

# Potentially Inappropriate Prescribing in Older Adults with Hypertension or Diabetes Mellitus and Hypertension in a Primary Care Setting in Bahrain

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## Significance of the Study

- The prevalence of potentially inappropriate prescribing for older adults with hypertension or diabetes mellitus and hypertension in Bahrain was 34.1%, it was more often for medications intended for acute medical illness, and it was unrelated to the training of primary care physicians. The quality of prescribing for older adults should be improved with appropriate interventions.

## Keywords

Screening Tool of Older Persons' Prescriptions criteria · Inappropriate prescribing · Family physicians · General practitioners

## Abstract

**Objectives:** The aims of this study were to evaluate: (1) the prevalence and types of potentially inappropriate prescribing in older adults with hypertension or diabetes mellitus and hypertension, and (2) whether or not differences in the training of primary care physicians were associated with potentially inappropriate prescribing. **Materials and Methods:** Primary care prescriptions issued by family physicians and general practitioners were audited using Screening Tool of Older Persons' Prescriptions criteria (version 1), with 18 out of 65 applicable criteria. Descriptive statistics were used to test the difference between proportions, and two-tailed *t* test was used for continuous variables. **Results:** A total of 2,090 outpatient prescriptions were written during the study period; of these, 712 (34.1%) were potentially inappropriate.

The mean number of drugs per patient was 6.03 ( $\pm 2.5$ ). Of the 712 prescriptions, 543 (76.3%) were used for the treatment of acute medical illnesses. The most common examples of potentially inappropriate prescribing were: orphenadrine ( $n = 174$ ; 8.33%), long-term nonsteroidal anti-inflammatory drugs for >3 months ( $n = 150$ ; 7.18%), proton pump inhibitors for >8 weeks ( $n = 135$ ; 6.46%), antihypertensive therapy duplication ( $n = 59$ ; 2.82%), long-acting glyburide ( $n = 48$ ; 2.29%), and chlorthalidone for >1 month ( $n = 44$ ; 2.11%). Family physicians showed a greater tendency toward potentially inappropriate prescribing compared to general practitioners, but the difference was nonsignificant ( $n = 514$  [34.75%] vs.  $n = 162$  [31.3%];  $p = 0.16$ ). **Conclusions:** The prevalence of potentially inappropriate prescribing (i.e., 34.1%) was within the spectrum reported worldwide and unrelated to the training backgrounds of physicians. Most of the identified potentially inappropriate prescribing (76.3%) in older adults was associated with medications for acute medical illnesses and hence inappropriate polypharmacy should be discouraged.

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## Introduction

The prescribing of medications is a critical component of the care of the older adults, and optimization of drugs prescribing has become an important public health concern [1, 2]. With emerging demographic transitions leading to an increasing proportion of older people worldwide, improvement of the quality and safety of prescribing, especially for older people, poses a global challenge [3]. There is evidence that inappropriate prescribing is common in older adults and is associated with adverse events, many of which require hospital admission [4]. Inappropriate prescribing has been recognized as one of the 5 most important quality-of-care problems in the older adults [5]. In addition to advanced age, multiple comorbidities and polypharmacy, or the concurrent use of multiple medications, are major risk factors for potentially inappropriate prescribing (PIP) in older adults [4, 6].

Polypharmacy by patients (notably older adults) and/or administration of more medications than are clinically indicated [4] is a common and growing global issue affecting the quality of health care in primary care [7] and secondary/tertiary care [8], particularly in those with multiple morbidities, and in residential care facilities for older people [9]. Although the term polypharmacy often implies criticism of the way medications have been prescribed, at times it is justified. Polypharmacy can be categorized into appropriate and inappropriate (problematic) polypharmacy [7]. Appropriate polypharmacy is defined as prescribing for an individual with complex clinical conditions or for multiple conditions in circumstances where the use of medication has been optimized and prescribed according to the best evidence [4]. In contrast, inappropriate polypharmacy is defined as prescribing of multiple medications inappropriately, or where the intended therapeutic benefit of the drug is not realized [4]. Inappropriate prescribing may be associated with non-evidence-based treatment, risk due to a drug that outweighs its benefit, clinical contraindication, the existence of a significant clinical drug-drug interaction potential, poor medication compliance, deterioration of the patient's quality of life, unnecessary drug costs, and potential omission of appropriate medication(s) from the patient's therapeutic regimen [10].

The Screening Tool of Older Persons' Prescriptions (STOPP) and the Screening Tool to Alert Doctors to the Right Treatment (START) [8] have been recommended for identifying older patients at risk of adverse effects and to reduce the risk of initiating a drug therapy likely to result in adverse events. The STOPP criteria (version 1)

comprise 65 clinically significant criteria for PIP in older patients, whereas the START criteria consist of 22 evidence-based prescribing indicators for common diseases in older adults to determine the omissions of potentially appropriate drugs. Both STOPP/START screening tools are explicit methods with well-defined criteria, based on physiological systems and accepted by geriatric pharmacotherapy specialists from the UK and Ireland on the basis of the Delphi consensus method [8]. The STOPP/START criteria have been used in numerous studies in several countries worldwide [11, 12], supported by the European Union of Geriatric Medicine Societies [12], and chosen for the evaluation of prescribing in patients with multiple chronic conditions [13]. Although these criteria are effective for the evaluation of prescribing quality, the clinical, human, and economic outcomes may not adequately address quality of care or mortality [14].

Therefore, the objectives of this study were to identify the prevalence and types of polypharmacy-based PIP among older adults with hypertension or both diabetes and hypertension in a primary care setting in Bahrain and to determine whether or not there are PIP differences between family physicians (FP) and general practitioners (GP) in a primary care practice.

## Materials and Methods

### *Setting*

This nationwide study was conducted in 22 out of 24 primary care health centers in Bahrain from December 2014 to May 2015. The Kingdom of Bahrain is a group of islands located in the Arabian Gulf with an approximate population of 1.36 million at the time of this study. A primary health care organization with a network of 24 health centers across 5 regions of the country provides subsidized curative and preventive services that include dispensing of essential drugs. The number of primary care physicians in each health center varied between 4 and 11, with a random ratio of FP and GP. Patients requiring special investigations and consultations or admission are referred to the Salmaniya Medical Complex, King Hamad University Hospital, and Bahrain Defense Forces Hospital for secondary/tertiary care.

### *Study Population and Variability*

The Research and Ethics Committees of the College of Medicine and Medical Sciences, Arabian Gulf University, and the Ministry of Health, Kingdom of Bahrain, approved this study.

Out of 8,746 prescriptions issued for patients with hypertension or with diabetes mellitus and hypertension, 2,090 met the inclusion criteria (age  $\geq 65$  years and either hypertension or both diabetes mellitus and hypertension). The patient's personal number, gender, category of primary care physicians (FP/GP), and medication-related data from prescriptions were entered for anal-

**Table 1.** Characteristics of study subjects, medications, and primary care physicians

Characteristic	Patients with hypertension	Patients with diabetes and hypertension	Primary care physicians		
			family physicians (n = 182)	general practitioners (n = 84)	all physicians (n = 266)
Patients	1,017	1,073	1,477	527	2,090
Males	488 (48.0)	471 (43.9)	626 (42.4)	290 (55.0)	959 (45.9)
Females	529 (52.0)	602 (56.1)	851 (57.6)	237 (45.0)	1,131 (54.1)
Age, years	72.6±6.8	71.7±6.5	72.0±6.6	72.5±6.6	72.1±6.6
Age range, years	65–108	65–103	65–108	65–103	65–108
<i>Drugs prescribed for chronic conditions</i>					
Total	3,636 (75.5)	6,595 (84.7)	7,461 (81.9)	2,379 (79.9)	10,231 (81.2)
Drugs per patient	3.6±1.7	6.2±1.8	5.1±2.2	4.5±2.1	4.9±2.2
Range	1–10	2–13	1–13	1–12	1–13
<i>Drugs prescribed for acute conditions</i>					
Total	1,180 (24.5)	1,191 (15.3)	1,650 (18.1)	600 (20.1)	2,371 (18.8)
Drugs per patient	1.2±1.3	1.1±1.3	1.1±1.3	1.1±1.3	1.1±1.3
Range	0–7	0–9	0–7	0–9	0–9
<i>Total number of drugs prescribed</i>					
Total	4,816 (100)	7,786 (100)	9,112 (100)	2,978 (100)	12,602 (100)
Drugs per patient	4.7±2.1	7.3±2.2	6.2±2.5	5.7±2.4	6.03±2.5
Range	1–13	2–16	1–15	1–16	1–16

n (%) or mean ± SD unless otherwise stated.

ysis on the basis of 18 out of 65 STOPP criteria applicable to prescription-based studies. PIP was identified and coded by K.A.J. The STOPP criteria (version 1) were used as a screening tool to identify PIP from a patient's therapeutic regimen [8].

#### Operational Definitions

In this study, a hypertensive patient was identified as one who received one or more antihypertensive drugs, and patients were identified as having diabetes with hypertension if they received one or more antihypertensive drugs together with one or more anti-diabetic drugs. Older adult or elderly was defined according to the World Health Organization as an individual aged ≥65 years. FP were those certified physicians who were trained for 4 years in Family Practice Residency Program (FPRP) in Bahrain recognized by the Arab Board Council for Family and Community Medicine and affiliated with the Irish College of General Practitioners and the Royal College of Surgeons, Ireland. A few of the FP were trained in other Eastern Mediterranean region countries. All other primary care physicians who were medical graduates and licensed to practice in Bahrain were categorized as GP [15].

#### Statistical Analysis

Descriptive statistics such as percentages, means, and SD were used to test the difference between proportions, and a two-tailed *t* test was used for continuous variables. A *p* < 0.05 was considered statistically significant. Statistical Package for Social Sciences (SPSS version 20) was used for data analysis.

## Results

### Study Population

The mean age of the older adults was 72.1 ± 6.6 years (range 65–108). The mean (±SD) number of drugs per patient with hypertension and patient with both diabetes and hypertension was 4.7 ± 2.1 and 7.3 ± 2.2, respectively (Table 1; *p* < 0.0001). The corresponding median number of drugs per patient was 5.0 and 7.0, respectively. In case of acute medical illness the mean (±SD) value of drugs per patient was 1.2 ± 1.3 (median 1.0) and 1.1 ± 1.3 (median 1.0), respectively, which represented 18.8% of the total drugs prescribed (Table 1).

### Potentially Inappropriate Prescribing

The PIP among older adults in a primary care setting are presented in Table 2. Based on 18 applicable STOPP criteria, the prevalence of PIP was 34.1% (712/2,090). Common PIP in older adults were: skeletal muscle relaxant orphenadrine as a component of Muscadol® (*n* = 174; 8.33%), long-term use of nonsteroidal anti-inflammatory drugs (NSAID) for >3 months (*n* = 150; 7.1%), proton pump inhibitors for >8 weeks (*n* = 135; 6.46%), antihy-

**Table 2.** Prevalence of PIP among elderly patients with hypertension or diabetes with hypertension in primary care using STOPP criteria version 1

STOPP criteria (applicable)	Clinical concerns [8, 25]	PIP in patients with hypertension	PIP in patients with diabetic hypertension	PIP in all patients	PIP by family physician	PIP by general practitioner	<i>p</i> value
<i>Cardiovascular system</i>							
Long-term digoxin >125 µg/day	increased risk of toxicity	3 (0.29)	0 (0)	3 (0.14)	2 (0.13)	0 (0)	1.0
Furosemide monotherapy for hypertension <sup>b</sup>	better alternatives are available	0 (0)	4 (0.37)	4 (0.19)	2 (0.13)	2 (0.38)	0.27
β-blocker in combination with verapamil	increased risk of heart block	1 (0.09)	0 (0)	1 (0.05)	1 (0.06)	0 (0)	1.0
β-blocker in patients with COPD	risk of bronchospasm	10 (0.98)	6 (0.56)	16 (0.77)	13 (0.88)	3 (0.58)	0.77
Vasodilators	risk of syncope, falls	11 (1.08)	16 (1.49)	27 (1.29)	16 (1.08)	4 (0.77)	0.79
Dipyridamole as monotherapy for cardiovascular secondary prevention	no evidence of efficacy	1 (0.09)	4 (0.37)	5 (0.24)	4 (0.27)	0 (0)	0.57
<i>Central nervous system</i>							
Chlordiazepoxide for >1 month <sup>c</sup>	sedation, confusion, falls, constipation	19 (1.87)	25 (2.33)	44 (2.11)	30 (2.03)	14 (2.70)	0.38
First-generation antihistamine for >1 week <sup>c</sup>	risk of sedation and anticholinergic side effects	6 (0.59)	4 (0.37)	10 (0.48)	7 (0.47)	3 (0.58)	0.72
Skeletal muscle relaxants (orphenadrine) <sup>c</sup>	risk of sedation and anticholinergic side effects	92 (9.05)	82 (7.64)	174 (8.33)	135 (9.14)	30 (5.80)	0.02 <sup>a</sup>
<i>Endocrine system</i>							
Glyburide in type 2 diabetes mellitus	prolonged hypoglycemia	–	48 (2.29)	48 (2.29)	38 (2.57)	9 (1.74)	0.31
<i>Gastrointestinal system</i>							
PPI at the full therapeutic dose for >8 weeks <sup>c</sup>	increased bone fractures, hyponatremia, hypomagnesaemia	60 (5.90)	75 (7.00)	135 (6.46)	101 (6.84)	26 (5.03)	0.17
Anticholinergic antispasmodic drugs <sup>c</sup>	sedation, confusion, falls, constipation	13 (1.28)	14 (1.30)	27 (1.29)	22 (1.49)	3 (0.58)	0.16
Loperamide for diarrhea of unknown etiology <sup>c</sup>	delayed diagnosis	0 (0)	1 (0.09)	1 (0.05)	0 (0)	1 (0.19)	1.0
<i>Musculoskeletal system</i>							
Long-term NSAID for >3 months <sup>c</sup>	risk of peptic ulcer	72 (7.08)	78 (7.27)	150 (7.18)	99 (6.7)	45 (8.7)	0.13
Long-term corticosteroids for >3 months	risk of side effects	3 (0.29)	1 (0.09)	4 (0.19)	4 (0.27)	0 (0)	0.57
NSAID with heart failure	exacerbation of heart failure	2 (0.20)	0 (0)	2 (0.10)	2 (0.13)	0 (0)	1.0
<i>Respiratory system</i>							
Theophylline monotherapy for COPD	risk of adverse effects	2 (0.20)	0 (0)	2 (0.10)	2 (0.13)	0 (0)	1.0
<i>Therapy duplication</i>							
Two β-blockers	risk of adverse effects	1 (0.09)	0 (0)	1 (0.05)	0 (0)	1 (0.19)	1.0
Two calcium channel blockers	risk of adverse effects	2 (0.20)	0 (0)	2 (0.10)	2 (0.13)	0 (0)	1.0
Two diuretics	risk of adverse effects	9 (0.88)	26 (2.42)	35 (1.67)	23 (1.56)	12 (2.32)	0.24
Two RAAS inhibitors	risk of adverse effects	1 (0.09)	15 (1.40)	16 (0.77)	8 (0.54)	8 (1.55)	0.04 <sup>a</sup>
Two NSAID	risk of adverse effects	4 (0.39)	1 (0.09)	5 (0.24)	3 (0.20)	1 (0.19)	1.0
Total		312 (30.64)	400 (35.08)	712 (34.09)	514 (34.75)	162 (31.3)	0.16

Values are presented as numbers (%). STOPP, Screening Tool of Older Person's Prescription; COPD, chronic obstructive pulmonary disease; NSAID, nonsteroidal anti-inflammatory drugs; PIP, potentially inappropriate prescribing; PPI, proton pump inhibitor; RAAS, renin-angiotensin-aldosterone system. <sup>a</sup> *p* < 0.05. <sup>b</sup> Can be used for both acute and chronic clinical conditions. <sup>c</sup> Drugs suggested for acute medical illness.

pertensive therapy duplication (*n* = 59; 2.82%), long-acting oral hypoglycemic glyburide (*n* = 48; 2.29%), and use of chlordiazepoxide as Librax<sup>®</sup> for >1 month (*n* = 44; 2.11%). Most of the identified PIP (76.3%) was for patients with acute medical illness for central nervous, gastrointestinal, and musculoskeletal system-related medications (Table 2). The classes of drugs according to the physiological systems, prescribed for acute illness and multiple chronic morbidities, are listed in Tables 3 and 4, respectively. The most common class of drugs used for

acute illness was acid-suppressing drugs, whereas the least common class was prokinetic drugs (Table 3). In contrast, in patients with multiple chronic morbidities the corresponding class of drugs was antihypertensives and antiarrhythmic drugs, respectively (Table 4).

#### PIP by FP and GP

Of the 2,090 prescriptions, 182 FP issued 1,477 prescriptions and 84 GP issued 517, whereas the identity of the prescribers in 96 prescriptions could not be estab-

**Table 3.** Classes of medications used for acute medical illnesses according to physiological systems

Acute medical conditions	Patients with hypertension	Patients with diabetes and hypertension
<i>Anti-infectives</i>		
Antimicrobial agents (systemic)	39 (0.81)	16 (0.21)
<i>Central nervous system</i>		
Long-acting benzodiazepine (chlordiazepoxide) in combination with clidinium (Librax <sup>®</sup> ) <sup>a</sup>	24 (0.50)	28 (0.36)
<i>Gastrointestinal system</i>		
Acid-suppressing drugs and mucosal protectants	236 (4.90)	274 (3.52)
Drugs for dyspepsia and gastroesophageal reflux disease	42 (0.87)	35 (0.45)
Laxatives	17 (0.35)	21 (0.27)
Antispasmodic	13 (0.27)	14 (0.18)
Prokinetics	4 (0.08)	2 (0.03)
<i>Musculoskeletal and joint diseases</i>		
Simple analgesic (paracetamol)	153 (3.18)	110 (1.41)
Nonsteroidal anti-inflammatory drugs	152 (3.16)	131 (1.68)
Skeletal muscle relaxant (Muscadol <sup>®</sup> ) <sup>b</sup>	92 (1.91)	82 (1.05)
<i>Nutrition and blood</i>		
Multivitamins	72 (1.50)	169 (2.17)
<i>Respiratory system</i>		
Antitussives and mucolytics	97 (2.01)	62 (0.80)
Antihistamines (first and second generations)	70 (1.45)	43 (0.55)
Topical preparations <sup>c</sup>	127 (2.64)	152 (1.95)
Miscellaneous drugs	42 (0.87)	52 (0.67)
Total	1,180 (24.50)	1,191 (15.30)

Values are presented as numbers (%). <sup>a</sup> Fixed dose combination of sedative/antianxiety chlordiazepoxide HCl 5 mg and anticholinergic clidinium bromide 2.5 mg (antispasmodic). <sup>b</sup> Fixed dose combination of paracetamol 450 mg plus orphenadrine 35 mg (skeletal muscle relaxant). <sup>c</sup> Includes tropical nasal decongestants, drugs used for nasal allergy, oropharyngeal anti-infective drugs, anti-infective eye preparations, and local preparations for rectal and vaginal disorders.

lished. The extent of PIP was generally similar between FP and GP, and the difference was statistically nonsignificant (34.75 vs. 31.3%;  $p = 0.16$ ; Table 2), although FP prescribed a higher number of drugs per patient compared to GP (mean  $6.2 \pm 2.5$  vs.  $5.7 \pm 2.4$ ;  $p < 0.0001$ ).

## Discussion

The current study identified the most common PIP by primary care physicians for patients with hypertension or both diabetes mellitus and hypertension in Bahrain. Studies identifying PIP on the basis of STOPP criteria among primary care or community-dwelling older individuals with multiple chronic morbidities are very scarce in Eastern Mediterranean region countries [8, 12, 16]. PIP is

highly prevalent in older adults and it is a major health care concern because of its association with negative health care outcomes such as adverse drug event-related morbidity [4]. Patients with hypertension or diabetes and hypertension are prescribed a variety of medications such as antihypertensive, antidiabetic, antidyslipidemic, anti-thrombotic, uric acid-lowering drug and others. This targeted age group with multiple chronic morbidities seems to be vulnerable to inappropriate prescribing.

In our study which included older adults with hypertension or diabetes and hypertension, often with other morbidities, the mean number of medications/patient prescribed for chronic (long-term) and acute (short-term) medical conditions appears to be comparable to that reported in Turkey [17] but less than that reported from Spain [18, 19] in studies on patients in the similar

**Table 4.** Classes of medications used to treat multiple chronic morbidities according to physiological systems

Chronic medical conditions	Patients with hypertension	Patients with diabetes and hypertension
<i>Cardiovascular system</i>		
Antihypertensive drugs	2,265 (47.03)	2,500 (32.11)
Lipid-regulating drugs	512 (10.63)	845 (10.85)
Antiplatelet drugs	302 (6.27)	582 (7.47)
Nitrovasodilators	109 (2.26)	104 (1.34)
Uric acid-lowering agents	105 (2.18)	123 (1.58)
Phlebotropic drugs <sup>a</sup>	13 (0.27)	8 (0.10)
Cytoprotective anti-ischemic agents <sup>b</sup>	12 (0.25)	15 (0.19)
Cardiac glycosides	8 (0.17)	3 (0.04)
Antiarrhythmic drugs	0 (0)	1 (0.01)
Hemorheologic agents <sup>c</sup>	0 (0)	4 (0.05)
<i>Central nervous system</i>		
Psychotropic drugs	28 (0.58)	84 (1.08)
<i>Endocrine system</i>		
Drugs used in diabetes	–	1,970 (25.30)
Thyroid hormonal replacement therapy	86 (1.79)	116 (1.49)
Antithyroid drugs	2 (0.04)	6 (0.08)
<i>Eye</i>		
Antiglaucoma	6 (0.12)	12 (0.15)
<i>Nutrition and blood</i>		
Calcium supplements	47 (0.98)	66 (0.85)
Anemia and other blood disorders	32 (0.66)	40 (0.51)
Vitamin D derivatives	14 (0.29)	33 (0.42)
<i>Respiratory system</i>		
Bronchodilators/anti-inflammatory agents	73 (1.52)	55 (0.71)
Miscellaneous drugs	22 (0.46)	28 (0.36)
Total	3,636 (75.50)	6,595 (84.69)

Values are presented as numbers (%). <sup>a</sup> Fixed dose combination of diosmin 450 mg plus hesperidin 500 mg (Daflon<sup>®</sup>) indicated for the treatment of chronic venous diseases. <sup>b</sup> Includes trimetazidine which is usually prescribed as a long-term treatment for angina pectoris in case of inadequate control by or intolerance to first-line antianginal therapies. <sup>c</sup> Includes pentoxifylline used in the treatment of circulatory ischemic disorders such as in intermittent claudication.

age group and care setting but without specifying the nature of chronic diseases.

Given the trend in prescribing according to evidence-based guidelines especially in older adults with multiple comorbidities, the definition of 5 or more medications as a threshold for polypharmacy seems too low [7]. Since approximately 80% of the drugs per patient were for multiple chronic morbidities, the value of 6 medications per patient found in our study suggests that prescriptions were likely evidence based. The current observational study revealed that the mean prevalence of  $\geq$ PIP was estimated to be 34.1%; only 27.7% (18 out of 65) of STOPP

criteria were applicable. Of note, authors of other recent studies who recruited patients in a similar age group, care-setting, and STOPP criteria reported a prevalence that ranged from 14.8 to 52.7% [2, 17, 18, 20–24]. The disparity in the prevalence rates could be attributed to variables such as the study design, the physician's prescribing behavior, the nature of the chronic morbidity, prescribing regulations, and the clinical setting [12, 18, 24]. Furthermore, the primary care essential drug list, the regional drug market situation, and country-specific PIP are other determinants of PIP prevalence and PIP subsets that can be identified using STOPP criteria.

The most frequent PIP was related to medications intended for chronic conditions that included duplication of antihypertensive therapy and use of glyburide, a long-acting oral hypoglycemic drug, whereas medications prescribed for acute medical illness were skeletal muscle relaxant orphenadrine (Muscadol®), long-term use of drugs such as NSAID, proton pump inhibitors, and chlordiazepoxide. Although medications prescribed for acute medical illnesses accounted for approximately one fifth of the overall prescribed drugs/patient, they contributed the most to PIP prevalence in older adults. Such medications should be judiciously prescribed in order to limit inappropriate polypharmacy in older adults.

Orphenadrine has been identified by both STOPP [8] and American Geriatric Society Beers criteria [25] as a potentially inappropriate medication to be avoided in patients aged  $\geq 65$  years. This is because orphenadrine has strong anticholinergic properties and increases the risk of sedation, confusion, falls, and fractures [8, 25]. None of the published primary care-based studies [2, 17, 18, 20–24] have identified PIP of orphenadrine. In contrast, orphenadrine was the most common PIP detected in our study. This observation supports the recommendation that there is a need to conduct country-specific PIP studies in older adults to gain a better global perspective [17]. Previous studies have confirmed that the dose and duration of NSAID significantly increased the risk of mortality in patients aged  $\geq 65$  due to gastrointestinal complications [26]. Long-term use of NSAID in our study was ranked as the second most common PIP trend; a similar trend has been reported in UK [2], Serbia [21], and Sweden [24]. In older adults, the long-term use of proton pump inhibitors at full therapeutic dose for  $>8$  weeks is deemed inappropriate and is best avoided unless otherwise justified. Such use may increase the risk of fracture, vitamin B<sub>12</sub> deficiency, hyponatremia, hypomagnesemia, and *Clostridium difficile* infection [8, 25]. Proton pump inhibitors ranked as the third most common PIP in our study, a trend reported from Ireland [22] and the UK [2] as well. Chlordiazepoxide, a long-acting benzodiazepine, has been identified as potentially inappropriate medication for older adults. Its use either alone or as a fixed-dose combination is best avoided because it can increase the risk of cognitive impairment, delirium, impaired balance, falls, and fractures [8, 25]. Long-acting benzodiazepine (chlordiazepoxide), identified as the fourth common PIP in our study, was the most common PIP reported in several European Union countries [2, 18, 20–22, 24].

We attempted to explore the differences in polypharmacy and PIP between FP and GP, the two categories of primary care physicians in Bahrain. More drugs per patient were prescribed by FP than by GP; such a difference can be attributed to the fact that most of the patients with both diabetes and hypertension and referral cases from secondary to primary care are managed at diabetes outpatient clinics by FP with in-depth diabetes care training. This explanation is further corroborated by findings that the proportion of patients with both diabetes and hypertension treated by FP was considerably higher than that of patients treated by GP (77.7 vs. 19.6%,  $\chi^2 = 1,630.57$ ;  $p < 0.0001$ ; data not shown). Although FP showed a slightly greater tendency towards PIP compared to GP, the difference was statistically nonsignificant. In older adults, orphenadrine intended mainly for short-term acute illnesses was favored by FP, whereas antihypertensive therapy duplication was by GP. Combination therapy with angiotensin-converting enzyme inhibitor and angiotensin II receptor blocker has been reported to increase the risk of hyperkalemia and renal failure [27].

The reasons for PIP in older adults by primary care physicians in Bahrain are uncertain. Previous studies in other countries have identified several risk factors linked to PIP in older adults: inadequate training of primary care practitioner in using STOPP or Beers criteria [28]; poor knowledge and awareness about PIP to older adults [28, 29]; inappropriate polypharmacy [29]; and short consultation times in older adults. A consultation time of less than 10 min/patient has been reported to be insufficient by primary care practitioners in many countries [28, 30, 31]; it was longer for patients in the older-age group and the length of consultation depended on the medical conditions of the patients [31]. The estimated consultation time of 8 min/patient in the primary care general clinic setting in Bahrain appears to be insufficient for older adults with multiple chronic morbidities. Addressing such organizational issues of primary care is critical for decreasing PIP and enhancing the overall quality of health care.

There are several limitations to the current study. During the data collection period, patients' data in the primary care setting in Bahrain was not digitized. Several PIP subsets of STOPP criteria cannot be identified by prescription audit alone and would require the patient's clinical and/or laboratory data. Some notable examples for such PIP are: NSAID given to patients with a history of peptic ulcer disease, moderate to severe hypertension, heart failure, or renal failure; long-term use of NSAID

(>3 months) for mild joint pain; use of metformin in patients with an estimated glomerular filtration rate <30 mL/min/1.73 m<sup>2</sup>; aspirin in patients with no history of coronary, cerebral, or peripheral arterial symptoms or occlusive arterial events; and thiazide diuretic in patients with a history of gout. Therefore, a prescription audit would not have identified these PIP comprehensively. Despite some notable differences in PIP among FP and GP, the study design did not have statistical power to confirm with certainty the differences. The lack of information about over-the-counter medications may have underestimated the overall PIP magnitude. The strength of this study is that it included a nationwide targeted sample, and the sample size is robust considering the demographic pattern of Bahrain.

## Conclusion

The prevalence of PIP in Bahrain was within the spectrum reported worldwide and it was found to be unrelated to the training background of primary care physicians. Most often PIP was for medications intended for acute medical illness in older adults. Educational interventions with an explicit emphasis on rational prescribing for older adults are recommended to reduce PIP and polypharmacy practice.

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## References

- Page RL, Linnebur SA, Bryant LL, et al: Inappropriate prescribing in the hospitalized elderly patient: defining the problem, evaluation tools, and possible solutions. *Clin Interv Aging* 2010;5:75–87.
- Hajjar ER, Haulon JT, Maher RL Jr: Adverse drug events, polypharmacy and medication management; in Hutchison LC, Sleeper RB (eds): *Fundamentals of Geriatric Pharmacotherapy*, ed 2. Bethesda, American Society of Health-System Pharmacists, 2015, pp 91–108.
- O'Connor MN, Gallagher P, O'Mahony D: Inappropriate prescribing: criteria, detection and prevention. *Drugs Aging* 2012;29:437–452.
- National Institute for Health and Care Excellence: Multimorbidity and polypharmacy – key therapeutic topic (KTT 18). 2017. <https://www.nice.org.uk/advice/ktt18> (accessed December 25, 2017).
- Campbell SM, Braspenning J, Hutchinson A, et al: Research methods used in developing and applying quality indicators in primary care. *Qual Saf Health Care* 2002;11:358–364.
- Yang P-J, Lee Y-T, Tzeng S-L, et al: Potentially inappropriate prescribing in disabled older patients with chronic diseases: a screening tool of older persons' potentially inappropriate prescriptions versus Beers 2012 criteria. *Med Princ Pract* 2015;24:565–570.
- Avery A, Barber N, Ghaleb M, et al: Investigating the prevalence and causes of prescribing errors in general practice: the PRACtCe Study. [www.gmc-UK.org/about/research/12996.asp](http://www.gmc-UK.org/about/research/12996.asp) (accessed October 17, 2016).
- Gallagher P, Ryan C, Byrne S, et al: STOPP (Screening Tool of Older Person's Prescriptions) and START (Screening Tool to Alert doctors to Right Treatment): consensus validation. *Int J Clin Pharmacol Ther* 2008;46:72–83.
- Barber ND, Alldred DP, Raynor DK, et al: Care homes use of medicines study: prevalence, causes and potential harm of medication errors in homes for older people. *Qual Saf Health Care* 2009;18:341–346.
- Steinman MA, Landefeld CS, Rosenthal GF, et al: Polypharmacy and prescribing quality in older people. *J Am Geriatr Soc* 2006;54:1516–1523.
- O'Mahony D, O'Sullivan D, Byrne S, et al: STOPP/START criteria for potentially inappropriate prescribing in older people: version 2. *Age Ageing* 2015;44:213–218.
- Hill-Taylor B, Sketris I, Hayden J, et al: Application of the STOPP/START criteria: a systematic review of the prevalence of potentially inappropriate prescribing in older adults, and evidence of clinical, humanistic and economic impact. *J Clin Pharm Ther* 2013;38:360–372.
- Alfaro Lara ER, Vega Coca MD, Banqueri MG, et al: Selection of tools for reconciliation, compliance and appropriateness of treatment in patients with multiple chronic conditions. *Eur J Intern Med* 2012;23:506–512.
- Hill-Taylor B, Walsh KA, Stewart S, et al: Effectiveness of the STOPP/START (Screening Tool of Older Persons' potentially inappropriate Prescriptions/Screening Tool to Alert doctors to the Right Treatment) criteria: systematic review and meta-analysis of randomized controlled studies. *J Clin Pharm Ther* 2016;41:158–169.
- Al Khaja KA, Sequeira RP, Al-Ansari TM, et al: Prescription writing skills of residents in a family practice residency programme in Bahrain. *Postgrad Med J* 2008;84:198–204.
- Lee CS, Liew TM: Inappropriate prescribing among older persons in primary care: protocol for systematic review and meta-analysis of observational studies. *BMJ Open* 2017;7:e015395.
- Bahat G, Bay I, Tufan A, et al: Prevalence of potentially inappropriate prescribing among older adults: a comparison of the Beers 2012 and Screening Tool of Older Person's Prescriptions criteria version 2. *Geriatr Gerontol Int* 2017;17:1245–1251.
- Blanco-Reina E, García-Merino MR, Ocaña-Riola R, et al: Assessing potentially inappropriate prescribing in community-dwelling older patients using the updated version of STOPP-START criteria: a comparison of profiles and prevalences with respect to the original version. *PLoS One* 2016;11:e0167586.
- Lesende IM, Crespo IM, López GM, et al: Potentiality of STOPP/START criteria used in primary care to effectively change inappropriate prescribing in elderly patients. *Eur Geriatr Med* 2013;4:293–298.
- Dalleur O, Boland B, De Groot A, et al: Detection of potentially inappropriate prescribing in the very old: cross-sectional analysis of the data from the BELFRAIL observational cohort study. *BMC Geriatr* 2015;15:156.
- Kovačević SV, Simišić M, Rudinski SS, et al: Potentially inappropriate prescribing in older primary care patients. *PLoS One* 2014;9:e95536.
- Ryan C, O'Mahony D, Kennedy J, et al: Potentially inappropriate prescribing in an Irish elderly population in primary care. *Br J Clin Pharmacol* 2009;68:936–947.



- 23 Oliveira MG, Amorim WW, de Jesus SR, et al: A comparison of the Beers and STOPP criteria for identifying the use of potentially inappropriate medications among elderly patients in primary care. *J Eval Clin Pract* 2015;21:320–325.
- 24 Hedna K, Hakkarainen KM, Gyllensten H, et al: Potentially inappropriate prescribing and adverse drug reactions in the elderly: a population-based study. *Eur J Clin Pharmacol* 2015;71:1525–1533.
- 25 American Geriatrics Society 2012 Beers Criteria Update Expert Panel: American Geriatrics Society updated Beers criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc* 2012;60:616–631.
- 26 Straube S, Tramèr MR, Moore RA, et al: Mortality with upper gastrointestinal bleeding and perforation: effects of time and NSAID use. *BMC Gastroenterol* 2009;9:41.
- 27 ONTARGET Investigators; Yusuf S, Teo KK, et al: Telmisartan, ramipril, or both in patients at high risk for vascular events. *N Engl J Med* 2008;358:1547–1559.
- 28 Maio V, Jutkowitz E, Herrera K, et al: Appropriate medication prescribing in elderly patients: how knowledgeable are primary care physicians? A survey study in Parma, Italy. *J Clin Pharm Ther* 2011;36:468–480.
- 29 Ramaswamy R, Maio V, Diamond JJ, et al: Potentially inappropriate prescribing in elderly: assessing doctor knowledge, confidence and barriers. *J Eval Clin Pract* 2011;17:1153–1159.
- 30 ICM Unlimited BMC: British Medical Association National Survey of GPs the future of general practice. 2015. <https://www.bma.org.uk//media/files/pdfs/working%20for%20change/negotiating%20for%20the%20profession/general%20practitioners/future%20of%20general%20practice%20full%20survey%202015.pdf> (accessed December 22, 2016).
- 31 Tähepold H, Maaros HL, Kalda R, et al: Structure and duration of consultations in Estonian family practice. *Scand J Prim Health Care* 2003;21:167–170.