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Polypharmacy and potentially inappropriate medications in older adults in primary health care

Polifarmácia e medicamentos potencialmente inapropriados em idosos assistidos pela atenção básica à saúde

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RESUMO
Objetivo: Avaliar a polifarmácia e os Medicamentos Potencialmente Inapropriados (MPI) direcionados a idosos assistidos pela Atenção Básica à Saúde (ABS) do Município de Campo Grande/MS, Brasil, a partir dos Critérios de Beers 2015. **Método:** Estudo quantitativo, realizado no período de dezembro/2015 a agosto/2016 com 150 Idosos atendidos em 5 Unidades de Saúde do Município de Campo Grande, Mato Grosso do Sul. Brasil **Resultados:** A idade média foi de 70,6 (±7,23). Dos idosos avaliados, 64% (n=96) encontravam-se submetidos à polimedicação. Foi identificado um total de 24 MPI (24,5%), prescritos 168 vezes. Cem idosos (66,7%) apresentaram pelo menos um MPI prescrito (n=57; 38%). Os MPI mais frequentes foram: insulina (n= 39; 23,2%), glibenclamida (n= 38; 22,6%), omeprazol (n= 27; 16,1%), metildopa (n= 13; 7,7%) e amitriptilina (n= 10; 5,9%). Oitenta e um idosos (54%) estavam submetidos à polifarmácia e estavam em uso de pelo menos um MPI. Considerando somente os pacientes que fizeram uso de pelo menos 1 (um) MPI (n= 100, 66,7%), 81% eram polimedicados. **Conclusão:** Aproximadamente três em cada cinco prescrições para idosos assistidos pela ABS de Campo Grande/MS e avaliados no presente estudo é inapropriada.

Palavras-chave: Serviços Farmacêuticos, Critérios de Beers, Assistência Integral à Saúde.

ABSTRACT
Objective: To assess polypharmacy and Potentially Inappropriate Medications (PIMs) prescribing in older adults in Primary Health Care (PHC) in the city of Campo Grande, Mato Grosso do Sul, Brazil, based on the 2015 Beers Criteria. **Methods:** Quantitative study conducted from December 2015 to August 2016 with 150 older adults attending 5 Health Care Centers of the city of Campo Grande, Mato Grosso do Sul, Brazil. **Results:** Participants' mean age was 70.6 (±7.23). 64% (n=96) of the older adults analyzed were submitted to polypharmacy. There were 24 PIMs (24.5%) prescribed 168 times. One hundred older adults (66.7%) had been prescribed at least one PIM (n=57; 38%). The most frequent PIMs were insulin (n=39; 23.2%), glibenclamide (n=38; 22.6%), omeprazole (n=27; 16.1%), methyldopa (n=13; 7.7%), and amitriptyline (n=10; 5.9%). Eighty-one older adults (54%) were submitted to polypharmacy and used at least one PIM. Considering only the patients who used at least 1 PIM (n=100, 66.7%), 81% were polymedicated. **Conclusion:** Approximately three out of five prescriptions for older adults in PHC in the city of Campo Grande, Mato Grosso do Sul, assessed in the present study are inappropriate.

Keywords: Pharmaceutical Services, Beers criteria, Comprehensive Health Care.

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1 INTRODUCTION

Brazil is experiencing a rapid aging of the population due reductions in fertility and mortality rates that have already been observed, particularly in Asia and Europe. The World Health Organization (WHO) considers the age of 65 as a definition of older person. However, the Brazilian government considers the age of 60 as the beginning of old age (WHO, 2005). According to the Brazilian Institute of Geography and Statistics (*Instituto Brasileiro de Geografia e Estatística – IBGE*), individuals aged 60 years and older accounted for 10.8% of the total population in 2010, and it is estimated that in 2050 such figure will be over 29.7% (BRAZIL, 2010).

Because of population aging, Brazil, as other developing countries, has undergone a change in the profile of public health problems, with a predominance of chronic noncommunicable diseases. The rise of chronic noncommunicable diseases in the older population increases the demand for medicines; however, aging leads to changes in the pharmacokinetics and pharmacodynamics of drugs.

Regarding pharmacokinetics, such changes are related to the parameters of drug absorption, distribution, metabolism, and elimination. Absorption is poorly affected by aging, i.e., although drug absorption is slow, retarding peak serum, bioavailability is not affected. As for distribution, there is an increase in body fat, a decrease in muscle mass, a decrease in total body water volume, a decrease in plasma albumin concentration, and an increase in the plasma concentration of alpha-1-glycoprotein. Such alterations affect the volume of distribution, which requires the monitoring of drugs with narrow therapeutic index. With regard to metabolism, hepatic blood flow, liver mass, enzymatic activity and first-pass metabolism may be decreased, which may compromise the metabolism of some drugs. Finally, regarding elimination, renal mass, number of glomeruli, renal blood flow and glomerular filtration rate are decreased and may interfere with the elimination of some drugs (GABARDI, TULLIUS, KRENZIEN, 2015).

Regarding pharmacodynamics, older people experience changes in their sensitivity profile, which lead to alterations in their response to drugs. When the same drug is administered to young and older patients, different responses are observed – older patients' response to the drug is often exacerbated, which demonstrates a greater sensitivity. This can be attributed to the decline in homeostasis maintenance and to changes in receptor affinity for drugs and in the number of receptors. Age-related changes in pharmacokinetic and pharmacodynamic parameters of drugs may influence the clinical outcomes achieved by this population. Thus, decision-making requires careful evaluation prior to the elaboration of therapeutic schemes targeted at older individuals (KLOTZ, MÖRIKE, SHI, 2008). The process of selecting drugs for older patients is complex and includes several aspects, such as deciding which drug is indicated, choosing the best drug, determining the appropriate dosage based

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on the patient's physiological state, monitoring for efficacy and toxicity, and informing the patient about adverse reactions and when to seek medical care (ROCHON, 2016).

Polypharmacy is defined as the use of multiple drugs by a patient. There is no consensus in the literature regarding the precise minimum number of drugs to define such practice, but it generally ranges from 5 to 10 (FERNER, ARONSON, 2006).

There are different instruments for assessing older people's pharmacotherapy, the Beers Criteria represent one of the most consulted sources about the safety of prescribing drugs for older people and are widely used in geriatric medicine and in the development of care quality indicators (AGS, 2015; LAROCHE, CHARMES, MERLE, 2007; HANLON et al., 1992; GALLAGHER et al., 2008; HOLT, SCHMIEDL, THURMANN, 2010; KIM, HEO, LEE, 2010; NAUGLER et al., 2000; SHRANK, POLINSKL, AVORN, 2007; BEERS, 1997).

The Beers Criteria were initially developed in 1991 in the United States. The first list included 19 inappropriate drugs and 11 drugs whose dose, frequency of use and duration of treatment were inappropriate for older people (BEERS et al., 1991). Its first update was published in 1997 and included non-institutionalized older adults in order to make it more applicable. The list included 28 inappropriate drugs and 35 drugs which were inappropriate for 15 specific pathological conditions (BEERS, 1997). In 2002, the list was updated again to assess potential adverse effects and to include new drugs. The new list included 48 inappropriate drugs and drugs which were not appropriate for 20 specific pathological conditions (FICK et al., 2003). The criteria were last updated in 2015 with the participation of 13 experts who identified more than 40 potentially inappropriate drugs or classes of drugs, which were organized into five lists. The new criteria included a specific list of drug interactions and another of drugs that should be avoided or have their dosages adjusted for patients with impaired renal function (AGS, 2015). It should be noted that some OTC drugs are included in the Beers Criteria; therefore, it is important to take them into account when reviewing older people's pharmacotherapy and to inform these patients about the potential problems related to their use.

According to the Beers Criteria, a Potentially Inappropriate Medication (PIM) for the older population is that whose use should be avoided in older adults in general and in those with certain diseases or syndromes, prescribed at reduced dosage or with caution or carefully monitored. Additionally, there is no sufficient supporting evidence on the benefits of such drugs and they increase the risk of adverse reactions. Moreover, there are safer alternative treatments (AGS, 2015).

Aging, which has been accompanied by an increase in the prevalence of chronic noncommunicable diseases, requires a pharmaceutical practice focused on the evaluation of the multidisciplinary team and at the provision of information to them and the patient regarding pharmacotherapy. Early identification of drug-related problems and the implementation of

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pharmaceutical interventions may contribute to better clinical outcomes and to the patients' quality of life (PERETTA, CICCIA, 2000).

Given the changes in pharmacokinetics and pharmacodynamics in older adults, Beers considers some categories of drugs to be inappropriate for use in this population either because of lack of therapeutic efficacy or because the increased risk of adverse effects do not outweigh benefits when compared to other categories of drugs (AGS, 2015). There is an inexpressive number of studies based on the 2015 Beers Criteria that have assessed older adults in PHC, which demonstrates the novelty, relevance, and scientific contribution of this proposal.

In this sense, the present study aimed to assess polypharmacy and Potentially Inappropriate Medications (PIM) in older adults in Primary Health Care in the city of Campo Grande, Mato Grosso do Sul, Brazil, according to the 2015 Beers Criteria; in addition, we sought to identify the presence of drug-drug interactions capable of causing significant harm to older adults, especially those requiring dose adjustment based on renal function.

2 MATERIAL AND METHODS

2.1 STUDY DESIGN AND SETTING

This is a quantitative, transversal, descriptive study carried out at Family Health Care Centers (*Unidades Básicas de Saúde da Família – UBSF*) and Primary Health Care Centers (*Unidades Básicas de Saúde – UBS*) located in the city of Campro Grande, Mato Grosso do Sul, Brazil. Five centers were analyzed: UBSF Portal Caiobá, UBSF Jardim Itamaracá, UBSF Estrela Dalva, UBSF Aero Itália, and UBS Cidade Morena.

2.2 INCLUSION CRITERIA

- Age equal to or over 60 years;
- Agreement to participate in the study by providing written informed consent;
- Patients with a medical prescription at the moment of data collection.

2.3 DATA COLLECTION PROCEDURES

The study included older adults who attended the pharmacies of the Health Care Centers where the study took place from December 2015 to August 2016.

Data were collected using an author-developed instrument. The following variables were assessed: gender, age, number of drugs prescribed, and presence of PIM in the prescription. The PIMs identified were classified according to the Beers Criteria into: a) potentially inappropriate

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medications for older adults, b) drug interactions capable of causing significant harm to older adults; c) medications that require dosage adjustment based on renal function; d) medications that are potentially inappropriate but can be used with caution by older adults; and e) medications that are potentially inappropriate for older adults because of drug-disease or drug-syndrome interaction that may exacerbate the disease or syndrome.

The quantification of the total number of medications and the analysis of the inadequacy of the use took into account the number of times the medication was prescribed, i.e., repeated use of a certain medication was counted in order to identify older adults' exposure to PIMs.

2.4 ANALYSIS OF RESULTS

Data were treated and interpreted using descriptive statistical analysis performed in Microsoft Excel® version 2010.

2.5 ETHICAL ISSUES

The present study was approved by the Ethics Committee of the Federal University of Mato Grosso do Sul (*Universidade Federal do Mato Grosso do Sul – UFMS*) under approval No. 1.311.257 (Annex A). All the participants were informed about the research and freely agreed to participate in the study.

3 RESULTS

Participants were 150 older people who had their medical prescriptions analyzed. Ninety-four belonged to the female gender (62,6%) and the mean age was 70.6 ($\pm$ 7,23). In relation to the age group we have the following proportion: 60 to 69 years (49,3%), 70 to 79 years (39,3%), 80 to 89 years (10,7%) and> 90 years (0,7 %).

In all, 48 health problems were identified in the population analyzed. The most frequent health problems were: systemic arterial hypertension (n= 140; 93.4%), type II diabetes mellitus (n= 82; 54.7%), dyslipidemias (n= 39; 26%), hypothyroidism (n= 22; 14.7%), and gastritis (n= 20; 13.4%).

Regarding aspects related to pharmacotherapy, 98 drugs were prescribed 858 times for the participants. Table 2 presents detailed information related to pharmacotherapy.

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Table 2 - Medications prescribed for older adults in Primary Health Care. Campo Grande, Mato Grosso do Sul, 2016.

	n	(%)
Most commonly prescribed drugs		
Losartan	88	10.3
Hydrochlorothiazide	83	9.8
Acetylsalicylic acid	79	9.3
Metformin	68	7.9
Insulin	39	4.5
Glibenclamide	38	4.4
Anlodipine	37	4.3
Potassium chloride	33	3.8
Simvastatin	33	3.8
Omeprazole	27	3.2
Number of drugs prescribed per older person		
1-4	54	36
5-10	88	58.7
>10	8	5.3
Total	**150**	**100**

Table 3 presents the assessment of PIM prescribing according to the Beers Criteria (2015).

Table 3 - Potentially Inappropriate Medications prescribed for older adults in Primary Health Care. Campo Grande, Mato Grosso do Sul, 2016.

Variables	n	(%)
Active Principle		
Appropriate	74	75.5
Inappropriate	24	24.5
Total Number of Medications Prescribed		
Appropriate	690	80.4
Inappropriate	168	19.6
Potentially Inappropriate Medications		
Insulin	39	23.2
Glibenclamide	38	22.6
Proton Pump Inhibitor	29	17.3
Methyldopa	13	7.7
Tricyclic antidepressants	12	7.1
Nonselective NSAIDs	9	5.4
First generation antihistamines	8	4.8
Benzodiazepines	5	2.9

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Antipsychotics	3	1.8
Amiodarone	3	1.8
Digoxin (>0.125mg)	3	1.8
Alpha blockers	3	1.8
Muscle relaxants	2	1.2
Phenobarbital	1	0.6
Total	**168**	**100**

Notes: Each older adult could have been prescribed more than one inappropriate drug class; NSAIDs: Nonsteroidal anti-inflammatory drugs; Proton pump inhibitor: omeprazole, pantoprazole; Tricyclic antidepressants: amitriptyline, clomipramine, imipramine; oral nonselective NSAIDs: diclofenac, ibuprofen, meloxicam; First generation antihistamines: dexchlorpheniramine, promethazine; Benzodiazepines: clonazepam, diazepam; Antipsychotics: haloperidol, risperidone, quetiapine; Alpha blockers: doxazosin; Muscle relaxants: carisoprodol, cyclobenzaprine, orphenadrine.

Of the 150 older adults analyzed, 36 (24%) were not submitted to polypharmacy and did not use PIMs. Eighteen older adults (12%) were not submitted to polypharmacy, but used at least one PIM. Fifteen older adults (10%) were submitted to polypharmacy, but did not use PIMs. In addition, 81 older adults (54%) were submitted to polypharmacy and used at least one PIM. Considering only the patients who used at least one PIM (n= 100; 66.7%), 81% were polymedicated. There was a higher frequency of PIMs in female older adults (n= 64; 68.1%).

Table 4 shows the drug-drug interactions identified in the prescriptions assessed. In all, 34 older adults (22.7%) presented interactions that should be avoided in their prescriptions.

Table 4 - Drug-drug interactions between medications prescribed for older adults in Primary Health Care. Campo Grande, Mato Gross do Sul, 2016.

Drug-drug Interactions	**n**	**(%)**
Antidepressants (tricyclic and SSRIs) x 2 or more drugs acting on the CNS	3	20
Corticosteroids x NSAIDs	1	6.7
Warfarin x NSAIDs	1	6.7
Anticholinergics x Anticholinergics	1	6.7
Antipsychotics x 2 or more drugs acting on the CNS	2	13.3
Benzodiazepines x 2 or more drugs acting on the CNS	7	46.6
Total	**15**	**100**

Note: Each older adult could present more than one drug-drug interaction. SSRIs: Selective serotonin re-uptake inhibitors; NSAIDs: Nonsteroidal anti-inflammatory drugs; CNS: Central Nervous System; Antidepressants: amitriptyline, clomipramine, imipramine, fluoxetine. Corticosteroids: prednisone, dexamethasone; NSAIDs: diclofenac, ibuprofen, meloxicam; Anticholinergics: dexchlorpheniramine, amitriptyline, orphenadrine, cyclobenzaprine, clomipramine,

imipramine, promethazine; Antipsychotics: haloperidol, risperidone, quetiapine, levomepromazine; Benzodiazepines: clonazepam, diazepam.

Table 5 presents the interactions identified based on the Beers Criteria (2015) for drug-disease or drug-syndrome interactions that may exacerbate the disease or syndrome in older adults.

Table 5 - Drug-disease or drug-syndrome interactions among medications prescribed for older adults in Primary Health Care. Campo Grande, Mato Grosso do Sul, 2016.

Drug Class / Drug x Disease / Syndrome	N	(%)
NSAIDs x CKD with CrCl <30mL/min/ heart failure/ gastric or duodenal ulcer	9	11.8
Drugs with strong anticholinergic properties x delirium / dementia or cognitive impairment / history of falls and fractures / benign prostatic hyperplasia	22	28.9
Corticosteroids x delirium	4	5.3
SSRIs x falls or fractures	2	2.6
Antipsychotics x syncope/ delirium/ dementia cognitive impairment/ history of falls and fractures / Parkinson's disease	4	5.3
H2-receptor antagonists x delirium/ dementia or cognitive impairment	6	7.9
Anticonvulsants x history of falls and fractures	12	15.8
Opioids x history of falls and fractures	2	2.6
Benzodiazepines x delirium/ dementia or cognitive impairment / history of falls and fractures	5	6.6
Antihistamines alone or in combination x delirium / dementia / fall or fracture / benign prostatic hyperplasia	5	6.6
Alpha blockers x Syncope	3	3.9
Tricyclic antidepressants x Syncope / history of falls or fractures / delirium / dementia / benign prostatic hyperplasia	12	15.8
Cilostazol x heart failure	4	5.3

CCB x heart failure	2	2.6

Nota: Each older adult could present more than one drug-disease or drug-syndrome interaction; NSAIDs: Nonsteroidal anti-inflammatory drugs; CKD: Chronic kidney disease; CrCl: creatinine clearance; SSRIs: Selective serotonin re-uptake inhibitors; CCB: Calcium channel blockers; NSAIDs: diclofenac, ibuprofen, meloxicam; Anticholinergics: dexchlorpheniramine, amitriptyline, orphenadrine, cyclobenzaprine, clomipramine, imipramine, promethazine; Corticosteroids: prednisone, dexamethasone; SSRIs: fluoxetine; Antipsychotics: haloperidol, risperidone, quetiapine, levomepromazine; H2-receptor antagonists: dexchlorpheniramine; Anticonvulsants: carbamazepine, clonazepam, diazepam, phenobarbital, gabapentin, pregabalin; Opioids: codeine; Benzodiazepines: clonazepam, diazepam; Alpha blockers: doxazosin; Tricyclic antidepressants: amitriptyline, clomipramine, imipramine; CCB: verapamil.

A total of 126 older adults (84.6%) were prescribed at least one PIM classified as medication that should be used with caution by older adults (Table 6).

Table 6 - Medications that should be used with caution prescribed for older adults in Primary Health Care. Campo Grande, Mato Grosso do Sul, 2016.

Drug Class/Drug	n	(%)
Diuretics	102	48.6
ASA	79	37.6
Tricyclic Antidepressants	12	5.7
Carbamazepine	7	3.3
Antipsychotics	4	1.9
Isosorbide Dinitrate	4	1.9
Fluoxetine	2	1.0
Total	**210**	**100**

Notes: Each older adult could have been prescribed more than one medication that should be used with caution. Diuretics: hydrochlorothiazide, furosemide, spironolactone; Tricyclic Antidepressants: amitriptyline, clomipramine, imipramine; Antipsychotics: haloperidol, risperidone, quetiapine, levomepromazine.

Fifteen older adults (10.0%) used at least one drug that should be avoided or adjusted based on renal function as recommended by the 2015 Beers Criteria. These drugs included spironolactone (n= 6; 37.5%), ranitidine (n= 6; 37.5%), pregabalin (n= 3; 18.75%), and gabapentin (n= 1; 6.25%).

All (n= 10; 100%) the PIMs identified present a strength of recommendation classified as strong, which means that the adverse events, burden, and risks outweigh the benefits of using such PIMs. Additionally, quality of evidence is high for 33.3% (n=8), moderate for 62.5% (n=15), and low for 4.2% (n=1).

4 DISCUSSION

Polypharmacy and PIM prescribing in older adults are public health problems and have been associated with adverse events such as falls, hospitalization, and death. In the present study, the mean PIM prescribing rate in the population was 66.7%, and approximately three out of five prescriptions for older adults in PHC were inappropriate.

Research has reported a mean PIM prescribing rate of 20.5% in older adults in primary care, and approximately one in five prescriptions for older adults in primary care is inappropriate (OPONDO et al., 2012). In this sense, assessing prescriptions and implementing pharmaceutical interventions can reduce inappropriate prescribing and the mean number of inappropriate drugs in the same prescription (CLYNE et al., 2015).

The study by Lopes et al. (2016) has associated the use of PIMs with polypharmacy and polymorbidity; in addition, it could be inferred from its results that the clinical consequences of the use of PIMs should be highlighted due to the greater risk of adverse events and the negative impact on the functionality of older adults.

In the present study, more than half of older adults in Primary Health Care used at least 1 PIM. In a study using the 2015 Beers Criteria, the PIM prescribing rate was 43% in older patients receiving hemodialysis (PARKER et al., 2016). However, in terms of comparison, no other study carried out with older adults in Primary Health Care using the Beers Criteria (2015) has been identified. The Brazilian model of access to public health care may justify such a particular concern with polypharmacy and PIM prescribing in older adults.

The World Health Organization reports that the average number of drugs used by older adults should be between 1.3 and 2.2 (WHO, 1993). However, the mean number of drugs found in the present study was 5.77. This result demonstrates the high rate of polypharmacy among the patients analyzed – 96 older adults (64%) were submitted to polypharmacy, i.e., the use of five or more drugs (FERNER, ARONSON, 2006).

A study carried out with older patients with cancer showed that 84% of the participants used five or more medications; of these, 43% used more than 10 medications (NIGHTINGALE et al., 2015). Other studies have found a prevalence of polypharmacy in older adults ranging from 39.3% to 91% (WAUTERS et al., 2016; MARTINS, et al., 2015; DALLEUR, et al., 2015; MUNCK, ARAÚJO, 2012; NASSUR, et al., 2010).

Nassur et al. (2010) reported that polypharmacy is directly related to the use of potentially inappropriate medications. In the present study, 54% of the patients used PIMs and were polymedicated. Considering only those who had been prescribed PIMs, 81 (81%) were polymedicated. Likewise, the rate of PIM use in a University Hospital of Juiz de Fora, Minas Gerais,

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was 95.9% (MUNCK, ARAUJO, 2012). Another study showed that PIM prescribing was associated with the number of medications prescribed (≥5 medications) and with the presence of cardiovascular or gastrointestinal diseases (WENG et al., 2013).

According to the literature, the clinical consequences of polypharmacy in older adults are related to increased risk of adverse events, increased hospital admission, increased potential drug interactions, increased PIM prescribing, increased odds of cascade iatrogenesis, problems adhering to treatment, and increased risk of falls (LU et al., 2015; WENG et al., 2013).

In this sense, considering the Beers Criteria for drugs that should be avoided or have their dosages adjusted based on renal function, spironolactone should be avoided when creatinine clearance is lower than 30 mL/min because it can lead to hyperkalemia in older adults. Reduction of gabapentin and pregabalin doses may be required when creatinine clearance is lower than 60 mL/min because they can exacerbate CNS-related adverse events. Finally, ranitidine dose should be reduced when creatinine clearance is lower than 50 mL/min because its use is associated with changes in the mental state of older adults (AGS, 2015; HANLON et al., 2009).

Potentially Inappropriate Medications that should be used with caution by older adults include ASA, which is recommended for primary prevention of cardiovascular events (not exceeding 325mg/day). However, there is no evidence of the benefits in relation to the risks regarding the use of ASA for primary prevention in individuals aged over 80 years (AGS, 2015). Despite that, 41.2% of the individuals over 80 years of age analyzed in the present study used ASA. A study using the 2012 Beers Criteria found rates of ASA use in older adults ranging from 30 to 80% in 3 long-term care institutions (GANASSIN, MATOS, TOFFOLI-KADRI, 2014).

ASA is indicated for secondary risk reduction in high-risk older patients with established cardiovascular disease. However, despite the benefits, there is also scarcity of data on its use for secondary prevention in individuals over 80 years of age. The follow-up of adverse events related to the use of ASA, such as gastrointestinal irritability and bleeding risk, is recommended given the increased vulnerability of this group, especially in the context of polypharmacy, to multiple comorbidities and frailty (DAMLUJI et al., 2015; LABUZ-ROSZAK et al., 2012). Considering the vasodilator drugs, the need for caution is related to the possibility of exacerbation of episodes of syncope in individuals with a previous history of such health problem. With regard to other drugs that should be used cautiously and that were prescribed in the present study (antipsychotics, selective serotonin re-uptake inhibitors, diuretics, tricyclic antidepressants and carbamazepine), the risks involved in their use are related to the possibility of exacerbation or development of the syndrome of inappropriate antidiuretic hormone secretion and hyponatremia. Patients who are prescribed such

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drugs should have their sodium levels monitored during treatment or when the dose changes (AGS, 2015).

Drug-drug interactions that should be avoided were identified in 34 older adults (22.7%) – the most common interaction was the use of benzodiazepines with 2 or more CNS drugs. The use of antidepressants, antipsychotics, or benzodiazepines with two or more CNS drugs should be avoided because of the increased risk of falls in older adults.

The interaction between two anticholinergic drugs is associated with a high risk of cognitive decline; therefore, the combination of drugs with these pharmacological properties should be avoided (AGS, 2015; FOX et al., 2014). In turn, the combination of corticosteroids and NSAIDs is associated with an increased risk of peptic ulcer and/or gastrointestinal bleeding and should be avoided when possible or used in the presence of a gastroprotective drug.

Finally, the combination of warfarin and NSAIDs raises the risk of bleeding by inhibiting platelet adhesion and aggregation and by promoting changes in the pharmacokinetics of warfarin, resulting in an increase in the international normalized ratio (INR) or in the prothrombin time; therefore, such combination should be avoided or monitored, if necessary, for the possibility of bleeding events (AGS, 2015; MICROMEDEX, 2016).

All PIM prescribing situations identified in the present study presented a strength of recommendation classified as strong. The strength of recommendation reported in the Beers Criteria is graded based on benefit-risk evidence. Situations in which the benefits clearly outweigh the harms, adverse events, and risks are classified as strong, and those in which benefits may not outweigh harms, adverse events, and risks are classified as weak.

Situations classified as insufficient refer to the fact that evidence is inadequate to determine net harms, adverse events, and risks. The quality of evidence relates to the type of study conducted and is classified as high, moderate and low. In this sense, 33.3% of the quality of evidence related to PIM prescribing in older adults in the present study was high, i.e., evidence includes well-designed and well-conducted studies that directly assess effects on the individual's health (AGS, 2015).

Brazil's Primary Health Care Model prioritizes actions targeted at Health Promotion, Prevention and Treatment of diseases, and Rehabilitation. However, given the pharmacotherapy prescribed for older adults in primary care, it was possible to verify that the care model is still centered on a little careful medical prescription, which can increase the demand for medium and high complexity health services due to harms resulting from Potentially Inappropriate Medications.

The training (structuring) and performance of a multidisciplinary team is of utmost importance for the formulation of action strategies targeted at early intervention to avoid health problems inherent to the aging process and to address the concept of the several lines of care.

COMPETING INTERESTS

REFERENCES

Alldred, D. P., Kennedy, M. C., Hughes, C., Chen, T. F., Miller, P. Interventions to optimize prescribing for older people in care homes. *Cochrane Database Syst Rev*, 2016.

American Geriatrics Society (Ags). American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *J Am Geriatr Soc*, 2015.

Beers, M. H., Ouslander, J. G., Rollingher, I., Reuben, D. B., Brooks, J., Beck, J. C. Explicit criteria for determining inappropriate medication use in nursing home residents. UCLA Division of Geriatric Medicine. *Arch Intern Med*, 1991; 151: 1825-1832.

Beers, M. H. Explicit criteria for determining potentially inappropriate medication use by the elderly. An update. *Arch Intern Med*, 1997; 157: 1531-1536.

Brasil. Instituto Brasileiro de Geografia e Estatística. Censo 2010. Available from: <www.ibge.gov.br>. Cited 2016 Dec 8.

Bowie, M. W., Slattum, P. W. Pharmacodynamics in older adults: a review. *Am J Geriatr Pharmacother*, 2007; 5: 263-303.

Cho, S., Lau, S. W., Tandon, V., Kumi, K., Pfuma, E., Abernethy, D. R. Geriatric drug evaluation: where are we now and where should we be in the future? *Arch Intern Med*, 2011; 171: 937-940.

Clyne, B., Smith, S. M., Hughes, C. M., Boland, F., Bradley, M. C., Cooper, et al., Effectiveness of a Multifaceted Intervention for Potentially Inappropriate Prescribing in Older Patients in Primary Care: A Cluster-Randomized Controlled Trial (OPTI-SCRIPT Study). *Ann Fam Med* , 2015; 13: 545-553.

Corsonello, A.; Pedone, C.; Incalzi, R.A. Age-related pharmacokinetic and pharmacodynamic changes and related risk of adverse drug reactions. *Curr Med Chem*, 2010; 17: 571-584.

Dalleur, O., Boland, B., De Groot, A., Vaes, B., Boeckxstaens, P., Azermai, M., et al., Detection of potentially inappropriate prescribing in the very old: cross-sectional analysis of the data from the BELFRAIL observational cohort study. *BMC Geriatr,* 2015; 15: 1-9.

Brazilian Journal of Development

Damluji, A. A., Ramireddy, A., Otalvaro, L., Forman, D. E. J Secondary cardiovascular prevention in older adults: an evidence based review. *J Geriatr Cardiol*, 2015; 12: 459-464.

Ferner, R. E., Aronson, J. K. Communicating information about drug safety**.** *BMJ,* 2006*;* 333:143-145.

Feng, X. R., Liu, M. L., Liu, F., Fan, Y., Tian, Q. P. Dose-response of aspirin on platelet function in very elderly patients. *Beijing Da Xue Xue Bao*, 2016; 48: 835-840.

Fick, D. M., Cooper, J. W., Wade, W. E., Waller, J. L., Et Al., Updating the Beers Criteria for potentially inappropriate medication use in older adults: results of a US consensus panel of experts. *Arch Intern Med*, 2003; 163: 2716-2724.

Gabardi, S., Tullius, S. G., Krenzien, F. Understanding alterations in drug handling with aging: a focus on the pharmacokinetics of maintenance immunosuppressants in the elderly. *Curr Opin Organ Transplant*, 2015; 20: 424-430.

Ganassin, A. R., Matos, V. T. G., Toffoli-Kadri, M. C. Potentially inappropriate medication use in institutionalized older adults according to the Beers Criteria. *Rer Bras Ciênc Farm*, 2014; 50: 827-837.

Klotz, U.; Mörike, K.; Shi, S. The clinical implications of aging for rational drug therapy. *Eur J Clin Pharmacol,* 2008; 64: 183–199.

Lojudice, D. C., Laprega, M. R., Rodrigues, R. A. P., Junior, A. L. R. Quedas de idosos institucionalizados: ocorrência e fatores associados. *Rev Bras Geriatr Gerontol,* 2010; 13: 403-412.

Lopes, L. M., Figueiredo, T. P., Costa, S. C., Reis, A. M. M. Utilização de medicamentos potencialmente inapropriados por idosos em domicílio. *Ciênc Saúde Coletiva*, 2016; 21: 3429-3438.

Lu, W. H., Wen, Y. W., Chen, L. K., Hsiao, F. Y. Effect of polypharmacy, potentially inappropriate medications and anticholinergic burden on clinical outcomes: a retrospective cohort study. *CMAJ*, 2015; 187: 130-137.

Marin, M. J. S., Cecílio, L. C. O., Perez, A. E. W. U. F., Santella, F., Silva, C. B. A., Gonçalves Filho, J. R., Roceti, L. C. Caracterização do uso de medicamentos entre idosos de uma unidade do Programa Saúde da Família. *Cad Saúde Pública*, 2008; 24: 1545-1555.

Martins, G. A., Acurcio, F. A., Franceschini, S. C. C., Priore, S. E., Ribeiro, A. Q. Uso de medicamentos potencialmente inadequados entre idosos do Município de Viçosa, Minas Gerais, Brasil: um inquérito de base populacional. *Cad Saúde Pública*, 2015; 31: 2401-2412.

Brazilian Journal of Development

Micromedex®, Truven Health Analytics. [Internet database]. Greenwood Village, Colo: Inc. Updated periodically. c1974-2016. Available: http://www. http://truvenhealth.com.

Munck, A. K. R., Araújo, A. L. A. Avaliação dos medicamentos inapropriados prescritos para pacientes idosos em um Hospital Universitário. *HU Rev*, 2012; 38.

Nassur, B. A., Braun, V., Devens, L. T., Morelato, R. L. Avaliação dos medicamentos inapropriados utilizados por idosos admitidos em hospital geral filantrópico. *Rev Bras Clín Méd*, 2010; 8: 208-211.

Nightingale, G., Hajjar, E., Swartz, K., Andrel-Sendecki, J., Chapman, A. Evaluation of a pharmacist-led medication assessment used to identify prevalence of and associations with polypharmacy and potentially inappropriate medication use among ambulatory senior adults with cancer. *J Clin Oncol*, 2015; 33: 1453-1459.

Nobrega, O. T.; Karnikowski, M. G. O. A terapia medicamentosa no idoso: cuidados na medicação. *Ciênc Saúde Coletiva*, 2005; 10: 309-313.

Obreli-Neto, P. R., Nobili, A., De Lyra, D. P. J., Pilger, D., Guidoni, C. M., De Oliveira, A. B., et al., Incidence and predictors of adverse drug reactions caused by drug-drug interactions in elderly outpatients: a prospective cohort study. *JPPS*, 2012; 15: 332-343.

Opondo, D., Eslami, S., Visscher, S., Rooij, S. E., Verheij, R., Korevaar, J. C., et al., A. Inappropriateness of Medication Prescriptions to Elderly Patients in the Primary Care Setting: A Systematic Review. *PloS one electronic resource*, 2012; 8: 43617.

Oms. Organización Mundial De La Salud. International drug monitoring: the role of national centers. Genebra: OMS, 1972.

Parker, K., Aasebo, W., Stavem, K. Potentially Inappropriate Medications in Elderly Haemodialysis Patients Using the STOPP Criteria. *Drugs - Real World Outcomes*, 2016; 3: 359-63.

Peretta, M.; Ciccia, G. Reengenharia farmacêutica - guia para implantar atenção farmacêutica. Brasília: *Ethosfarma*, 2000; 45-64.

Rochon, P. A. Drug prescribing for older adults. *UpToDate*, 2016. Available from: < http://www.uptodate.com/contents/drug-prescribing-for-older-adults>. Cited 2016 Nov 24.

Secoli, S. R. Polifarmácia: interações e reações adversas no uso de medicamentos por idosos. *Rev Bras Enf,* 2010; 63: 136-140.

Shi, S.; Morike, K.; Klotz, U. The clinical implications of ageing for rational drug therapy. *Eur J Clin Pharmacol*, 2008; 64: 183-199.
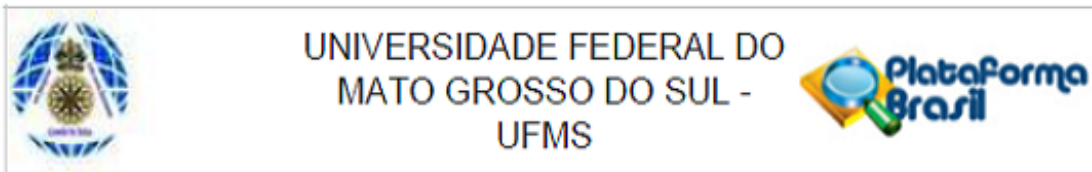
Brazilian Journal of Development

Tan, J. L., Eastment, J. G., Poudel, A., Hubbard, R. E. Age-Related Changes in Hepatic Function: An Update on Implications for Drug Therapy. *Drugs & Aging*, 2015; 32: 999-1008.

Wauters, M., Elseviers, M., Vaes, B., Degryse, J., Dalleur, O., Vander, R., et al., Too many, too few, or too unsafe? Impact of inappropriate prescribing on mortality, and hospitalization in a cohort of community-dwelling oldest old. *British J Clin Pharmacol*, 2016; 82: 1382–1392.

Weng, M. C., Tsai, C. F., Sheu, K. L., Lee, Y. T., Lee, H. C., Tzeng, S. L., et al ., The impact of number of drugs prescribed on the risk of potentially inappropriate medication among outpatient older adults with chronic diseases. *J* Assoc Physicians, 2013; 106: 106-109.

WHO. Envelhecimento ativo: uma política de saúde. Brasília: *Org Pan-Americana de Saúde*, 2005.

WHO. How to Investigate Drug Use in Health Facilities: Selected Drug Use Indicators. *World Health Organization*, 1993; 92.

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ANNEX A- UFMS RESEARCH ETHICS COMMITTEE APPROVAL LETTER

	UNIVERSIDADE FEDERAL DO MATO GROSSO DO SUL - UFMS	Plataforma Brasil

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: Cuidado farmacêutico na atenção básica para pacientes com doenças crônicas não transmissíveis

Pesquisador: Camila Guimarães Polisel

Área Temática:

Versão: 1

CAAE: 50091615.0.0000.0021

Instituição Proponente: Universidade Federal de Mato Grosso do Sul - UFMS

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 1.311.257

Apresentação do Projeto:

Trata-se de um estudo analítico e com abordagem quantitativa, desenhado com o propósito de avaliar parâmetros relacionados ao cuidado farmacêutico em pacientes com doenças crônicas não transmissíveis (DCNT).

Objetivo da Pesquisa:

Avaliar parâmetros relacionados ao cuidado farmacêutico em pacientes cadastrados no Plano de Ações Estratégicas para o Enfrentamento das Doenças Crônicas Não Transmissíveis de Unidades Básicas de Saúde de Campo Grande/MS: 1) Coletar dados do perfil do paciente, de sua história clínica, social e relacionada aos medicamentos que utiliza;2) Aferir a circunferência abdominal e a pressão arterial dos participantes; 3) Avaliar a adesão do participante ao tratamento.

Avaliação dos Riscos e Benefícios:

Os riscos são relativamente pequenos (responder a um questionário com questões objetivas) e os benefícios são muito satisfatórios.

Comentários e Considerações sobre a Pesquisa:

A pesquisa será realizada em Unidades Básicas de Saúde (UBS) localizadas no município de Campo Grande/MS e que possuam grupos de acompanhamento de pacientes com DCNT. As UBS envolvidas no estudo serão indicadas pela Secretaria Municipal de Saúde (SESAU), de acordo com o

Endereço: Pró Reitoria de Pesquisa e Pós Graduação/UFMS	
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Telefone: (67)3345-7187 Fax: (67)3345-7187	E-mail: bioetica@propp.ufms.br

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Continuação do Parecer: 1.311.257

interesse e demandas do serviço, a cada ano. O projeto será desenvolvido durante os anos de 2015-2017.

Considerações sobre os Termos de apresentação obrigatória:

Apresenta "Declaração de interesse em projeto de pesquisa" assinada pela Coordenadoria de Assistência
Farmacêutia (CAF-SESAU).Apresenta os instrumentos de coleta de dados.

Recomendações:

Não há

Conclusões ou Pendências e Lista de Inadequações:

Não há.

Considerações Finais a critério do CEP:

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_604369.pdf	11/10/2015 15:52:09		Aceito
Declaração de Instituição e Infraestrutura	SESAU.pdf	11/10/2015 15:51:10	Camila Guimarães Polisel	Aceito
Projeto Detalhado / Brochura Investigador	Projeto_Detalhado.docx	11/10/2015 15:48:34	Camila Guimarães Polisel	Aceito
Folha de Rosto	folha.pdf	09/10/2015 15:54:39	Camila Guimarães Polisel	Aceito
Outros	Adesao.docx	08/10/2015 11:55:24	Camila Guimarães Polisel	Aceito
Outros	ficha.docx	08/10/2015 11:54:46	Camila Guimarães Polisel	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TCLE.doc	07/10/2015 15:06:32	Camila Guimarães Polisel	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não