

Polypharmacy and potentially inappropriate medications for elder people in gerontological nursing

Polifarmácia e medicamentos potencialmente inapropriados para idosos na enfermagem gerontológica
Polifarmacia y medicamentos potencialmente inapropiados para ancianos en la enfermería gerontológica

Gabrielle Ferreira Melo Marques¹, Danielle Mayara Rodrigues Palhão de Rezende¹, Iara Pereira da Silva¹, Priscila Carolina de Souza¹, Suzi Rosa Miziara Barbosa¹, Ramon Moraes Penha¹, Camila Guimarães Polisel¹

¹ Universidade Federal de Mato Grosso do Sul. Campo Grande, Mato Grosso do Sul, Brazil.

How to cite this article:

Marques GFM, Rezende DMRP, Silva IP, Souza PC, Barborsia SRM, Penha RM, et al. Polypharmacy and potentially inappropriate medications for elder people in gerontological nursing. Rev Bras Enferm [Internet]. 2018;71(5):2440-6. DOI: <http://dx.doi.org/10.1590/0034-7167-2017-0211>

Submission: 03-15-2017

Approval: 01-27-2018

ABSTRACT

Objective: To identify polypharmacy and potentially inappropriate medications (PIM) for elder people with chronic health situations and its implications for gerontological nursing. **Method:** Descriptive and transversal study, conducted from March to September 2016 by pharmaceutical residents in the clinic of Endocrinology of a hospital in Mid-West region of Brazil. **Results:** 44 elder people with an average age of 69.5 (\pm 6.79) years old had their assessed prescriptions. We identified 65 medications prescribed 253 times, in which 10 PIM (15.4%) were prescribed 51 times. 33 seniors (72.7%) had at least one PIM, of those, 66.7% were polymedicated. Of the total, 22 elder people (50%) were subjected to polypharmacy and made use of at least one PIM. **Conclusion:** The results showed high incidence of PIM and polypharmacy, as well as their physiological impacts to the elder population. The study provokes discussions about that the trained nurse in human aging has skills and competencies able to enhance interventions related to pharmacotherapy.

Descriptors: Elder People; Use of Medications; Polymedication; List of Potentially Inappropriate Medications; Geriatric Nursing.

RESUMO

Objetivo: Identificar polifarmácia e medicamentos potencialmente inapropriados (MPI) para idosos com situações crônicas de saúde e suas implicações para enfermagem gerontológica. **Método:** Estudo descritivo, transversal, realizado de março a setembro de 2016 por residentes farmacêuticos, no ambulatório de endocrinologia de um hospital no Centro-Oeste do Brasil. **Resultados:** Quarenta e quatro idosos com idade média de 69,5 (\pm 6,79) anos tiveram suas prescrições avaliadas. Identificaram-se 65 medicamentos prescritos 253 vezes, sendo que 10 MPI (15,4%) foram prescritos 51 vezes. Trinta e três idosos (72,7%) apresentaram pelo menos um MPI, desses, 66,7% eram polimedicados. Do total, 22 idosos (50%) estavam submetidos à polifarmácia e faziam uso de pelo menos um MPI. **Conclusão:** Os resultados evidenciaram alta incidência de MPI e polifarmácia, bem como seus impactos fisiológicos à população idosa. O estudo provoca discussões acerca de que enfermeiro capacitado sobre o envelhecimento humano possui habilidades e competências capazes de potencializar intervenções relacionadas à farmacoterapia.

Descritores: Idoso; Uso de Medicamentos; Polimedição; Lista de Medicamentos Potencialmente Inapropriados; Enfermagem Geriátrica.

RESUMEN

Objetivo: Identificar polifarmacia y medicamentos potencialmente inapropiados (MPI) para ancianos con situaciones crónicas de salud y sus implicaciones para enfermería gerontológica. **Método:** Estudio descriptivo, transversal, realizado de marzo a septiembre de 2016 por residentes farmacéuticos, en el ambulatorio de endocrinología de un hospital en el Centro-Oeste de Brasil. **Resultados:** Cuarenta y cuatro ancianos con edad media de 69,5 (\pm 6,79) años tuvieron sus prescripciones evaluadas. Se identificaron 65 medicamentos prescritos 253 veces, siendo que 10 MPI (15,4%) fueron prescritos 51 veces. Treinta y tres ancianos (72,7%) presentaron al menos un MPI, de los que el 66,7% eran polimedicados. Del total, 22 ancianos (50%) estaban sometidos

a la polifarmacia y utilizaban al menos un MPI. **Conclusión:** Los resultados evidenciaron alta incidencia de MPI y polifarmacia, así como sus impactos fisiológicos a la población anciana. El estudio provoca discusiones acerca de que el enfermero capacitado sobre el envejecimiento humano tiene habilidades y competencias que potencializan intervenciones relacionadas a la farmacoterapia. **Descriptores:** Anciano; Utilización de Medicamentos; Polifarmacia; Lista de Medicamentos Potencialmente Inapropiados; Enfermería Geriátrica.

CORRESPONDING AUTHOR Gabrielle Ferreira Melo Marques E-mail: ghabi_ms@hotmail.com

INTRODUCTION

Decision-making on pharmacotherapy in elder people is complex and includes several aspects, such as deciding which medicine is more indicated, determining the appropriate dosage according to the physiological condition of the patient, monitoring the effectiveness and toxicity and educating them about the adverse reactions and when to seek medical care⁽¹⁾. In addition, the pharmacological response in the elder people is different to that of young adults, which requires different prescriptions in both groups⁽²⁾, considering that the pre-commercialization clinical trials of medications generally exclude elder people, and this leads to the approval of doses that may not be appropriate to this population, contributing to the challenges of prescription⁽³⁾. It is necessary to also balance between insufficient and excessive prescription, since many medicines are sometimes necessary for the management of the multiple comorbidities in the elderly^(1,4).

Polypharmacy is defined as the use of multiple medications by a patient. There is no consensus in the literature about the exact minimum number of medicines to define such practice, but it usually varies from 5 to 10⁽⁵⁾. Polypharmacy refers, generally, to prescription drugs; however, it is important to consider the use of non-prescription drugs, in addition to herbs and supplements⁽¹⁾.

A lot of attention has been directed to excessive prescription of potentially inappropriate medications (PIM) for elder people⁽¹⁾. Although there are different instruments for the evaluation of pharmacotherapy for the elder population, the Beers Criteria represent one of the most consulted sources about the safety of prescription drugs for the elderly and are widely used in geriatric clinic and development of indicators of quality of care. According to the Beers Criteria, the PIM for elder people is the one whose use should be avoided in the elder person in general and in people with certain diseases or syndromes, and must be prescribed in low doses, with caution or carefully monitored. In addition, such medicines do not have enough evidence of benefits, have increased risk of adverse reactions and/or there are safer therapeutic alternatives⁽⁶⁾.

By looking on issues related to polypharmacy and to the PIM for elder people, taking into account the process of the professional pharmacist within the clinic, it is possible to recognize that consultation and pharmaceutical guidelines are potentiated in the technical aspect, but limited in the continuity of appropriate use of prescription drugs. In this sense, there is compelling evidence that the gerontological nursing can corroborate on minimization of damage associated with PIM, especially by being the health care profession that has advanced the most on solidification of interventions aimed at human aging, whereas this is a dynamic and complex process that combines biological, psychological, spiritual/religious and

socioeconomic aspects as components of the current health status of individuals seeking health services⁽⁷⁾. So, if on one hand the pharmacist's work seems to be confined to the recognition of drug inconsistencies, gerontological nursing, on the other hand, has interventive resources effective in minimizing the direct and indirect complications associated with prescription drugs.

In this context, considering that there is an unimpressive number of studies outlined from the Beers Criteria 2015 that have evaluated elder people in clinical setting, the aim of this study is to identify the polypharmacy and the PIM for elder people with chronic health situations, and to stimulate discussion about the need of multidisciplinary practice specialized in the integral medical care to the elder person.

OBJECTIVE

To analyze the polypharmacy and potentially inappropriate medications prescribed for elder people in chronic health situations from the multidisciplinary perspective specializing in full medical service to the elder person.

METHOD

Ethical aspects

The study met the standards of the Ethics and Research Committee of the Federal University of Mato Grosso do Sul (CEP/UFMS) and was approved.

Design, study site and period

This was a descriptive study with transversal design, carried out in the period of March to September 2016, by pharmaceutical residents of a Multiprofessional Residence Program in Long-term Care. The location of the study was the clinic of Endocrinology of a non-profit hospital located in the Central-West region of Brazil that provides basic medical care in various specialties, through an agreement with the Unified Health System (SUS).

Population or sample; inclusion and exclusion criteria

The sample was composed by free demand, considering the demand for services provided by the clinic, making unnecessary the sample calculation, but meeting strict inclusion criteria: age equal to or more than 60 years old, diagnosis of at least one chronic not transmittable disease, to perform pharmacological treatment and have available medical prescription.

Study protocol

Data collection occurred through pharmaceutical consultations carried out twice a week, in the morning period and

in private environment. The pharmaceutical consultation is institutionalized as a routine of the pharmaceutical action in the site in which the study was conducted. Thus, to obtain the proposed variables for this study, researchers have used this feature, which is guided by the following steps: 1) Introduction; 2) Data Collection and Problem Identification; 3) Actions/Solutions and 4) Closing of the consultation. To do so, the data obtained were considered in step 2.

The strategy to select the participants involved screening of charts the day before the medical consultation. Subsequently, a list containing the name of the preselected participants was delivered to the ambulatory care team so that, at the end of medical care, they were forwarded to the pharmaceutical consultation. At the beginning of the service, they received information about the study and were invited to participate, with no loss in receiving the service in case they disagree. Individuals who have shown interest in participating in the study were included only after the signing of the informed consent.

The data were collected from the Guide of Pharmaceutical Consultation, initially created and validated by Abdel-Tawab and collaborators, as recommended by the Ministry of Health for deployment of Clinical Pharmaceutical Services⁽⁶⁾. Therefore, the guide has instruments for evaluation and survey problems, already validated and consecrated to the pharmacy area.

Through pharmaceutical consultations, the following variables were analyzed: gender, age, number of prescribed drugs and presence of PIM in prescribing. The PIM identified were categorized into: a) potentially inappropriate medications for elder people; b) potentially inappropriate medications but can be used with caution in elder people; and c) medications which require dose adjustment based on renal function. For the quantification of the total number of medicines and analysis of the inadequacy of the use, it was considered the number of times that the drug was prescribed, i.e. accounted for the repetitions of the same medicine to identify elderly exposure to PIM.

Analysis of the results and statistics

For the analysis of the results, the variables were tabulated and interpreted by descriptive statistics. To this end, the Microsoft Excel program, 2010 version, was used.

RESULTS

The total of 44 elderly people with an average age of 69.5 (\pm 6.79) years old were included in the study, and therefore had their drug prescriptions evaluated. Of the 44 seniors, 63.6% were female, and 54.6% were aged between 60 to 69 years old, as Table 1 shows.

Considering the aspects related to pharmacotherapy, 65 drugs were prescribed 253 times to the participants. Table 2 presents, in detail, the data related to pharmacotherapy.

From the evaluation of the Beers Criteria, 10 PIM (15.4%) were prescribed 51 times. 33 seniors (72.7%) had at least one PIM prescribed. The PIM most commonly prescribed were: insulin (n = 19; 37.3%), omeprazole (n = 11; 21.6%), glibenclamide (n = 9; 17.6%), amitriptyline (n = 5; 9.8%) and methyl dopa (n = 2; 3.9%). Table 3 presents, in detail, the PIM prescribed.

Table 1 – Profile of elder people with chronic health situations assisted in an ambulatory hospital setting, Brazil, 2017

Variables	n	(%)
Gender		
Female	28	63.6
Male	16	36.4
Average age (\pm SD)		
69.5 (6.79 \pm)		
Age group		
60 to 69	24	54.6
70 to 79	17	38.6
\geq 80	3	6.8

Note: * SD – Standard Deviation.

Table 2 – Profile of prescription drugs for the elder people with chronic health situations assisted in an ambulatory hospital setting, Brazil, 2017

Variables	n	(%)
Drugs most commonly prescribed		
Simvastatin	22	8.7
Metformin	21	8.3
Insulin	19	7.5
Losartan	17	6.7
Acetylsalicylic acid	16	6.3
B Complex	12	4.7
Omeprazole	11	4.3
Glibenclamide	9	3.5
Hydrochlorotiazida	9	3.5
Levothyroxine	8	3.2
Vildagliptin	8	3.2
Number of drugs prescribed for elder people		
1-4	19	43.2
5-10	21	47.7
> 10	4	9.1
Total	44	100

Of 44 elder people assessed, nine (20.45%) were not subjected to polypharmacy and did not make use of PIM. On the other hand, 11 elder people (25%) were not subjected to polypharmacy but used at least one PIM. Among the elder people polymedicated, two (4.55%) did not use PIM, while 22 (50%) used it. Considering the individuals that were in use of at least one PIM (n = 33, 72.7%), 66.7% were polymedicated.

When stratified by gender, it was observed that the frequency of prescription of PIM was higher in the elderly male (n = 12; 75%). In addition, 60% of the female elder people (n = 12) and 58.3% of the male elder people (n = 7) made use of 1 PIM; 21.4% (n = 6) of female gender and 41.7% (n = 5) of the male gender made use of 2 PIM; 5% (n = 1) of female gender made use of 3 PIM and 5% (n = 1) of female gender made use of 5 PIM.

The total of 29 elder people (65.9%) had at least one PIM prescribed that fits in the use with caution class in the elderly population. The most commonly prescribed drug class were diuretics (n = 17; 42.5%), as Table 4 shows.

Table 3 – Potentially inappropriate medications prescribed for the elderly with chronic health situations assisted in an ambulatory hospital setting, Brazil, 2017

Variables	n	(%)
Active ingredient		
Appropriate	55	84.6
Inappropriate	10	15.4
Total number of prescribed drugs		
Appropriate	202	79.8
Inappropriate	51	20.2
Potentially inappropriate medications		
Insulin	19	37.3
Omeprazole	11	21.6
Glibenclamide	9	17.7
Amitriptyline	5	9.8
Non-selective NSAID COX	3	5.9
Methyldopa	2	3.9
Carisoprodol	1	1.9
Propatitnitate	1	1.9
Total	51	100

Note: Each elder person could have more than one pharmacological inappropriate prescribed class; NSAIDS: non-steroidal anti-inflammatory; Non-selective NSAID COX, oral: diclofenac, naproxen, meloxicam.

Table 4 – Medicines to be used cautiously prescribed for elder people with chronic health situations assisted in an ambulatory hospital, Brazil, 2017

Class/Medicine	n	(%)
Diuretics	17	42.5
Acetylsalicylic acid	16	40.0
Amitriptyline	5	12.5
Fluoxetine	2	5.0
Total	210	100

Note: Each elder person could have more than one medicine to be used with caution. Diuretics: hydrochlorothiazide, furosemide, spironolactone.

Table 5 presents the medicines prescribed to five (11.4%) elder people of this study and that, from 2015 Beers Criteria, should be avoided or have its dose adjusted according to renal function in the elderly.

Table 5 – Medicines to be avoided or have its dose adjusted for renal function, prescribed for elder people with chronic health situations assisted in an ambulatory hospital setting, Brazil, 2017

Class/Medicine	n	(%)
Ranitidine	3	60.0
Amiloride	1	20.0
Spironolactone	1	20.0
Total	210	100

Note: Each elder person could have more than one medicine to be avoided or have its dose adjusted for renal function prescribed.

DISCUSSION

Polypharmacy and prescribing potentially inappropriate medications for elder people are public health problems and have been associated with adverse events such as falls, hospitalization and death. In this study, the average prescription of PIM for the population evaluated was 72.7%. Accordingly, the assessment of prescriptions and the implementation of pharmaceutical interventions can reduce in the number of inappropriate prescriptions and the average number of inappropriate medications in a same prescription. They can contribute, for example, with the reduction in prescription proton pump inhibitors and other drugs widely used, despite the absence of indication in polymedicated patients⁽⁹⁾.

A study by Lopes and collaborators⁽¹⁰⁾ associated the use of PIM with polypharmacy, polypathology and arterial hypertension and inferred that the clinical consequences of the use of PIM are important due to the increased risk of adverse events and adverse impact in the functionality of the elder person. They also concluded that the actions of promotion of the rational use of medicines are important in care to the elder person to ensure access to safe drugs and appropriate to physiological characteristics of this population.

In this study, 32 elder people (72.7%) were using at least one PIM. However, only one study using the 2015 Beers Criteria has been identified in the literature. In it, the frequency of prescription of PIM was 43% of the elder people on hemodialysis assessed⁽¹¹⁾. Furthermore, no study published considering current knowledge dealt to assess elder people with chronic health conditions in outpatient setting from the 2015 Beers Criteria, which demonstrates the originality, relevance and scientific contribution of this proposal.

The World Health Organization recommends that the average number of medicines used by the elder people is between 1.3 to 2.2⁽¹²⁾. However, the average number found in this study was six drugs. This result demonstrates the high polymedication rate among the evaluated patients, since 25 seniors (56.8%) were submitted to polymedication, considering the polypharmacy as using five or more drugs⁽⁵⁾. A study of elder outpatients with cancer showed that 84% of the evaluated used five or more medicines, with 43% used more than ten medicines⁽¹³⁾. Other studies have found prevalence of polypharmacy in elder people ranging from 39.3% to 91%⁽¹⁴⁻¹⁹⁾.

Nassur and collaborators⁽¹⁹⁾ reported that polypharmacy is directly related to the use of potentially inappropriate medications. In this study, 50% of the patients made use of at least one PIM and were polymedicated at the same time. Considering only the elder people who received prescriptions of PIM, 22 (66.7%) were polymedicated. Similarly, the frequency of polymedicated patients in use of PIM in a university hospital of Juiz de Fora (MG) was 95.9%⁽¹⁷⁾. Another study showed that the presence of PIM in prescription was associated with the number of prescribed medications (five or more medications) and with the presence of cardiovascular or gastrointestinal diseases⁽²⁰⁾.

The clinical impact of polypharmacy in elder people are related to increased risk of adverse events, of hospital admission, of the potential of drug interactions, of the number of PIM, of the

possibility of iatrogenic cascade, by problems of adherence to the treatment and considerable risk of falls⁽²⁰⁻²⁴⁾. So, in addition to direct damages caused by the action of drugs in the body of the elder person, the falls by balance changes are important consequences of the misuse of drugs or interactions between them. Its implications vary from slight abrasions to death, reflecting in large economic impacts for the family and negative impacts on the quality of life of the elder person⁽²⁵⁾. The aging process promotes a functional impairment in multiple organ systems, primarily in the gastrointestinal tract, kidneys, liver, skeletal muscle, cardiovascular system and Central Nervous System (CNS)⁽²⁶⁾. In addition, it promotes physiological changes such as: reduced of hepatic clearance, of glomerular filtration capacity and of muscle mass⁽²⁷⁾, which can influence the parameters of pharmacokinetics and pharmacodynamics of medicines in use by this population. Of the pharmacokinetic processes, the metabolization and excretion are the most affected processes by the aging process. In the hepatic metabolism, we observe reduction of the ability of the liver to inactivate toxins according to age, which contributes to a pro-inflammatory state, regulating negatively the metabolism of medicines⁽²⁸⁾. In renal excretion, we observe reduction in clearance of drugs, which can provide an increase in plasmatic half-life, most likely to cause toxic effects⁽²⁹⁾.

In this sense, considering the recommendations of the 2015 Beers Criteria relating to medications that should be avoided or reduced dose according to its kidney function, the ranitidine must have its dose reduced from a creatinine clearance less than 50 ml/min, because its use is associated with changes in the mental state of the elder person. As for the spironolactone should be avoided when the creatinine clearance is less than 30 ml/min, since can lead to hyperkalemia in the elder people. Finally, the amiloride should be avoided when the creatinine clearance is less than 30 ml/min, because it can lead to hyperpotassemia and hyponatremia in elder person^(6,30).

Among the PIM that can be used with caution in the elderly, we highlight the use of AAS for the primary prevention of cardiac events (not exceeding 325 mg/day). However, the use of AAS for primary prevention in elder people aged over 80 years old has no evidence of benefit in relation to the risk⁽⁶⁾. Despite this, 100% of the elder people aged over 80 years old participants of this survey were making use of AAS. A study using as reference the 2012 Beers Criteria found frequency of use of AAS for the elderly ranging between 30 and 80%, in three long-stay institutions⁽³¹⁾.

In high-risk elder people with established cardiovascular disease, the AAS is indicated for reducing the secondary risk. However, despite the benefits, there is not much data for secondary prevention in the elder people over 80 years old. The monitoring of adverse events related to the use of AAS, such as gastrointestinal irritability and bleeding risk, is indicated due to the increased vulnerability of this group, especially in the context of polypharmacy, multiple comorbidities and weakness⁽³²⁻³³⁾. Considering what we exposed, Feng and collaborators⁽³⁴⁾ propose that reducing the dose of the AAS of 100 mg/day to 40 mg/day reduces the risk of gastrointestinal bleeding and improves symptoms related to the upper gastrointestinal tract, while maintaining the effectiveness of the platelet aggregation in elder people.

Although the problems associated with the use of proton pump inhibitors (PPI) in elder people are widely discussed in the current literature, this study identified 11 elder people (25.0%) using this pharmacological class, corroborating with the results of other recently published studies^(11,15). It is worth mentioning that the PPI were included in the 2015 Beers Criteria, under recommendation of avoiding its prolonged use (over eight weeks) depending on the risk of *Clostridium difficile* infection (caused by the reduction of the gastric acidity), bone loss and fractures (due to the reduction of bone density and reduction of intestinal calcium absorption). In addition, its use is also linked to increased risk of chronic kidney disease because of acute renal injury of repetition and hypomagnesemia, as well as increased rates of pneumonia, generated by the reduction of the gastric acidity and increasing bacterial colonization in stomach^(6,35). Haenisch and collaborators⁽³⁶⁾ reported that chronic use of PPI can raise the rates of incidence of dementia in elder people for up to 44%, possibly due to its ability to cross the blood-brain barrier and to interact with brain enzymes.

The Geriatric Nursing takes unique role in caring for the elder people, especially in the sense that the human aging brings with it comorbidities requiring pharmacological technologies for treatment or palliation. From the results of this study, it was possible to observe that the Beers Criteria are consistent not only to establish PIM, but its application articulates interprofessional relations increasing nursing care targeted to this population.

To the extent that the prescriptive practice seems to be common polypharmacy in the geriatric attention, PIM surely identified give to the nursing care plan, targeted to the elder person assisted in clinic, adequate foundation so to highlight the factors related to acute secondary complications to medication in course, favoring actions of nursing policies, as well as giving the professional nurse better governance regarding the goals in the plan of gerontogeriatric care.

Limitations of the study

A limitation of the study was transversal design adopted in the methodology, which hindered the pharmacotherapy follow-up of attended individuals and, consequently, the realization of potential interventions to minimize health risks. In addition, the absence of a trained nurse in the process of elder care has made it difficult for interprofessional practice to achieve better clinical outcomes in chronic health conditions.

Contributions to the field of nursing, health or public policy

This study contributes to the nursing in order to offer subsidy to building situational diagnostics and support actions directed to the complexity that involves polypharmacy and potentially inappropriate medications for elder people. It supports the emerging area of Gerontological Nursing from the pharmaceutical perspective by showing the need for better multidisciplinary joint service in individual and collective needs.

CONCLUSION

The results showed the stability of 2015 Beers Criteria in the identification and classification of PIM, as well as the high

incidence and the physiological impacts of prescription drugs to the elder population studied. However, far beyond the technical aspects related to the non-conformities of medications, this study promotes the discussion about that, even though the professional pharmacist within its inherent skills can intervene through pharmaceutical consultation on prescriptions with PIM and polypharmacy, the professional nurse, qualified from the

global perspective (gerontological), and not purely functional (geriatric) about the human aging, seems to possess skills and abilities that potentialize damage-reducing interventions associated with pharmacotherapy. The field of study is open, especially for studies with longitudinal design enabling the pharmacotherapy follow-up of individuals and interprofessional activities with emphasis on interventions aimed at minimizing health risks.

REFERENCES

1. Rochon PA. Drug prescribing for older adults. UpToDate[Internet]. 2016 [cited 2016 Nov 24]. Available from: <http://www.uptodate.com/contents/drug-prescribing-for-older-adults>
2. Vaz CSSB. Medicamentos potencialmente inapropriados em idosos: a realidade de um serviço de medicina [Dissertação]. Faculdade de Farmácia da Universidade de Coimbra; 2012.
3. Cho S, Lau SW, Tandon V, Kumi K, Pfüma E, Abernethy DR. Geriatric drug evaluation: where are we now and where should we be in the future? Arch Intern Med[Internet]. 2011[cited 2016 Nov 24];171(10): 937-40. Available from: <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/227393>
4. Boyd CM, Darer J, Boulton C, Fried LP, Boulton L, Wu AW. Clinical practice guidelines and quality of care for older patients with multiple comorbid diseases: implications for pay for performance. JAMA [Internet]. 2005[cited 2016 Nov 24];294(6):716-24. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/16091574>
5. Ferner RE, Aronson JK. Communicating information about drug safety. BMJ [Internet]. 2006[cited 2016 Nov 24];333(7559):143-5. Available from: <https://www.bmj.com/content/333/7559/143.long>
6. American Geriatrics Society-AGS. American Geriatrics Society 2015: updated beers criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc[Internet]. 2015[cited 2016 Nov 24];63(11):2227-46. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/26446832>
7. Santos SSC. Theoric-philosophic conceptions about aging, old age, aged and gerontogeriatric nursing. Rev Bras Enferm[Internet]. 2010[cited 2016 Nov 24];63(6):1035-39. Available from: <http://www.scielo.br/pdf/reben/v63n6/25.pdf>
8. Brasil. Ministério da Saúde. Secretaria de Ciência, Tecnologia e Insumos Estratégicos. Departamento de Assistência Farmacêutica e Insumos Estratégicos. Serviços farmacêuticos na atenção básica à saúde. Cuidado farmacêutico na atenção básica, caderno 2. Brasília; 2014. 308p.
9. Clyne B, Smith SM, Hughes CM, Boland F, Bradley MC, Cooper JA, 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[Internet]. 2015[cited 2016 Nov 24];13(6):545-53. Available from: <http://www.annfam.org/content/13/6/545.long>
10. Lopes LM, Figueiredo TP, Costa SC, Reis AMM. Use of potentially inappropriate medications by the elderly at home. Ciênc Saúde Colet[Internet]. 2016[cited 2016 Nov 24];21(11):3429-38. Available from: http://www.scielo.br/pdf/csc/v21n11/en_1413-8123-csc-21-11-3429.pdf
11. Parker K, Aasebo W, Stavem K. Potentially inappropriate medications in elderly haemodialysis patients using the STOPP criteria. Drugs Real World Outcomes[Internet]. 2016[cited 2016 Nov 24];3(3):359-63. Available from: <https://link.springer.com/article/10.1007%2Fs40801-016-0088-z>
12. World Health Organization-WHO. How to investigate drug use in health facilities: selected drug use indicators. WHO; 1993. 92 p.
13. Nightingale G, Hajjar E, Swartz K, Andrei-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[Internet]. 2015[cited 2016 Nov 24];33(13):1453-59. Available from: <http://ascopubs.org/doi/pdf/10.1200/JCO.2014.58.7550>
14. 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. Br J Clin Pharmacol[Internet]. 2016[cited 2016 Nov 24];82(5):1382-92. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5061799/>
15. Martins GA, Acúrcio FA, Franceschini SCC, Priore SE, Ribeiro AQ. Uso de medicamentos potencialmente inadequados entre idosos do Município de Viçosa, Minas Gerais, Brasil: um inquérito de base populacional. Cad Saúde Pública[Internet]. 2015[cited 2016 Nov 24];31(11):2401-12. Available from: <http://www.scielo.br/pdf/csp/v31n11/0102-311X-csp-31-11-2401.pdf>
16. Dalleur O, Boland B, De Groot A, Vaes B, Boeckstaens 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[Internet]. 2015[cited 2016 Nov 24];15(156):1-9. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4668646/>
17. Munck AKR, Araújo ALA. Avaliação dos medicamentos inapropriados prescritos para pacientes idosos em um Hospital Universitário.

- HU Rev[Internet]. 2012[cited 2016 Nov 24];38(2). Available from: <https://hurevista.ufjf.emnuvens.com.br/hurevista/article/view/2143>
18. Sousa-Munoz RL, Ibiapina GR, Gadelha CS, Maroja JLS. Prescrições geriátricas inapropriadas e polifarmacoterapia em enfermarias de clínica médica de um Hospital-Escola. *Rev Bras Geriatr Gerontol*[Internet]. 2012[cited 2016 Nov 24];15(2):315-24. Available from: <http://www.scielo.br/pdf/rbgg/v15n2/14.pdf>
 19. Nassur BA, Braun V, Devens LT, Morelato RL. Avaliação dos medicamentos inapropriados utilizados por idosos admitidos em hospital geral filantrópico. *Rev Bras Clin Med*[Internet]. 2010[cited 2016 Nov 24]; 8(3):208-11. Available from: <http://files.bvs.br/upload/S/1679-1010/2010/v8n3/a005.pdf>
 20. Weng MC, Tsai CF, Sheu KL, Lee YT, Lee HC, Tzeng SL, et al. The impact of number of drugs prescribed on the risk of potentially inappropriate medication among outpatient older adults with chronic diseases. *QJM* [Internet]. 2013[cited 2016 Nov 24];106(11):1009-15. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/23836694>
 21. Lu WH, Wen YW, Chen LK, Hsiao FY. Effect of polypharmacy, potentially inappropriate medications and anticholinergic burden on clinical outcomes: a retrospective cohort study. *Can Med Assoc J*[Internet]. 2015[cited 2016 Nov 24];187(4):130-7. Available from: <http://www.cmaj.ca/content/187/4/E130.long>
 22. Fried TR, O'leary J, Towle V, Goldstein MK, Trentalange M, Martin DK. Health outcomes associated with polypharmacy in community-dwelling older adults: a systematic review. *J Am Geriatr Soc*[Internet]. 2014[cited 2016 Nov 24];62(12):2261-72. Available from: <https://doi.org/10.1111/jgs.13153>
 23. Lai SW, Liao KF, Liao CC, Muo CH, Liu CS, Sung FC. Polypharmacy correlates with increased risk for hip fracture in the elderly: a population-based study. *Med*[Internet]. 2010[cited 2016 Nov 24];89(5):295-9. Available from: <https://www.ncbi.nlm.nih.gov/pubmed/20827106>
 24. Rochon PA, Gurwitz JH. Optimising drug treatment for elderly people: the prescribing cascade. *Br Med J*[Internet]. 1997[cited 2016 Nov 24];315 (7115):1096-9. Available from: <https://doi.org/10.1136/bmj.315.7115.1096>
 25. Lojudice DC, Laprega MR, Rodrigues RAP, Rodrigues Jr AL. Quedas de idosos institucionalizados: ocorrência e fatores associados. *Rev Bras Geriatr Gerontol*[Internet]. 2010[cited 2016 Nov 24];13(3):403-12. Available from: www.scielo.br/pdf/rbgg/v13n3/a07v13n3.pdf
 26. Shi S, Morike K, Klotz U. The clinical implications of ageing for rational drug therapy. *Eur J Clin Pharmacol*[Internet]. 2008[cited 2016 Nov 24];64(2):183-199. Available from: <https://dx.doi.org/10.1007/s00228-007-0422-1>
 27. Corsonello A, Pedone C, Incalzi RA. Age-related pharmacokinetic and pharmacodynamic changes and related risk of adverse drug reactions. *Curr Med Chem*[Internet]. 2010[cited 2016 Nov 24];17(6):571-84. Available from: <http://www.eurekaselect.com/70931/article>
 28. Tan JL, Eastment JG, Poudel A, Hubbard RE. Age-Related changes in hepatic function: an update on implications for drug therapy. *Drugs Aging*[Internet]. 2015[cited 2016 Nov 24];32(12):999-1008. Available from: <https://dx.doi.org/10.1007/s40266-015-0318-1>
 29. Nobrega OT, Karnikowski MGO. A terapia medicamentosa no idoso: cuidados na medicação. *Ciênc Saúde Coletiva*[Internet]. 2005[cited 2016 Nov 24];10(2):309-13. Available from: www.scielo.br/pdf/csc/v10n2/a08v10n2
 30. Hanlon JT, Aspinall SL, Semla TP, Weisbord SD, Fried LF, Good CB, et al. Consensus guidelines for oral dosing of primarily renally cleared medications in older adults. *J Am Geriatr Soc*[Internet]. 2009[cited 2016 Nov 24];57(11):335-40. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2640432/>
 31. Ganassin AR, Matos VTG, Toffoli-Kadri MC. Potentially inappropriate medication use in institutionalized older adults according to the Beers Criteria. *Braz J Pharm Sci*[Internet]. 2014[cited 2016 Nov 24];50(4):827-837. Available from: <http://www.scielo.br/pdf/bjps/v50n4/1984-8250-bjps-50-04-00827.pdf>
 32. Damluji AA, Ramireddy A, Otalvaro L, Forman DEJ. Secondary cardiovascular prevention in older adults: an evidence based review. *J Geriatr Cardiol*[Internet]. 2015[cited 2016 Nov 24];12(5):459-464. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4605938/>
 33. Labuz-Roszak B, Pierzchala K, Skrzypek M, Swiech M, Machowska-Majchrzak A. Oral anticoagulant and antiplatelet drugs used in prevention of cardiovascular events in elderly people in Poland. *BMC Cardiovasc Disord*[Internet]. 2012[cited 2016 Nov 24];12(98):12-98. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/23114009/>
 34. Feng XR, Liu ML, Liu F, Fan Y, Tian QP. Dose-response of aspirin on platelet function in very elderly patients. *Beijing Da Xue Xue Bao*[Internet]. 2016[cited 2016 Nov 24];48(5):835-840. Available from: <http://xuebao.bjmu.edu.cn/fileup/PDF/201648835.pdf>
 35. Schoenfeld AJ, Grady D. Adverse effects associated with proton pump inhibitors. *JAMA Inter Med*[Internet]. 2016[cited 2016 Nov 24];176(2):172-4. Available from: <https://archinte.jamanetwork.com/article.aspx?doi=10.1001/jamainternmed.2015.7927>
 36. Haenisch B, Von Holt K, Wiese B, Prokein J, Lange C, Ernst A, et al. Risk of dementia in elderly patients with the use of proton pump inhibitors. *Eur Arch Psychiatry Clin Neurosci*[Internet]. 2015[cited 2016 Nov 24];265(5):419-428. Available from: <https://dx.doi.org/10.1007/s00406-014-0554-0>