Advances in Medical, Pharmaceutical and Dental Research Journal (AMPDR)- ISSN 2812-4898
http://dx.doi.org/10.21622/AMPDR.2025.05.2.1365

June 2025
Volume 5
Issue 2

Geriatric prescribing patterns: A Beers 2023 criteria pharmacoepidemiologic analysis, Alexandria, Egypt

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Received on, 22 May 2025 - Accepted on, 09 July 2025 - Published on, 18 August 2025

ABSTRACT:

Background: *In the geriatric population, the appropriateness of medication requires meeting multiple criteria, such as having a clear evidence-based indication, being well-tolerated by the majority, and being sufficiently cost-effective. In African countries, standardized Potentially Inappropriate Medication use criteria are rarely used.*

Aim: *We aimed in this study to estimate the prevalence of inappropriate medication prescribing patterns among geriatric patients aged 65 years or more in Alexandria, Egypt, and to determine the characteristics and risk factors for such patterns.*

Methods: *Cluster sampling was used as the sampling technique, and the sample size reached 1,000 prescriptions representing all districts of the Alexandria governorate. The updated 2023 Beers Criteria were utilized to identify potentially inappropriate prescribing. Inappropriate prescribing was considered if at least one inappropriate medication fell into at least one of the categories mentioned in the 2023 Beers Criteria.*

Results: *About 64.1% of prescriptions included three or more medications. Notably, 31.8% of prescriptions contained three medications, while 25.5% included four medications. A total of 463 (46.3%) prescriptions were potentially inappropriate. The full logistic regression model, which included all predictors, was statistically significant, χ^2 (20, N=1147) = 372.825, p < .001. Several independent variables made a unique statistically significant contribution to the model, including district, physician grade, and the number of medications prescribed.*

Conclusion: *It is advisable to standardize prescribing systems, particularly for the older population.*

KEYWORDS:

Geriatric, Prescribing patterns, Beers, Pharmacoepidemiologic, Egypt.

1. Background:

In the geriatric population, the judgment of whether a medication is appropriate necessitates fulfilling a multitude of criteria such as having a clear evidence-based indication, being well-tolerated by the majority, and being sufficiently cost-effective. Appropriate prescribing in older people also encompasses considering an individual patient's life expectancy, avoiding preventive therapies in those with a poor survival prognosis, and promoting drugs with favorable risk-benefit ratios. Conversely, medicines that are potentially inappropriate in geriatrics either lack a clear evidence-based indication, carry a substantially higher probable risk of adverse events compared to younger people, or lack considerable cost-effectiveness. [1]

With the ongoing change in demographics and the increasing number of older patients, medication use has gradually turned into polypharmacy, which is the prescribing of multiple medications, most commonly defined as ≥ 5 medications for the older patients' therapeutic management. This, in turn, increases the risk of associated adverse events, causing morbidity and even leading to mortality. Consequently, polypharmacy has become a major concern worldwide, especially in Low- and Middle-Income Countries (LMICs). [2,3]

Prescribers for the geriatric population with multiple comorbidities have a heightened potential to commit various types of prescribing

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errors. Several complex and interrelated factors contribute to these errors, including a lack of knowledge about the unique physiology of older adults, principles of geriatric medicine, and their implications for pharmacotherapy in this population. Overprescribing often results in inappropriate prescribing, while underprescribing can lead to the omission of necessary medications. [4,5]

Several countries have developed their standards for identifying potentially inappropriate medication prescribing errors in the older population, providing a clinical reference. The American Geriatrics Society's (AGS) Beers Criteria (Beers Criteria) is one such standard, designed to assess potentially inappropriate medication use in the older population. It is extensively used by clinicians, researchers, medical administrative staff, educators, and regulators. The criteria primarily focus on the safety of medication use in the older population. An advantage of the Beers Criteria is that it is evidence-based and utilizes the Delphi validation approach to reach expert consensus, thereby creating a list of inappropriate drugs for older patients. [6]

The recently updated version of the Beers Criteria was launched in 2023. The updated Beers Criteria defines the drugs and drug lists that the AGS and its panel of experts have reached a consensus to consider as potentially inappropriate for use in older patients. The panel categorized these drugs into the same five main categories developed in the previous 2019 update: medications considered potentially inappropriate, medications considered potentially inappropriate for patients with specific diseases or syndromes, medications to be used with caution, medications with potentially inappropriate drug-drug interactions, and medications requiring dose adjustment based on renal function. [7,8]

A recent systematic review on the prevalence of Potentially Inappropriate Medication (PIM) use among the older population revealed that African countries rarely use standardized PIM use criteria. The findings suggest that this may be the highest contributor to the high prevalence of PIM use in this region. [9] These findings represent a milestone that highlights the emerging need for a thorough evaluation of PIM use among the older population in African countries. They have mobilized our enthusiasm to start with Egypt as a prototype for such an evaluation in our diligent pursuit to minimize PIM use in the older population.

In Egypt, to the best of our knowledge, there are no available studies that specifically address inappropriate medication prescribing in older adults, despite the increasing proportion of this population segment. According to World Bank/ United Nations (UN) data accessed via FRED, individuals aged 65 years and older constituted approximately 4.97% of the total population in 2023, reflecting a gradual but significant demographic shift toward an aging society. [10]

Defining inappropriate medications using explicit lists of criteria, such as the Beers Criteria, may miss some issues like therapeutic duplication within a drug class.

Therapeutic duplication in drug class prescriptions (also called therapeutic duplicates) increases the potential risk of adverse drug reactions without providing any additional therapeutic benefits. Therefore, it is crucial to pay close attention to each prescribed drug due to the evidence-supported increase in both the risk of adverse drug events and the associated costs, which consequently contribute to the economic burden. Identifying therapeutic duplication is essential for optimizing polypharmacy. [11]

In this study, we aim to estimate the prevalence of inappropriate medication prescribing patterns among geriatric patients aged 65 years or older in Alexandria, Egypt, and to determine the characteristics and risk factors for such patterns.

2. Methods:

a. *Study population:*

The total number of medication prescriptions for geriatric patients aged 65 years and older resides in the nine districts of Alexandria governorate, Egypt. The geographical distribution of these districts was obtained from the official Alexandria governorate website. Our sample size calculations included 1000 prescriptions, representing the study population. Data collection and assessment of medication prescriptions were conducted at community pharmacies within each district.

b. *Sample size calculation:*

Sample size estimation depends on the statistical analysis type. We planned to use three different types, calculating the minimum required sample size for each to ensure adequate power and precision:

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i. For prevalence estimation, we employed the formula [12]:

$$n = \frac{Z^2 P(1-P)}{d^2}$$

Where: n sample size, **Z**= Z statistic for level of confidence, **p**=expected prevalence or proportion, **d**= precision.

Accepting 5% error in our estimate and to achieve a study power of 80%, with a 95% confidence level, Z= 1.96, d= .05, and p= 0.5 (the safest choice for estimating population proportion is 0.5 as it presents the largest sample size to be estimated). [13]

The estimated sample size calculated was 384 but as we used a sampling method other than simple random sampling a larger sample size was to be needed because of the "design effect", for a cluster sampling strategy the design effect might be estimated as 2 [13], so the calculated sample size after adjustment for "design effect" was 768.To reduce sampling error, a round figure for sample size of 1000 had been taken.

For Chi-square analysis: we consulted sample size estimation tables [14], aiming for 80% power, 5% significance level, 8 degrees of freedom (based on up to 9 categories for a variable), and an expected effect size of 0.2 [14]. The calculated sample size was 376, confirming that our selected sample size of 1000 is sufficient for conducting Chi-square analyses between each pair of selected categorical variables.

For multiple logistic regression: In logistic regression, a common guideline suggests that you need approximately 10 events for each variable to achieve reasonably stable estimates of the regression coefficients. [15]

We expected that the proportion of inappropriate medication prescribing would be at least 24%, comparable to the proportion studied for community-dwelling patients in the United States. [16] Consequently, there would be at least 240 events in our sample size of 1000. Therefore, adhering to the rule of thumb, we can conduct a multiple logistic regression analysis with up to 24 independent variables. In our case, we have only five independent variables, which means we have approximately 48 events or outcomes per variable. Thus, a sample size of 1000 would be adequate to perform a multiple logistic regression analysis.

c. Sampling technique:

To select a sample of medication prescriptions depending on the principle of simple random sampling we should get a list or sampling frame for these medication prescriptions (population of N units) and a sample of n units is selected randomly from that population of N units without replacement so that each of the possible samples has the same probability of selection.

As there is no available sampling frame for the population of medication prescriptions in the visited community pharmacies in each defined district, so it is justified to use the principle of cluster sampling.

Cluster sampling is most useful when the homogeneity among units within clusters is not more than the homogeneity among units in the population as a whole and this was evident for the present study because the variability between the individual prescriptions within each district-specific community pharmacy is almost the same between the individual prescriptions within all the visited community pharmacies in all districts (whole population) and this is due to the presence of the same market drug list available for prescription. In such instances, cluster sampling can result in a considerable reduction in sampling frame construction without resulting in a significant increase in sampling errors. [17]

d. Data collection:

i. Basic data collection:

At each visit, the following data had been documented from each sampled prescription through prescription reviewing: ***1. Patient characteristics:*** patient name, patient age, patient sex, and diagnosis. ***2. Physician characteristics:*** Clinic specialty (Orthopedic, Internal medicine, etc.), and physician grade [General Practitioner (GP), specialist, or consultant]. ***3. Prescription characteristics:*** Number of medications, name of medications, dose of medications, presence of at least one drug–drug interaction, presence of at least one drug class duplication.

ii. Assessment for drug class duplication or drug-drug interactions:

The American Hospital Formulary Services (AHFS) Pharmacologic-Therapeutic Classification serves as a reliable reference for assessing therapeutic duplication.

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The AHFS Pharmacologic-Therapeutic Classification was developed and is maintained by the American Society of Health-System Pharmacists, the national professional association representing pharmacists who practice in inpatient, outpatient, home-care, and long-term-care settings. The American Society of Health-System Pharmacists has a long history of fostering evidence-based medication use and patient medication safety. [18] The assessment for drug class duplication was conducted according to the AHFS classification.

Drug-drug interactions were determined through screening the entire list of medications in the prescription against a reliable checking tool, ***Lexicomp's online Comprehensive Interaction Analysis Program***, which is a complete drug and herbal interaction analysis program. One can enter a patient's entire regimen, identify potential interactions, and obtain appropriate patient management steps. The analysis includes a summary of drug interactions with an assigned risk rating to identify the action steps necessary. Each letter designation (A, B, C, D, X) represents the severity level of the identified interaction. A detailed interaction monograph is displayed by clicking on the interacting drug name. Lexicomp's online Comprehensive Interaction Analysis Program excelled as a personal digital assistant pharmacopoeia for assessing drug interactions, thoughtfully designed to provide quickly accessible, exceptionally reliable information. A drug-drug interaction is defined as having at least one either D or X risk rating interaction using Lexicomp's online Comprehensive Interaction Analysis Program. [19]

iii. Assessment of inappropriate medication prescribing:

The medications were reviewed by the investigator using the updated 2023 Beers Criteria to identify potentially inappropriate prescribing. Inappropriate prescribing was considered if at least one inappropriate medication was identified in the prescription, falling into at least one of the mentioned categories stated in the 2023 Beers Criteria: medications considered potentially inappropriate, medications deemed potentially inappropriate for patients with specific diseases or syndromes, medications that should be used with caution, and medications with potentially inappropriate drug-drug interactions. [8]

e. Statistical analysis:

Statistical analysis was conducted using IBM® SPSS® Statistics version 27. Data integrity was checked and verified via the frequency checks for the qualitative variables, as well as minimum and maximum checks for the quantitative variables, ensuring that no errors or missing values are present. Descriptive statistics were utilized to present qualitative variables in terms of frequencies and percentages. For the analytical statistics, a multivariate logistic regression analysis was conducted to examine the associations between the independent variables—' Patient age,' 'Patient gender,' 'Physician grade,' 'Clinical specialty,' and 'Number of prescription medications'—and the outcome variable, inappropriate medication prescribing according to the 'Beers Criteria 2023." The regression coefficients (βs) indicate the magnitude of increase or decrease in the log odds of the outcome variable for each unit change in the independent variable, while keeping all other variables constant. The Standard Error (SE) estimates the variability (precision) of the regression coefficient.

Selecting a model-building strategy is closely tied to the choice of independent variables. In logistic regression, two approaches are commonly employed, each having its own focus and purpose: direct (also known as full, standard, or simultaneous) and stepwise (known as Statistical). [20] These strategies are not necessarily interchangeable, as they can generate different model fit statistics and independent variable estimates from the same data. Thus, it is crucial to identify the appropriate model that aligns with one's research objectives. The direct approach is a default of sorts, as it enters all independent variables into the model at the same time and makes no assumptions about the order or relative worth of these variables. The direct approach is best if there is a priori knowledge of the independent variables and their relevance to the outcome variable. [21]

Stepwise regression identifies independent variables to keep or remove from the model based on predefined statistical criteria influenced by the unique characteristics of the sample being analyzed. Although stepwise regression is frequently used in clinical research, its use is somewhat controversial because it relies on automated variable selection that tends to take advantage of random chance factors in a given sample. Additionally, stepwise regression may produce models that do not seem entirely reasonable from a biological perspective. Given these concerns, some argue that stepwise regression is best reserved for preliminary screening or hypothesis testing only, such as with novel outcomes and limited understanding of independent variable contributions. Accordingly, we preferred to use the direct (enter) method for model building in our study. [22]

6. Results:

Our study included a total of 1,000 patient prescriptions, of which 580 patients were males (58%) and 420 were females (42%). The mean age of the patients was 71.85 ± 4.3 years, ranging from 63 to 86 years. The majority of the patients (76.3%) were between 66 and 80 years old. Patients were almost evenly distributed across the nine districts, each accounting for approximately 11% of the total population. **Table 1** shows the demographics of the study patients according to their assessed prescriptions.

The majority of assessed prescriptions (72.4%) were issued by specialist physicians, with internal medicine being the most common specialty (42.8%), as shown in **Table 2**. Additionally, 64.1% of prescriptions included three or more medications. Notably, 31.8% of prescriptions contained three medications, while 25.5% included four medications. These findings highlight the significant role of specialists in the prescribing process and the widespread occurrence of polypharmacy in older patients.

Table 1. Demographic characteristics for patients whose prescriptions were assessed

Patient demographics	(Mean ± SD)	(Min. - Max.)	Frequency (%)
Gender			
Males			580 (58)
Females			420 (42)
Age in years:	**(71.93 ± 4.24)**	**(65 - 86)**	
65 – 70			456 (45.6)
71 – 75			332 (33.2)
76 – 80			152 (15.2)
81 – 85			57 (5.7)
86 – 90			3 (0.3)
District			
Al Montazah Awal			111 (11.1)
Al Montazah Tany			111 (11.1)
Eastern District			111 (11.1)
Central District			111 (11.1)
Western District			111 (11.1)
Al Gomrok			111 (11.1)
Al Amreya			110 (11.0)
Al Agamy			112 (11.2)
Borg Al Arab			112 (11.2)

Table 2. Characteristics of prescriptions included in the study

Prescription characteristics	Frequency (%)
Prescribing Physician Grade	
General Practitioner (GP)	46 (4.6)
Specialist	724 (72.4)
Consultant	230 (23)
Prescription specialty	
Internal medicine	428 (42.8)
Neuro-psychiatry	88 (8.8)
Urology	125 (12.5)
Orthopedic	57 (5.7)
Chest	145 (14.5)
General Surgery	71 (7.1)
E.N.T.	40 (4.0)
Ophthalmology	46 (4.6)
Prescription's number of medications	
One	26 (2.6)
Two	244 (24.4)
Three	318 (31.8)
Four	255 (25.5)
Five	83 (8.3)
Six	49 (4.9)
Seven	24 (2.4)
Eight	1 (0.1)

The full model containing all predictors was statistically significant, χ^2 (20, N=1147) = 372.825,

Advances in Medical, Pharmaceutical and Dental Research Journal (AMPDR)- ISSN 2812-4898
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$p < .001$, indicating that the model was able to distinguish between respondents who were compliant versus non-compliant with Beers criteria 2023. The model explained between 31.1% (Cox & Snell R^2) and 41.6% (Nagelkerke R^2) of the variance in compliance status and correctly classified 77.5% of cases. The Hosmer-Lemeshow test was non-significant, χ^2 (8) = 14.954, p = .060, indicating good model fit. [21,22]

As shown in **table 3**, several independent variables made a unique statistically significant contribution to the model (district, physician grade, and the number of medications prescribed).

The findings show that the strongest predictor of non-compliance with Beers criteria 2023 among assessed prescriptions was the number of medications prescribed, recording an odds ratio of 3.234. This indicates that the odds of non-compliance are 3.234 times higher for each additional medication prescribed, while controlling for all other factors included in the model.

The findings show that the strongest predictor of non-compliance with Beers Criteria 2023 among assessed prescriptions is the number of medications prescribed, with an odds ratio of 3.234. This indicates that the odds of non-compliance are 3.234 times higher for each additional medication prescribed, while controlling for all other factors included in the model. Although the odds ratio for physician grade General Practitioner (GP) is higher in value, at 10.105, indicating that physicians with a grade of 1 have significantly higher odds of having non-compliant prescriptions, this higher odds ratio reflects a specific subgroup effect rather than a general trend applicable to all cases. The Beers criteria 2023 appropriateness status for the significant contributors is shown in **Table 4**, and a general Beers criteria 2023 appropriateness distribution according to the physician grade is shown in **Figure 1**.

Table 3: Logistic Regression Predicting Likelihood of Compliance with Beers Criteria

Predictor	β	SE	P-value	Odds Ratio	95% CI for Odds Ratio
District (Al Montazah Tany)	0.879	0.340	0.010	2.409	1.236 – 4.695
District (Eastern District)	1.177	0.339	0.001	3.245	1.678 – 6.277
District (Central District)	1.109	0.341	0.001	3.032	1.568 – 5.862
District (Western District)	0.973	0.332	0.003	2.646	1.400 – 5.000
Physician Grade (GP)	2.313	0.438	<0.001	10.105	4.288 – 23.799
Physician Grade (Specialist)	0.806	0.209	<0.001	2.240	1.496 – 3.355
Number of Medications Prescribed	1.174	0.085	<0.001	3.234	2.746 – 3.812
Constant	-6.939	1.419	<0.001	0.001	

Table 4: Beers criteria 2023 categories appropriateness status for significant contributors

Predictor	Potentially Inappropriate medication n (%)		Potentially Inappropriate medication for a certain disease n (%)		Medication should be used with caution n (%)		The medication dose should be adjusted n (%)		Potential drug-drug interaction n (%)		Duplication n (%)	
	Appropriate	Inappropriate	Appropriate	Inappropriate	Appropriate	Inappropriate	Appropriate	Inappropriate	Appropriate	Inappropriate	Appropriate	Inappropriate
District												
Al Montazah Awal	99 (89.2)	12 (10.8)	98 (88.3)	13 (11.7)	89 (80.2)	22 (19.8)	98 (88.3)	13 (11.7)	95 (85.6)	16 (14.4)	99 (89.2)	12 (10.8)
Al Montazah Tany	79 (71.2)	32 (28.8)	91 (82)	20 (18)	88 (79.3)	23 (20.7)	94 (84.7)	17 (15.3)	93 (83.8)	18 (16.2)	91 (82)	20 (18)
Eastern District	86 (77.5)	25 (22.5)	86 (77.5)	25 (22.5)	98 (88.3)	13 (11.7)	97 (87.4)	14 (12.6)	93 (83.8)	18 (16.2)	99 (89.2)	12 (10.8)
Central District	83 (74.8)	28 (25.2)	86 (77.5)	25 (22.5)	91 (82)	20 (18)	95 (85.6)	16 (14.4)	89 (80.2)	22 (19.8)	94 (84.7)	17 (15.3)
Western District	87 (78.4)	24 (21.6)	90 (81.1)	21 (18.9)	96 (86.5)	15 (13.5)	100 (90.1)	11 (9.9)	89 (80.2)	22 (19.8)	104 (93.7)	7 (6.3)
Al Gomrok	93 (83.8)	18 (16.2)	89 (80.2)	22 (19.8)	99 (89.2)	12 (10.8)	100 (90.1)	11 (9.9)	94 (84.7)	17 (15.3)	104 (93.7)	7 (6.3)
Al Amreya	90 (81.8)	20 (18.2)	87 (79.1)	23 (20.9)	94 (85.5)	16 (14.5)	99 (90)	11 (10)	93 (84.5)	17 (15.5)	103 (93.6)	7 (6.4)
Al Agamy	97 (86.6)	15 (13.4)	91 (81.3)	21 (18.8)	99 (88.4)	13 (11.6)	103 (92)	9 (8)	97 (86.6)	15 (13.4)	106 (94.6)	6 (5.4)
Borg Al Arab	92 (82.1)	20 (17.9)	93 (83)	19 (17)	89 (79.5)	23 (20.5)	98 (87.5)	14 (12.5)	92 (82.1)	20 (17.9)	107 (95.5)	5 (4.5)
Physician Grade												
GP	33 (71.7)	13 (28.3)	33 (71.7)	13 (28.3)	31 (67.4)	15 (32.6)	43 (93.5)	3 (6.5)	33 (71.7)	13 (28.3)	40 (87)	6 (13)
Specialist	583 (80.5)	141 (19.5)	575 (79.4)	149 (20.6)	598 (82.6)	126 (17.4)	633 (87.4)	91 (12.6)	602 (83.1)	122 (16.9)	654 (90.3)	70 (9.7)
Consultant	190 (82.6)	40 (17.4)	203 (88.3)	27 (11.7)	214 (93)	16 (7)	208 (90.4)	22 (9.6)	200 (87)	30 (13)	213 (92.6)	17 (7.4)
Number of prescription medications												
1 - 3	533 (90.6)	55 (9.4)	523 (88.9)	65 (11.1)	560 (95.2)	28 (4.8)	558 (94.9)	30 (5.1)	574 (97.6)	14 (2.4)	581 (98.8)	7 (1.2)
4 - 6	265 (68.5)	122 (31.5)	269 (69.5)	118 (30.5)	277 (71.6)	110 (28.4)	306 (79.1)	81 (20.9)	257 (66.4)	130 (33.6)	320 (82.7)	67 (17.3)
7 - 8	8 (32)	17 (68)	19 (76)	6 (24)	6 (24)	19 (76)	20 (80)	5 (20)	4 (16)	21 (84)	6 (24)	19 (76)

Advances in Medical, Pharmaceutical and Dental Research Journal (AMPDR)- ISSN 2812-4898
http://dx.doi.org/10.21622/AMPDR.2025.05.2.1365

Table 5. Frequency distribution of the inappropriate medications identified based on the Beers criteria 2023

Drug name	Frequency	%
Indomethacin	281	28.13
Nitrofurantoin	130	12.96
Hyoscyamine	78	7.83
Amitriptyline	69	6.91
Ketorolac	22	2.18
Nifedipine (immediate release)	26	2.55
Chlorpheniramine	57	5.65
Thioridazine	18	1.82
Diphenhydramine (oral)	15	1.46
Methyldopa	30	3
Amiodarone	34	3.37
Metoclopramide	91	9.11
Digoxin	77	7.75
Spironolactone > 25 mg/day	32	3.18
Benztropine	16	1.63
Haloperidol	12	1.19
Chlorzoxazone	5	0.46
Orphenadrine	8	0.82

Table 6. List of the most frequent drug-drug interactions detected according to Beers criteria 2023

Drug – drug interaction	Frequency	%	Risk category
Amiodarone + Digoxin	25	14.5	D
Diclofenac + Furosemide	19	11	D
Carbamazepine + Phenytoin	13	7.5	D
Amiodarone + Warfarin	9	5.2	D
Captopril + Allopurinol	8	4.6	D
Others	99	57.5	

Table 7. List of the most frequent five drug class duplications detected according to the Beers criteria 2023

Drug class duplication	Frequency	%	AHFS* Code
Diclofenac + Ibuprofen	41	16.9	28:08.04.92
Allopurinol + Colchicine	35	14.4	92:16
Nitrofurantoin + Trimethoprim	25	10.3	8:36
Diclofenac + Indomethacin	24	9.9	28:08.04.92
Amitriptyline + Clomipramine	12	4.9	28:16.04.28
Others	106	43.6	

*American Hospital Formulary Services

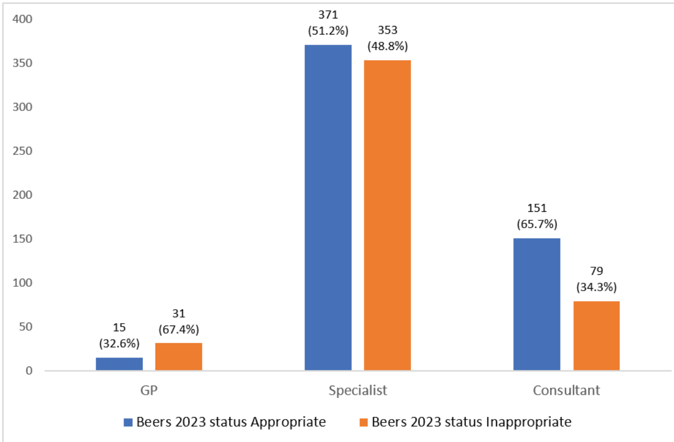

Figure 1. Distribution of appropriateness according to Beers criteria 2023 by physician grade

7. Discussion:

Inappropriate prescribing can be attributed to various factors that must be addressed to optimize current prescribing approaches. Conceptually, prescribing can be seen as a function influenced by the patient, the prescriber, and the environment.

The primary factor in prescribing decisions should be the clinical needs of the patient. Prescribing should prioritize evidence-based therapies and minimize the use of medications that lack clinical necessity or proven efficacy. Additionally, patients' expectations can considerably influence these decisions. [23]

Prescribing is primarily the responsibility of physicians who rely on their clinical experience and personal attitudes to make final decisions. Inadequate training in geriatric pharmacotherapy is a significant factor that can heavily contribute to inappropriate prescribing. For instance, some prescribers may avoid prescribing a medication or increasing its dose simply because the patient is an older patient, a practice known as ageism.

Additionally, inappropriate prescribing can arise from a lack of communication between physicians practicing in different settings or even between specialists practicing in the same setting. [23,24]

The environment in which the prescriber operates can significantly influence prescribing decisions. For instance, acute care settings often do not prioritize the review of patients' chronic and preventive medications. Additionally, a lack of systems or structures for sharing drug-related information during transitions between care settings can negatively impact the quality of care provided. [25]

It should be noted that several medications were not evaluated for various reasons. Some medications, such as Trimethobenzamide, Mesoridazine, and Desiccated Thyroid extract, were not available in Egypt. Additionally, some medications, such as Pentazocine and Amphetamines, are classified as controlled substances by the Egyptian Ministry of Health (MOH) and, consequently, cannot be dispensed at ordinary community pharmacies. These factors may contribute to the underestimation of inappropriate prescriptions. In our study, we identified the most prevalent potentially inappropriate medications according to the Beers Criteria 2023. This included indomethacin, a non-steroidal anti-inflammatory drug (NSAID); nitrofurantoin (antimicrobial); hyoscyamine (antispasmodic); amitriptyline (antidepressant); amiodarone (antiarrhythmic); methyldopa (antihypertensive); and chlorpheniramine (antihistamine). Together, these drugs accounted for approximately 87% of all potentially inappropriate medications. **(Table 5)**

The study identified that the most frequent drug–drug interaction (DDI) was between amiodarone and digoxin, accounting for 14.5% of all interactions. This combination significantly increases the risk of digoxin toxicity due to amiodarone's inhibition of P-glycoprotein, which reduces digoxin clearance. Clinical consequences may include bradycardia, arrhythmias, and gastrointestinal disturbances, necessitating close monitoring of serum digoxin levels and dose adjustments [26,27].

Other notable DDIs included diclofenac with furosemide (11%) and carbamazepine with phenytoin (7.5%). Diclofenac may blunt the diuretic and antihypertensive effects of furosemide, posing risks of fluid retention, hypertension, and renal impairment, particularly in elderly or renally compromised individuals [28]. The carbamazepine-phenytoin combination presents risks of central nervous system toxicity, sedation, and potential hepatic enzyme induction, leading to altered plasma levels and reduced seizure control [29]. All of these interactions fall under risk category D, as per standard drug interaction classifications, indicating the need for careful monitoring and potential therapy modification (Table 6).

In terms of drug class duplications, the most frequent combination was diclofenac and ibuprofen, observed in 16.9% of duplication events. Both agents belong to the NSAID class, and their concurrent use substantially increases the risk of gastrointestinal bleeding, cardiovascular complications, and renal dysfunction, concerns explicitly highlighted in the American Geriatrics Society (AGS) 2023 Beers Criteria [8].

Other frequently observed duplications included allopurinol with colchicine (14.4%), which may enhance the risk of myopathy, bone marrow suppression, and gastrointestinal intolerance, especially in patients with impaired renal function [30]. The combination of nitrofurantoin with trimethoprim (10.3%) may lead to additive nephrotoxicity and hematological adverse effects, and nitrofurantoin in particular is contraindicated in older adults with poor renal function [8,32].

Of special concern is the duplication of tricyclic antidepressants, such as amitriptyline with clomipramine (4.9%), which amplifies anticholinergic burden, increasing the risk of delirium, falls, and cognitive decline in older patients [8,33].

These findings underscore the critical importance of integrating comprehensive medication reviews, clinical decision support tools, and evidence-based resources such as the Beers Criteria into routine practice. Doing so can significantly reduce the risk of preventable

Advances in Medical, Pharmaceutical and Dental Research Journal (AMPDR)- ISSN 2812-4898
http://dx.doi.org/10.21622/AMPDR.2025.05.2.1365

adverse drug events, particularly among older adults and those with complex medication regimens.

Comparing our findings with existing literature, we observed that indomethacin, amitriptyline, methyldopa, and antihistamines are consistently identified as potentially inappropriate medications, aligning with previous studies [33-35]. However, there were differences in other medications, highlighting the variability in the application of the Beers Criteria across different countries.

The odds ratio of 10.105 for physician grade (GP) indicates significantly higher odds of non-compliant prescriptions. However, this effect is specific to a particular subgroup and should not be generalized across all study cases. This distinction underscores the difference between "general applicability" and "subgroup effect".

"General Applicability" means that the number of medications prescribed, as a continuous variable, is a universal predictor of non-compliance with the 2023 Beers criteria. This implies that as the number of medications increases, the likelihood of non-compliance rises for all patients, regardless of other factors. Conversely, "Subgroup Effect" refers to the physician grade (GP) being a categorical variable with a higher odds ratio, but its influence is specific to a subset of the data (patients treated by grade GP physicians). While the impact of physician grade is significant, it is limited to a particular group of patients, rather than being a universal factor across all patient prescriptions. [20]

The number of medications prescribed has a cumulative effect, with each additional medication increasing the odds of non-compliance by a factor of 3.234. This incremental increase quickly compounds, making it a strong predictor of non-compliance. On the other hand, the odds ratio of 10.105 for physician grade (GP) reflects a single comparative effect rather than an accumulating risk. The number of medications prescribed likely varies widely and frequently among patients, exerting a more consistent influence on compliance compared to the relatively stable category of physician grades.

In summary, the number of medications prescribed is considered the strongest predictor of non-compliance with the Beers criteria 2023 due to its broad applicability, cumulative impact, and consistent influence across the entire patient population, despite the higher odds ratio associated with physician grade (GP).

Managing the complexity of medication regimens is hence crucial for improving compliance with the 2023 Beers criteria. Roux et al. (2020) conducted a retrospective population-based cohort study using the Quebec Integrated Chronic Disease Surveillance System (QICDSS). This system monitors drug claims for older adults aged 65 and above, living in the community, who have chronic diseases or are at risk of developing them, and are covered by public drug insurance plans. The study found that having more medications and multiple chronic diseases, especially mental disorders (RR: 1.50; 95% CI: 1.49–1.51), significantly affected medication management. [36]

The overall findings in assessing compliance with the Beers Criteria 2023 clearly emphasize the significance of regional variations, physician qualification levels, and the complexity of prescribed medication regimens in determining the prescription status as either compliant or non-compliant with the Beers Criteria 2023. By focusing on these areas, interventions may increase adherence and lead to better patient outcomes.

A systematic review by Garcia (2006) identified five strategies to minimize inappropriate prescribing in older adults: seeking pharmacist recommendations, using computerized alerts, reviewing patient medications, applying Beers' criteria, and educating patients to enhance compliance. [37] Other research has shown that methods like geriatric medicine services, pharmacist participation in patient care, and computerized decision support can improve prescribing appropriateness for older patients in various settings. [38, 39].

8. Conclusions:

Building on these findings and recommendations, we propose standardizing prescribing systems, particularly for the older population, to minimize inappropriate prescribing practices. Integrating updated Beers criteria into the prescribing systems for older patients to serve as reliable clinical decision support tools could be very beneficial, especially given the implementation of Egypt's universal health insurance system. This approach aims to achieve the ultimate objective of reducing the economic burden and improving patient well-being by avoiding inappropriate prescribing in the older population.

List of abbreviations:

LMICs	Low- and Middle-Income Countries
AGS	American Geriatrics Society
PIM	Potentially Inappropriate Medication
GP	General Practitioner
AHFS	American Hospital Formulary Services
SE	Standard Error
MOH	Ministry of Health
NSAID	Non-steroidal anti-inflammatory drug
QICDSS	Quebec Integrated Chronic Disease Surveillance System
(UN)	United Nations

Declarations:

Ethics approval and consent to participate:

"An ethical approval was obtained and uploaded as a supplementary file."

Consent for publication:

'Not applicable'

Consent:

'Not applicable'

Availability of data and materials:

All data generated or analysed during this study are included in this published article [and its supplementary information files].

Competing interests:

'Not applicable'

Funding:

'Not applicable'

Authors contributions:

Both authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by both authors. The first draft of the manuscript was written by **Hesham Metwalli Abd El Moneim Mousli** and both authors commented on previous versions of the manuscript. both authors read and approved the final manuscript.

Acknowledgements:

'Not applicable'

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