Title: Potentially Inappropriate Medications in Chinese Older Outpatients according to Beers Criteria: A Cross-sectional Study

Short Title: PIM in Chinese Older Outpatients

Fangyuan Tian*, Haixia Li*, Zhaoyan Chen, Ting Xu

Department of Pharmacy, West China Hospital, Sichuan University, Chengdu, China.

* These authors contributed equally to this work

Frist author name: Fangyuan Tian.

From Department of Pharmacy, West China Hospital, Sichuan University, Chengdu, 610041, Sichuan, China P.R.

Email: tianfangyuan0608@163.com

ORCID ID: https://orcid.org/0000-0002-5187-0386

Tel: +0086 028-85422965

Fax: +0086 028-85422965

Haixia Li

From Department of Pharmacy, West China Hospital, Sichuan University, Chengdu, 610041, Sichuan, China P.R.

Email: 1542436704@qq.com

Tel: +0086 028-85422965

Fax: +0086 028-85422965

Zhaoyan Chen

From Department of Pharmacy, West China Hospital, Sichuan University, Chengdu, 610041, Sichuan, China P.R.

Email: chenzhaoyan1993@163.com

Tel: +0086 028-85422965

Fax: +0086 028-85422965

Corresponding Authors: Dr. Ting Xu.

Institute: Department of Pharmacy, West China Hospital, Sichuan University

Adress: Department of Pharmacy, West China Hospital, Sichuan University, No.37, Guoxue Lane, Chengdu, Sichuan, China

E-mail: tingx2009@163.com

Tel: +0086 028-85422664

Fax: +0086 028-85422664

Abstract

Objectives: Multimorbidity and polypharmacy in older adults always increase the prevalence of potentially inappropriate medications (PIMs) and affect the quality of life of the older adults. The purposes of this study were aimed to investigate the prevalence of PIMs prescription and the most frequent PIMs among outpatients according to Beers criteria and to explore related risk factors for PIMs prescription.

Methods: The cross-sectional retrospective study was conducted among elderly outpatients in Chengdu (a city in China) from January 2018 to December 2018. The 2015 Beers criteria was used to assess PIMs in

elderly outpatients. Univariate analysis and multivariate logistic regression analysis were adopted to determine the factors that may affect the prevalence of PIMs in elderly outpatients.

Results: A total of 15523 patient prescriptions were enrolled, of which 4654 (29.98%) were identified with at least one PIM based on Beers criteria, and 6460 PIMs were detected. Of these PIM prescriptions, 76.32% were detected to receive 1 PIM, 16.54% were detected to receive 2 PIMs, and only 7.13% were found to have at least 3 PIMs. Benzodiazepines (2371, 50.95%), diuretics (1197, 25.72%), and selective serotonin reuptake inhibitors (439, 9.43%) were three common types of drugs that were the most frequent PIMs used. Sex, age, number of

diseases, number of medications, and diseases or disease states were risk factors for PIMs in outpatients.

Conclusion: The results of the study showed that the phenomenon of PIM was common among elderly outpatients in Chengdu. Risk factors for PIM in elderly outpatients include gender, age, number of diseases, number of medications, and sleep disorder.

Keywords: Beers criteria, cross-sectional study, older, potentially inappropriate medications

What is already known about this topic?

- Multimorbidity and polypharmacy in older adults always increase the prevalence of potentially inappropriate medications and affect the quality of life of the older adults.

- Potentially inappropriate medications increases the risk of adverse events, especially in the elderly

What does this study add?

- This is the first study conducted in Chengdu to identify predictors of potentially inappropriate medications in the hospital setting that could help identify high-risk individuals.
- The results of the study showed that the phenomenon of PIM was common among elderly outpatients in Chengdu.
- Risk factors for PIM in elderly outpatients include gender, age, number of diseases, number of medications, and sleep disorder.

Introduction

According to statistics from the World Health Organization (WHO) [1], the proportion of the world's population over 60 years old will nearly double from 12% to 22% between 2015 and 2050. By 2050, the total number of people aged 60 years and older in the world is expected to reach 2 billion, and the elderly population aged 80 years and older in China will reach 120 million. China has the largest elderly population in

the world. In China, the national population exceeds 1.4 billion in the end of 2019, of which the population aged ≥ 60 years accounts for 18.1% (254 million) of the total population, up from 126 million in 2000 [2]. As the proportion of the elderly population continues to increase, the degree of aging in China will continue to deepen.

The elderly become a group that is susceptible to multiple diseases due to aging, especially chronic diseases. WHO data show that 41 million people die from chronic diseases each year, equivalent to 71% of the total global deaths, and the death toll from chronic diseases in China accounts for 89% of all deaths [3-4]. Currently, the coexistence of multiple diseases in the elderly is common, compared with the young, they often

take many different medicines, which will further increase the burden on the liver and kidney function. And changes in pharmacokinetics and pharmacodynamics have led to an increased risk of drug-drug interactions and drug-disease interactions [5-6]. Potential inappropriate medication (PIM) is a public health challenge that refers to the potential adverse risk of patients may outweigh the expected clinical benefit, which is closely associated with adverse clinical outcomes, such as adverse drug events, hospitalization, mortality, and health care costs [7-9]. Therefore, it is of great significance to pay attention to the PIM of the elderly.

Although there are many criteria in the world, only the Beers criteria and the STOPP/START criteria are widely used globally. The Beers

criteria is the world's oldest drug evaluation tool for the elderly. It was initially published in 1991 by American Geriatrics Society (AGS) and was subsequently updated in 1997, 2003, 2012, 2015, and 2019 based on literature evidence [10-15]. Compared with the 2012 Beers criteria, the 2015 Beers criteria has made some changes and newly added two major components: medications that should be avoided by the elderly due to drug-drug interactions and medications that should be avoided or the dose need to be adjusted based on kidney functions.

The research on the prevalence of PIMs in elderly patients is increasing in China according to updated version of the 2015 Beers criteria, but the study sample size is small and most studies mainly focus on the drugs'

use of inpatients in a hospital [16-18]. There is lack of data on outpatients in China, and no large-scale cross-sectional research. Therefore, the purposes of this study were: 1) to determine the prevalence of PIMs and the most frequent PIMs among outpatients in China according to Beers criteria; 2) to explore related risk factors for PIMs.

Methods

Setting and sample

The retrospective study was conducted in hospitals in Chengdu, the capital city of Sichuan Province in China. Chengdu covers an area of 12,390 square kilometers, with a permanent population of 16.0 million in 2017 [19]. The patient prescriptions came from the "Cooperation Project

of Hospital Prescription Analysis" and used random sampling method to extract prescriptions from outpatients of geriatrics in hospitals in Chengdu. All hospitals involved in the Chengdu area were tertiary hospitals.

Older adults (aged 60 and older) that visited the outpatient clinics of the geriatric departments or geriatric centers between January 1, 2018, and December 31, 2018, were included in the study.

Prescriptions with missing or incomplete information were excluded, including gender, diagnosis, medication, and dosage. It didn’t include solvent substances such as water for injection and 0.9% sodium chloride while calculating the number of medications.

Data collection

The data collection were as follows: (1) basic information (region, year, hospital, department, source); (2) patient characteristic (prescription number, age, sex, diagnosis); (3) patient medication (generic name, trade name, specification, dosage form, administration route, number of prescriptions, dosage, frequency of administration).

Evaluation criteria

The AGS 2015 updated Beers criteria was used to evaluate the PIMs for elderly patients [14]. A total of 101 drug criteria in 5 categories were included: (1) 40 medications or medication classes that elderly should avoid; (2) medications or medication classes that elderly should avoid

under the 12 diseases/conditions; (3) 16 medications or medication classes to be used with caution; (4) 13 non-anti-infective drug-drug interactions; and (5) 20 non-anti-infective medications that should be avoided or the dosage of which should be adjusted based on kidney function. All drugs included in the Beers criteria were evaluated based on availability in China. Because of the lack of data on the level of kidney function in outpatients, the last major component cannot be evaluated, so this study mainly evaluated the content of Beers criteria (1)-(4).

Ethics approval

This study was approved by the West China Hospital Research Ethics Board.

Statistical analysis

Patient prescriptions were classified according to their characteristics, including region, year, prescription number, department, source, common name, trade name, drug specifications, administration route, sex, age, diagnosis. The Microsoft Excel software was used to process the prescription data, excluded the blank information prescription through the screening option, and combined manual reading to eliminate the incomplete information prescription.

Statistical analysis was conducted using the SPSS software (version 25.0). Categorical data were described using frequency, and the chi-squared test was used to compare between groups of categorical

variables. Continuous data were expressed as the mean ± standard deviation, otherwise the median ± interquartile range (IQR) were used for description, and statistical analysis using the Student's t-test or non-parametric test, respectively. The presence of PIM as the dependent variable, age (60-69 years, 70-79 years, and ≥ 80 years), sex (male and female), diseases (the top 10 common chronic diseases in the elderly involved in the prescriptions), number of diseases (1-2 diseases and ≥ 3 diseases) and number of medications (1-4 medications, 5-9 medications, and ≥ 10 medications) as independent variables. Univariate analysis was used to determine the association of the two variables. Multivariate logistic regression analysis was performed on independent variables with

statistical significance in univariate analysis. The variables that entered multivariate logistic regression analysis will output the odds ratio (OR), 95% confidence intervals (95%CI), and *p*-value of each subgroup relative to the reference group.

Results

Basic characteristics of patients

A total of 50492 prescription entries were included initially in the study. 609 entries were excluded, and finally 49883 entries were obtained to analysis, with a total of 15523 patient (aged 60 years and older) prescriptions (Fig 1). The 15523 patient prescriptions involved nine tertiary hospitals in Chengdu. Table 1 listed basic characteristics of

patients. Of these patient prescriptions, 60.97% (9464/15523) were for male patients, and the median age was 74 (IQR 67, 84) years, of which 35.08% (5446/15523) were 80 years and above. The median number of diseases in per patient was 2 (IQR 1, 3). 57.21% (8881/15523) of the prescriptions were prescribed to patients who suffered from at least 2 diseases, and 14.27% (2215/15523) were prescribed to patients who suffered from at least 5 diseases. Hypertension, coronary heart disease, diabetes, and sleep disorders were the four most common diseases in the elderly, which were 54.13% (8402/15523), 23.48% (3645/15523), 20.56% (3192/15523), and 18.86% (2927/15523), respectively. The median number of medications per patient was 3 (IQR 2, 4), and 21.16%

(3285/15523) were polypharmacy (number of medications were 5 drugs and above). Cardiovascular system drugs, central nervous system drugs and endocrine system drugs were the three most common types of drugs, of which cardiovascular system drugs had the largest number, accounting for 65.75% (10206/15523).

Prevalence of PIMs and the most frequent PIMs

Among the 15523 patient prescriptions, 4654 (29.98%) were identified with at least one PIM based on Beers criteria, and 6460 PIMs were detected (Table 2). Of the patient prescriptions with PIM, 76.32% (3552/4654) were found to receive 1 PIM, 16.54% (770/4654) were found to receive 2 PIMs, and only 7.13% (332/4654) were detected to

have at least 3 PIMs.

A total of 21 medications or medication classes were involved, and 3649 PIMs were detected using medications that the elderly should be avoided; the most frequent PIMs were benzodiazepines (2378, 65.17%), first-generation antihistamines (392, 10.74%), and Z-drugs (265, 7.26%). A total of 279 PIMs were detected with drugs related to disease/symptom in the elderly, and the most PIMs were detected in dementia/cognitive impairment (93, 33.33%), heart failure (69, 24.73%), and insomnia (61, 21.86%), of which benzodiazepines (39, 41.94%), nonsteroidal anti-inflammatory drugs (NSAIDs, 62, 89.86%), and decongestants (31, 50.82%) were the most relevant, respectively. There were a total of 10

medications or medication classes using cautiously by the elderly, and 2298 PIMs were detected. The most frequently detected drugs were diuretics (1414, 62.53%), selective serotonin reuptake inhibitors (SSRIs, 443, 19.28%), and antipsychotic drugs (206, 8.96%). A total of 234 PIMs were detected among non-anti-infective drug-drug interactions in the elderly, involving 6 pairs of drug-drug interactions, of which (antidepressants/ antipsychotics/benzodiazepines/Z-drugs + ≥ 2 other central nervous system active drugs) was the most detected (190, 81.20%).

Among the 4654 patient prescriptions with PIM, benzodiazepines (2371, 50.95%) were the most frequent PIMs, of which eszolam (1585, 66.85%) and alprazolam (692, 29.19%) were the most common; followed by diuretics (1197, 25.72%) and SSRIs (439, 9.43%), and

hydrochlorothiazide (786, 65.66%) and sertraline (151, 34.40%) were detected the most, respectively.

Factors associated with PIM use

The univariate analysis showed that of all factors, compared with the non-PIM group, besides the factor of COPD ($P>0.05$), other factors including age, sex, number of diseases, number of medications, hypertension, coronary heart disease, diabetes, sleep disorder, hyperlipidemia, cerebral infarction, osteoporosis, benign prostatic hyperplasia, and renal insufficiency in the PIM group were statistically different ($P<0.05$), as shown in Table 1.

On the multivariate analysis, the sex, age, number of diseases, number of medications, and diseases or disease states were risk factors for PIM in

outpatients ($P<0.05$). Patients with female, aged 80 year and older, number of diseases≥3, number of medications≥5, sleep disorder were found to more likely have PIMs. The results of the multivariate analysis are shown in Table 3.

Discussion

This study mainly reports the prevalence and risk factor of PIMs in 15523 elderly outpatients in Chengdu. The results showed that the prevalence of PIMs among elderly outpatients according to Beers criteria version 2015 was 29.98%, and a total of 6,460 PIMs were detected. 76.32% of the patient prescriptions in PIM were found to receive 1 PIM, and only 7.13% were found to have at least 3 PIMs. Benzodiazepines,

diuretics, and SSRIs were the most frequent PIMs. The sex, age, number of diseases, number of medications, and diseases or disease states were risk factors for PIMs in outpatients, and PIM use was closely related to the number of medications.

The incidence of PIMs in elderly outpatients in this study was 29.98%, which was similar to or lower than that the results reported in previous studies based on 2015 Beers criteria, and their study reported that the prevalence of PIMs in elderly outpatients was 29.6%~62.5% [20-23]. This difference in the incidence of PIM might be related to the regionality of diseases and drugs, because the prevalence of certain diseases was different, and the range of drugs available and used by elderly patients

were also different [24]. Furthermore, the aim population in these studies was aged ≥ 60 years or ≥ 65 years in elderly outpatients. It is worth noting that the Beers criteria is designed to focus on elderly patients aged ≥ 65 years, while the current internationally recognized age limit for the elderly is different, with developed country ≥ 65 years old and developing countries ≥ 60 years old. Meanwhile, the elderly refers to people aged ≥60 years according to Chinese national conditions that China is the largest developing country. Therefore, the study took elderly patients aged 60 year and over as the research objective and reported the prevalence of PIMs in outpatients based on the specific conditions. The difference in the age classification of the elderly might also cause the

difference in prevalence of PIMs. To our knowledge, no studies have reported the prevalence of PIMs among elderly outpatients in Chengdu using the 2015 Beers criteria, so it is impossible to compare whether the results are similar.

From the results obtained in the study, it is found that benzodiazepines were the drugs with a higher incidence of PIMs, and the finding was similar to most studies [20,25,26]. The high prescription rate of benzodiazepines could be attributed to the high prevalence of insomnia in the elderly. More than 80% of patients were prescribed for insomnia, but most of the newly prescribed benzodiazepines and sedative hypnotics might be inappropriate [27]. Due to the gradual aging of the functions of

various organs and tissues, the elderly are more sensitive to drugs, and although benzodiazepines are thought to be associated with increased risk of cognitive impairment, falls, and fractures, they are still common in the elderly [28]. Guidelines recommended the use of non-drug treatment for the treatment of insomnia at first, including sleep hygiene, stimulation control, sleep restriction, relaxation training, and cognitive behavioral therapy [29-30]. A review reported that sleep hygiene and cognitive behavioral therapy were considered initial treatments for insomnia, and the use of benzodiazepines in the elderly was discouraged, especially for long-term use [31]. Compared with benzodiazepines, Z-drugs were regarded as first-line drugs for patients with chronic insomnia due to their

more favorable pharmacokinetic characteristics and safety. But research evidence showed that [32] they had similar adverse drug reaction (ADR) risks, such as impairing body balance and increasing the risk of falls in the elderly. The results of a study comparing zolpidem with benzodiazepines revealed that [33] compared with patients using alprazolam and lorazepam, the risk of fractures caused by zolpidem was higher. Diuretics and SSRIs were also the most common PIMs, ranking second only to benzodiazepines. These two drugs belong to the third part of the Beers criteria that to be used with caution by the elderly. Among them, diuretics are the basic drugs for the treatment of patients with heart failure, which can eliminate edema and maintain a stable blood flow,

mainly including furosemide, hydrochlorothiazide and spironolactone. They are commonly used drugs for patients with cardiovascular diseases. Diuretics related hyponatremia is a prevalent cause for admission. A study reported [34] that hydrochlorothiazide and indapamide were the most common drugs that caused hyponatremia. Because it can cause or aggravate syndrome of inappropriate antidiuretic hormone secretion or hyponatremia, electrolyte levels such as sodium, potassium, and chloride should be monitored during clinical use. SSRIs are commonly used antidepressants. Citalopram, escitalopram, fluoxetine, paroxetine, and sertraline were highly prevalent in the study population. One Study revealed [35] that second-generation antidepressants represented by

SSRIs and SNRIs could significantly increase the risk of hospital admission due to hyponatremia in the elderly, and the relative risk was nearly 5 times higher, but the absolute risk was less than 2%. There are uncertainties in the balance of pros and cons of the drugs in this section. Although there is no sufficient evidence to support the benefits or risks, clinicians still need to pay attention to their potential risks when using them, especially elderly patients with risk factors should use it with caution.

According to the results of factor analysis, patients with female, aged ≥ 80 years, number of diseases ≥ 3, and combined medications ≥ 5 were more likely to receive PIMs when prescribed. Consistent with research at

home and abroad, female patients had a higher risk of PIM than male patients, and was not restricted by PIM evaluation tools such as Beers criteria and STOPP/START criteria [21,36]. Similar to the results reported by other scholars [37,38], the number of drugs was associated with the high detection rate of PIM prescriptions. Compared with patients with 1 to 4 drugs, patients with 5 to 9 drugs had 3.455 times the risk of PIM, and patients with 10 or more drugs had 15.164 times the risk of PIM. However, elderly patients are affected by factors such as reduced physiological function and coexistence of multiple diseases, and are very easy to use multiple drugs, and the phenomenon of multiple drugs is common. In this study, the polypharmacy of elderly outpatients was

21.16%, which was similar to the results of Moon et al. [39]. The number of chronic diseases was a risk factor for polypharmacy in the elderly. It can be seen that the number of diseases not only affect the number of drugs used, but also is a factor for PIM in elderly patients. In addition, another important finding was that sleep disorder was also a risk factor that might affect the prevalence of PIMs in elderly outpatients. Sleep disorder was obviously associated with more PIMs prescription due to the use of sedative hypnotics, such as benzodiazepines and Z-drugs that were involved in the Beers criteria. The various factors are closely linked and influence each other. Therefore, it is necessary to start clinically from many aspects, focusing on female patients with advanced age, multiple

diseases, and multiple medications, and strengthen drug management.

This study was a retrospective study conducted in a specific department of tertiary hospitals in Chengdu. Based on the outpatient electronic prescription database, the study with a large sample size for analysis could better reflect the drug use of the elderly. The 2015 Beers criteria was used for the first time to evaluate the prevalence of PIMs among elderly outpatients in Chengdu, and analyzed the status of PIM through large samples and explored the influencing factors of PIM in elderly patients.

Although the research sample was large and involved data from 9 hospitals in Chengdu, there were still some deficiencies in this study due

to the limitations of research type and data. First of all, the patient's relevant medical records, examination data, and medication information were limited, and the patient's personal information and out-of-hospital data cannot be obtained, such as weight, smoking history, past medical history, current medical history, medication history, ADR occurrence history. Therefore, on the one hand, the detection rate of PIM prescriptions reported in the study may be underestimated, on the other hand, it has failed to assess its association with PIM. Secondly, the study only focused on the drugs in the Beers criteria, and the follow-up could be combined with the STOPP/START criteria to analyze the status of PIM in the elderly, increase drug sensitivity and enrich the detection types.

Finally, all data were from HIS, and some interference factors, such as accuracy and completeness, cannot be excluded.

Conclusion

Our study demonstrated that the prevalence of PIMs use was high among elderly outpatients in Chengdu. The sex, age, number of diseases, number of medications, and sleep disorder varieties affect the occurrence of PIMs in elderly outpatients to varying degrees. The research results suggest that effective intervention and management of PIM in elderly patients should be conducted in the future.

Acknowledgements

We thank the participants in our study.

Conflicts of interests

The authors declare that they have no competing interests.

Author Contributions

FY Tian: Developing design, literature search, manuscript writing. HX Li: developing design, literature search, manuscript writing. ZY Chen and T Xu: Developing design, literature search, manuscript writing, and analysis of results. All authors read and approved the final manuscript.

Funding

This work was supported by Sichuan Science and Technology Program (Project number: 2020JDR0143 and 2020JDR0144).

Availability of data and materials

The datasets used for the current study are available from the

corresponding author upon reasonable request.

Ethics approval and consent to participate

Ethics approval was obtained form the Institutional Review Boards of

West China Hospital, Sichuan University.

Consent for publication

Not applicable.

ORCID

Fangyuan Tian: https://orcid.org/0000-0002-5187-0386

References

World Health Organization. Ageing and health; 2018 [cited 2020 Jul 26]. Available from: https://www.who.int/news-room/fact-sheets/detail/ageing-and-health#.X
ce.cn. [Zhang Yi: The growth rate of the total population slows down, and the level of urbanization continues to rise]; 2020 [cited 2020 Jul 26]. Available from: http://www.ce.cn/xwzx/gnsz/gdxw/202001/19/t20200119_34154542.shtml. X
World Health Organization. Noncommunicable diseases; 2018 [cited 2020 Jul 26]. Available from: https://www.who.int/news-room/fact-sheets/detail/noncommunicable-diseases. X
World Health Organization. World Health Organization-NCD Country Profile, 2018

[cited 2020 Jul 26]; Available from: https://www.who.int/nmh/countries/chn_zh.pdf. X
Payne RA. The epidemiology of polypharmacy. *Clin Med (Lond)*. 2016, 16(5): 465-469. https://doi.org/10.7861/clinmedicine.16-5-465 PMID: 27697812X
Fried TR, O'Leary J, Towle V, et al. Health outcomes associated with polypharmacy in community-dwelling older adults: a systematic review. *J Am Geriatr Soc*, 2014, 62(12): 2261-72. https://doi.org/10.1111/jgs.13153 PMID: 25516023X
Wallace E, McDowell R, Bennett K, et al. Impact of Potentially Inappropriate Prescribing on Adverse Drug Events, Health Related Quality of Life and Emergency Hospital Attendance in Older People Attending General Practice: A Prospective Cohort Study. *J Gerontol A Biol Sci Med Sci*, 2017, 72(2): 271-277. https://doi.org/10.1093/gerona/glw140 PMID: 27466245 X
Muhlack DC, Hoppe LK, Weberpals J, et al. The Association of Potentially Inappropriate Medication at Older Age With Cardiovascular Events and Overall Mortality: A Systematic Review and Meta-Analysis of Cohort Studies. *J Am Med Dir Assoc*, 2017, 18(3): 211-220. https://doi.org/10.1016/j.jamda.2016.11.025 PMID: 28131719 X
Hyttinen V, Jyrkkä J, Valtonen H. A Systematic Review of the Impact of Potentially Inappropriate Medication on Health Care Utilization and Costs Among Older Adults. *Med Care*, 2016, 54(10): 950-64. https://doi.org/10.1097/MLR.0000000000000587 PMID: 27367864X
Beers MH, Ouslander JG, Rollingher I, et al. Explicit criteria for determining inappropriate medication use in nursing home residents. UCLA Division of Geriatric Medicine. *Arch Intern Med*, 1991, 151(9): 1825-1832. PMID: 1888249
Beers MH. Explicit criteria for determining potentially inappropriate medication use by the elderly. An update. *Arch Intern Med*, 1997, 157(14): 1531-1536. PMID: 9236554
Fick DM, Cooper JW, Wade WE, 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(22): 2716-2724. https://doi.org/10.1001/archinte.163.22.2716 PMID: 14662625X
Campanelli CM. American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc*, 2012, 60(4): 616-631. https://doi.org/10.1111/j.1532-5415.2012.03923.x PMID: 22376048 X
Samuel MJ. American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. *J Am Geriatr Soc*, 2015, 63(11): 2227-2246. https://doi.org/10.1111/jgs.13702 PMID: 26446832X
2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. *J Am Geriatr Soc*, 2019, 67(4): 674-694. https://doi.org/10.1111/jgs.15767 PMID: 30693946 X
Zhang X, Zhou S, Pan K, et al. Potentially inappropriate medications in hospitalized older patients: a cross-sectional study using the Beers 2015 criteria versus the 2012 criteria. *Clin Interv Aging*, 2017, 12: 1697-1703. https://doi.org/10.2147/CIA.S146009 PMID: 29066875 X

Ma Z, Zhang C, Cui X, et al. Comparison of three criteria for potentially inappropriate medications in Chinese older adults. *Clin Interv Aging*, 2018, 14: 65-72. https://doi.org/10.2147/CIA.S190983 PMID: 30643395 X

Wang P, Wang Q, Li F, et al. Relationship Between Potentially Inappropriate Medications And The Risk Of Hospital Readmission And Death In Hospitalized Older Patients. *Clin Interv Aging*, 2019, 14: 1871-1878. https://doi.org/10.2147/CIA.S218849 PMID: 31806945X

Statistic bureau of chengdu, NBS survey office in chengdu. Chengdu Statistical yearbook. In: Population and Labor Force. *China Statistics Press*; 2018. P. 54.

Bhatt AN, Paul SS, Krishnamoorthy S, et al. Potentially inappropriate medications prescribed for older persons: A study from two teaching hospitals in Southern India. *J Family Community Med*, 2019, 26(3): 187-192. PMID: 31572049

Al-Azayzih A, Alamoori R, Altawalbeh SM. Potentially inappropriate medications prescribing according to Beers criteria among elderly outpatients in Jordan: a cross sectional study. *Pharm Pract (Granada)*, 2019, 17(2): 1439. https://doi.org/10.18549/PharmPract.2019.2.1439 PMID: 31275497X

Saka SA, Oosthuizen F, Nlooto M. Potential inappropriate prescribing and associated factors among older persons in Nigeria and South Africa. *Int J Clin Pharm*, 2019, 41(1): 207-214. https://doi.org/10.1007/s11096-018-0770-1 PMID: 30610546X

Awad A, Hanna O. Potentially inappropriate medication use among geriatric patients in primary care setting: A cross-sectional study using the Beers, STOPP, FORTA and MAI criteria. *PLoS One*, 2019, 14(6): e0218174. https://doi.org/10.1371/journal.pone.0218174 PMID: 31194800X

Azoulay L, Zargarzadeh A, Salahshouri Z, et al. Inappropriate medication prescribing in community-dwelling elderly people living in Iran. *Eur J Clin Pharmacol*, 2005, 61(12): 913-9. https://doi.org/10.1007/s00228-005-0036-4 PMID: 16307268X

Grina D, Briedis V. The use of potentially inappropriate medications among the Lithuanian elderly according to Beers and EU(7)-PIM list - a nationwide cross-sectional study on reimbursement claims data. *J Clin Pharm Ther*, 2017, 42(2): 195-200. https://doi.org/10.1111/jcpt.12494 PMID: 28155237 X

Roux B, Sirois C, Simard M, et al. Potentially inappropriate medications in older adults: a population-based cohort study. *Fam Pract*, 2020, 37(2): 173-179. https://doi.org/10.1093/fampra/cmz060 PMID: 31602472X

Pek EA, Remfry A, Pendrith C, et al. High Prevalence of Inappropriate Benzodiazepine and Sedative Hypnotic Prescriptions among Hospitalized Older Adults. *J Hosp Med*, 2017, 12(5): 310-316. https://doi.org/10.12788/jhm.2739 PMID: 28459898 X

de Groot MH, van Campen JP, Moek MA, et al. The effects of fall-risk-increasing drugs on postural control: a literature review. *Drugs Aging*, 2013, 30(11): 901-20. https://doi.org/10.1007/s40266-013-0113-9 PMID: 24005984 X

Qaseem A, Kansagara D, Forciea MA, et al; Clinical Guidelines Committee of the American College of Physicians. Management of Chronic Insomnia Disorder in Adults: A Clinical Practice Guideline From the American College of Physicians. *Ann Intern Med*, 2016, 165(2): 125-33. https://doi.org/10.7326/M15-2175 PMID:

27136449 X
Samir Kumar Praharaj, Ravi Gupta, Navendu Gaur. Clinical Practice Guideline on Management of Sleep Disorders in the Elderly. *Indian J Psychiatry*, 2018, 60(Suppl 3): S383-S396. PMID: 29535472
Schroeck JL, Ford J, Conway EL, et al. Review of Safety and Efficacy of Sleep Medicines in Older Adults. *Clin Ther*. 2016, 38(11): 2340-2372. https://doi.org/10.1016/j.clinthera.2016.09.010 PMID: 27751669 X
Donnelly K, Bracchi R, Hewitt J, et al. Benzodiazepines, Z-drugs and the risk of hip fracture: A systematic review and meta-analysis. *PLoS One*, 2017, 12(4): e0174730. https://doi.org/10.1371/journal.pone.0174730 PMID: 28448593 X
Finkle WD, Der JS, Greenland S, et al. Risk of fractures requiring hospitalization after an initial prescription for zolpidem, alprazolam, lorazepam, or diazepam in older adults. *J Am Geriatr Soc*, 2011, 59(10): 1883-90. https://doi.org/10.1111/j.1532-5415.2011.03591.x PMID: 22091502 X
Barber J, McKeever TM, McDowell SE, et al. A systematic review and meta-analysis of thiazide-induced hyponatraemia: time to reconsider electrolyte monitoring regimens after thiazide initiation?. *Br J Clin Pharmacol*, 2015, 79(4): 566-77. https://doi.org/10.1111/bcp.12499 PMID: 25139696 X
Gandhi S, Shariff SZ, Al-Jaishi A, et al. Second-Generation Antidepressants and Hyponatremia Risk: A Population-Based Cohort Study of Older Adults. *Am J Kidney Dis*, 2017, 69(1): 87-96. https://doi.org/10.1053/j.ajkd.2016.08.020 PMID: 27773479X
Nam YS, Han JS, Kim JY, et al. Prescription of potentially inappropriate medication in Korean older adults based on 2012 Beers Criteria: a cross-sectional population based study. *BMC Geriatr*, 2016, 16: 118. https://doi.org/10.1186/s12877-016-0285-3 PMID: 27255674 X
Fadare JO, Desalu OO, Obimakinde AM, et al. Prevalence of inappropriate medication prescription in the elderly in Nigeria: A comparison of Beers and STOPP criteria. *Int J Risk Saf Med*, 2015, 27(4): 177-89. https://doi.org/10.3233/JRS-150660 PMID: 26756891X
Arai S, Ishikawa T, Kato H, et al. Multidrug use positively correlates with high-risk prescriptions in the Japanese elderly: a longitudinal study. *J Pharm Health Care Sci*, 2019, 5: 20. https://doi.org/10.1186/s40780-019-0150-6 PMID: 31497309 X
Moon JH, Huh JS, Won CW, et al. Is Polypharmacy Associated with Cognitive Frailty in the Elderly? Results from the Korean Frailty and Aging Cohort Study. *J Nutr Health Aging*, 2019, 23(10): 958-965. https://doi.org/10.1007/s12603-019-1274-y PMID: 31781725X