

# Potentially inappropriate medications use and its associated factors among geriatric patients: a cross-sectional study based on 2019 Beers Criteria

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## Abstract

The aims of this study were to estimate the prevalence of potentially inappropriate medications (PIMs) in a community-dwelling Jordanian population of geriatrics according to the 2019 American Geriatrics Society Beers Criteria, to identify the most used PIMs and factors independently associated with PIMs use.

This was an observational, descriptive, cross-sectional study. The sample population included 386 participants. Data were collected by face-to-face interviews. A total of 2894 medications were evaluated. The prevalence of patients using at least one PIM was 49.2%. The most used PIMs were proton pump inhibitors (24.6%) and long-acting sulfonylurea (20.5%). Participants who had diabetes mellitus, peptic ulcer, or irritable bowel syndrome had significantly higher numbers of PIMs.

The use of PIMs was high in Jordanian geriatric patients. The results of this study might help healthcare providers to detect high-risk patients and reconsider the necessity of using PIMs to decrease the risk of adverse drug events.

## Keywords

AGS Beers Criteria, Geriatrics, Jordan, Potentially inappropriate medications

## Introduction

Geriatrics are at increased risk of drug-related problems due to age-related changes in drugs pharmacokinetics and pharmacodynamics, the use of multiple medications for prevention and treatment of their age-related medical conditions, and the absence of sufficient specialized guidelines for the treatment of geriatric comorbidities.

Altered pharmacokinetics and pharmacodynamics affect the clinical response to a drug in geriatric patients. Age-related changes in drugs pharmacokinetics are related to changes in hepatic function and renal clearance (Shi and Klotz 2011). For instance, renal drug clearance is decreased with age even in the absence of renal diseases (Rowe et al. 1976). The changes in blood flow, protein binding, and body composition also affect the volume

of distribution of several drugs such as benzodiazepines and digoxin (Reidenberg et al. 1978; Hilmer 2008). Besides, drug pharmacodynamics can be altered with age, especially drugs effects on the central nervous system and cardiovascular system due to downregulation of receptors or an increase in receptors' sensitivity (Bowie and Slattum 2007; Trifiró and Spina 2011).

Furthermore, polypharmacy is an important issue that increases the risk of drug-related problems. The precise number of medications that define polypharmacy is variable but it is usually defined as 5 or more medications (Gnjidic et al. 2012). Polypharmacy is common in geriatrics; who are using either prescription, over-the-counter or herbal medications to manage their morbidities (Maher et al. 2014). It is important to reconsider medication appropriateness for geriatrics to decrease the risk for inappropriate drug use, suboptimal drug use, drug-drug interactions, and adverse drug events.

Various criteria have been developed to assess drug appropriateness for older adults (Hanlon et al. 1992; Gallagher et al. 2008). The most widely used criteria is Beers Criteria, which is firstly developed by Mark Beers and colleagues in 1991 (Beers et al. 1991), and then transitioned to the American Geriatric Society (AGS) in 2011. It has been updated every 3 years since 2011 (Fick et al. 2012; Samuel 2015) and the latest update was published in 2019 (Fick et al. 2019). The Beers Criteria is a list of medications considered potentially inappropriate for use in geriatric patients independent of their conditions or in patients with specific diseases or conditions; mostly due to high risk for adverse events. Although it is supported by evidence, Beers Criteria should never solely dictate how medications are prescribed for geriatrics and healthcare providers should always use clinical judgment and evidence-based guidelines to select therapies for their patients.

Since developed, several studies have been published using Beers Criteria (Goltz et al. 2012; Napolitano et al. 2013; Davidoff et al. 2015; Zhao et al. 2021). The prevalence of potentially inappropriate medications (PIMs) varied based on study design, population studied, and the different updates of Beers criteria. In this study, PIMs were assessed in community-dwelling elderly patients in Jordan based on the latest Beers Criteria; 2019 AGS Beers Criteria (Fick et al. 2019). The primary objective of this study was to estimate the prevalence of PIMs among Jordanian geriatrics independent of diagnosis or drug-drug interactions. The other objectives were to identify the most common PIMs that were used, and to investigate the association between participants' factors and the use of PIMs.

## Experimental part

### Study design and setting

This was an observational, descriptive, cross-sectional study that took place between October and December 2020 exploring PIMs use among community-dwelling elderly patients in Jordan. Elderly patients aged 65 years

or older from the community were eligible to participate in this study. Convenience sampling method was used to select participants in this study. A total of 386 geriatric patients were face-to face interviewed by pharmacy students who were well-trained to conduct and fill out the questionnaire. To prevent any potential source of bias, they were not aware of the intended outcome measure of the study at the time of data collection. The questionnaire contains three main parts; the first part comprises the demographic characteristics of participants, the second part covers the past medical history and acute conditions that needed nonprescription drug use in the last three months, and the third part is about the current medications used and duration of their use; for both regularly prescribed medications and as needed (PRN) medications.

Medications used by participants were reviewed based on the 2019 AGS Beers Criteria to identify PIMs, and the prevalence ratio was calculated as the number of patients who were using one or more PIMs divided by the total number of patients participated in the study.

### Ethical approval

This study received ethical approval from the Institutional Review Board (IRB) of the Hashemite University, Jordan (Ref. No. 1/14/2019/2020). Participants in their communities were reached out by researchers and asked to participate in this study. Verbal approval was taken before filling the questionnaire. All participants were informed that participation in the study is voluntary and were assured of the anonymity and confidentiality of their data.

### Statistical analysis

Following data collection, data was analyzed using statistical package for social science (SPSS) version 24. Continuous variables were presented as mean and standard deviation. Categorical variables were presented as frequencies and percentages. When there was any missing data, valid percentages were reported. Independent-sample t-test was used to assess the association between categorical variables and mean number of PIMs used. All the test requirements were met; there were no outliers in the data, as assessed by inspection of a boxplot for values greater than 1.5 box-lengths from the edge of the box. The difference scores for the number of PIMs between the two groups were normally distributed, as assessed by visual inspection of a Normal Q-Q Plot, and there was homogeneity of variances, as assessed by Levene's test for equality of variances. Chi-square test of homogeneity was used to test for potential association between categorical variables and PIMs use. P-value of < 0.05 was considered to be statistically significant for all analyses. A linear regression was performed to understand the effect of age and number of medications (regular and/or as needed) on the number of PIMs. Based on a margin of error of 5% and confidence interval of 95%, the minimum sample size that was accepted to get relevant data is 377.

## Results

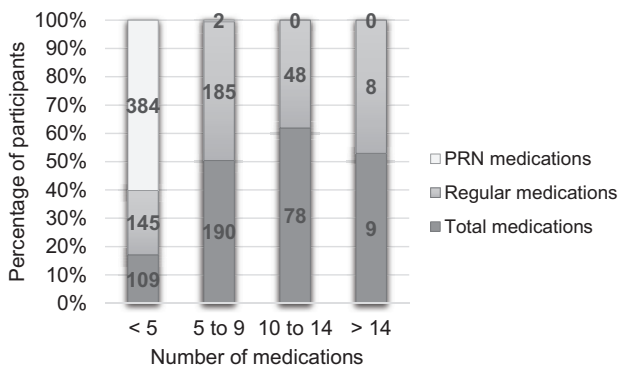
### Participants descriptive characteristics

A total of 386 community-dwelling geriatric patients were participated in this study. Participants' age ranged from 65 to 97 years with an average age of 71.89 ( $\pm 6.19$ ) years. About 43.6% of the participants were male. Regarding their education level; around 40% of the participants did not attend school and around 30% received high school education while 23% were college graduate and 4.2% received advanced degree. Around two-third of them (around 70%) were married and majority of them (91.1%) were not working.

The most common chronic diseases presented in this population were hypertension (78.5%), diabetes mellitus (DM) (60.4%) and dyslipidemia (57.3%). Other chronic diseases were heart failure (12.4%), ischemic heart diseases (13.7%), peptic ulcer (PU) (18.9%), and around 23% of male patients had benign prostatic hyperplasia. The history of falls and fracture was around 12% (Table 1).

### Medication use

In this study, information about both regularly scheduled and PRN medications were collected. A total of 2894 medications were reviewed for the 386 included patients (2609 regular medications and 285 PRN medications). These medications included 264 different active ingredients. The average number of total medications used per patient was 7.5 ( $\pm 3.039$ ) with a minimum of 3 medications and a maximum of 21 medications; of which around 6.76 ( $\pm 2.848$ ) were ones that are used on a regular basis (Table 1). Almost all patients (384/386) were using less than 5 PRN medications, around 37.6% (145/386) were using less than 5 regular medications, and 28.2% (109/386) were using less than 5 medications in total (regular and PRN), i.e., around seventy-two percent (277/386) of the participants were using polypharmacy (five or more medications) (Figure 1).



**Figure 1.** Number of medications used by participants. PRN: as needed.

### Prevalence of PIMs

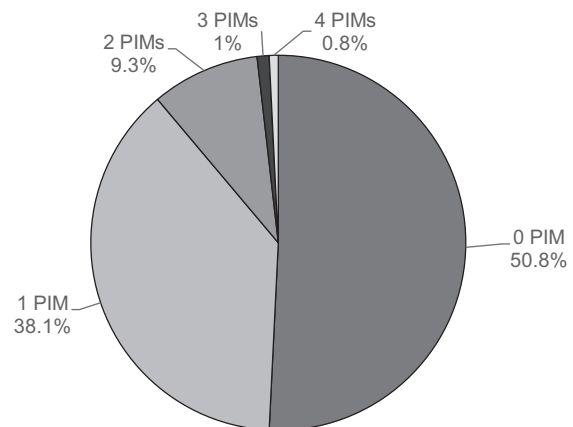
In this study, the prevalence of PIMs use was 49.2%. The prevalence was calculated by the number of patients taking

**Table 1.** Demographic and clinical characteristics of the study participants (N = 386) <sup>a</sup>.

Parameters	n (%)	Mean (SD)
<b>Gender</b>		
Male	167 (43.6)	
Female	216 (56.4)	
<b>Age</b>		71.89 ( $\pm 6.19$ )
<b>Education</b>		
Did not attend school	161 (42.7)	
Primary school	1 (0.3)	
High school	111 (29.4)	
College graduate	88 (22.8)	
Advanced degree	16 (4.2)	
<b>Marital status</b>		
Never married	7 (1.9)	
Married	272 (72.1)	
Divorced	6 (1.6)	
Separated	2 (0.5)	
Widowed	90 (23.9)	
<b>Current working</b>	34 (8.9)	
<b>Chronic diseases</b>		
Hypertension	303 (78.5)	
Diabetes Mellitus	233 (60.4)	
Dyslipidemia	221 (57.3)	
Benign prostatic hyperplasia	38/167 male (22.8)	
Peptic ulcer	73 (18.9)	
Ischemic heart disease	53 (13.7)	
Heart failure	48 (12.4)	
History of falls and fractures	46 (11.9)	
Gout	37 (9.6)	
Hypothyroidism	32 (8.3)	
Osteoporosis	28 (7.3)	
Asthma	25 (6.5)	
Anemia	24 (6.2)	
Stroke	19 (4.9)	
Osteoarthritis	18 (4.7)	
Chronic kidney disease	15 (3.9)	
Irritable bowel syndrome	15 (3.9)	
Rheumatoid arthritis	14 (3.6)	
Urinary incontinence	12 (3.1)	
<b>Medication use per patient</b>		
No of total medications		7.50 ( $\pm 3.039$ )
No of regular medications		6.76 ( $\pm 2.848$ )
No of PRN medications		0.74 ( $\pm 1.072$ )

<sup>a</sup> Sample size varied due to missing data (n = 377–386). PRN: as needed.

at least one PIM divided by the total number of patients participated in the study. Of the identified patients who were using PIMs, most of them were using 1 PIM (Figure 2).



**Figure 2.** Percentage of participants using potentially inappropriate medications (PIMs) based on 2019 American Geriatrics Society Beers criteria (AGS Beers criteria).

In this study, we identified 25 medications that are classified as PIMs according to 2019 AGS Beers Criteria. The most common were the prolonged (more than 8 weeks) use of proton pump inhibitors (lansoprazole, pantoprazole, rabeprazole, omeprazole, and esomeprazole) and long-acting sulfonylureas (glimepiride and glyburide) with a percentage of 24.6% and 20.5%, respectively. Other groups of medications that are considered as PIMs and were commonly used by participants were benzodiazepines (5.7%), muscle relaxants (5.7%), antispasmodics (5.4%), and first-generation antihistamines (2.4%) (Table 2).

**Table 2.** Classes of most frequently used PIMs among the study participants (N = 386).

Therapeutic category	Drugs	n (%)
Proton pump inhibitors for more than 8 weeks	Lansoprazole	95 (24.6)
	Pantoprazole	
	Rabeprazole	
	Omeprazole	
	Esomeprazole	
Long acting sulfonylurea	Glimepiride	79 (20.5)
	Glyburide	
Benzodiazepines	Chlordiazepoxide	22 (5.7)
	Alprazolam	
	Diazepam	
	Clonazepam	
Muscle relaxants	Chlorzoxazone	22 (5.7)
	Orphenadrine	
Antispasmodics	Clidinium	21 (5.4)
	Scopolamine	
First generation antihistamines	Chlorpheniramine	9 (2.3)
	Promethazine	

PIMs: potentially inappropriate medications.

## Factors independently associated with PIMs use

In our study, using chi-square test of homogeneity, participants who had DM, PU and irritable bowel syndrome (IBS) were more likely to have PIMs compared to those without these diseases (Table 3).

**Table 3.** Variables associated with the presence of PIMs.

Independent variable	PIMs n (%)		P value
	Yes	No	
DM	Yes	129 (55.4%)	0.003
	No	61 (39.9%)	
PU	Yes	54 (74.0%)	0.001
	No	136 (43.5%)	
IBS	Yes	13 (86.7%)	0.003
	No	177 (47.7%)	

PIMs: potentially inappropriate medications, DM: diabetes mellitus, PU: peptic ulcer, IBS: irritable bowel syndrome.

There were 233 (60.4%) diabetics and 153 (39.6%) non-diabetic patients. An independent-samples t-test was performed to determine if there were differences in the number of PIMs between diabetic and non-diabetic patients. The mean of number of PIMs among diabetic patients was higher ( $0.71 \pm 0.78$ ) than non-diabetics ( $0.51 \pm 0.72$ ), a statistically significant difference of 0.20 (95% CI, 0.04 to 0.35),  $t(384) = 2.365$ ,  $p = 0.012$  (Table 4).

**Table 4.** Variables associated with a significant higher number of PIMs.

Independent variable	Participants n (%)	No. of PIMs (Mean $\pm$ SD)	Means difference (95% CI)	P value
DM	Yes	233 (60.4%)	$0.71 \pm 0.78$	0.20 (0.04–0.35)
	No	153 (39.6%)	$0.51 \pm 0.72$	
PU	Yes	73 (18.9%)	$1.01 \pm 0.81$	0.47 (0.29–0.66)
	No	313 (80.1%)	$0.54 \pm 0.72$	
IBS	Yes	15 (3.9%)	$1.73 \pm 1.03$	1.15 (0.77–1.52)
	No	371 (96.1%)	$0.58 \pm 0.71$	

PIMs: potentially inappropriate medications, DM: diabetes mellitus, PU: peptic ulcer, IBS: irritable bowel syndrome.

There were 73 (19%) participants having PU disease. The mean number of PIMs among patients with PU was significantly higher ( $1.01 \pm 0.81$ ) than those without PU ( $0.54 \pm 0.72$ ),  $p = 0.001$ . Moreover, there were 15 (3.9%) participants having IBS. The mean number of PIMs among patients with IBS was higher ( $1.73 \pm 1.03$ ) than those without IBS ( $0.58 \pm 0.71$ ),  $p = 0.001$  (Table 4).

A linear regression was run to test the effect of age and number of medications (regular and/or as needed) on the number of PIMs. Some of the test assumptions were violated and there was no significant relationship between these tested variables and PIMs (data not shown).

## Discussion

This is the first Jordanian study that evaluates PIMs use in community-dwelling geriatrics based on the latest version of AGS Beers Criteria (2019 AGS Beers Criteria). About 49.2% of patients were using one or more PIMs. Diagnosis with DM, PU or IBS were identified as significant predictors of PIMs use in this study. These findings would be the first step for evaluating future interventions to decrease PIMs use among geriatric patients.

The prevalence of PIMs varies according to criteria used and participant's characteristics (Goltz et al. 2012; Napolitano et al. 2013; Davidoff et al. 2015; Zhao et al. 2021). In this study the prevalence was 49.2%. This is the first study in Jordan to evaluate PIMs use based on 2019 AGS Beers Criteria. There was one study conducted in Jordan that evaluated PIMs use according to 2015 AGS Beers Criteria based on outpatient electronic medical records and the prevalence was 62.5% (Al-Azayzih et al. 2019), which is higher than what we found in our study. However, the comparison could be difficult due to differences in the data collection method. In this study, it was face-to-face interview included nonprescription as well as prescription medications and the difference in the AGS Beers Criteria versions used for assessment (2015 vs 2019).

In other studies conducted worldwide for the use of PIMs according to 2019 AGS Beers Criteria, the prevalence ranged from 34.1 to 68.8%. These studies were conducted in Lebanon (34.1%) (Chahine 2020), in USA (34.4%) (Clark et al. 2020), in China (35.0%) (Huang et al. 2020), in Switzerland (53%) (Achterhof et al. 2020), and in Spain (68.8%) (Lopez-Rodriguez et al. 2020). The

difference in prevalence is predicted and comparing other studies should be made with caution due to differences in population studied, time of the study, source of patient information, healthcare setting, and medication availability and accessibility in different countries.

Our results show that the most prescribed PIMs were PPIs and long-acting sulfonylureas. The use of PPIs coincides with other studies (Fralick et al. 2020; Lopez-Rodriguez et al. 2020; Roux et al. 2020; He et al. 2021). Overuse of PPIs is a problem worldwide (Forgacs and Loganayagam 2008; Voukelatou et al. 2019) as it is in Jordan (Alqudah et al. 2016) due to their relative superior efficacy and high safety compared to H2 receptor blockers. However, their use for more than 8 weeks should be avoided because they are associated with *Clostridium difficile* infection and bone loss and fracture (Fick et al. 2019). Patient education and increasing healthcare knowledge about long-term side effects of PPIs is necessary especially that studies show a lack of awareness of inappropriate use PPIs and their related adverse events among patients (Rababa and Rababa'h 2020) and healthcare providers including physicians, pharmacists and nurses (Luo et al. 2019; Asdaq et al. 2021).

Long-acting sulfonylureas were of highly prescribed PIMs in this study however, they were not reported in similar studies. One explanation for this result is the high percentage of diabetic patients in this study (60.4%), which is higher than the reported prevalence in the same age group (Sinclair et al. 2020). The small size of our study compared to disease prevalence studies may explain this difference. High percentage of diabetic patients in this study increases the use of antidiabetic medications and this raises the chance of using long-acting sulfonylureas. Long-acting sulfonylureas are considered PIMs due to their high risk of severe prolonged hypoglycemia (Fick et al. 2019). Elderly are more vulnerable to hypoglycemia due to age-related physiologic changes that alter the counter-regulatory mechanisms to hypoglycemia; elderly have lower glucagon and growth hormone responses but higher epinephrine and cortisol responses than age-matched healthy individuals (Mathur et al. 2015). Moreover, elderly patients are less aware of symptoms of hypoglycemia (Pegg et al. 1991). Therefore, long-acting sulfonylurea should be avoided in elderly and, if used, patient education about their risk of hypoglycemia and symptoms of hypoglycemia is vital, as well as the risk of disulfiram-like reactions in concomitant alcohol use.

In this study, Seventy-two percent of participants were using polypharmacy, which coincides with previous study conducted to estimate the prevalence of polypharmacy among elderly in Jordan (74.9%) (Al-Qerem et al. 2018) and Oman (76.3%) (Al-Hashar et al. 2016). Polypharmacy have been linked to several negative outcomes. i.e., mortality, falls, cognitive impairment and drug-related problems (Wastesson et al. 2018). Although in other similar studies, number of medications used per patient were identified as predictors of PIMs use (Achterhof et al. 2020; Wang et al. 2020; Jungo et al. 2021; Zhao et al. 2021), in this study, it was not identified as associated factor.

The factors associated with PIMs use in this study were diagnosis with DM, PU, or IBS. Other similar studies identified DM, hypertension, coronary artery diseases (Alyazeedi et al. 2019) and heart failure (Alyazeedi et al. 2019; Wang et al. 2020) as predictors of PIMs. The commonly identified PIMs in this study were PPIs and long-acting sulfonylureas, which are used for management of PU and DM, respectively. Identifying subcategories of geriatrics who are at increased risk of using PIMs helps prescribers giving more attention to disease management protocols for geriatric patients with emphasis to decrease the prescription of PIMs.

Among all healthcare providers, pharmacists are the ones who interact most frequently with patients especially in community pharmacy. Being a medication expert, they have central role in monitoring and assessing the use of PIMs, increasing the patient awareness of PIMs and educating them about potential adverse effects or interactions.

The strengths of this study are (1) being the first study to detect PIMs use and associated factors in community-dwelling geriatrics in Jordan based on the latest update of Beers Criteria. (2) being conducted in the community by face-to-face interview and it is not based on registries or electronic questionnaire, which allowed for collecting data about all medications used by patients including nonprescription ones and medications prescribed from different clinics. The results of this study may be representative of the largest proportion of geriatrics; who lives in the community, regardless of their demographic, social or clinical conditions.

One limitation of this study is being an observational study and therefore, future prospective studies are required to correlate the use of PIMs with adverse drug events, morbidities and hospitalization among geriatric population in Jordan. Besides, interventional strategies directed to healthcare professionals and general populations are needed to increase the awareness about PIMs and their drug-related problems. Healthcare professionals should be aware of PIMs risks and fully evaluate all geriatrics medications to de-prescribe the potentially inappropriate ones or switch to safer alternative medications whenever applicable.

## Conclusion

Based on 2019 Beers Criteria, the prevalence of PIMs use is high in elderly patients in Jordan. PPIs and long-acting sulfonylureas are the most prescribed PIMs. Diagnosis with DM, PU or IBS are predictors of PIMs use. Increase the knowledge about PIMs and their potential side effects among patients and healthcare providers is warranted.

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## References

- Achterhof AB, Rozsnyai Z, Reeve E, Jungo KT, Floriani C, Poortvliet RKE, Rodondi N, Gussekloo J, Streit S (2020) Potentially inappropriate medication and attitudes of older adults towards de-prescribing. *PLoS ONE* 15: e0240463. <https://doi.org/10.1371/journal.pone.0240463>
- Al-Azayzih A, Alamoori R, Altawalbeh SM (2019) Potentially inappropriate medications prescribing according to beers criteria among elderly outpatients in Jordan: A cross sectional study. *Pharmacy Practice* 17: 1–7. <https://doi.org/10.18549/PharmPract.2019.2.1439>
- Al-Hashar A, Al Sinawi H, Al Mahrizi A, Al-Hatrushy M (2016) Prevalence and covariates of polypharmacy in elderly patients on discharge from a tertiary care hospital in Oman. *Oman Medical Journal* 31: 421–425. <https://doi.org/10.5001/omj.2016.85>
- Al-Qerem W, Jarrar YB, Al-Sheikh I, Elmaadani A (2018) The prevalence of drug-drug interactions and polypharmacy among elderly patients in Jordan. *Biomedical Research (India)* 29: 2561–2569. <https://doi.org/10.4066/biomedicalresearch.29-18-618>
- Alqudah MAY, Al-Azzam S, Alzoubi K, Alkhatatbeh M, Rawashdeh N (2016) Overuse of proton pump inhibitors for stress ulcer prophylaxis in Jordan. *International Journal of Clinical Pharmacology and Therapeutics* 54: 597–602. <https://doi.org/10.5414/CP202533>
- Alyazeedi A, Algendy AF, Sharabash M, Karawia A (2019) Prevalence, determinants and associated risk of potentially inappropriate prescribing for older adults in qatar: A national retrospective study. *Clinical Interventions in Aging* 14: 1889–1899. <https://doi.org/10.2147/CIA.S222532>
- Asdaq SMB, ALbasha M, Almutairi A, Alyabisi R, Almuhaisni A, Faqih R, Alamri AS, Alsanie WF, Alhomrani M (2021) Use of proton pump inhibitors: An exploration of awareness, attitude and behavior of health care professionals of Riyadh, Saudi Arabia. *Saudi Pharmaceutical Journal* 29: 713–718. <https://doi.org/10.1016/j.jsps.2021.04.033>
- Beers MH, Ouslander JG, Rollingher I, Reuben DB, Brooks J, Beck JC (1991) Explicit Criteria for Determining Inappropriate Medication Use in Nursing Home Residents. *Archives of Internal Medicine* 151: 1825–1832. <https://doi.org/10.1001/archinte.1991.00400090107019>
- Bowie MW, Slattum PW (2007) Pharmacodynamics in Older Adults: A Review. *American Journal Geriatric Pharmacotherapy* 5: 263–303. <https://doi.org/10.1016/j.amjopharm.2007.10.001>
- Chahine B (2020) Potentially inappropriate medications prescribing to elderly patients with advanced chronic kidney by using 2019 American Geriatrics Society Beers Criteria. *Health Science Reports* 3: e214. <https://doi.org/10.1002/hsr.2.214>
- Clark CM, Shaver AL, Aurelio LA, Feuerstein S, Wahler RG, Daly CJ, Jacobs DM (2020) Potentially Inappropriate Medications Are Associated with Increased Healthcare Utilization and Costs. *Journal of the American Geriatrics Society* 68: 2542–2550. <https://doi.org/10.1111/jgs.16743>
- Davidoff AJ, Miller GE, Sarpong EM, Yang E, Brandt N, Fick DM (2015) Prevalence of potentially inappropriate medication use in older adults using the 2012 beers criteria. *Journal of the American Geriatrics Society* 63: 486–500. <https://doi.org/10.1111/jgs.13320>
- Fick D, Semla T, Beizer J, Brandt N, Dombrowski R, DuBeau CE, Flanagan N, Hanlon J, Hollmann P, Linnebur S, Sandhu S, Steinman M (2012) American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. *Journal of the American Geriatrics Society* 60: 616–631. <https://doi.org/10.1111/j.1532-5415.2012.03923.x>
- Fick DM, Semla TP, Steinman M, Beizer J, Brandt N, Dombrowski R, DuBeau CE, Pezzullo L, Epplin JJ, Flanagan N, Linnebur S, Sandhu S (2019) American Geriatrics Society 2019 updated AGS Beers Criteria for potentially inappropriate medication use in older adults. *Journal of the American Geriatrics Society* 67: 674–694. <https://doi.org/10.1111/jgs.15767>
- Forgacs I, Loganayagam A (2008) Overprescribing proton pump inhibitors. *BMJ* 336: 2–3. <https://doi.org/10.1136/bmj.39406.449456.BE>
- Fralick M, Bartsch E, Ritchie CS, Sacks CA (2020) Estimating the use of potentially inappropriate medications among older adults in the United States. *Journal of the American Geriatrics Society* 68: 2927–2930. <https://doi.org/10.1111/jgs.16779>
- Gallagher P, Ryan C, Byrne S, Kennedy J, O'Mahony D (2008) STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment). Consensus validation. *International Journal of Clinical Pharmacology and Therapeutics* 46: 72–83. <https://doi.org/10.5414/CP46072>
- Gnjidic D, Hilmer SN, Blyth FM, Naganathan V, Waite L, Seibel MJ, McLachlan AJ, Cumming RG, Handelsman DJ, Le Couteur DG (2012) Polypharmacy cutoff and outcomes: Five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. *Journal of Clinical Epidemiology* 65: 989–995. <https://doi.org/10.1016/j.jclinepi.2012.02.018>
- Goltz L, Kullak-Ublick GA, Kirch W (2012) Potentially inappropriate prescribing for elderly outpatients in Germany: A retrospective claims data analysis. *International Journal of Clinical Pharmacology and Therapeutics* 50: 185–194. <https://doi.org/10.5414/CP201441>
- Hanlon JT, Schmader KE, Samsa GP, Weinberger M, Uttech KM, Lewis IK, Cohen HJ, Feussner JR (1992) A method for assessing drug therapy appropriateness. *Journal of Clinical Epidemiology* 45: 1045–1051. [https://doi.org/10.1016/0895-4356\(92\)90144-C](https://doi.org/10.1016/0895-4356(92)90144-C)
- He D, Zhu H, Zhou H, Dong N, Zhang H (2021) Potentially inappropriate medications in Chinese older adults: a comparison of two updated Beers criteria. *International Journal of Clinical Pharmacy* 43: 229–235. <https://doi.org/10.1007/s11096-020-01139-5>
- Hilmer SN (2008) ADME-tox issues for the elderly. *Expert Opinion on Drug Metabolism and Toxicology* 4: 1321–1331. <https://doi.org/10.1517/17425255.4.10.1321>
- Huang Y, Zhang L, Huang X, Liu K, Yu Y, Xiao J (2020) Potentially inappropriate medications in Chinese community-dwelling older adults. *International Journal of Clinical Pharmacy* 42: 598–603. <https://doi.org/10.1007/s11096-020-00980-y>
- Jungo KT, Streit S, Lauffenburger JC (2021) Patient factors associated with new prescribing of potentially inappropriate medications in multimorbid US older adults using multiple medications. *BMC Geriatrics* 21: e163. <https://doi.org/10.1186/s12877-021-02089-x>
- Lopez-Rodriguez JA, Rogero-Blanco E, Aza-Pascual-Salcedo M, Lopez-Verde F, Pico-Soler V, Leiva-Fernandez F, Daniel Prados-Torres J, Prados-Torres A, Cura-Gonzalez I (2020) Potentially inappropriate prescriptions according to explicit and implicit criteria in patients with multimorbidity and polypharmacy. MULTIPAP: A cross-sectional study. *PLoS ONE* 15: e0237186. <https://doi.org/10.1371/journal.pone.0237186>

- Luo H, Fan Q, Bian T, Li X, Chen K, Zhang Q, Wei Y, Xiao Y, Li Y (2019) Awareness, attitude and behavior regarding proton pump inhibitor among medical staff in the Southwest of China. *BMC Health Services Research* 19: e880. <https://doi.org/10.1186/s12913-019-4725-6>
- Maher RL, Hanlon J, Hajjar ER (2014) Clinical consequences of polypharmacy in elderly. *Expert Opinion on Drug Safety* 13: 57–65. <https://doi.org/10.1517/14740338.2013.827660>
- Mathur S, Zammitt NN, Frier BM (2015) Optimal glycaemic control in elderly people with Type 2 Diabetes: What does the evidence say? *Drug Safety* 38: 17–32. <https://doi.org/10.1007/s40264-014-0247-7>
- Napolitano F, Izzo MT, Di Giuseppe G, Angelillo IF (2013) Frequency of inappropriate medication prescription in hospitalized elderly patients in Italy. *PLoS ONE* 8: e82359. <https://doi.org/10.1371/journal.pone.0082359>
- Pegg A, Fitzgerald F, Wise D, Singh BM, Wise PH (1991) A community-based study of diabetes-related skills and knowledge in elderly people with insulin-requiring diabetes. *Diabetic Medicine* 8: 778–781. <https://doi.org/10.1111/j.1464-5491.1991.tb01700.x>
- Rababa M, Rababa'h A (2020) Community-dwelling older adults' awareness of the inappropriate use of proton pump inhibitors. *BMC Geriatrics* 20: e431. <https://doi.org/10.1186/s12877-020-01844-w>
- Reidenberg MM, Levy M, Warner H, Coutinho CB, Schwartz MA, Yu G, Cheripko J (1978) Relationship between diazepam dose, plasma level, age, and central nervous system depression. *Clinical Pharmacology and Therapeutics* 23: 371–374. <https://doi.org/10.1002/cpt1978234371>
- Roux B, Sirois C, Simard M, Gagnon ME, Laroche ML (2020) Potentially inappropriate medications in older adults: a population-based cohort study. *Family Practice* 37: 173–179. <https://doi.org/10.1093/fampra/cmz060>
- Rowe JW, Andres R, Tobin JD, Norris AH, Shock NW (1976) The effect of age on creatinine clearance in men: a cross sectional and longitudinal study. *Journals of Gerontology* 31: 155–163. <https://doi.org/10.1093/geronj/31.2.155>
- Samuel MJ (2015) American Geriatrics Society 2015 updated beers criteria for potentially inappropriate medication use in older adults. *Journal of the American Geriatrics Society* 63: 2227–2246. <https://doi.org/10.1111/jgs.13702>
- Shi S, Klotz U (2011) Age-related changes in pharmacokinetics. *Current Drug Metabolism* 12: 601–610. <https://doi.org/10.2174/138920011796504527>
- Sinclair A, Saeedi P, Kaundal A, Karuranga S, Malanda B, Williams R (2020) Diabetes and global ageing among 65–99-year-old adults: Findings from the International Diabetes Federation Diabetes Atlas, 9<sup>th</sup> edn. *Diabetes Research and Clinical Practice* 162: 108078. <https://doi.org/10.1016/j.diabres.2020.108078>
- Trifiró G, Spina E (2011) Age-related changes in pharmacodynamics: Focus on drugs acting on central nervous and cardiovascular systems. *Current Drug Metabolism* 12: 611–620. <https://doi.org/10.2174/138920011796504473>
- Voukelatou P, Vrettos I, Emmanouilidou G, Dodos K, Skotsimara G, Kontogeorgou D, Kalliakmanis A (2019) Predictors of inappropriate proton pump inhibitors use in elderly patients. *Current Gerontology and Geriatrics Research* 2019: e7591045. <https://doi.org/10.1155/2019/7591045>
- Wang F, Ma Z, Liu M, Wu X (2020) Potentially inappropriate medications at admission and discharge in older adults: A comparison of the beers 2019 and 2015 criteria. *International Journal of Clinical Pharmacology and Therapeutics* 58: 299–309. <https://doi.org/10.5414/CP203638>
- Wastesson JW, Morin L, Tan ECK, Johnell K (2018) An update on the clinical consequences of polypharmacy in older adults: a narrative review. *Expert Opinion on Drug Safety* 17: 1185–1196. <https://doi.org/10.1080/14740338.2018.1546841>
- Zhao M, Song J-X, Zheng F-F, Huang L, Feng Y-F (2021) Potentially inappropriate medication and associated factors among older patients with chronic coronary syndrome at hospital discharge in Beijing, China. *Clinical Interventions in Aging* 16: 1047–1056. <https://doi.org/10.2147/CIA.S305006>