



Potentially Inappropriate Medication Use among Elderly Inpatients at a Teaching Hospital in South India

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ABSTRACT

BACKGROUND: Use of inappropriate medications among elderly is common. An association between potentially inappropriate medication (PIM) use in elderly and adverse outcomes such as impaired muscle strength, functional status, increased healthcare expenditure, and increased risk of hospitalization and death has been demonstrated. Yet there are few studies addressing this issue.

OBJECTIVE: This study focuses on the prevalence of the use of potentially inappropriate medications in hospitalized elderly.

DESIGN: A retrospective observational study was done between June and December 2012 involving 150 patients. Patient data including period of hospital stay, medical illnesses and medication list at discharge were obtained from the in-patient records. The chi-squared test for categorical variables was used to compare the characteristics of participants receiving and not receiving inappropriate medications.

SETTING: The study collected data from 150 patients admitted to a teaching hospital at Bangalore, Karnataka.

PATIENTS: The sample was composed of 150 patients aged > 60 years admitted with multiple co morbidities.

MEASUREMENTS: The percentage of patients prescribed PIMs as defined using a modified Beers list was measured. Multivariable-adjusted odds ratios for PIM use were computed.

RESULTS: Of the 150 patients, 17.3% received at least 1 PIM, and 7% received 3 or more. Most common category of PIM use were Prazosin, followed by benzodiazepines

PIM use was directly associated with no: of comorbidities and Polypharmacy

CONCLUSION: There is a widespread use of potentially inappropriate medications among elderly patients in the population studied. Physicians should be more aware of the Beer's criteria when treating the elderly.

KEYWORDS: Potentially inappropriate medications (PIM), Beers criteria (BC), Polypharmacy, geriatric, elderly.

INTRODUCTION

India, now home to 1.2 billion people, is projected to overtake China in about a decade to become the world's most populous country. Between 2010 and 2050, the number of those aged above 60 years is also expected to increase from 7 percent to 14 percent of the total population. Presently we have about 100 million elderly in India. Elderly suffer from multiple illnesses both acute and chronic, requiring multiple hospital visits and medications from multiple specialists.

Medications can be considered inappropriate when their risk outweighs their benefit. The pharmacokinetics and pharmacodynamics of drugs is different in elderly and knowledge of geriatric pharmacology is of utmost importance in prescribing for the elderly.

The Beers criteria, named after Mark Beers, MD, lists medications that should generally be avoided in older adults. First evolved in 1991 by 13 pharmaco therapeutic and geriatric specialists as a tool for safer medication prescribing in frail older adults residing in nursing homes, it was revised in 1997 and again in 2003 to apply to all persons aged ≥ 65 years, and was most recently updated in 2012. The final updated Beers criteria encompasses fifty-three medications or medication classes, which are divided into three categories: potentially inappropriate medications (PIM) and classes to avoid in older adults, those to avoid in older adults with certain diseases and syndromes that these drugs can exacerbate, and finally medications to be used with caution in older adults.^{1, 1}

Polypharmacy (defined as the concurrent use of multiple medications) is common in the elderly and its prevalence ranges from 33% to 58%.^{1, 2} Unfortunately, polypharmacy may cause problems such as drug-drug interactions, non-adherence to therapy and adverse drug effects.

Objective of Study:

An association between potentially inappropriate medication (PIM) use in elderly and adverse outcomes such as impaired muscle strength and functional status, increased healthcare expenditure, and increased risk of hospitalization and death has been demonstrated.^{3 4 5} Use of inappropriate medications among elderly is common both in ambulatory and hospitalized settings.^{6 7} Yet there are few studies addressing this issue among the elderly in India.

Our objectives were to study the prevalence and predictors of the use of potentially inappropriate medications in hospitalized elderly and the associations between PIM use and comorbidities, polypharmacy, and duration of hospitalization.

MATERIALS AND METHODS

This is a retrospective study conducted in a 1200 bedded tertiary care teaching hospital in Karnataka, South India.

150 patients discharged from medical wards between June and December 2012 were included. Patient data including period of hospital stay, medical illnesses and medication list at discharge were obtained from the in-patient records.

Wherever the medication list at discharge was unavailable, medications ordered on the last day of admission were analyzed. The medication appropriateness was decided according to Beers criteria. The number of

discharge medications included not only oral and parenteral medications but also inhalers, and topical medicines. Combination medications were counted separately; insulin and multivitamins were counted as a single medication.

The patients were grouped according to their age into young old (65-74 yrs), old old (75-85yrs) and oldest old (>85 yrs). The presence of chronic medical illnesses like diabetes, hypertension, chronic obstructive pulmonary disease, cerebrovascular disease and ischemic heart disease were identified and the use of inappropriate medications was assessed in each group.

Whenever a potentially inappropriate medicine was identified, it was classified according to the Beers criteria into the three categories mentioned above. The drugs were not counted as inappropriate if they were used in a palliative setting or if there was no other alternative to its use.

Polypharmacy was considered as the administration of ≥ 5 drugs per day.

Data was assessed using the statistical package for social sciences, version 16. The chi-squared test for categorical variables was used to compare the characteristics of participants receiving and not receiving inappropriate medications. A probability value of less than 0.05 was considered statistically significant.

RESULTS

Patient characteristics (Table 1)

A total of 150 patient records were analyzed. Out of the total 150 patients, 120 (80%) were aged 60-74 years (young old), 22 (14.7%) were in the age group of 75-84 years (old old), and 8 (5.3%) were aged above 85 years (oldest old). The mean age of the patients in the study group was 67.8 years. Of the 150 patients, 56 (37.3%) were females and 94 (62.6%) were males.

The average number of chronic co-morbid medical illnesses per patient was 4.28 (± 2.235). The commonest co-morbid illnesses were hypertension (n=80) (53%) and diabetes (n=78) (52%).

The average duration of hospital stay was 8.06 days (mean duration =8 days)

Polypharmacy (Table 2)

110 (73.3%) patients were subject to polypharmacy.. The mean number of medications consumed per day by the patients in the study group was 6.7 \pm 3.1. 40 patients consumed <5 medications, 84 consumed between 5 to 10 medications, and 26 regularly consumed ≥ 10 medications per day.

The average number of medications taken by elderly men (n=94) was 6.79 (± 3.2) per day and elderly women (n=56) were taking 6.62 (± 2.9) medications per day. The patients of the oldest old category (≥ 85 years n=8) had an average of 7.38 medications/day. The young old (n=120) had a mean of 6.72 medications per day and the old old (n=22) had a mean of 6.5 medications per day.

The prevalence of polypharmacy was higher in those patients who had multiple co morbid illnesses. 110 patients were subject to polypharmacy. A patient who was subject to polypharmacy had an average of 4.9 comorbid illnesses, whereas the others had an average of 2.5 comorbid illnesses.

Potentially inappropriate medications (Table 3)

Of the total number of 150 patients in the study group, one of six (26) were taking a potentially inappropriate medication according to the Beers' list. (p=0.830)

Of the 26 patients taking a PIM, men constituted the majority, 17 (65.3%) compared to women, 9 (34.7%). Eighteen of them belonged to the young old (n=120), 3 of the old old (n=22) and 5 of them belonged to the oldest old category (n= 8).

Nineteen (73%) were prescribed a single inappropriate medication, one of five (5) patients were prescribed 2 potentially inappropriate medicines and one of thirteen (2) were taking 3 drugs that were potentially inappropriate.

Among the potentially inappropriate medications, the most common ones belonged to those that acted on the cardiovascular system, (13) (50%), of which antihypertensives (prazosin) constituted the majority (6)(46%) followed by anti arrhythmic (amiodarone)(5) (38.4%) and vasodilators (hydralazine and nitrates)(2)(15.3%) . The second commonest inappropriately prescribed drugs were those that acted on the central nervous system (30%), chiefly benzodiazepines (6) (alprazolam) followed by anticholinergics. (amitriptyline).

The maximum duration of hospital stay by any patient was 55 days, (0.7%) with most patients staying on an average duration of 8.1 (range 1- 55). PIM users stayed on a higher average of 8.7 days when compared to the non- PIM users. (Mean=7.93) (p=0.602)

The average number of medical illnesses seen in the group inappropriately prescribed was 5.7 (4.7, 6.7), whereas the group without any inappropriate medication was 3.97 (3.6, 4.3) (p<0.001).

Of the 26 PIM users, majority (22) (84.6%) were hypertensives (Odds Ratio 6.3; C.I 1.9-22.8), 10 (38.4%) had Ischemic heart disease,(Odds ratio 3.9; C.I 1.4-11.1), 18 (69%) had diabetes, and the proportion of patients with chronic obstructive pulmonary disease and cerebrovascular disease were 9 (34.6%) and 2 (7.6%) respectively. Of these, Hypertension, (84.6%) (p <0.001) ischemic Heart disease (38.4%) (p=0.009) were significantly associated with the use of inappropriate medications.

The prevalence of PIM use varied according to the co morbid illnesses. PIM use was highest in those with ischemic heart disease (10 of 27) (37%)(p=0.009), hypertension (22 of 80) (27.5%)(p=0.000) followed by diabetes (18 of 78)(23%)(p =0.053) and chronic lung disease (2 of 13)(15%) (p=0.88)

PIM and polypharmacy

Of the 110 patients who were subject to polypharmacy, 21 (19.09%) were using an inappropriate medication. Of the 40 patients who were not on polypharmacy, five had PIM use. (p = 0.34)

The maximum number of medications a patient was prescribed was 16. (Range 1-16, Mean 6.73 ± 3.09) 25 were prescribed ≥ 10 medicines, and 85 were prescribed ≥ 5 medicines. Of the 26 PIM users, 21 (80.7%) were subject to polypharmacy with an average of 8 medicines (mean 8.12 ± 3.36) as compared to the non PIM users (Mean 6.44 ± 2.92).

DISCUSSION

The study demonstrates that of the total number of patients discharged from medical wards, 17.3 % were taking at least one inappropriate medication. (p=0.830). The prevalence of PIM use was significantly associated with increasing age (p <0.001)

The prevalence of PIM use was lower than in international studies conducted on the use of inappropriate medications conducted among hospitalized elderly patients in Ireland (32%)⁸, France (66%),⁹ Switzerland (22.1%)¹⁰, and Taiwan (23.7%)¹¹ . Among studies conducted in India, our results were lower compared to ones conducted in other teaching hospitals in Karnataka- Bangalore ¹², Mysore ¹ but comparable to studies conducted in Punjab (18%) ². The difference could be probably due to the differences in patient and disease characteristics, prescribing patterns, study settings and availability of medications listed in BC.

As in other studies, the prescription of inappropriate medication had a significant association with increasing co morbidity.^{3 4}. The average number of medical illnesses seen in the group inappropriately prescribed was 5.77, whereas the group without any inappropriate medication was 3.97 ±2.05) Hypertension, (84.6%)(p

<0.001) ischemic Heart disease (38.4%)($p < 0.001$) were significantly associated with the use of inappropriate medications

Among the chronic illnesses, Essential hypertension and Ischemic heart disease increased the odds of use of PIM, similar to other studies in India ^{20,5}

The most commonly prescribed inappropriate medication in our study were antihypertensives, chiefly prazosin (46%), antiarrhythmics, amiodarone (38%) followed by drugs acting on the CNS, benzodiazepines (19%), and anticholinergics (15%). This was different from other studies ^{19-21,23} where drugs acting on the respiratory system comprised the majority of the inappropriate medications. The difference was probably due to the increased prevalence of hypertensives (53%) in the population.

As in other studies, prescription of inappropriate medications had a statistically significant association with increasing age (>84 years), ²¹ with 5 of 8 patients receiving inappropriately prescribed medications. ($p < 0.001$).

Contrary to other studies, ^{21, 22, 23} we did not find any statistically significant association with inappropriate medication use and duration of hospital stay.

Studies have shown that use of inappropriate medications is significantly associated with increased duration of hospital stay. ^{21,22,23} We did not find such an association, This could be attributed to improved drug monitoring or other factors that could influence duration of hospital stay e.g social factors, costs of hospitalization etc.

Polypharmacy

Our study found a higher prevalence of polypharmacy; compared to previous studies¹ in northern India 110 (73.3%) ($p < 0.001$). The ninety –four elderly men in the study population consumed a higher average number of medications compared to that of the elderly women (mean 6.85 vs 6.53, respectively). ($p > 0.001$)

The presence of diabetes, (n=78; mean 7.26), hypertension (n=80; mean 7.9), ischemic heart disease (n=27; mean 8.07) and chronic pulmonary illness (n= 33; mean 7.97) had a statistically significant association with polypharmacy use when compared to the patients with other co morbid illnesses. Of these, hypertension appeared to be the most important predictor of polypharmacy ($p < 0.001$)

A higher prevalence of potentially inappropriate medication use was seen among those with increasing number of medications. 26 patients who were taking inappropriate medicines were prescribed a higher average number of medications (mean 8.12 ± 3.36) when compared to among the 124 non PIM users. (Mean 6.44 ± 2.92) ($p < 0.02$)

Of the 26 patients who were inappropriately prescribed, 21 (80.7%) were subject to polypharmacy, although they formed only 19% of the study population ($p = 0.346$)

Inappropriate prescription was directly linked to polypharmacy. The prescription of inappropriate medications increased as the number of concurrent medications increased. This was similar to studies conducted in other hospital in Karnataka^{19,20}. When polypharmacy was defined as the use of 5 or more drugs, this association differed markedly. Only 21 of the total 110 were prescribed more than 5 medications, which was statistically insignificant, suggesting that a quantitative definition for polypharmacy was questionable.⁶

Polypharmacy was however rampant in the study group, as is known from previous studies^{7,8} and this was directly linked to morbidity in our study group.

This study is important because it shows that despite the existence of Beers criteria since 1987 and its regular updation, last in 2012, it still has not found its way into mainstream practice. Hence, the elderly continue to be prescribed those medicines that are known to have adverse effects in them. Every adverse event could be misdiagnosed and another drug added to alleviate the new symptom and this leads to the

prescribing cascade,⁹ subsequently adding to polypharmacy. Patients are at an increased risk of receiving an inappropriate medication and having an adverse drug reaction (ADR), which may impact a patient's adherence to his or her medication regimen. Polypharmacy has also been reported to increase the risk of geriatric syndromes and morbidity/ mortality.^{27,10}

The prevalence of the use of inappropriate medications is a concern, because studies have shown to have negative consequences such as increased risk of falls¹¹, impaired activities of daily living¹², non adherence to medication¹³ and increased medical costs.¹⁴

The increased prescription of inappropriate medications in patients with hypertension and diabetes points to the increased prevalence of these illnesses in the Indian elderly population. Although our study did not prove any statistical association, the use of inappropriate medications increases with the increased duration of hospital stay²³, and was known to have significant association with adverse effects such as falls^{32, 15}, and cognitive dysfunction¹⁶.

Our study also had certain limitations. This was a retrospective study, based on a small sample size of 150 patients, with information on drugs prescribed obtained from case records. The drug prescription was obtained from the discharge summaries, and where the same was not available, from the last day of inpatient admission. This may not have been a true representation of inappropriate medication use, since the medication list at discharge would have largely been modified to suit the chronic illness, rather than during the acute period.

The prescription of inappropriate medicine among the elderly was based on the updated Beers' criteria 2012. Beers' criteria do not address several other important aspects of inappropriate prescribing in older people, e.g. duplicate drug class prescriptions, harmful drug-drug interactions, inappropriate duration and frequency of therapy, and perhaps most importantly, drugs that are often omitted from older people's prescriptions. Beers' criteria are not organized in such a way as to make them quick and easy for the busy prescribing physician or dispensing pharmacist to use. Further, errors in prescription writing, errors of commission and omission were not looked into. Other tools for drug prescription in the elderly such as START¹⁷, STOPP¹⁸ and IPET¹⁹ (Improved Prescription in the Elderly Tool) would provide more insight on the use of inappropriate prescriptions in the elderly.

Our data was obtained from patients admitted and discharged from medical wards. A review of the discharge medications of patients admitted from surgical specialties would probably have shown different results. Patients with chronic illnesses like osteoarthritis, osteoporosis were not represented adequately, not only because such patients visited the orthopedic department more frequently, but also because they were probably undiagnosed in the medical wards.

Adverse drug events can be a cause and effect of inappropriate medication use. There was no data obtainable from the discharge records, and hence drug related events to inappropriate medications could not be studied.

CONCLUSION

Pharmacotherapy in the elderly requires a balance between inappropriate medication use and under-treatment. Interventions aimed at rational medication use in elderly Indians should focus on the predictors of use of inappropriate drugs. The need of physicians trained in Geriatric medicine is rising due to the changing patient characteristics in the Indian population scenario. Geriatricians are more likely to be aware of geriatric pharmacotherapy and its effects²⁰. There is a great scope for conducting intense research to determine inappropriate medication use and its health-related adverse consequences in the increasing Indian elderly population.

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GRAPHICS

Table 1: Clinical and demographic characteristics of study subjects (n=150)

Characteristics ¹	Frequencies
Ag category	
60-74	120 (80.0)
75-84	22 (14.7)
>84	8 (5.3)
Sex	
Male	56 (37.3)
Female	94 (62.7)
Polypharmacy Used	
Less than 5	40 (26.7)
More than 5	110 (73.3)
Number of PIMS	
0	124 (82.7)
1	19 (12.7)
2	5 (3.3)
3	2 (1.3)
PIM	
No	124 (82.7)
Yes	26 (17.3)
Presence of co-morbidities	
Presence of Diabetes	78 (52.0)
Presence of hypertension	80 (53.3)
Presence of chronic lung disease	33 (22.0)
Presence of IHD	27 (18.0)
Presence of BPH	13 (8.7)
Presence of stroke	13 (8.7)

Presence of chronic kidney disease	11 (7.3)
Presence of heart failure	9 (6.0)
Lower urinary tract symptoms	27 (18.0)
Presence of Parkinson's disease	8 (5.3)
Presence of seizures	6 (4.0)
Presence of peptic ulcer	3 (2.0)
Presence of delirium	3 (2.0)
History of falls or fractures	
Present	4 (2.7)
Presence of Syncope	1 (0.7)
Presence of dementia	1 (0.7)
Presence of insomnia	
Absent	150 (100)
Presence of urinary incontinence	
Absent	150 (100)
Presence of constipation	
Absent	150 (100)
Stress or mixed urinary incontinence	
Absent	150 (100)
Duration of hospital stay*	8.1 ± 7.5
	6 (4,9)
Total number of problems*	4.3 ± 2.2
	4(3, 6)
Number of medicines Used*	6.7 ± 3.1
	7 (4, 9)

¹ Reported as number within parenthesis percentages; *-mean ± SD, median (25th & 75th percentile)

Table 2: Factors associated with poly –pharmacy used:

Characteristics	Poly-pharmacy used		p value
	Less than 5 n=40	More than 5 n=110	
Age category			
60-74	32 (80.0)	88 (80.0)	0.72
75-84	5 (12.5)	17 (15.5)	
>84	3 (7.5)	4 (4.5)	
Sex			
Male	17 (42.5)	39 (35.5)	0.43
Female	23 (57.5)	71 (64.5)	
Number of PIMS			
0	35 (87.5)	89 (80.9)	
1	5 (12.5)	14 (12.7)	0.44
2	0	5 (4.5)	
3	0	2 (1.8)	
Pim			
0	35 (87.5)	89 (80.9)	0.34
1	5 (12.5)	21 (19.1)	
Presence of diabetes			
Present	15 (37.5)	63 (57.3)	0.03
Absent	25 (62.5)	47 (42.7)	
Presence of hypertension			
Present	10 (25.0)	70 (63.6)	<0.001
Absent	30 (75.0)	40 (36.4)	
Presence of Chronic lung disease			
Present			
Absent	3 (7.5)	30 (27.3)	0.01
	37 (92.5)	80 (72.7)	
Presence of IHD			
Present	1 (2.5)	26 (23.6)	0.003
Absent	39 (97.5)	84 (76.4)	
Duration of hospital stay*	5.5 ±2.5	9.0 ± 8.3	0.007
	5 (4, 7)	6 (4,10)	

Total number of problems*	2.5 ± 1.3	4.9 ± 2.1	<0.001
	3 (1, 3)	5 (3, 6)	
Number of medicines used*	3.1 ± 0.92	8.1 ± 2.4	<0.001
	3 (3, 4)	7 (6, 9)	

Reported as number within parenthesis percentages; *-mean ± SD, median (25th & 75th percentile); p values using chi-square

Table 3: Factors Associated With PIM:

Characteristics	PIM		OR	p value
	Yes	No	95% C.I	
Age category				
	60-74	18(69.2)	102(82.3)	0.002
	75-84	3(11.5)	19(15.3)	
	>84	5(19.2)	3(2.4)	
Sex				
	Male	18(69.2)	76(61.3)	0.447
	Female	8(30.8)	48(38.7)	
Poly pharmacy				
	0	5(19.2)	35(28.2)	0.346
	1	21(80.8)	89(71.8)	
Presence of diabetes				
	Present	18(69.2)	60(48.4)	2.4
	Absent	8(30.8)	64(51.6)	0.9 – 6.5
Presence of hypertension				
	Present	22(84.6)	58(46.8)	6.3
	Absent	4(15.4)	66(53.2)	1.9 – 22.8
Presence of Chronic lung disease				
	Present	9(34.6)	24(19.4)	2.2
	Absent	17(65.4)	100(80.6)	0.8 – 6.1

Presence of IHD	10(38.5)	17(13.7)	3.9	0.009
Present	16(61.5)	107(86.3)	1.4 – 11.1	
Absent				
Duration of hospital stay*	8.7±6.54	7.9±7.65		0.449
	6.5(4,11)	6(4,8)		
Total number of problems	5.77±2.50	3.97±2.05		<0.001
Number of medicines used*	6.4±2.97	8.1±3.36		0.011
	6(4,8)	9(5.75,10.25)		

Reported as number within parenthesis percentages; *-mean ± SD, median (25th & 75th percentile); p values using chi-square

APPENDIX I

BEERS' CRITERIA FOR POTENTIALLY INAPPROPRIATE MEDICATION USE IN OLDER ADULTS

TABLE 1: 2012 AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults

Organ System/ Therapeutic Category/Drug(s)	Recommendation, Rationale, Quality of Evidence (QE) & Strength of Recommendation (SR)
Anticholinergics (excludes TCAs)	
First-generation antihistamines (as single agent or as part of combination products)	Avoid.
<ul style="list-style-type: none"> • Brompheniramine • Carbinoxamine • Chlorpheniramine • Clemastine • Cyproheptadine • Dexbrompheniramine • Dexchlorpheniramine • Diphenhydramine (oral) • Doxylamine • Hydroxyzine • Promethazine • Triprolidine 	Highly anticholinergic; clearance reduced with advanced age, and tolerance develops when used as hypnotic; increased risk of confusion, dry mouth, constipation, and other anticholinergic effects/toxicity. Use of diphenhydramine in special situations such as acute treatment of severe allergic reaction may be appropriate. QE = High (Hydroxyzine and Promethazine), Moderate (All others); SR = Strong
Antiparkinson agents	Avoid.
<ul style="list-style-type: none"> • Benztropine (oral) • Trihexyphenidyl 	Not recommended for prevention of extrapyramidal symptoms with antipsychotics; more effective agents available for treatment of Parkinson disease. QE = Moderate; SR = Strong

Antispasmodics <ul style="list-style-type: none"> • Belladonna alkaloids • Clidinium-chlordiazepoxide • Dicyclomine • Hyoscyamine • Propantheline • Scopolamine 	Avoid except in short-term palliative care to decrease oral secretions. Highly anticholinergic, uncertain effectiveness. QE = Moderate; SR = Strong
Antithrombotics Dipyridamole, oral short-acting* (does not apply to the extended-release combination with aspirin)	Avoid. May cause orthostatic hypotension; more effective alternatives available; IV form acceptable for use in cardiac stress testing. QE = Moderate; SR = Strong
Ticlopidine*	Avoid. Safer, effective alternatives available. QE = Moderate; SR = Strong
Anti-infective Nitrofurantoin	Avoid for long-term suppression; avoid in patients with CrCl <60 mL/min. Potential for pulmonary toxicity; safer alternatives available; lack of efficacy in patients with CrCl <60 mL/min due to inadequate drug concentration in the urine. QE = Moderate; SR = Strong
Cardiovascular Alpha1 blockers <ul style="list-style-type: none"> • Doxazosin • Prazosin • Terazosin 	Avoid use as an antihypertensive. High risk of orthostatic hypotension; not recommended as routine treatment for hypertension; alternative agents have superior risk/benefit profile. QE = Moderate; SR = Strong
Alpha agonists <ul style="list-style-type: none"> • Clonidine • Guanabenz* • Guanfacine* • Methyldopa* • Reserpine (>0.1 mg/day)* 	Avoid clonidine as a first-line antihypertensive. Avoid others as listed. High risk of adverse CNS effects; may cause bradycardia and orthostatic hypotension; not recommended as routine treatment for hypertension. QE = Low; SR = Strong
Antiarrhythmic drugs (Class Ia, Ic, III) <ul style="list-style-type: none"> • Amiodarone • Dofetilide • Dronedarone • Flecainide • Ibutilide • Procainamide • Propafenone • Quinidine • Sotalol • Disopyramide* 	Avoid antiarrhythmic drugs as first-line treatment of atrial fibrillation. Data suggest that rate control yields better balance of benefits and harms than rhythm control for most older adults. Amiodarone is associated with multiple toxicities, including thyroid disease, pulmonary disorders, and QT interval prolongation. QE = High; SR = Strong
Dronedarone	Avoid. Disopyramide is a potent negative inotrope and therefore may induce heart failure in older adults; strongly anticholinergic; other antiarrhythmic drugs preferred. QE = Low; SR = Strong Avoid in patients with permanent atrial fibrillation or heart failure. Worse outcomes have been reported in patients taking dronedarone who have permanent atrial fibrillation or heart failure. In general, rate control is preferred over rhythm control for atrial fibrillation. QE = Moderate; SR = Strong

Digoxin >0.125 mg/day	Avoid. In heart failure, higher dosages associated with no additional benefit and may increase risk of toxicity; decreased renal clearance may increase risk of toxicity. QE = Moderate; SR = Strong
Nifedipine, immediate release*	Avoid. Potential for hypotension; risk of precipitating myocardial ischemia. QE = High; SR = Strong
Spirolactone >25 mg/day	Avoid in patients with heart failure or with a CrCl <30 mL/min. In heart failure, the risk of hyperkalemia is higher in older adults if taking >25 mg/day. QE = Moderate; SR = Strong
Central Nervous System	
Tertiary TCAs, alone or in combination:	Avoid.
<ul style="list-style-type: none"> • Amitriptyline • Chlordiazepoxide- • Amitriptyline • Clomipramine • Doxepin >6 mg/day • Imipramine • Perphenazine-amitriptyline • Trimipramine 	Highly anticholinergic, sedating, and cause orthostatic hypotension; the safety profile of low-dose doxepin (≤ 6 mg/day) is comparable to that of placebo. QE = High; SR = Strong
Antipsychotics, first- (conventional) and second- (atypical) generation (see online for full list)	Avoid use for behavioral problems of dementia unless non-pharmacologic options have failed and patient is threat to self or others. Increased risk of cerebrovascular accident (stroke) and mortality in persons with dementia. QE = Moderate; SR = Strong
Thioridazine	Avoid.
Mesoridazine	Highly anticholinergic and greater risk of QT-interval prolongation. QE = Moderate; SR = Strong
Barbiturates	Avoid.
<ul style="list-style-type: none"> • Amobarbital* • Butabarbital* • Butalbital • Mephobarbital* • Pentobarbital* • Phenobarbital • Secobarbital* 	High rate of physical dependence; tolerance to sleep benefits; greater risk of overdose at low dosages. QE = High; SR = Strong

Benzodiazepines	Avoid benzodiazepines (any type) for treatment of insomnia, agitation, or delirium.
Short- and intermediate-acting:	Older adults have increased sensitivity to benzodiazepines and decreased metabolism of long-acting agents. In general, all benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle accidents in older adults.
<ul style="list-style-type: none"> Alprazolam Estazolam Lorazepam Oxazepam Temazepam Triazolam 	May be appropriate for seizure disorders, rapid eye movement sleep disorders, benzodiazepine withdrawal, ethanol withdrawal, severe generalized anxiety disorder, perioperative anesthesia, end-of-life care.
Long-acting:	QE = High; SR = Strong
<ul style="list-style-type: none"> Chlorazepate Chlordiazepoxide Chlordiazepoxide-amitriptyline Clidinium-chlordiazepoxide Clonazepam Diazepam Flurazepam Quazepam 	
Chloral hydrate	Avoid. Tolerance occurs within 10 days and risk outweighs the benefits in light of overdose with doses only 3 times the recommended dose. QE = Low; SR = Strong
Meprobamate	Avoid. High rate of physical dependence; very sedating. QE = Moderate; SR = Strong
Nonbenzodiazepine hypnotics	Avoid chronic use (>90 days) Benzodiazepine-receptor agonists that have adverse events similar to those of benzodiazepines in older adults (e.g., delirium, falls, fractures); minimal improvement in sleep latency and duration. QE = Moderate; SR = Strong
<ul style="list-style-type: none"> Eszopiclone Zolpidem Zaleplon 	
Ergot mesylates*	Avoid.
Isoxsuprine*	Lack of efficacy. QE = High; SR = Strong
Endocrine	
Androgens	Avoid unless indicated for moderate to severe hypogonadism. Potential for cardiac problems and contraindicated in men with prostate cancer. QE = Moderate; SR = Weak
<ul style="list-style-type: none"> Methyltestosterone* Testosterone 	
Desiccated thyroid	Avoid. Concerns about cardiac effects; safer alternatives available. QE = Low; SR = Strong
Estrogens with or without progestins	Avoid oral and topical patch. Topical vaginal cream: Acceptable to use low-dose intravaginal estrogen for the management of dyspareunia, lower urinary tract infections, and other vaginal symptoms. Evidence of carcinogenic potential (breast and endometrium); lack of cardioprotective effect and cognitive protection in older women. Evidence that vaginal estrogens for treatment of vaginal dryness is safe and effective in women with breast cancer, especially at dosages of estradiol <25 mcg twice weekly. QE = High (Oral and Patch), Moderate (Topical); SR = Strong (Oral and Patch), Weak (Topical)

Growth hormone	Avoid, except as hormone replacement following pituitary gland removal. Effect on body composition is small and associated with edema, arthralgia, carpal tunnel syndrome, gynecomastia, impaired fasting glucose. QE = High; SR = Strong
Insulin, sliding scale	Avoid. Higher risk of hypoglycemia without improvement in hyperglycemia management regardless of care setting. QE = Moderate; SR = Strong
Megestrol	Avoid. Minimal effect on weight; increases risk of thrombotic events and possibly death in older adults. QE = Moderate; SR = Strong
Sulfonylureas, long-duration <ul style="list-style-type: none"> • Chlorpropamide • Glyburide 	Avoid. Chlorpropamide: prolonged half-life in older adults; can cause prolonged hypoglycemia; causes SIADH Glyburide: higher risk of severe prolonged hypoglycemia in older adults. QE = High; SR = Strong
Gastrointestinal Metoclopramide	Avoid, unless for gastroparesis. Can cause extrapyramidal effects including tardive dyskinesia; risk may be further increased in frail older adults. QE = Moderate; SR = Strong
Mineral oil, given orally	Avoid. Potential for aspiration and adverse effects; safer alternatives available. QE = Moderate; SR = Strong
Trimethobenzamide	Avoid. One of the least effective antiemetic drugs; can cause extrapyramidal adverse effects. QE = Moderate; SR = Strong
Pain Medications Meperidine	Avoid. Not an effective oral analgesic in dosages commonly used; may cause neurotoxicity; safer alternatives available. QE = High; SR = Strong
Non-COX-selective NSAIDs, oral <ul style="list-style-type: none"> • Aspirin >325 mg/day • Diclofenac • Diflunisal • Etodolac • Fenoprofen • Ibuprofen • Ketoprofen • Meclofenamate • Mefenamic acid • Meloxicam • Nabumetone • Naproxen • Oxaprozin • Piroxicam • Sulindac • Tolmetin 	Avoid chronic use unless other alternatives are not effective and patient can take gastroprotective agent (proton-pump inhibitor or misoprostol). Increases risk of GI bleeding/peptic ulcer disease in high-risk groups, including those ≥ 75 years old or taking oral or parenteral corticosteroids, anticoagulants, or antiplatelet agents. Use of proton pump inhibitor or misoprostol reduces but does not eliminate risk. QE = Moderate; SR = Strong

<ul style="list-style-type: none"> • Indomethacin • Ketorolac, includes parenteral 	<p>Avoid.</p> <p>Increases risk of GI bleeding/peptic ulcer disease in high-risk groups (See Non-COX selective NSAIDs)</p> <p>Of all the NSAIDs, indomethacin has most adverse effects.</p> <p>QE = Moderate (Indomethacin), High (Ketorolac); SR = Strong</p>
Pentazocine*	<p>Avoid.</p> <p>Opioid analgesic that causes CNS adverse effects, including confusion and hallucinations, more commonly than other narcotic drugs; is also a mixed agonist and antagonist; safer alternatives available.</p> <p>QE = Low; SR = Strong</p>
Skeletal muscle relaxants	<p>Avoid.</p> <p>Most muscle relaxants poorly tolerated by older adults, because of anticholinergic adverse effects, sedation, increased risk of fractures; effectiveness at dosages tolerated by older adults is questionable.</p> <p>QE = Moderate; SR = Strong</p>
<ul style="list-style-type: none"> • Carisoprodol • Chlorzoxazone • Cyclobenzaprine • Metaxalone • Methocarbamol • Orphenadrine 	

*Infrequently used drugs. Table 1 Abbreviations: ACEI, angiotensin converting-enzyme inhibitors; ARB, angiotensin receptor blockers; CNS, central nervous system; COX, cyclooxygenase; CrCl, creatinine clearance; GI, gastrointestinal; NSAIDs, nonsteroidal anti-inflammatory drugs; SIADH, syndrome of inappropriate antidiuretic hormone secretion; SR, Strength of Recommendation; TCAs, tricyclic antidepressants; QE, Quality of Evidence

TABLE 2: 2012 AGS Beers Criteria for Potentially Inappropriate Medication Use in Older Adults Due to Drug-Disease or Drug-Syndrome Interactions That May Exacerbate the Disease or Syndrome

Disease or Syndrome	Drug(s)	Recommendation, Rationale, Quality of Evidence (QE) & Strength of Recommendation (SR)
Cardiovascular		
Heart failure	<p>NSAIDs and COX-2 inhibitors</p> <p>Nondihydropyridine CCBs (avoid only for systolic heart failure)</p> <ul style="list-style-type: none"> • Diltiazem • Verapamil <p>Pioglitazone, rosiglitazone</p> <p>Cilostazol</p> <p>Dronedarone</p>	<p>Avoid.</p> <p>Potential to promote fluid retention and/or exacerbate heart failure.</p> <p>QE = Moderate (NSAIDs, CCBs, Dronedarone), High (Thiazolidinediones (glitazones)), Low (Cilostazol); SR = Strong</p>
Syncope	<p>Acetylcholinesterase inhibitors (AChEIs)</p> <p>Peripheral alpha blockers</p> <ul style="list-style-type: none"> • Doxazosin • Prazosin • Terazosin <p>Tertiary TCAs</p> <p>Chlorpromazine, thioridazine, and olanzapine</p>	<p>Avoid.</p> <p>Increases risk of orthostatic hypotension or bradycardia.</p> <p>QE = High (Alpha blockers), Moderate (AChEIs, TCAs and antipsychotics); SR = Strong (AChEIs and TCAs), Weak (Alpha blockers and antipsychotics)</p>
Central Nervous System		
Chronic seizures or epilepsy	<p>Bupropion</p> <p>Chlorpromazine</p> <p>Clozapine</p> <p>Maprotiline</p> <p>Olanzapine</p> <p>Thioridazine</p> <p>Thiothixene</p> <p>Tramadol</p>	<p>Avoid.</p> <p>Lowers seizure threshold; may be acceptable in patients with well-controlled seizures in whom alternative agents have not been effective.</p> <p>QE = Moderate; SR = Strong</p>

Delirium	All TCAs Anticholinergics Benzodiazepines Chlorpromazine Corticosteroids H2-receptor antagonist Meperidine Sedative hypnotics Thioridazine	Avoid. Avoid in older adults with or at high risk of delirium because of inducing or worsening delirium in older adults; if discontinuing drugs used chronically, taper to avoid withdrawal symptoms. QE = Moderate; SR = Strong
Dementia & cognitive impairment	Anticholinergics Benzodiazepines H2-receptor antagonists Zolpidem Antipsychotics, chronic and as-needed use	Avoid. Avoid due to adverse CNS effects.
History of falls or fractures	Anticonvulsants Antipsychotics Benzodiazepines Nonbenzodiazepine hypnotics <ul style="list-style-type: none"> • Eszopiclone • Zaleplon • Zolpidem TCAs/SSRIs	Avoid unless safer alternatives are not available; avoid anticonvulsants except for seizure. Ability to produce ataxia, impaired psychomotor function, syncope, and additional falls; shorter-acting benzodiazepines are not safer than long-acting ones. QE = High; SR = Strong
Insomnia	Oral decongestants <ul style="list-style-type: none"> • Pseudoephedrine • Phenylephrine Stimulants • Amphetamine • Methylphenidate • Pemoline Theobromines • Theophylline • Caffeine 	Avoid. CNS stimulant effects. QE = Moderate; SR = Strong
Parkinson's disease	All antipsychotics (see online publication for full list, except for quetiapine and clozapine) Antiemetics <ul style="list-style-type: none"> • Metoclopramide • Prochlorperazine • Promethazine 	Avoid. Dopamine receptor antagonists with potential to worsen parkinsonian symptoms. Quetiapine and clozapine appear to be less likely to precipitate worsening of Parkinson disease. QE = Moderate; SR = Strong
Gastrointestinal		

Chronic constipation	<p>Oral antimuscarinics for urinary incontinence</p> <ul style="list-style-type: none"> • Darifenacin • Oxybutynin (oral) • Solifenacin • Tolterodine • Trospium • Nondihydropyridine CCB • Diltiazem • Verapamil <p>First-generation antihistamines as single agent or part of combination products</p> <ul style="list-style-type: none"> • Brompheniramine • Chlorpheniramine • Cyproheptadine • Dexchlorpheniramine • Diphenhydramine • Doxylamine • Hydroxyzine • Promethazine <p>Anticholinergics/antispasmodics</p> <ul style="list-style-type: none"> • Antipsychotics • Belladonna alkaloids • Clidinium-chlordiazepoxide • Dicyclomine • Hyoscyamine • Propantheline • Scopolamine • Tertiary TCAs 	<p>Avoid unless no other alternatives. Can worsen constipation; agents for urinary incontinence: antimuscarinics overall differ in incidence of constipation; response variable; consider alternative agent if constipation develops. QE = High (For Urinary Incontinence), Moderate/Low (All Others); SR = Strong</p>
History of gastric or duodenal ulcers	<p>Aspirin (>325 mg/day) Non-COX-2 selective NSAIDs</p>	<p>Avoid unless other alternatives are not effective and patient can take gastroprotective agent (proton-pump inhibitor or misoprostol). May exacerbate existing ulcers or cause new/additional ulcers. QE = Moderate; SR = Strong</p>
Kidney/Urinary Tract Chronic kidney disease stages IV and V	<p>NSAIDs Triamterene (alone or in combination)</p>	<p>Avoid. May increase risk of kidney injury. May increase risk of acute kidney injury. QE = Moderate (NSAIDs), Low (Triamterene); SR = Strong (NSAIDs), Weak (Triamterene)</p>
Urinary incontinence (all types) in women	<p>Estrogen oral and transdermal (excludes intravaginal estrogen)</p>	<p>Avoid in women. Aggravation of incontinence. QE = High; SR = Strong</p>
Lower urinary tract symptoms, benign prostatic hyperplasia	<p>Inhaled anticholinergic agents Strongly anticholinergic drugs, except antimuscarinics for urinary incontinence (see Table 9 for complete list).</p>	<p>Avoid in men. May decrease urinary flow and cause urinary retention. QE = Moderate; SR = Strong (Inhaled agents), Weak (All others)</p>
Stress or mixed urinary incontinence	<p>Alpha-blockers</p> <ul style="list-style-type: none"> • Doxazosin • Prazosin • Terazosin 	<p>Avoid in women. Aggravation of incontinence. QE = Moderate; SR = Strong</p>

Table 2 Abbreviations: CCBs, calcium channel blockers; AChEIs, acetylcholinesterase inhibitors; CNS, central nervous system; COX, cyclooxygenase; NSAIDs, nonsteroidal anti-inflammatory drugs; SR, Strength of Recommendation; SSRIs, selective serotonin reuptake inhibitors; TCAs, tricyclic antidepressants; QE, Quality of Evidence

TABLE 3: 2012 AGS Beers Criteria for Potentially Inappropriate Medications to Be Used with Caution in Older Adults	
Drug(s)	Recommendation, Rationale, Quality of Evidence (QE) & Strength of Recommendation (SR)
Aspirin for primary prevention of cardiac events	Use with caution in adults ≥ 80 years old. Lack of evidence of benefit versus risk in individuals ≥ 80 years old. QE = Low; SR = Weak
Dabigatran	Use with caution in adults ≥ 75 years old or if CrCl < 30 mL/min. Increased risk of bleeding compared with warfarin in adults ≥ 75 years old; lack of evidence for efficacy and safety in patients with CrCl < 30 mL/min QE = Moderate; SR = Weak
Prasugrel	Use with caution in adults ≥ 75 years old. Greater risk of bleeding in older adults; risk may be offset by benefit in highest-risk older patients (eg, those with prior myocardial infarction or diabetes). QE = Moderate; SR = Weak
Antipsychotics	Use with caution.
Carbamazepine	May exacerbate or cause SIADH or hyponatremia; need to monitor sodium level closely when starting or changing dosages in older adults due to increased risk.
Carboplatin	
Cisplatin	
Mirtazapine	QE = Moderate; SR = Strong
SNRIs	
SSRIs	
TCAs	
Vincristine	
Vasodilators	Use with caution. May exacerbate episodes of syncope in individuals with history of syncope. QE = Moderate; SR = Weak

Table 3 Abbreviations: CrCl, creatinine clearance; SIADH, syndrome of inappropriate antidiuretic hormone