

## Prevalence of Polypharmacy and Potentially Inappropriate Medications Prescribed among Elderly Inpatients in a Primary Care Setting of Pokhara, Nepal

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### ABSTRACT

**Introduction:** Polypharmacy, referred to as prescription several medications is major concern in the elderly population. Potentially inappropriate medications (PIMs) are those medications that should be avoided due to their adverse clinical effects. This study aimed to estimate the prevalence of polypharmacy and identify PIMs in primary care practice using Beer's criteria and the Screening Tool of Older People's Potentially Inappropriate Prescription (STOPP) criteria.

**Methods:** This was an observational cross-sectional study. A total of 102 elderly patients aged  $\geq 65$  years were enrolled in the study from a primary care centre in Pokhara, Nepal. A questionnaire comprising sociodemographic and prescribed medication information was used for data collection. Potentially inappropriate prescriptions were assessed using Beer's and STOPP criteria.

**Results:** The majority of the study population were females (53%) age group 65-74 years (74.5%). Comorbidities were common in 69% of the elderly, and major polypharmacy was prevalent in approximately 73% of the elderly. PIM prevalence rates of 36.12% and 6.86% were identified using the Beer's criteria and STOPP criteria, respectively.

**Conclusion:** This study reports the prevalence of polypharmacy and PIM prescriptions among elderly patients. Appropriate drug therapy can be achieved by using appropriate tools for the detection of PIM use in elderly patients. Further research on interventions related to PIMs is warranted to prevent adverse

**Keywords:** Adverse drug events, Beer's criteria, Elderly population, Polypharmacy, Potentially inappropriate medications, STOPP criteria

### INTRODUCTION

With increasing age organ functions is reduced leading to the emergence of different diseases.<sup>1</sup> For the prevention, treatment and rehabilitation of the illnesses, elderly people must take many medicines as a result of concurrent disorders.<sup>2</sup> Polypharmacy is defined as the concurrent use of multiple medications by the same patient and is most commonly defined as the use of  $\geq 5$  medicines.<sup>3,4</sup>

Polypharmacy poses a great risk to the elderly population owing to age-related changes that lead to altered pharmacokinetics and pharmacodynamics of medicine.<sup>1</sup> The consequences of polypharmacy include adverse drug events, medication cascade effects and drug interactions.<sup>5</sup> Polypharmacy is also linked with increased suffering from symptoms and decreased quality of life (QOL) in adults with advanced illness.<sup>6</sup>

Potentially inappropriate medicines (PIMs) refer to the use of medications whose actual

or potential harm exceeds the actual or potential benefits when equally or more effective therapeutic alternatives are available.<sup>7</sup> Medications that increase the likelihood of drug interactions and those misused, overused and underused are included in PIMs.<sup>8</sup> Various tools have been developed to enable healthcare professionals to verify potentially inappropriate medications. Beer's criteria and the Screening Tool of Older Person's Potentially Inappropriate Prescriptions (STOPP) are two widely recognized standard for PIMs.<sup>9</sup>

Safe and effective prescribing in the elderly population are particularly challenging. The exploration of polypharmacy and PIMs help to monitor the economic and disease burden.<sup>10</sup> To date, some studies<sup>11,12,13</sup> have investigated PIMs among geriatric patients.

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have investigated PIMs among geriatric patients. Studies found that 34.67%<sup>11</sup> and 21.6 %<sup>12</sup> had at least one PIM as identified by the 2012 and 2015 Beers criteria respectively. There is a scarcity of available literature that identifies the polypharmacy and investigate PIM using updated Beer's criteria and STOPP criteria. Therefore, this study was performed to explore the prevalence of polypharmacy and PIM prescribing for elderly inpatients in a primary care setting of Pokhara, Nepal.

## METHODS

The study was conducted on patients in a primary care hospital of ward number 30, Pokhara Metropolitan city. This study used an observational cross-sectional design. A Convenience sampling technique was applied for this study. As convenience sampling can lead to selection bias this technique was utilized as it is not time consuming. The study was carried out from January 28, 2020 to April 22, 2020. The target population was patients aged  $\geq 65$  years who attended healthcare centre. A sample size of  $>100$ , as suggested by WHO,<sup>14</sup> were included in the study by collecting data from all eligible participants.

The data were collected prospectively by using the data collection form. After obtaining informed consent from patients, they were asked the questions to assess sociodemographic characteristics (age, gender, medical history) in the data collection form. Medication data were gathered from the participant's medical records. Polypharmacy was categorized as: a. no polypharmacy ( $<2$  medications), b. minor polypharmacy (2-3 medications), c. moderate polypharmacy (4-5 medications), and major polypharmacy ( $>5$  medications).<sup>15</sup> We applied the American Geriatrics Society 2019 Beers Criteria and the STOPP criteria for the detection of PIM. Detection was based on the patient's medications used in the study period.

Permission to conduct this study was obtained from the Institutional Review Committee of Pokhara University, Nepal (Reference Number:130/076/077) and study approval was obtained from the study site.

Participants were informed about all aspects of the study before data collection. Signed informed

consent was obtained from each participant following a detailed explanation of the research purpose. The data from the study was entered in MS Excel and analyzed using SPSS version 20. Descriptive analyses were used to describe the patient's characteristics, prevalence of polypharmacy and potentially inappropriate medications. The concordance between the two PIM criteria was calculated using kappa tests. Statistical significance was set at  $p < 0.05$ .

## RESULTS

A total of 102 patients aged 65 years and above participated in the study (Table 1). Approximately 53% of the participants were females. The distribution of patients according to age group revealed that 74.5% of patients were 65-74 years old, while 18% and 8% were 75-84 years and 85 or above years, respectively. Most of the patients (69%) presented with comorbidities.

Table 1: Sociodemographic characteristics of patients attending the primary care hospital

Sociodemographic Variables	Frequency (%)
<b>Sex</b>	
Male	48 (47.1)
Female	54 (52.9)
<b>Age classification</b>	
65-74	76 (74.5)
75-84	18 (17.6)
$\geq 85$	8 (7.8)
<b>Smoking History</b>	
Yes	37 (36.3)
No	65 (63.7)
<b>Alcohol Intake</b>	
Yes	41 (40.2)
No	61 (59.8)
<b>Comorbidity</b>	
Yes	70 (68.6)
No	32 (31.4)

The number of medications prescribed for elderly individuals ranged from 3 to 15, with a total of 770 drugs prescribed to the study participants. Approximately 73% of the patients were prescribed six or more drugs (major polypharmacy) whereas the remaining patients were prescribed up to five drugs (minor or moderate polypharmacy) (Table 2).

Table 2: Prevalence of polypharmacy among elderly participants

Polypharmacy	Frequency (%)
Minor	4 (3.9)
Moderate	24 (23.5)
Major	74 (72.5)

Based on STOPP criteria, four PIM were identified among the elderly participants, which included metoprolol, prednisolone, tamsulosin, and cefixime + (ceftriaxone) (Table 3).

Table 3: List of Potential Inappropriate Medications (PIM) identified according to STOPP criteria

Drug Name	Frequency of PIMs	Reasons for inappropriateness
Metoprolol	3	Risk of masking hypoglycaemic symptoms
Prednisolone	2	Unnecessary exposure to long term side effects of systemic steroids
Tamsulosin	1	Risk of urinary frequency and worsening of incontinence
Cefixime + (Ceftriaxone)	1	Prescribing from the same class

The medications while reviewing through Beers Criteria identified proton pump inhibitors (e.g., pantoprazole, rabeprazole, omeprazole) as the most frequent PIMs (29 cases) whereas digoxin and nitrofurantoin as PIM shared 4 cases each (Table 4)

Drugs	Frequency	Reason for inappropriateness	Recommendation
<b>Pantoprazole</b>	24		Avoid scheduled use for >8 weeks unless for high-risk patients (e.g., oral corticosteroids or chronic NSAID use), erosive esophagitis, Barrett esophagitis, pathological hypersecretory condition, or demonstrated need for maintenance treatment
<b>Rabeprazole</b>	4		
<b>Omeprazole</b>	1	Risk of <i>Clostridium difficile</i> infection and bone loss and Fractures	
<b>Prazosin</b>	2	High risk of orthostatic hypotension and associated harms, especially in older adults; not recommended as routine treatment for hypertension; alternative agents	Avoid use as an antihypertensive
<b>Diazepam</b>	1	Older adults have increased sensitivity to benzodiazepines and decreased metabolism of long-acting agents; in general, all benzodiazepines increase the risk of cognitive impairment, delirium, falls, fractures, and motor vehicle crashes in older adult	Avoid
<b>Lorazepam</b>	1		

<b>Digoxin</b>	4	Use in atrial fibrillation: should not be used as a first-line agent in atrial fibrillation, because there are safer and more effective alternatives for rate control supported by high-quality evidence. Use in heart failure: evidence for benefits and harms of digoxin is conflicting and of lower quality	Avoid this rate control agent as first-line therapy for atrial fibrillation Avoid as first-line therapy for heart failure If used for atrial fibrillation or heart failure, avoid dosages >0.125 mg/day
<b>Nitrofurantoin</b>	4	Potential for pulmonary toxicity, hepatotoxicity, and peripheral neuropathy especially with long term use	Avoid in individuals with creatinine < 30 mL/min or for long term suppression
<b>Ketorolac</b>	3	Increased risk of gastrointestinal bleeding or peptic ulcer disease and acute kidney injury in older adults	Avoid chronic use
<b>Amiodarone</b>	2	Effective for maintaining sinus rhythm but has greater toxicities than other antiarrhythmics used in atrial fibrillation	Avoid as first-line therapy for atrial fibrillation unless the patient has heart failure or substantial left ventricular hypertrophy
<b>Cyproheptadine</b>	1	Highly anticholinergic; clearance reduced with advanced age	Avoid

There was no significant difference between the PIM identified using Beer's criteria and STOPP criteria ( $p=0.157$ ). The concordance between the two criteria was calculated using kappa tests where poor agreement between the two criteria ( $\kappa=0.102$ ) was observed as shown in Table 5.

Table 5: Concordance between Beers and STOPP criteria

Beers criteria PIM	STOPP criteria PIM		$\kappa$	p value
	Yes	No		
Yes	4	43	0.102	0.157
No	10	45		

## DISCUSSION

In this study, the prevalence of polypharmacy and PIM prescribed among the elderly population admitted to the primary care hospital of Pokhara, Nepal, was evaluated. Identification of inappropriate medications is very useful because this will help prevent overprescribing. This will help both the healthcare practitioners and the patients as well.

The majority of the study participants (53%) were females. This distribution pattern correlates with the male and female population ratio of Nepal (Census, 2021). The descending order of age groups, based on enrolled patient frequency, followed the pattern 65-74 years >75-84 years >85 or above years. The life expectancy of Nepal is around 71 years<sup>16</sup> and hence the majority of the elderly population were of the age group 65-74 years. The percentage of study participants who consumed alcohol (40%) was similar to the study results obtained for alcohol consumption patterns in western Nepal.<sup>17</sup> Furthermore, owing to 36% of participants with a smoking history, a similar prevalence was observed in a cross-sectional study among adults from Kathmandu, Nepal.<sup>18</sup> Most patients (69%) were presented with comorbidities attributable to the reduction of different organ functions with an increase in age.<sup>1</sup>

The number of medications prescribed for an elderly individual ranged from 3 to 15 drugs. Major polypharmacy (>5 medications) was prevalent among the elderly patients (73%) enrolled in our study. A cross-sectional study, performed in the United States with an aging population, determined



major polypharmacy in 36.8% of participants.<sup>15</sup> Previous study conducted by Giri et al identified that the prevalence of polypharmacy among 49.13% of patients.<sup>12</sup> Variations in the number of prescribed medications may result from differences in the prevalence of comorbidities, prescribing patterns, and health insurance policies that cover expenses.

The PIM poses a great clinical challenge for the optimal treatment of elderly patients. STOPP criteria identified PIMs in 6.86% of cases. In our study, the most frequently used PIM based on STOPP criteria was metoprolol. It is advised not to prescribe this drug because of the risk of masking the hypoglycemic symptoms.<sup>19</sup> Other PIMs included prednisolone (unnecessary exposure to long-term side effects of systemic steroids),<sup>20</sup> tamsulosin (risk of urinary frequency and worsening of incontinence),<sup>21</sup> and cefixime + (ceftriaxone) (prescribed from the same class).<sup>22</sup>

Alternatively, Beer's criteria identified PIMs in 39.2% of cases. This value is slightly higher than that reported in a study conducted in a tertiary Care hospital of western Nepal<sup>12</sup> while other reported similar results to the present study.<sup>11</sup> This discrepancy might be due to the difference in prescribing patterns and the nature of patients that are available in primary care and tertiary care centres. The most common PIMs, based on Beer's criteria were proton pump inhibitors followed by insulin, digoxin, and nitrofurantoin. This is consistent with the study done in India.<sup>23</sup> The Proton pump inhibitors, approved for the reduction of gastric acid production, are considered PIM attributable to their association with the risk of *Clostridium difficile* infection<sup>24</sup> and a potential increase in bone loss and fractures.<sup>25</sup> A study in Nepal<sup>26</sup> showed that prazosin was the most frequently prescribed drug followed by nitrofurantoin and amitriptyline. This variation in the findings may be due to the reason that the study is being conducted in different regions and prescription may vary according to region and time of the study.

The PIMs identified by STOPP criteria were significantly less than those identified by Beer's criteria. This observation complies with the study results in Lebanon<sup>27</sup> and Italy.<sup>28</sup> Consideration of the clinical

situation of patients in Beer's criteria makes it less specific as compared to STOPP criteria<sup>29</sup> resulting in more PIMs using Beer's criteria. A poor concordance was observed between Beers criterium and STOPP criteria as observed by the  $\kappa$  value  $< 0.40$ .<sup>30</sup> The low concordance suggests that the applicability of tools depends upon the specific population, setting and country in which it is used. This also suggests a need for a country-specific PIM list.

The use of PIMs is associated with a higher risk of adverse drug reactions and drug interactions in elderly.<sup>31</sup> Therefore, the utilization of suitable criteria (e.g., Beers and STOPP criteria) is important for the identification of PIM. Timely evaluation of PIMs and appropriate intervention is critical to avoid unwarranted therapeutic failure, avoid loss of time and money for nonoptimal healthcare, and improve the quality of life of the elderly.<sup>32,33</sup>

Our study had some limitations. The limited size of the study population may have affected the results. Since the tool we employed is used in USA and European countries the medications listed on the criteria may not have the same adverse effects in different population.

This study examined the profile of patients in primary healthcare facilities so the findings may not be applicable to the broader population. Further studies in the secondary and tertiary healthcare facilities are needed.

## CONCLUSION

The research indicates that use of polypharmacy was frequently employed among elderly individuals. It was demonstrated that PIMs were prevalent in less than half of the elderly in our sample. Appropriate tools for the detection of PIM use in elderly patients will be useful in identifying inappropriate prescriptions. It is necessary to employ an interdisciplinary approach to monitor the utilization of medication in elderly population.

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**CONFLICT OF INTEREST**

The author declares no conflict of interest, financial or otherwise.

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**REFERENCES**

1. Drenth-van Maanen AC, Wilting I, Jansen PA. Prescribing medicines to older people—How to consider the impact of ageing on human organ and body functions. *British journal of clinical pharmacology*. 2020 Oct; 86(10):1921-30.
2. Nobili A, Garattini S, Mannucci PM. Multiple diseases and polypharmacy in the elderly: challenges for the internist of the third millennium. *Journal of comorbidity*. 2011;1(1):28-44.
3. Abdulah R, Insani WN, Destiani DP, Rohmaniasari N, Mohenathas ND, Barliana MI. Polypharmacy leads to increased prevalence of potentially inappropriate medication in the Indonesian geriatric population visiting primary care facilities. *Therapeutics and clinical risk management*. 2018 Sep 4:1591-7.
4. Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. *BMC geriatrics*. 2017 Dec;17: 1-0.
5. Salazar JA, Poon I, Nair M. Clinical consequences of polypharmacy in elderly: expect the unexpected, think the unthinkable. *Expert opinion on drug safety*. 2007 Nov 1;6(6):695-704.
6. Schenker Y, Park SY, Jeong K, Pruskowski J, Kavalieratos D, Resick J, Abernethy A, Kutner JS. Associations between polypharmacy, symptom burden, and quality of life in patients with advanced, life-limiting illness. *Journal of general internal medicine*. 2019 Apr 15;34:559-66.
7. Zhang X, Zhou S, Pan K, Li X, Zhao X, Zhou Y, Cui Y, Liu X. Potentially inappropriate medications in hospitalized older patients: a cross-sectional study using the Beers 2015 criteria versus the 2012 criteria. *Clinical interventions in aging*. 2017 Oct 12:1697-703.
8. Spinewine A, Schmader KE, Barber N, Hughes C, Lapane KL, Swine C, Hanlon JT. Appropriate prescribing in elderly people: how well can it be measured and optimised?. *The Lancet*. 2007 Jul 14;370(9582):173-84.
9. Vatcharavongvan P, Prasert V, Ploylearmsang C, Puttawanchai V. Prevalence and factors that influence potentially inappropriate medication use among Thai elderly in primary care settings. *Canadian Geriatrics Journal*. 2021 Dec;24(4):332.
10. Unutmaz GD, Soysal P, Tuven B, Isik AT. Costs of medication in older patients: before and after comprehensive geriatric assessment. *Clinical interventions in aging*. 2018 Apr 9:607-13.
11. Basnet S, Paudel KR, Sah AK, Jha RK, Sah P, Adhikari S, Shrestha S. Prescribing pattern, polypharmacy and potentially inappropriate prescribing in hospitalized elderly patients: a retrospective study in a teaching hospital in Nepal. *Int J Sci Rep*. 2016 Jan 2;2(1):7-12.
12. Giri SA, Khan GM. Prescribing pattern and appropriateness of prescription among elderly patients in a tertiary care hospital of Western Nepal—a prospective cross-sectional study. *Asian J Pharm Clin Res*. 2020;13(4):126-31.
13. Rijal S, Adhikari K, Sigdel D, Mallik SK. Prescribing pattern of drugs in geriatrics patients using beers criteria. *Journal of Nepal Health Research Council*. 2019; 17 (2), 153-157
14. Sisay M, Mengistu G, Molla B, Amare F, Gabriel T. Evaluation of rational drug use based on World Health Organization core drug use indicators in selected public hospitals of eastern Ethiopia: a cross sectional study. *BMC health services research*. 2017 Dec;17(1):1-9.
15. Young EH, Pan S, Yap AG, Reveles KR, Bhakta K. Polypharmacy prevalence in older adults seen in United States physician offices from 2009 to 2016. *PLoS One*. 2021 Aug 3;16(8):e0255642.
16. Yadav UN, Yadav OP, Singh DR, Ghimire S, Rayamajhee B, Mistry SK, Rawal LB, Ali AM, Tamang MK, Mehta S. Perceived fear of COVID-19 and its associated factors among Nepalese older adults in eastern Nepal: A cross-sectional study. *Plos one*. 2021 Jul 26;16(7):e0254825.
17. Adhikari TB, Rijal A, Kallestrup P, Neupane D. Alcohol consumption pattern in western Nepal: findings from the COBIN baseline survey. *BMC psychiatry*. 2019 Dec;19:1-8.

18. Simkhada R, Wasti SP, Gc VS, Lee AC. Prevalence of depressive symptoms and its associated factors in older adults: a cross-sectional study in Kathmandu, Nepal. *Aging & mental health*. 2018 Jun 3;22(6):802-7.
19. Dungan K, Merrill J, Long C, Binkley P. Effect of beta blocker use and type on hypoglycemia risk among hospitalized insulin requiring patients. *Cardiovascular diabetology*. 2019 Dec;18:1-9.
20. Waljee AK, Rogers MA, Lin P, Singal AG, Stein JD, Marks RM, Ayanian JZ, Nallamothu BK. Short term use of oral corticosteroids and related harms among adults in the United States: population based cohort study. *bmj*. 2017 Apr 12;357.
21. Kakizaki H, Lee KS, Yamamoto O, Jong JJ, Kattou D, Sumarsono B, Uno S, Yamaguchi O. Mirabegron add-on therapy to tamsulosin for the treatment of overactive bladder in men with lower urinary tract symptoms: a randomized, placebo-controlled study (MATCH). *European Urology Focus*. 2020 Jul 15;6(4):729-37.
22. Regnier B. Comparative study of intravenous ceftriaxone followed by oral cefixime versus ceftriaxone alone in the treatment of severe upper urinary tract infections. *Presse Medicale* 1989 Oct 1;18(32):1617-21.
23. Sharma R, Bansal P, Garg R, Ranjan R, Kumar R, Arora M. Prevalence of potentially inappropriate medication and its correlates in elderly hospitalized patients: A cross-sectional study based on Beers criteria. *Journal of Family & Community Medicine*. 2020 Sep;27(3):200.
24. Freedberg DE, Salmasian H, Friedman C, Abrams JA. Proton pump inhibitors and risk for recurrent *Clostridium difficile* infection among inpatients. *The American journal of gastroenterology*. 2013 Nov;108(11):1794-1801.
25. Yang YX, Lewis JD, Epstein S, Metz DC. Long-term proton pump inhibitor therapy and risk of hip fracture. *Jama*. 2006 Dec 27;296(24):2947-53.
26. Koirala B, Rauniyar GP, Sharma SK, Analysis of inappropriate medication use and drug interaction in older people visiting tertiary care centre of eastern Nepal. *International Journal of Basic and Clinical Pharmacology* 2022; 11;219-222
27. Sakr S, Hallit S, Haddad M, Khabbaz LR. Assessment of potentially inappropriate medications in elderly according to Beers 2015 and STOPP criteria and their association with treatment satisfaction. *Archives of Gerontology and Geriatrics*. 2018 Sep 1; 78:132-8.
28. Di Giorgio C, Provenzano A, Polidori P. Potentially inappropriate drug prescribing in elderly hospitalized patients: an analysis and comparison of explicit criteria. *International journal of clinical pharmacy*. 2016 Apr; 38:462-8.
29. Hajjar ER, Cafiero AC, Hanlon JT. Polypharmacy in elderly patients. *The American journal of geriatric pharmacotherapy*. 2007 Dec 1;5(4):345-51.
30. Ma Z, Zhang C, Cui X, Liu L. Comparison of three criteria for potentially inappropriate medications in Chinese older adults. *Clinical interventions in aging*. 2019 Dec 28;65-72.
31. Miller MG, Kneuss TG, Patel JN, Parala-Metz AG, Haggstrom DE. Identifying potentially inappropriate medication (PIM) use in geriatric oncology. *Journal of Geriatric Oncology*. 2021 Jan 1;12(1):34-40.
32. O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. *Age and ageing*. 2014 Oct 16;44(2):213-8.
33. Saka SA, Nlooto M, Oosthuizen F. American Geriatrics Society-Beers Criteria and adverse drug reactions: a comparative cross-sectional study of Nigerian and South African older inpatients. *Clinical Interventions in Aging*. 2018 Nov 19;2375-87.