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7	Prevalence, Characteristics and Determinants of Polypharmacy Among
8	Elderly Patients Attending Primary Health Care Centers in Bahrain
9	A cross-sectional study
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17 Abstract

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Objectives: This study aims to determine the prevalence, characteristics and determinants of 18 polypharmacy among elderly patients in Bahrain. *Methods*: A cross-sectional study was conducted 19 20 in the period between March and April 2022 in all primary healthcare centres in Bahrain. A simple random sample was obtained. An elderly patient was defined as a patient aged 60 years or above. 21 22 In addition, polypharmacy was defined as the concomitant use of 5 medications or more and 23 excessive polypharmacy was defined as the concomitant use of 10 medications or more. *Results:* 24 A total of 977 patients were included, more than half of them were females (n=533, 54.44%) and the mean age of the participants was 67.90 ± 6.87 years. Essential hypertension, hyperlipidemia 25 and diabetes mellitus were the most common comorbidities among the participants (61.51%, 26 27 57.63% and 53.22%, respectively). Of the cohort, 443 were on 5 or more medications i.e., polypharmacy (45.34%), and around 7% were on at least 10 medications (n=66, 6.76%). A 28 29 multivariate analysis revealed that patients with diabetes (OR=5.836, CI 4.061-8.385, P<0.001), hypertension (OR=6.231, CI= 4.235-9.168, P<0.001), hyperlipidemia (OR 3.999, 95% CI 2.756-30 5.802, P<0.001), cardiovascular diseases (OR 3.589, 95 CI 1.787-7.205, P<0.001) and asthma (OR 31

3.148, 95% CI 1.646-6.019, P<0.001) were significantly more likely to suffer from polypharmacy. 32 *Conclusion:* Polypharmacy was prevalent among elderly patients in Bahrain, particularly among 33 those with non-communicable diseases. Polypharmacy should be considered while delivering 34 elderly healthcare services, especially in patients with non-communicable diseases. 35 Keywords: Aged, Bahrain, Elderly, Polymorbidity, Polypharmacy. 36 37 **Advances in Knowledge** 38 This study revealed a high prevalence of polypharmacy and excessive polypharmacy 39 among elderly patients in Bahrain. It is the first study to assess polypharmacy among 40 elderly patients in Bahrain. 41 A significantly higher prevalence of polypharmacy was seen in patients with non-42 43 communicable diseases. 44 **Application to Patient Care** 45 46 The findings of this study describe the magnitude and determinants of polypharmacy 47 among old patients and the importance of deprescribing and avoiding unnecessary 48 medications in this group. 49 Elderly patients with chronic diseases are at a higher risk of polypharmacy and might 50 51 benefit more from any intervention to minimize polypharmacy. 52 Introduction 53 Globally, there is a rapid increase in the elderly population that is attributed to improvements in 54 55 medical services, better hygiene practices, availability of immunization and antimicrobials, and improvements in work and home environments.^{1, 2} It is projected that the number of old people 56 will increase from one billion in 2020 to more than two billion in 2050.³ According to United 57 Nations and World Health Organization, people aged 60 years are considered elderly.⁴ According 58 59 to the Bahrain National Health Survey 2018, the overall number of elderly individuals was 86,986, and around 2.8% of the population belongs to the age group of 65 years old and above.⁵ 60

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There is a substantial variation in defining an elderly population in the literature. Some studies and organizations use the age of 60 years to define old age, while other studies use the age of 65 years, 70 years and even 80 years to define old age. ^{6,7} This heterogeneity in the definition of old age results in different rates of diseases and outcomes across the studies.⁸

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Elderly patients are at risk of polymorbidity, defined as the presence of two or more chronic diseases. Non-communicable diseases including essential hypertension, diabetes mellitus, lipid disorders, and cardiac diseases are common among older individuals.⁹ Frailty and psychiatric disorders like dementia also increase with ageing.¹⁰ These diseases often require several medications for treatment, control and prevention.¹¹⁻¹²

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Considering the deterioration in the physiological and functional abilities of old people, drugrelated adverse effects and drug-drug interactions are frequent in this age category.¹³ Thus, using the minimum number of medications and frequent monitoring for such interactions is often necessary among the elderly, especially for medications with a narrow therapeutic index. ¹⁴ Several guidelines were published to address polypharmacy and prescribing issues in the elderly.^{14, 15, 16}

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79 Polypharmacy, commonly defined as the concomitant use of five or more medications by one patient, is a consequence of polymorbidity and a major issue in the management of patients with 80 chronic diseases.¹⁷ Older patients are at even higher risk of polypharmacy due to their 81 multimorbidity, decline in physical, physiological, sensory and cognitive functions and their 82 vulnerability to prescription cascade.¹⁸ Healthcare system and healthcare provider factors could 83 also potentially contribute to the high prevalence of polypharmacy among the elderly. Factors like 84 poorly maintained records, automated medication refill and absence of prescription guidelines are 85 liked to a higher risk of polypharmacy.¹⁹ 86

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Polypharmacy negatively affects patients' prognosis and disease outcomes. Polypharmacy in old
 age lowers functionality and increases the risk of mortality as found by some systematic reviews.^{20,}
 ²¹ Polypharmacy was linked to a higher risk of hip fractures, inappropriate prescribing and
 hospitalization. ^{22, 23}

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Many studies reported high rates of polypharmacy in old patients. A large cohort study of more 93 than 1.5 million elderly patients, concluded that the prevalence of polypharmacy was 44.0%, while 94 the prevalence of excessive polypharmacy was 11.7%.²⁴ In Qatar, polypharmacy was seen in 95 75.5% of elderly people. Female sex and the presence of chronic diseases were strong determinants 96 of higher risks of polypharmacy in these studies.²⁵ A study conducted in Saudi Arabia revealed 97 that as high as 55% of the elderly suffered from polypharmacy.²⁶ A large systematic review of 27 98 studies and more than nine thousand participants found that 49% of old people were on 5 or more 99 medications and 31% were on more than 10 medications.²⁷ 100

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This study aimed to determine the prevalence, characteristics and determinants of polypharmacy
in elderly patients attending primary healthcare centers in Bahrain. To the best of our knowledge,
no previous studies were conducted to assess the prevalence and characteristics of polypharmacy
among elderly patients attending primary healthcare centers in Bahrain.

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107 Methods

108 Study setting and design

A cross-sectional study was conducted among elderly patients attending primary healthcare centers in Bahrain. There are 27 primary health centres and five health regions in Bahrain. Elderly patients attending all health centers were considered for eligibility. Research approval was obtained from the Research and Ethics Committees of Primary Healthcare in Bahrain, and informed written consent was taken from all participants in the study.

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115 **Population and sampling**

In the period between March and April 2022, 15666 elderly patients visited primary healthcare
centers in Bahrain. Considering the total number of the elderly population in Bahrain (n=48053),
95% confidence interval, 5% precision level and a predicted prevalence of polypharmacy of 50%,
a sample size of 385 was targeted to determine statistical significance. A computer-based random
sample was taken from the pool of the patients (n=15666).

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122 **Operational definitions**

An elderly patient was defined as a patient aged 60 years or above. Polypharmacy was defined as the concomitant use of 5 medications or more at the selected clinical encounter (the 1st visit in the period between March and April 2022) and excessive polypharmacy was defined as the concomitant use of 10 medications or more at the selected visit during the same period. Topical agents including ear drops, nasal drops, inhalers and urgent injections were not considered as regular medications. Non-prescription medications, herbals, and vitamins were not assessed. All diagnoses were based on International Classification of Diseases (ICD-10).

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131 Inclusion and exclusion criteria

Adult patients aged 60 years or above who attended primary care centers in the period between
March and April 2022 were eligible for inclusion. If the patient had several visits in the selected
period, data of the first visit only were retrieved from the electronic records.

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136 Data collection instrument

A data collection tool was formulated. The tool consisted of 3 parts; the first part of the tool composed of sociodemographic characteristics of the patients and included age, sex, nationality and marital status; the second part assessed patients' comorbidities including diabetes mellitus, essential hypertension, hyperlipidemia, cerebrovascular accident and chronic kidney disease. The third part assessed all the medications available at primary care centers and included name and category of the medication according to anatomical therapeutic chemical classification system.

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144 Data analysis procedure

Frequencies and percentages were computed for categorical variables while means and standard deviations were computed for continuous variables. T-tests were used to compare differences in means between two independent groups, while categorical variables were compared using chisquare test. The data was analyzed using Statistical Package for Social Sciences software, version 26.0. In all tests, a p-value of less than 0.05 was statistically considered significant.

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151 **Results**

152 *Baseline characteristics of the participants*

A total of 977 patients were randomly selected and included in the study. The mean age of the participants was 67.90 ± 6.87 years and more than half of them were females (n=533, 54.44%). The majority of patients were Bahraini (94.37%) and married (74.51%). Regarding comorbidities, essential hypertension, hyperlipidemia and diabetes mellitus were the most common comorbidities among the participants (61.51%, 57.63% and 53.22%, respectively). Table (1).

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159 *Medication characteristics*

160 As shown in Table (2), metformin was the most commonly used medication among elderly 161 patients, followed by atorvastatin (n=296, 30.30%) and perindopril (n=248, 25.38%).

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As shown in Table (3), most patients were taking less than 5 medications (n=534, 54.66%), and the average number of medications was 4.36 medications per patient. In addition, 45.34% of the participants were on 5 or more medications and around 7% were taking 10 medications or more (n=66, 6.76%).

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168 Association between baseline characteristics of the participants and polypharmacy status

169 Univariate analysis showed that patients with advanced age (P=0.001), diabetes mellitus 170 (<0.001), essential hypertension (P<0.001), hyperlipidemia (P<0.001), cardiovascular diseases 171 (P<0.001), bronchial asthma (P<0.001) and hypothyroidism (P=0.010) were more likely to suffer 172 from polypharmacy. Table (4).

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The results of the multivariate analysis are shown in Table 5. Patients with diabetes mellitus were 174 6 times more likely to suffer from polypharmacy compared to patients without diabetes 175 (OR=5.836, CI 4.061-8.385, P<0.001). Similarly, patients with hypertension were more likely to 176 177 have polypharmacy than normotensive patients (OR=6.231, CI= 4.235-9.168, P<0.001). In 178 addition, polypharmacy rate was four times higher among patients with hyperlipidemia (OR 3.999, 95% CI 2.756-5.802, P<0.001) and cardiovascular diseases (OR 3.589, 95 CI 1.787-7.205, 179 180 P<0.001). Patients' age and presence of hypothyroidism did not influence the polypharmacy 181 status.

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183 Discussion

The results of this study revealed that almost half of the studied cohort suffered from polypharmacy. Additionally, the results showed that polypharmacy was significantly higher among patients with non-communicable diseases including diabetes mellitus, hypertension, hyperlipidemia, cardiovascular disease, bronchial asthma and hypothyroidism.

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Similar to the findings of this study, several regional studies reported high rates of polypharmacy 189 among old patients. ²³⁻²⁵ Internationally, lower rates of polypharmacy were reported. A cohort 190 study conducted in Iran reported a lower prevalence of polypharmacy among people aged 60 years 191 and above (23,1%).²⁸ The estimated prevalence of polypharmacy in Brazil was 13.5%.²⁹ In the 192 193 United States of America, a national health survey determined that the prevalence of polypharmacy among the elderly tripled from 12.8% in 1988 to 39.0% in 2010.³⁰ Furthermore, a 194 large multi-centre study was conducted in primary healthcare centers across Europe and reported 195 a polypharmacy prevalence of 27.2% (range between 16.4% and 60.8%).³¹ 196

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The variability in the reported prevalence rates of polypharmacy among elderly patients is 198 199 multifactorial. One of the reasons is the heterogeneity in the definition of polypharmacy among the studies. Some studies assessed the accumulative number of medications during a specific 200 period while other studies assessed the concurrent use of the medications. Another reason is the 201 heterogeneity in the definition of an elderly patient. Specifically, some studies considered the 202 chronological age of 60 years to define old age, while other studies considered the age of 65 years 203 to define old age.^{25,27} Additionally, study settings and methodologies were variable among the 204 studies. 6,7,11 205

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The high prevalence of polypharmacy in this study could be attributed to the high prevalence of 207 208 non-communicable diseases among the studied subjects. More than half of the studied patients 209 were suffering from diabetes mellitus, hypertension, and hyperlipidemia. This finding is in line with the results of Bahrain National Health Survey 2018 which showed that more than 76% of 210 those above 60 years old suffer from diabetes and more than 54% were hypertensive.⁵ These 211 conditions have a similar risk profile, tend to occur together and increase with age. Most of these 212 conditions require several medications to achieve adequate control. This is further supported by 213 214 the finding that metformin, atorvastatin, and perindopril were the three most prescribed

medications in this age group. Another explanation of the high rate of polypharmacy is the prescribing of medications for preventive use. Medications like statins and aspirin are commonly used for primary and secondary prevention purposes. Furthermore, there are no national or institutional guidelines to encourage deprescription among this group of patients in Bahrain. This might have had an impact on the rate of polypharmacy in the present study.

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Consistent with many studies, the results in the current study revealed a significant association
between polypharmacy and non-communicable diseases and showed that diabetes mellitus,
hypertension, hyperlipidemia, cardiovascular diseases and asthma were predictors of
polypharmacy. ^{24, 27, 30}

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Although the multivariate analysis in this study showed no association between polypharmacy 226 and patient's age, such finding was reported in the literature.²⁵ This association could be explained 227 228 by the fact that the number of chronic conditions usually increase with age with its concomitant need for drug treatment. In addition, no significant differences between male and female elderly 229 subjects and the risk of polypharmacy were found in this study. The studies are inconsistent 230 regarding the influence of the patient's sex on the risk of polypharmacy. While some studies 231 232 reported no significant differences between males and females in regard to polypharmacy, some studies reported a higher rate of polypharmacy among elderly females.^{24,30} 233

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Considering the negative consequences of polypharmacy and the increasing number of elderly 235 people in Bahrain, this study emphasizes the importance of practicing deprescription and 236 avoidance of unnecessary medications in this age group especially among patients with non-237 communicable diseases. Since primary healthcare is the first encounter for elderly patients in 238 Bahrain and is the optimal setting for prevention, quaternary prevention should be continuously 239 240 considered by family physicians while prescribing medications to elderly patients especially with the implementation of the "choose your doctor" program, a new program that allows each patient 241 to choose a family physician who would provide therapeutic and preventive services to him/her. 242 It will link each patient with one family physician instead of different family physicians, which 243 could minimize the prescription of unnecessary medications among elderly patients in particular.³² 244 245 Family physicians should periodically review the indication and importance of each medication and discontinue unneeded medications while treating elderly patients. In addition, polypill use can
minimize the risk of polypharmacy and simplify management regimens; therefore, polypill should
be considered by family physicians while treating elderly patients with chronic conditions.³³

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This study has several strengths. Firstly, all primary care centers were included in the study. Secondly, a simple random sample was obtained from the data pool which minimized the risk of selection bias. However, this study has some limitations. Only patients attending primary healthcare centers were included in the study. This may have overestimated the prevalence of polypharmacy among elderly patients. In addition, medications prescribed by the private sector and military hospitals were not assessed. Hence, the prevalence of polypharmacy may have been underestimated.

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258 Conclusion

In conclusion, this study revealed a high prevalence of polypharmacy among old people attending 259 primary healthcare services. Polypharmacy was significantly more common among patients with 260 non-communicable diseases like diabetes mellitus, essential hypertension, hyperlipidemia, 261 cardiovascular diseases and bronchial asthma. The high rate of polypharmacy must raise concerns 262 about its impact on patients' outcomes, morbidity and mortality. Considering the high prevalence 263 of polypharmacy, the rising number of elderly populations, the associated polymorbidity and 264 frailty and the consequences of polypharmacy, rational use of medicines guidelines and targeted 265 educational programs for general practitioners and family physicians should be developed. 266 Studies to assess the influence of polypharmacy on medication-taking behaviours among elderly 267 patients and its control of their medical conditions are needed. 268

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270 Authors' Contribution

271 MA, and FH conceptualized and designed the study. EA, ED and MAB reviewed the literature

- and prepared the first draft of the study. MA analyzed and interpreted the data. All authors
- 273 drafted the manuscript, read and approved the final version of the manuscript.
- 274

275 **Conflict of Interest**

276 The authors declare no conflicts of interest.

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Baseline characteris	n (%)	
Corr	Male	444 (45.45)
Sex	Female	533 (54.55)
Age, mean ± SD		67.90 ± 6.87
Nationality	Bahraini	922 (94.37)
Nationality	Non-Bahraini	55 (5.63)
	Single	43 (4.40)
Marital Status	Married	728 (74.51)
Marital Status	Divorced	54 (5.53)
	Widowed	152 (15.56)
	Essential hypertension	601 (61.51)
	Hyperlipidemia	563 (57.63)
	Diabetes Mellitus	520 (53.22)
	Hypothyroidism	121 (12.38)
Comorbidities	Bronchial asthma	80 (8.19)
	Cardiovascular diseases	79 (8.09)
	Psychiatric disorders	34 (3.48)
	Chronic kidney diseases	9 (0.92)
	Stroke	3 (0.31)

Table (1): Baseline characteristics of the participants

1 abie (2). Whose presenteed medications to enderry patients	Table (2): Most	prescribed medications	to elderly patients
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Medications	n (%)
Metformin (Glucophage)	422 (43.19)
Atorvastatin (Lipitor)	296 (30.30)
Perindopril (Coversyl)	248 (25.38)
Amlodipine (Norvasc)	227 (23.23)
Valsartan (Diovan)	215 (22.01)
Aspirin	215 (22.01)
Gliclazide (Diamicron)	181 (18.53)
Simvastatin (Zucor)	151 (15.46)
Pantoprazole (Proton)	146 (14.94)
Bisoprolol (Concor)	145 (14.84)
Rabeprazole (Pariet)	126 (12.90)
Hydrochlorothiazide	123 (12.59)
Thyroxine	119 (12.18)
Insulin Glargine (Lantus)	108 (11.05)
Rosuvastatin (Crestor)	105 (10.75)

Number of medications	Number of patients (%)
<5	534 (54.66)
5 to 9	377 (38.59)
10 or more	66 (6.76)
The average number of medications	4.36

Table (3): Number of medications used by the participants

Table (4): Associations between baseline characteristics of the participants and polypharmacy status

status		Polypharmacy, TN=443	No polypharmacy, TN=534	Р
		n (%)	n (%)	r value
	Male	195 (44.02)	249 (46.63)	vulue
Sex	Female	· · · · · ·		0.414
A company L CD	remaie	$248 (55.98) \\ 68.67 \pm 6.99$	285 (53.37)	0.001
Age, mean \pm SD	D 1 ' '		67.26 ± 6.71	0.001
Nationality	Bahraini	421 (95.03)	501 (93.82)	0.413
	Non-Bahraini	22 (4.97)	33 (6.18)	
	Single	21 (4.74)	22 (4.12)	_
Marital Status	Married	310 (69.98)	418 (78.28)	0.024
manua status	Divorced	28 (6.32)	26 (4.87)	0.021
	Widowed	84 (18.96)	68 (12.73)	
Diabetes Mellitus	Yes	358 (80.81)	162 (30.34)	<0.001
Diabetes Menitus	No	85 (19.19)	372 (69.66)	<0.001
Essential	Yes	385 (86.91)	216 (40.45)	<0.001
hypertension	No	58 (13.09)	318 (59.55)	
**	Yes	373 (84.20)	190 (35.58)	0.004
Hyperlipidemia	No	70 (15.80)	344 (64.42)	<0.001
Cardiovascular	Yes	64 (14.45)	15 (2.81)	0.001
diseases	No	379 (85.55)	519 (97.19)	<0.001
Cture las	Yes	2 (0.45)	1 (0.19)	0 457
Stroke	No	441 (99.55)	533 (99.81)	0.457
	Yes	53 (11.96)	27 (5.06)	.0.001
Bronchial asthma	No	390 (88.04)	507 (94.94)	<0.001
Chronic kidney	Yes	6 (1.35)	3 (0.56)	0.107
diseases	No	437 (98.65)	531 (99.44)	0.197
Psychiatric	Yes	20 (4.51)	14 (2.62)	0.455
disorders	No	423 (95.49)	520 (97.38)	0.108
TT (1 '1'	Yes	68 (15.35)	53 (9.93)	0.01
Hypothyroidism	No	375 (84.65)	481 (90.07)	0.01

	Odds ratio	95% Confidence interval	P value
Age	1.007	0.982-1.033	0.588
Marital Status (Compared to single)			
Marital Status (Married)	0.744	0.287-1.931	0.543
Marital Status (Divorced)	0.691	0.425-1.123	0.136
Marital Status (Widowed)	0.881	0.369-2.101	0.775
Diabetes Mellitus	5.836	4.061-8.385	<0.001
Essential hypertension	6.231	4.235-9.168	<0.001
Hyperlipidemia	3.999	2.756-5.802	<0.001
Cardiovascular diseases	3.589	1.787-7.205	<0.001
Bronchial asthma	3.148	1.646-6.019	<0.001
Hypothyroidism	1.643	0.985-2.739	0.057

Table (5): Logistic regression analysis of polypharmacy determinants