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Monteiro, Francelle Adorno Sôffa Guimarães; Pontes, Gabriela Mesquita; Sampaio, Gilsiane de Sousa; Oliveira, Maria Eugênia Ribeiro Carvalho de; Lima, Paulo Marcelo de Andrade

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Safety assessment of medicines available in the 'Brazilian list of essential medicines' in the older persons according to the Beers Criteria

Avaliação da segurança dos medicamentos disponíveis na 'Relação nacional de medicamentos essenciais' em idosos de acordo aos critérios de Beers

Francelle Adorno Sôffa Guimarães Monteiro[a], Gabriela Mesquita Pontes[a], Gilsiane de Sousa Sampaio[a], Maria Eugênia Ribeiro Carvalho de Oliveira[a], Paulo Marcelo de Andrade Lima[a]

[a] Núcleo de Pesquisa da Faculdade de Medicina (NUPMA), Universidade de Rio Verde, Campus Aparecida Extensão Goiânia – Goiânia (GO), Brazil.

Correspondence data
Paulo Marcelo de Andrade Lima – Avenida T-13 Qd. S-06, Lts. 08/13 – Setor Bela Vista – CEP: 74823-440 – Goiânia (GO), Brazil.
E-mail: paulo.lima@unirv.edu.br

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Abstract

Objective: To describe the safety of medicines available in the "Brazilian List of Essential Medicines" (RENAME/2022) for the main comorbidities that affect older persons according to the Beers criteria 2019.

Methods: Medicines listed in RENAME and recommended by the respective Brazilian medical guidelines for the treatment of hypertension, heart failure, diabetes, and neurological/psychiatric diseases were evaluated for their safety profiles according to the Beers criteria 2019.

Results: Fifty-eight out of 529 medicines in RENAME were evaluated. Of these, 29 were included in any of the Beers criteria: 20 were classified as potentially inappropriate, 17 should be avoided due to disease exacerbation, and 14 needed to be used with caution. Considering drugs used to treat cardiovascular, diabetes, and neurological/psychiatric disorders, 40.00, 37.50 and 60.00% respectively, had some criterion for their appropriate use in older persons.

Conclusion: RENAME presents alternatives for the safe treatment of older patients. In the treatment of cardiovascular diseases, diabetes, and neurodegenerative diseases, the first-choice recommendations are available in RENAME. Regarding psychiatric disorders, safe pharmacological alternatives are still scarce and need to be better discussed.

Keywords: Beers criteria; potentially inappropriate medication list; rename; aged; polypharmacy.

Resumo

Objetivo: Descrever a segurança dos medicamentos disponíveis na *Relação Nacional de Medicamentos Essenciais* (RENAME/2022) para as principais comorbidades que acometem os idosos segundo os critérios de Beers 2019.

Metodologia: Os medicamentos listados na RENAME e recomendados pelas respectivas diretrizes médicas brasileiras para o tratamento de hipertensão, insuficiência cardíaca, diabetes e doenças neurológicas/psiquiátricas foram avaliados quanto ao seu perfil de segurança de acordo com os critérios de Beers 2019.

Resultados: Foram avaliados 58 dos 529 medicamentos da RENAME. Deles, 29 foram incluídos em algum dos critérios de Beers: 20 foram classificados como potencialmente inapropriados, 17 deveriam ser evitados em razão da exacerbação da doença e 14 precisavam ser usados com cautela. Considerando-se os medicamentos utilizados para tratar doenças cardiovasculares, diabetes e distúrbios neurológicos/psiquiátricos, 40,00, 37,50 e 60,00%, respectivamente, tinham algum critério para o seu uso adequado em idosos.

Conclusão: A RENAME apresenta alternativas para o tratamento seguro de pacientes idosos. No tratamento de doenças cardiovasculares, diabetes e doenças neurodegenerativas, as recomendações de primeira escolha estão disponíveis na RENAME. Com relação aos transtornos psiquiátricos, alternativas farmacológicas seguras ainda são escassas e precisam ser mais bem discutidas.

Palavras-chave: critérios de Beers; lista de medicamentos potencialmente inapropriados; rename; idosos; polifarmácia.

INTRODUCTION

Excessive and frequent consumption of drugs with or without professional guidance is an important public health problem worldwide.[1] To mitigate the risks related to this practice and safely meet the needs of most individuals to have access to their medications, the concept of "essential medicines" was proposed by the World Health Organization (WHO).[1] The term "essential" is related to the premise that some medicines are more important than others and that access to these should be strengthened.[2] The WHO has a list of essential medicines that can be adapted according to each country's needs.[2] Within this concept, the RENAME list (in Brazilian Portuguese, *Relação Nacional de Medicamentos Essenciais*) was elaborated in 1975 in Brazil.[3]

RENAME consists of a list of essential medicines and supplies available at the Unified Health System for the main pathologies of the Brazilian population. This list, planned on the basis of effectiveness, cost and benefit, and availability of supplies, has as its fundamental aim to nationally standardize the medicines available to the population, being used to guide the production, distribution, and purchase of medicines in the country.[3]

The older population is part of a public with a high demand for drugs available at the public health system. Multimorbidity (ie, the coexistence of two or more chronic conditions) is common among older adults and leads to the use of multiple medications, known as polypharmacy;[4] moreover, older people show age-related physiology changes that affect the pharmacokinetic and pharmacodynamic profiles of drugs.[5] Thus, due to the combination of these conditions, many drugs are considered unsuitable for the older population, being named potentially inappropriate medications (PIMs).[6]

Medications are considered potentially inappropriate for use in older adults if the potential adverse risk of patients outweighs the expected clinical benefit, or when a better-tolerated or safer alternative is available.[6] PIMs have been found to be closely associated with an increased risk of poor health outcomes, including increased incidence rates of adverse drug events, hospitalization, and health-related costs and an economic burden for older patients.[7]

As a strategy to prevent medication-related harms, several assessment tools based on implicit or explicit approaches have been developed to avoid PIM use in older patients.[8] While the explicit criteria are based on standardized lists of inappropriate medicines applicable to the general population, implicit tools are based on the clinician's assessment of each patient.[8]

The Beers criteria are the most frequently used and validated explicit criteria for the detection of PIMs in older adults. The first version was developed by Dr. Mark Beers and, from 2012 on, the American Geriatrics Society (AGS) has been responsible for the updates. The new version contains five types of criteria, including:

1. PIMs in older adults,
2. PIM use in older adults due to drug-disease or drug-syndrome interactions that may exacerbate the disease or syndrome,
3. Drugs to be used with caution in older adults,
4. Drug-drug interactions, and
5. Drugs to avoid or adjust for dosage in varying stages of kidney function.[9]

Brazil is going through a process of demographic transition where the aging rate is increasing with a concomitant decrease in fertility and mortality rates. According to population census data from the Brazilian Institute of Geography and Statistics, in 2021, out of 213.3 million Brazilians, 37.7 million are aged over 60 years. Thus, considering the impact of prescribing quality determining the increased well-being of older patients, the present study aimed to describe the safety profile, in the older population, of medications listed in the standardized Brazilian List of Essential Medicines — RENAME/2022 — according to the Beers criteria 2019.

METHODS

This is a descriptive study that evaluated the safety profile, in older patients, of medications available in RENAME/2022 according to the Beers criteria 2019. This study was conducted in three phases.

First, the medications included in the RENAME/2022 list were reviewed and then classified according to the Anatomical Therapeutic Chemical (ATC) classification system.

Subsequently, all medications recommended in the treatment of hypertension and heart failure, diabetes, and neurological (including Parkinson's and Alzheimer's diseases) and psychiatric diseases (including anxiety, depressive, and psychotic disorders) which were listed in RENAME/2022 were selected for comparative analysis with the Beers criteria. The choice of these clinical conditions was based on the systematic literature review conducted by Sinnige et al., who showed that the most common disease clusters in the older population were diabetes, hypertension, and psychiatric/neurological diseases, mainly depression and dementia.[10] In Brazil, these diseases are also among the most common in older adults. Among the 10 most common diseases, cardiovascular disease ranks first, followed by diabetes; Parkinson's disease and Alzheimer's disease are in the fourth and eighth

places, respectively; depression is the sixth most common disease in this age group.

Drug selection was standardized according to the most recent medical guidelines and/or protocols for each clinical condition developed by the competent medical entities referring to each specialization, ie, "Brazilian Guidelines of Hypertension",[11] "Emerging Topics Update of the Brazilian Heart Failure Guideline",[12] "Brazilian Diabetes Society Guidelines",[13] "Clinical Protocol and Therapeutic Guidelines for Parkinson's Disease",[14] and "Clinical Protocol and Therapeutic Guidelines for Alzheimer's Disease".[15]

After selecting specific drugs for the most prevalent clinical conditions, categorization was performed according to 3 (out of 5) Beers criteria:

1. Potentially inappropriate medication,
2. Potentially inappropriate medication due to drug-disease or drug-syndrome interactions that may exacerbate the disease or syndrome, and
3. Drugs to be used with caution in older adults.

The last 2 criteria (drug-drug interactions and PIMs based on kidney function) were not evaluated since they would fit into a subgroup of older patients with special characteristics, which could alter the interpretation of results being analyzed for the general geriatric population, without particularities. The reasons for the inclusion of drugs in each criterion were analyzed, as well as the therapeutic alternatives for the treatment of each clinical condition.

RESULTS

RENAME/2022 contains 529 medications distributed in 15 categories according to the ATC (Figure 1). Of these, 147 medications were analyzed and distributed into 3 categories: 40 referring to the "cardiovascular system", 47 referring to the "digestive system and metabolism", and 60 to the "nervous system". These categories cover the drugs intended for the treatment of the main comorbidities that affect the older population (ie, hypertension, heart failure, diabetes, and neurological/psychiatric diseases).

Among the medications included in the "cardiovascular system" category, 20 are present among the drugs indicated by the "Brazilian Guidelines of Hypertension"[11] and "Emerging Topics Update of the Brazilian Heart Failure Guideline"[12] for the treatment of hypertension and heart failure. In the group of medications listed in the "digestive system and metabolism" category, 8 drugs are indicated for the treatment of diabetes according to the "Brazilian Diabetes Society Guidelines"[13]. In the "nervous system" category, 5 are antidepressants, 4 are benzodiazepines, and 7 are antipsychotics; moreover, 10 are recommended for the treatment of Parkinson's disease and 4 are recommended for the treatment of Dementia diseases

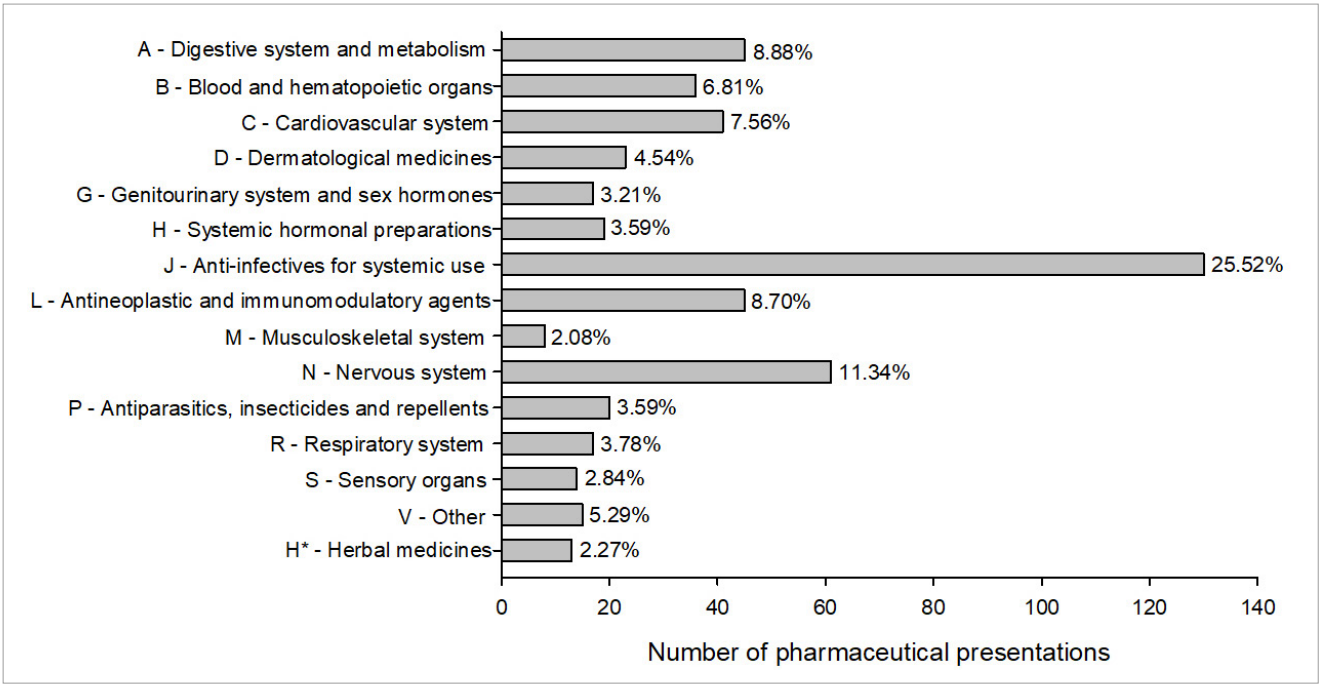

FIGURE 1. Number of pharmaceutical preparations available in RENAME/2022 distributed in their respective categories, according to the Anatomical Therapeutic Chemical classification system.

(Alzheimer's Disease), according to the "Clinical Protocol and Therapeutic Guidelines of Parkinson's disease"[14] and "Clinical Protocol and Therapeutic Guidelines of Alzheimer's disease"[15], respectively (Table 1). Among 58 medications present in RENAME/2022 and approved, according to medical guidelines, for the treatment of diseases with the highest prevalence in older persons, 29 (50%) medications are included in one of the Beers criteria. Among these medications, 20 were considered potentially inappropriate for older patients (criterion 1), 17 should be avoided because they exacerbate certain diseases

TABLE 1. Medications available in RENAME/2022 with indications for each comorbidity according to Brazilian guidelines.

Comorbidity	Medications
Cardiovascular system Hypertension Heart failure	Calcium channel blockers (CCB) Anlodipine, nifedipine, verapamil Diuretics (DIU) Hydrochlorothiazide, furosemide, spironolactone Angiotensin converting enzyme inhibitors (ACEi) Captopril, enalapril Angiotensin II AT1 receptor blockers (ARB) Losartan Beta blockers (BB) Atenolol, metoprolol (succinate and tartrate), carvedilol, propranolol Central alfa-2 agonists (AA) Methyldopa Alpha-1 blockers (AB) Doxazosin mesylate Direct vasodilators (DV) Hydralazine, isosorbide dinitrate Digitalics (DIG) Digoxin ARB + Neprilysin inhibitor (ARB/NI) Sacubitril/valsartan
Digestive system and metabolism Diabetes	Insulins Long-acting insulin analog, rapid-acting insulin analog, human insulin NPH, Human regular insulin Biguanides Metformin Sulfonylureas Glibenclamide, gliclazide SGLT-2 inhibitors Dapagliflozin
Nervous system Anxiety disorders Depressive disorders Psychotic disorders Parkinson's disease Alzheimer's disease	Antidepressants Tricyclics (TCA): amitriptyline, clomipramine, nortriptyline Selective 5-HT reuptake inhibitor (SSRI): fluoxetine Atypical: bupropion Benzodiazepines Clobazam, clonazepam, diazepam, midazolam Antipsychotics Typical: chlorpromazine, haloperidol Atypical: olanzapine, quetiapine, clozapine, ziprasidone, risperidone Anticholinesterases/Dementia diseases (Alzheimer's disease) Galantamine, donepezil, rivastigmine, memantine Antiparkinsonians NMDA antagonist: amantadine MAO inhibitors: selegiline, rasagiline COMT inhibitors: entacapone DA precursor + AADC inhibitors: levodopa + benserazide/carbidopa DA receptor agonists: pramipexole Anticholinergics: trihexyphenidyl, biperiden (hydrochloride and lactate)

(criterion 2), and 14 need to be used with caution (criterion 3). Some medications appear in more than one of the criteria (Table 2). Table 3 summarizes the safety profile of medications available in RENAME/2022 for older patients. The term "total" represents the number of medications selected for the clinical conditions according to medical guidelines. The term "appropriate" was assigned to those drugs that did not meet the Beers criteria, while the term "inappropriate" consisted of drugs that met Beers criteria 1, 2, and/or 3. Considering the most prevalent clinical conditions among the older population, there is a greater proportion of pharmacological alternatives, in RENAME/2022, for the treatment of hypertension and heart failure (60.00%) and diabetes (62.50%) when compared to neurological and psychiatric disorders (40.00%).

TABLE 2. Medications available in RENAME/2022 classified into the Beers criteria 2019.

Comorbidity	Criterion 1 Potentially inappropriate medication (PIM)	Criterion 2 PIM due to drug-disease/ syndrome interactions that may exacerbate the disease/syndrome	Criterion 3 Drugs to be used with caution in older adults
Cardiovascular system			
Hypertension/heart failure	Doxazosin. Methyldopa. Nifedipine. Digoxin.	Verapamil → heart failure. Doxazosin → syncope, urinary incontinence.	Diuretics.
Digestive system and metabolism			
Diabetes	Glibenclamide. Insulin regimens containing only short- or rapid-acting insulin without concurrent use of basal or long-acting insulin.	-	-
Nervous system			
Psychotic disorders	Antipsychotics (chlorpromazine, haloperidol, olanzapine, quetiapine, clozapine, ziprasidone, risperidone).	Antipsychotics → delirium, dementia or cognitive impairment, history of falls and fractures, Parkinson's disease (except quetiapine and clozapine). Chlorpromazine and olanzapine → syncope.	Antipsychotics.
Anxiety disorders	Benzodiazepines (clonazepam, diazepam).	Benzodiazepines → delirium, dementia or cognitive impairment, history of falls and fractures.	-
Depressive disorders	Tricyclic antidepressant (amitriptyline, clomipramine, nortriptyline).	Tricyclic antidepressant → syncope, delirium, history of falls and fractures.	Tricyclic antidepressant. Selective 5-HT reuptake inhibitor (fluoxetine).
Alzheimer's disease	-	-	-
Parkinson's disease	Trihexyphenidyl.	Anticholinergics → delirium, dementia, or cognitive impairment.	-

TABLE 3. Safety profile of medications available in RENAME/2022 according to the Beers criteria 2019, in each category.

Category	Total	Appropriate	Inappropriate	Inappropriate (%)
Cardiovascular system				
CCB	3	1	2	66.67
DIU	3	0	3	100.00
ACEi	2	2	0	0.00
ARB	1	1	0	0.00
BB	5	5	0	0.00
AA	1	0	1	100.00
AB	1	0	1	100.00
DV	2	2	0	0.00
DIG	1	0	1	100.00
ARB/NI	1	1	0	0.00
Total	20	12	8	40.00

Continue...

TABLE 3. Safety profile of medications available in RENAME/2022 according to the Beers criteria 2019, in each category.

Category	Total	Appropriate	Inappropriate	Inappropriate (%)
Digestive system and metabolism				
Insulins	4	2	2	50.00
Biguanides	1	1	0	0.00
Sulfonylureas	2	1	1	50.00
SGLT-2 inhibitors	1	1	0	0.00
Total	8	5	3	37.50
Nervous system				
Antidepressants	5	1	4	80.00
Benzodiazepines	4	0	4	100.00
Antipsychotics	7	0	7	100.00
Anti-dementia	4	4	0	0.00
Anti-parkinsonians	10	7	3	30.00
Total	30	12	18	60.00

Acronyms: CCB: calcium channel blockers; DIU: diuretics; ACEi: angiotensin-converting enzyme inhibitors; ARB: angiotensin II AT1 receptor blockers; BB: beta blockers; AA: central alfa-2 agonists; AB: alpha-1 blockers; DV: direct-acting vasodilators; DIG: digitalics; ARB/NI: ARB + neprilysin inhibitor.

DISCUSSION

The present study evaluated the safety profile of medications available in the "Brazilian List of Essential Medicines" for the most prevalent clinical conditions among older patients, which are cardiovascular diseases (especially hypertension and heart failure), diabetes, and neurodegenerative (Alzheimer's disease and Parkinson's disease) and psychiatric (anxiety and depression) disorders. The medications available in RENAME/2022 were selected according to the recommendations for use by the Brazilian medical guidelines for all the comorbidities reported above and were then compared to the explicit tool for evaluating the safety of drugs in older persons: the Beers criteria.

Hypertension is a common problem in the older population, affecting up to 80% of the population over 65 years old. Drugs for cardiovascular diseases are the most prescribed medications in older persons, and problems related to PIM in older people are common. The most frequent adverse effects due to the use of antihypertensives in older people include postural hypotension, increased risk of falls, electrolyte disturbances, and cognitive impairment.[16]

The RENAME list includes 20 medications, distributed among 10 classes, used to treat hypertension and heart failure according to the "Brazilian Guidelines of Hypertension"[11] and "Emerging Topics Update of the Brazilian Heart Failure Guideline",[12] respectively. Among them, 5 classes showed some criteria for inclusion as PIMs, ie, central alpha-2 agonists (eg, methyldopa), alpha-1 blockers (eg, doxazosin), calcium channel blockers (eg, nifedipine and verapamil), diuretics (eg, hydrochlorothiazide, furosemide, and spironolactone), and digitalis (eg, digoxin).

The AGS Beers Criteria strongly advises that central alpha-2 agonists and alpha-1 blockers should be avoided as routine therapy for hypertension.[9] Both classes frequently cause orthostatic hypotension and reflex tachycardia due to their vasodilating effects; moreover, central alpha-2 agonists can also cause sedation, headache, dizziness, and weakness. The association between hypotension and sedation increases the risk of falls and their complications, including hospitalizations or death.[16]

Calcium channel blockers are a versatile class of antihypertensive drugs; while the dihydropyridines subtype acts preferentially on vascular smooth muscle, the nondihydropyridines subtype is more cardioselective.[16] Nifedipine, which presents greater affinity for vascular calcium channels, is not recommended in older patients due to the risk of hypotension and myocardial ischemia;[9] it also has potential side effects including congestive heart failure due to systolic dysfunction, constipation, edema in the lower extremities, a negative inotropic effect in the presence of cardiac failure, and gastroesophageal reflux.[16] Verapamil, another calcium channel blocker with greater affinity for cardiac channels, should be avoided in heart failure with reduced ejection fraction.[9]

Diuretics, despite being basic drugs for the treatment of heart failure and hypertension due to their capacity to eliminate edema and maintain a stable blood flow,[16] belong to the third section of the Beers criteria (ie, drugs to be used with caution in older adults). The reasons include the increased risk to cause or aggravate the syndrome of inappropriate antidiuretic hormone secretion and hyponatremia.[9]

Digoxin, a cardiac glycoside used for rate control in patients with heart failure and atrial fibrillation, has a narrow safety

margin due to its adverse effects (mostly nausea, vomiting, weakness, loss of appetite, diarrhea, restlessness, and rhythm disorders).[17] The AGS Beers Criteria strongly advises that digoxin should not be used as a first-line agent in heart failure, because there are safer and more effective alternatives for rate control.[9] More recently, the medication that brings the association sacubitril (neprilysin inhibitor) and valsartan (angiotensin II AT1 receptor blocker) for the treatment of heart failure was inserted in RENAME and in the Brazilian medical guidelines.

In accordance with the Beers Criteria, the 'Brazilian Guidelines on Hypertension" recommends that some antihypertensive classes, such as centrally acting drugs (eg, methyldopa) and direct-acting vasodilators (eg, doxazosin and nifedipine), should be seen as an exception and unusual for the treatment of older patients.[11] The guidelines recommend that the initial treatment of hypertension in older patients should start with a thiazide diuretic (eg, hydrochlorothiazide) or a blocker of the renin-angiotensin-aldosterone system: an angiotensin-converting enzyme inhibitor (eg, captopril and enalapril) or an angiotensin II AT1 receptor blocker (eg, losartan). Beta-blockers (eg, atenolol, metoprolol, carvedilol, and propranolol) should not be used as initial monotherapy in older patients, except in the presence of some comorbidities in which they may even have a mandatory indication, such as heart failure or acute coronary insufficiency.[11]

In the "Digestive system and metabolism" category, medications used for the treatment of diabetes were highlighted. Diabetes has been described as a 21st century epidemic in developed countries, and the aging of populations is considered one of the most important causes. The prevalence of type 2 diabetes is predicted to increase to 628.6 million in 2045, with the greatest increase in prevalence in those over 65 years old.[13] The pharmacological management of diabetes and its complications is particularly challenging in older adults.

The RENAME list includes 8 medications distributed among 4 antidiabetic classes: insulins, biguanides, sulfonylureas, and SGLT-2 inhibitors. Among the 8 medications, 3 (rapid-acting insulin, regular human insulin, and glibenclamide) showed some criteria of unsafety for use in older patients because they can induce prolonged hypoglycemia, which in turn, depending on its severity, can increase the incidence of neurological sequelae, acute myocardial infarction, stroke, and falls.[9] Short- and rapid-acting insulins are also contraindicated in a single regimen (ie, if not associated with basal or long-acting insulin).[9] Among sulfonylureas, gliclazide has a lower risk of hypoglycemia when compared to glibenclamide, making it a safer therapeutic option. Metformin has a potential advantage due to its greater tolerability, lower risk of hypoglycemia, and causes less weight gain.[18]

The latest RENAME update included dapagliflozin, an SGLT-2 inhibitor. It has a low risk of hypoglycemia but must be adjusted according to renal function once its mechanism of action is based on glycosuria.[19] An additional benefit of decreasing cardiovascular risk and lowering blood pressure[20] suggests what can be a safe strategy in the treatment of diabetes among the older population.

The safety of drugs in the "nervous system" category was also evaluated in this study as psychiatric illnesses are common in older adults; they mainly include anxiety, sleep disorders, mood disorders, and dementia.[21] Antidepressants, benzodiazepines, and antipsychotics are used as psychotropic medications for these disorders.

Benzodiazepine use is widespread among older adults, being a public health problem worldwide.[22] Four benzodiazepines are present in the RENAME list; however, the Beers criteria recommend avoiding all benzodiazepines in older adults due to risks of cognitive impairment, delirium, falls, and fractures.[9] Alternative medications for treating insomnia and anxiety in older adults should be considered, eg, sedative antidepressants such as mirtazapine or selective serotonin reuptake inhibitors (SSRI) such as escitalopram[23] — unfortunately, neither of them are included in RENAME.

Regarding antidepressants, the use of tricyclic antidepressants (TCA) and serotonin and norepinephrine reuptake inhibitors (SNRI) has been associated with substantial anticholinergic effects (ie, confusion, dry mouth, sedation, and orthostatic hypotension).[24] Beers criteria recommend that all TCA, SSRI, and SNRI in older adults with syncope should be avoided; particularly TCA should also be avoided in older adults with history of falls or fractures.[9] Bupropion, an atypical antidepressant, is the only antidepressant available in RENAME that is not included in the Beers criteria.

SSRI and SNRI antidepressants are currently considered first-choice treatment; however, as discussed, anticholinergic adverse effects have an important impact in the older population. In a meta-analysis study that compared these antidepressant drugs, sertraline had the lowest risk of dizziness when compared to placebo, followed by fluoxetine, citalopram, and escitalopram; duloxetine and venlafaxine showed the worst results.[25]

Seven antipsychotic drugs are listed in RENAME; however, the Beers criteria recommends that, regardless of the diagnosis and conditions, they should be avoided in older adults. Antipsychotics showed strong anticholinergic effects

and extrapyramidal side effects[26] that increase the risks of dementia, cognitive impairment, history of falls or fractures, and delirium.[9] When comparing antipsychotic drugs in the older population, a recent systematic review showed that quetiapine had a lower risk of mortality, reduced rate of cerebrovascular events, increased rate of falls and injury, and lower rates of metabolic disorders when compared with olanzapine; however, when compared to risperidone, quetiapine showed higher rates of metabolic disorders.[27]

The number of older people living with Alzheimer's disease and related dementias (ADRD) is high. According to data from the Global Burden of Disease Study 2016, Brazil had the second highest age-standardized prevalence, with 1037 cases of dementia per 100,000 inhabitants.[28] The RENAME list includes 4 medications for the treatment of ADRD in accordance with "The Brazilian Clinical Protocol and Therapeutic Guidelines for Alzheimer's Disease". Although none of these medications are present in the Beers criteria, it is important to note that older adults with ADRD have a variety of symptoms (agitation, aggression, or sleep disturbances) for which pharmacotherapy is necessary, thus the risks associated with many of these medications may outweigh their clinical benefit.[28]

Another common neurological condition among older persons, as the second most prevalent neurodegenerative disease, is Parkinson's disease.[14] Typically, persons with Parkinson's disease show motor and cognitive impairment, and dysfunctional dopaminergic and cholinergic systems explain the basis of its pathophysiology.[29] The RENAME includes 10 drugs for the treatment of Parkinson's disease, where 7 have properties that potentiate dopaminergic neurotransmission and 3 are anticholinergic agents. The Beers criteria recommend that all anticholinergic agents should be avoided in older adults with delirium, dementia, and cognitive deficit; no recommendations are stated for dopaminergic agents.[9] Likewise for Alzheimer's disease, mood disorders, in particular depression and anxiety, are common in Parkinson's disease; it is plausible that the use of psychotropic drugs with anticholinergic, antidopaminergic, and GABAergic properties is avoided in the older population.[29]

CONCLUSION

The evaluation conducted in this study can conclude that the medications available in RENAME have a good safety profile for the treatment of the main comorbidities that affect older patients. Despite the existence of many PIMs, we verified the possibility of therapeutic alternatives for most of these clinical conditions, and recommendations of first-line treatments for each of them have been relatively safe for older patients.

In the management of hypertension, among antihypertensive agents, low doses of thiazides and agents acting on the renin-angiotensin system appear to show the lowest risks in older patients. Regarding the treatment of diabetes, the main concern regarding the use of antidiabetic drugs is the occurrence of hypoglycemia: avoiding the use of short-acting insulins in monotherapy and sulfonylureas is thus a basic premise; metformin and dapagliflozin have been presented as the best options.

There is no contraindication for antidementia agents in RENAME; for Parkinson's disease, among antiparkinsonian agents, the main recommendation is to avoid the use of anticholinergic agents.

Greater care is needed in the treatment of anxiety and depressive disorders. Although there is a considerable number of drugs aimed at the treatment of neuropsychiatric diseases in RENAME, there is a lack of safe options for older patients. Virtually all drugs with anxiolytic, antidepressant, and antipsychotic activity meet the criteria for inclusion as PIMs. The use of benzodiazepines should always be avoided, and non-pharmacological treatment should be stimulated for insomnia treatment. Antidepressants with less anticholinergic activity may be encouraged when compared to benzodiazepines and antipsychotics for the treatment of mood disorders in the older population.

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Conflict of interest

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Authors' contributions

FASGM: conceptualization, data curation, formal analysis, investigation, methodology, writing – review & editing. GMP: conceptualization, data curation, formal analysis, investigation, methodology, writing – review & editing. GSS: conceptualization, data curation, formal analysis, investigation, methodology, writing – review & editing. MERCO: conceptualization, data curation, formal analysis, investigation, methodology, writing – review & editing PMAL: conceptualization, project administration, resources, supervision, validation, writing – original draft.

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