmacotherapy, including drug interactions, adverse effects, higher rates of hospitalizations and use of health resources[3,4].

In this scenario, studies explicitly point to specific medications or categories of potentially inappropriate medications (PIM) that elderly individuals should avoid consuming or doing so with caution[5,6]. PIM are those in which the risks associated with its use may be greater than the therapeutic benefits, especially when more effective alternatives are available[7]. Despite the evidence associated with negative outcomes, they continue prescribed and used in the elderly with high prevalence[8-10]. It is noteworthy that the criteria are an indicator of inadequate management of the elderly, but do not replace individualized clinical judgment.

In several countries, the prevalence of PIM is high, varying, according to the screening tool used, between 33.9% and 58% in the home context and between 42.4% and 60.5% in hospitalized patients[11]. At the national level, the prevalence is also high, reaching 59.2% in the home context[12] and 85.9% in hospitals[13]. The use of PIM in the hospital context is associated with several unfavorable outcomes, including increased hospitalization time and higher mortality in this population[14,15]. In this scenario, studies evaluating the prevalence of PIM in hospitalized elderly are fundamental, due to their greater vulnerability in this situation.

There are different screening tools to identify and evaluate the prevalence of PIM in elderly patients who establish explicit evaluation criteria. Screening Tool *o*f Older Persons' Prescriptions (STOPP)[6] and the Beers Criteria[5,16] stand out. The latter are the most used in the world and have become a useful tool for evaluating the quality of prescription scare scans for the elderly, including specific geriatric assessments regarding the use of medications. These criteria seek to describe the medications avoided by the elderly and elaborated by Beers et al.[16], in 1991. They expanded and revised more recently in 2012[17], 2015[18] and 2019[5], by the American Society of Geriatrics to applied to all people aged ≥65 years, following an evidence-based approach, except for the elderly in palliative care. The use of a tool widely used in the world allows a broader knowledge of the real situation of the use of inappropriate medications by the elderly and allows the comparison of studies conducted in different geographical regions.

Scientific evidence, based on studies conducted using standardized methods[19] and using explicit criteria for evaluating drug therapy for the elderly, is fundamental to improve the selection of medications; educate health professionals and patients; reduce adverse events; and serve as a tool to assess the quality of care, costs and patterns of medication use in older adults[18]. In the current literature, none systematic review on the use of PIM in the hospitalized elderly population that used the Beers criteria was identified. In this sense, the aim of this study was to conduct a systematic review to identify and evaluate the prevalence of PIM prescription, according to the Beers Criteria, in elderly hospitalized at ≥65 years.

Method

A specific protocol was designed by the researchers to structure the systematic review and registered in PROSPERO, available in: http://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42019133367. The protocol included the stages of defining the theme and preparing the research question, "What is the prevalence of PIM prescription, according to the Beers Criteria, in hospitalized elderly aged ≥65 years?"; preparation of eligibility, inclusion and exclusion criteria for studies; survey of publications in databases; categorization and analysis of the information found in the publications and descriptive evaluation of the selected studies.

The following combination of descriptors (MeSH) in English was used to conduct the search in the MEDLINE database, as well as in the other databases, with minor adaptations, according to their specificities: ("Beers Criteria") and ("Potentially Inappropriate Medication List") and ("Beers Potentially *Prescribing*") and ("Beers Potentially *Criteria*" or "Beers *Criteria* of," or "Beers Inappropriate *Medications*"), with the date limits [01/02/2012 to 31/05/2019]. A librarian was consulted to promote rigor in the search process. Five databases used: Virtual Health Library of the Ministry of Health (VHL/

MS); Cochrane Library; Cumulative Index to Nursing & Allied Health Literature (CINAHL); Medical Literature Analysis and Retrieval System Online (MEDLINE) and Web of Science. The search for the studies was conducted in the month of May 2019.

The eligibility criteria were observational and experimental studies, conducted between 2012 and 2019; patients aged ≥65 years hospitalized in hospitals; studies that analyzed drug prescriptions using the Beers Criteria in the 2012 or 2015 versions, without language restriction. Abstracts of conference articles, theses and dissertations and studies that included joint data analysis with more than one criterion for the evaluation of PIM was excluded. The 2019 update of the Beers Criteria was not included due to its recent publication and lack of published studies with its application.

The studies were selected following two steps. First, two trained reviewers (R1 and R2) read and evaluated independently the titles and abstracts of the articles identified in the electronic databases. According to the eligibility criteria, they selected the articles for full reading. Subsequently, the articles read in full and final inclusion. When there was no consensus among the reviewers on the inclusion and final selection of the studies, the opinion of a third reviewer (R3) considered. The methodological quality of observational studies was analyzed using the Newcastle-Ottawa Scale, which scores three components: group selection (0-4 points), quality of adjustment for confusion (0-2 points) and exposure evaluation after outcome (0-3 points). The satisfactory quality of this scale should ≥6, in which the score of 9 points represents high methodological quality[20].

For systematization of data extraction a specific form was used containing: title, journal, author, year, country, type of publication; study design: type of study, objectives, data collection and sampling method, eligibility criteria, use of instruments; participants: number of study participants; identification of PIM for the elderly according to beers criteria (2012 or 2015 versions); limitations: risk of bias. The process of searching and selecting the studies followed the recommendations PRISMA[21] and represented in Figure 1.

The evidence of PIM prescriptions identified, explored, and synthesized narratively with tabulation of the results of the included studies. Some did not identify the prevalence of prescriptions that contained PIM, making it impossible to calculate and directly compare the results, so the performance of a meta-analysis would not recommend. It is also noteworthy that the 2012 and 2015 versions of the Beers criteria present differences regarding the categories of PIM, which makes it difficult to jointly analyze the data. In this sense, the prevalence of PIM analyzed in general, regardless of the inclusion of the drug in each category. Thus, the results conducted from descriptive analysis and synthesized, according to the prevalence of PIM.

Results

The search process resulted in the identification of 721 studies and after the selection steps 19 observational studies was included (Figure 1).

Among the selected studies, 17 (89.5%) were retrospective cohort observational studies published from 2013 to 2019. China stood out with the highest number of publications (n=4; 21.0%). The sample size ranged from 104 to 313,733 patients and the duration of the studies from three to thirty-five months. The mean age was 78.2 years (71.5-84.8). The most used criterion for the identification of PIM for the elderly was Beers 2015 (n=11; 57.9%). All studies showed good methodological quality according to the Newcastle-Ottawa scale. The general characteristics of the studies are summarized in Table 1.

The mean prevalence of PIM was 65.0% (28.7-95.3%), in which 221,879 elderly people used inappropriate medications. Prescription for the gastrointestinal system (15.3%), pain medications (10.5%) and central nervous system (9.7%) (Table 1). The main PIM prescribed were proton pump inhibitors - PPI (27.7%), opioids (27.2%) and benzodiazepines (19.0%) (Table 2).

Discussion

This systematic review allowed the determination of the prevalence of PIM prescribed for hospitalized elderly. The identification of these drugs is relevant and enables the current knowledge of drug therapy in this specific population. The high prevalence of PIM observed (65.0%) is worrying, indicating the importance of interventions for its reduction. Studies conducted in Canada[23] and in the USA[30], indicated rates higher than 90.0%. In Brazil, Japan and Italy, a prevalence of 47.3% was identified[41], 56.1%[42] and 31.1%[40], respectively. Comparing the results of studies conducted worldwide is not simple, due to variations in the methods used. Thus, there is a difference in the

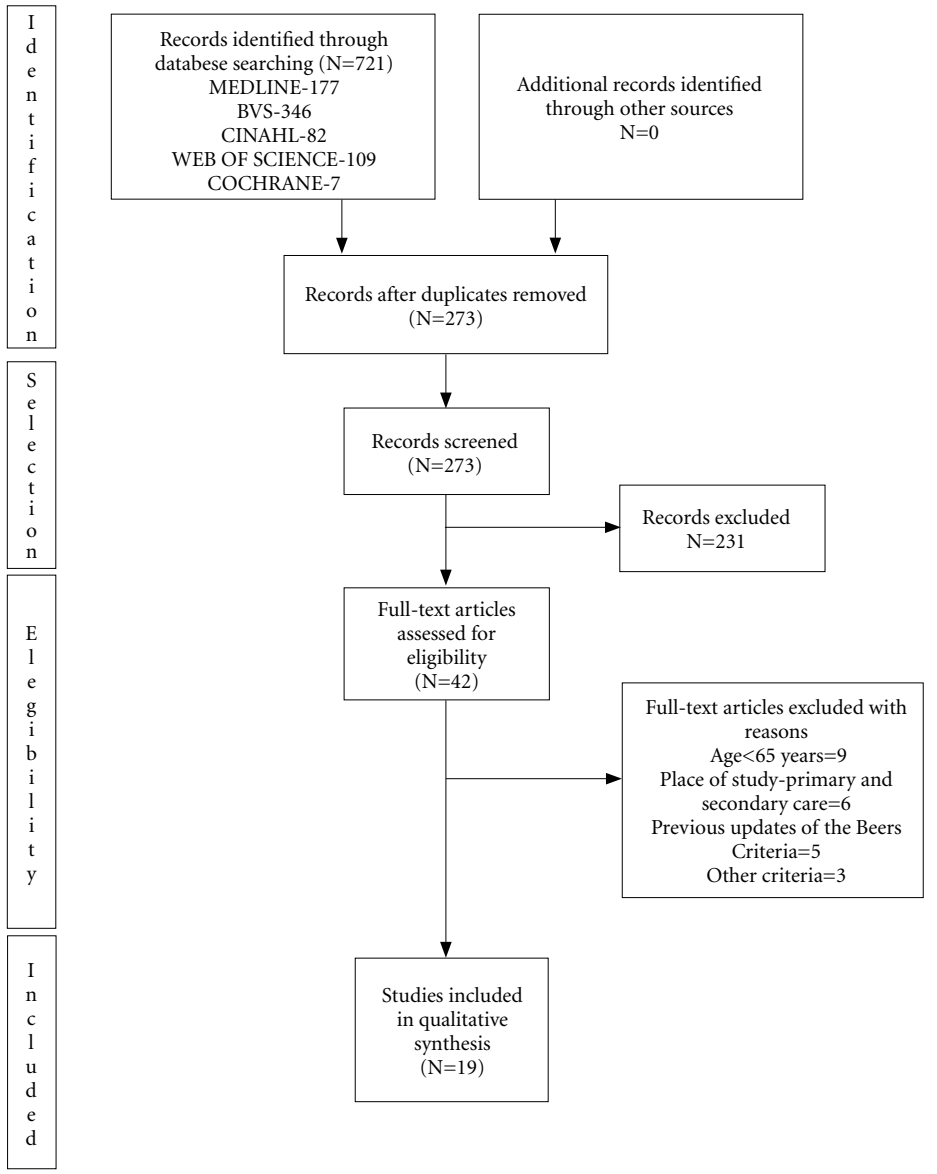

Figure 1. Study selection flowchart.

Source: Elaborated by the authors adapted from Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA).

prevalence of these prescriptions, which may also be related to the organization of health care delivery systems and with specific clinical practice environments in each country[40].

Included in the 2015 update of the Beers Criteria[18], the PPI s were the main PIM prescribed. Such medications are important for the treatment of diseases related to gastric acid, such as gastroesophageal reflux diseases and peptic ulcer[24]. However, its use of more than eight weeks not recommended, except in specific circumstances, when long-term acid suppression therapy is indicated[18]. Prolonged use of PPI compromises the safety of the elderly and can cause, among

Table 1. Characteristics of the studies included in the systematic review.

Study/Year	Country	Type of study	Sample n	Average age (years)	Beer's criteria	PIM/Patient Prevalence N (%)	Quality score
Chukwulebe et al., 2019[22]	United States	Cohort	11,822	71.5 (67.0-78.0)	2015	3,392 (28.7)	6
Lester et al., 2019[23]	Canada	Transverse	319	76.0 (75.0-76.8)	2015	304 (95.3)	6
Ma et al., 2019[24]	China	Transverse	863	75.4 (65.0-98.0)	2015	501 (58.1)	6
Chang et al., 2018[25]	Taiwan	Transverse	313,733	76.7	2015	199,882 (63.7)	7
Komagamine, 2018[26]	Japan	Transverse	689	82.0 (76.0-88.0)	2015	330 (47.9)	6
Komagamine et al., 2018[27]	Japan	Transverse	136	81.1	2015	105 (77.2)	6
Najjar et al., 2018[28]	Saudi Arabia	Cohort	200	78.0	2015	122 (61.0)	7
Sarwar et al., 2018[29]	Pakistan	Transverse	385	78 (65.0-85.0)	2015	342 (88.8)	6
Sharma et al., 2018[30]	United States	Transverse	104	82 (70.0-90.0)	2015	104 (91.3)	6
Komagamine e Hagane, 2017[31]	Japan	Cohort	158	84.8	2015	124 (78.4)	6
Li et al., 2017[32]	China	Transverse	6,337	81.3	2012	4,593 (72.5)	7
Zhang et al., 2017[33]	China	Transverse	456	81.8 (65.0-103.0)	2015	244 (53.5)	6
Arellano et al., 2016[34]	Chile	Cohort	250	77.5 (65.0-97.0)	2012	198 (79.2)	6
Di Giorgio et al.,2016[35]	Italy	Cohort	1,027	73.3	2012	507 (49.0)	7
Rongen et al., 2016[36]	Holland	Transverse	164	74.9 (65.0-92.0)	2012	77 (47.0)	6
Yang et al., 2015[37]	China	Transverse	141	81.5 (65.0-97.0)	2012	94 (66.7)	6
Matanovic e Vlahovic-Palcevski, 2014[38]	Croatia	Cohort	454	74.0	2012	263 (57.9)	6
Tosato et al., 2014[39]	Italy	Cohort	871	80.2	2012	509 (58.4)	7
Napolitano et al., 2013[40]	Italy	Transverse	605	76.7	2012	188 (31.1)	6

Source: Elaborated by the authors.

other problems, fractures[43], diarrhea associated with Clostridium difficile[44] and increased risk of pneumonia[45]. When prolonged use required, opportunities for suspension or dose reduction should considered.

Prescriptions for opioid drugs and non-steroidal anti-inflammatory drugs (NSAIDs) also highlighted. Opioids have added to the list of central nervous system (CNS) medications that should avoided in the elderly due to their association with the risk of falls or fractures[46]. In a study conducted, patients using opioids were 2.4 times more likely to have a fall and higher risk of in-hospital death (CR=1.58; 95%CI=1.34-1.86)

Table 2. Prevalence of potentially inappropriate drugs for the elderly, according to the Beers Criteria of the American Society of Geriatrics (2012 and 2015).

Organ System, Therapeutic Category	Mean prevalence (%)	Medication (%)	Mean prevalence (%)
Anticholinergics	5.7	Diphenhydramine	7.9
		Anticholinergics	7.2
		First-generation antihistamines	6.9
		Antispasmodic	6.7
Antithrombotics	5.1	Ticlopine	6.3
		Antithrombotics	3.9
Anti-infectious	2.8	Anti-infectious	5.1
		Nitrofurantoin	0.5
Cardiovascular	8.1	Cardiac medicines	27.0
		Amiodarone	12.4
		Spironolactone	12.1
		Antiarrhythmic	11.1
		Doxazosin	7.6
		Clonidine	7.4
		Terazosin	5.3
		Alpha1 blockers	4.0
		Niphedipine	4.3
		Digoxin	3.2
		Verapamil	2.0
		Propafenone	1.1
Central nervous system	9.7	Central nervous system medications	33.8
		Benzodiazepines	19.0
		TCA tertiaries	16.5
		Antipsychotics	16.4
		Hypnotics (non-benzodiazepines)	14.0
		Antidepressants	11.7
		Selective Serotonin Reuptake Inhibitors	6.6
		Barbiturates	6.5
		Anticonvulsant medications	4.6
		Diazepam	4.3
		Promazine	4.2
		Lorazepam	3.9
		Haloperidol	1.6
		Olanzapine	1.5
		Meprobamate	1.0
Endocrine	7.8	Insulin	14.0
		Long-term sulfonylureas	8.6
		Megestrol	5.27
		Endocrine medicines	3.4
Gastrointestinal	15.3	Gastrointestinal medicines	28.9
		PPI	27.7
		Metoclopramide	12.7
		Ranitidine	6.3
		Petroleum jelly oil	1.0
Pain medications	10.5	Opioids	27.2
		NSAIDs (0.4-87.7%)	15.9
		Meperidine	5.5
		Pain medications	3.4
		Skeletal muscle relaxant	0.6

Notes: TCA: tricyclic antidepressant, PPI: proton pump inhibitor, NSAIDs: non-steroidal anti-inflammatory drugs.

Source: Elaborated by the authors.

after the event[47]. NSAIDs commonly used by the elderly for chronic musculoskeletal pain[48], however, there is a high risk for gastrointestinal toxicity. The elderly using NSAIDs are at higher risk of serious complications, e.g., hemorrhage or gastric perforation[49]. Recently, the use of NSAIDs has been related to cardiovascular side effects[50]. It recommended, then, the use of these drugs in minimum effective doses for the shortest possible time[51].

Benzodiazepines have also been frequently prescribed. With aging, older people suffer from insomnia and depression, causing such drugs to be prescribed more frequently. Studies show that the use of these drugs increases the incidence of falls, hip fractures, altered mental status and delirium in the elderly[52] and is associated with a 3.6% higher frequency of return visits to the emergency department[22]. In this context, non-pharmacological therapy has been suggested as the initial method in the treatment of insomnia or delirium[32]. When the deprecation of the drug is not possible, monitoring of efficacy and possible adverse drug reaction (ADR) becomes essential.

In this regard, it found that the use of medications included in the Beers Criteria may be necessary at certain times. These criteria created not only to identify PIM, but also to support the discussion about the reasons why these drugs prescribed and the situations in which their use may bring greater or lesser risk to the elderly. Therefore, the criteria aim to support, rather than having dominion over a good clinical judgment[53].

Interesting discussions have been added by the studies reviewed. Polypharmacy was associated with an increased risk for the use of PIM[38], which can lead to a higher occurrence of ADR and consequently to increased hospitalization time and higher costs to health systems[54,55]. Tosato et al.[39] observed that the use of PIM was associated with ADR or decline in physical function (CR=1.74; 95%CI=1.06-2.85). Lester et al.[23] identified that the number of PIM prescribed not altered during hospitalization of the patient and their use was associated with an incidence rate of 1.46 (95%CI=1.13 to 1.88) for the duration of the stay. The authors report that there may be no effective medication reviews or that prescribers are unaware of the Beers Criteria and the existence of more appropriate medications for use in the elderly[23].

Faced with this situation, educational interventions to raise awareness among prescribers about these criteria are relevant. Studies have shown that there is a decrease in PIM prescribed after educational processes. Najjar et al.[28] showed that there was a significant decrease in the incidence rate of PIM from 61% to 29.5% during hospitalization ($p<0.001$); Komagamine and Hagane[31] pointed out that the proportion of patients who took any PIM decreased significantly from 93.5% on admission to 51.6% at discharge ($p<0.001$). It emphasized that the interventions described cannot confirm the clinical benefits obtained, since they not evaluated using clinically relevant results, such as mortality and quality of life. However, the interventions described may improve prescription and increase safety in the use of medications. These results state that the Beers Criteria stand out as an important tool for the detection of PIM and guide the change in the pattern of prescriptions, to ensure greater safety in the use of medications.

Other important initiatives to reduce the use of PIM are the revision of prescription with drug deprescription and computerized systems[23,31]. Deprescription aims at the planned and gradual withdrawal of PIM for each patient and requires monitoring of adverse events or rebound symptoms[56,57]. This attitude is effective in reducing inadequate polypharmacy and reducing harm to the patient[57]. Decision making based on computerized tools also stands out. Through the digital means, prescribing professionals can access all information about the medication therapy of patients and at the time of completion of the prescription, risk alerts and information about drug interactions are issued[2,53,58,59]. Despite the positive results, all studies make it clear that, in order to maintain the success of interventions, it is essential to engage and accept the prescriber in changing its practice and the participation of a multidisciplinary team, in specific nurses, clinical pharmacists and physicians. Thus, the guarantee of the common goal, which is the improvement in the quality of the prescription and the rational use of medicines in the elderly population, can achieved.

When interpreting the results of the included articles, it is worth mentioning some limitations to the method that could influence the estimates. Most studies were retrospective and in a single hospital. The use of only one PIM identification tool – Beers Criteria – may have underestimated the frequency of inadequacy, since some medications, especially those not used in the United States of America, not included.

We also highlight the updating of the Beers criteria in 2012 and 2015, generating two dif-

ferent versions. The first with three categories: medications or classes of inappropriate medications, regardless of diagnosis, their potential risks and some of their dosages; medicines that should avoided in specific clinical situations; and medicines or classes of medicines that should use with caution. The 2015 version, in addition to the three categories mentioned above, presents a fourth, referring to drugs whose doses should adjusted, depending on the creatinine clearance of the patient, and a fifth list, with drugs that should avoided in combination due to drug-drug interactions. Thus, there was the exclusion and inclusion of medications in the 2015 version[18], which may have interfered in the prevalence of PIM found in this study. Due to the lack of studies using the 2019 version, not evaluated in this review, which may have compromised the current identification of the prevalence of PIM. However, even with these limitations, it is believed there is no harm to the results and conclusions.

Conclusions

The evidence found in the studies shows that there is a high prevalence of prescribed PIM. The Beers Criteria allowed the identification of medications that should avoided in the elderly, have explicit criteria and their use can help in the prevention of adverse events resulting from inadequate drug therapy. Health professionals will be able to use the results of this review for decision-making to avoid the administration of PIM and propose best practices that ensure the safety of the hospitalized elderly.

The small number of studies identified by the systematic review in elderly aged ≥65 years in a hospital environment draws attention to the need for more cohort studies and randomized clinical trials that use the Beers criteria as a measure of the quality of hospital care. Only in this way will the predictive validity of these criteria proven in this scenario. However, such studies should follow standardized methods to validate the use of the criteria in the countries of their application, thus enabling the results of the different studies to be more comparable to each other.

Collaborations

CFM Lima and MFS Praxedes were responsible for the conception, research, methodology and final writing of the article. GCS Pereira, JS Berhends and DB Santos responsible for the methodology and critical review.

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