

Prevalence, Characteristics and Determinants of Polypharmacy Among Elderly Patients Attending Primary Healthcare Centres in Bahrain

A cross-sectional study

*Mahmood Alawainati,^{1,2} Fatima Habib,¹ Eman Ateya,¹ Eman Dakheel,¹ Muneera Al-Buainain¹

ABSTRACT: Objectives: This study aimed to determine the prevalence, characteristics and determinants of polypharmacy among elderly patients in Bahrain. **Methods:** This cross-sectional study was conducted between March and April 2022 in all primary healthcare centres in Bahrain. A simple random sample was obtained. An elderly patient was defined as one aged ≥ 60 years and polypharmacy was defined as the concomitant use of 5 or more medications, with excessive polypharmacy defined as the concomitant use of 10 or more medications. **Results:** A total of 977 patients were included, with more than half of them being females ($n = 533$, 54.55%) and the mean age of the participants at 67.90 ± 6.87 years. Essential hypertension, hyperlipidaemia and diabetes mellitus were the most common comorbidities among the participants (61.51%, 57.63% and 53.22%, respectively). Among the cohort, 443 (45.34%) were on 5 or more medications and of those 66 (6.76%) were on at least 10 medications. A multivariate analysis revealed that patients with diabetes (odds ratio [OR] = 5.836, 95% confidence interval [CI]: 4.061–8.385; $P < 0.001$), hypertension (OR = 6.231, 95% CI: 4.235–9.168; $P < 0.001$), hyperlipidaemia (OR = 3.999, 95% CI: 2.756–5.802; $P < 0.001$), cardiovascular diseases (OR = 3.589, 95% CI: 1.787–7.205; $P < 0.001$) and asthma (OR = 3.148, 95% CI: 1.646–6.019; $P < 0.001$) were significantly more likely to suffer from polypharmacy. **Conclusion:** Polypharmacy is prevalent among elderly patients in Bahrain, particularly among those with non-communicable diseases. Polypharmacy should be considered while delivering healthcare services to the elderly, especially those with non-communicable diseases.

Keywords: Aged; Elderly; Polypharmacy; Bahrain.

ADVANCES IN KNOWLEDGE

- This study revealed a high prevalence of polypharmacy and excessive polypharmacy among elderly patients in Bahrain.
- This is the first study to assess polypharmacy among elderly patients in Bahrain.
- A significantly higher prevalence of polypharmacy was observed among patients with non-communicable diseases.

APPLICATION TO PATIENT CARE

- The findings of this study describe the prevalence and determinants of polypharmacy among elderly patients and the importance of deprescribing and avoiding unnecessary medications in this group.
- Elderly patients with chronic diseases are at a higher risk of polypharmacy and might benefit more from interventions to minimise polypharmacy.

GLOBALLY, THERE IS A RAPID INCREASE in the elderly population, attributable to improvements in medical services, better hygiene practices, availability of immunisation and antimicrobials and improvements in the work and home environments.^{1,2} The elderly population is expected to increase from 1 billion in 2020 to more than 2 billion in 2050.³ According to the United Nations and World Health Organization, people aged ≥ 60 years are considered elderly.⁴ According to the Bahrain National Health Survey 2018, the overall number of elderly individuals was 86,986 and around 2.8% of the population was aged 65 years and above.⁵

There is a substantial variation in the definition of an elderly population in the literature. Some studies and organisations use the age of 60 to define old age,

while others use 65 years, 70 years and even 80 years to mark old age.^{6,7} This heterogeneity in the definition of old age has resulted in different rates of diseases and outcomes across studies.⁸

Elderly patients are at risk of polymorbidity, which is defined as the presence of 2 or more chronic diseases. Non-communicable diseases, including essential hypertension, diabetes mellitus, lipid disorders and cardiac diseases, are common among older individuals.⁹ The prevalence of frailty and psychiatric disorders such as dementia also increases with age.¹⁰ These diseases often require several medications for their treatment, control and prevention.^{11,12}

Considering the deterioration in the physiological and functional abilities of old people, drug-related adverse effects and drug–drug interactions are frequent

¹Family Medicine, Primary Healthcare Centers, Manama, Bahrain; ²Family Medicine, Royal College of Surgeons in Ireland - Medical University of Bahrain, Muharraq, Bahrain.

*Corresponding Author's e-mail: mja91@live.com

in this age category.¹³ Thus, using the minimum number of medications possible and frequently monitoring for such interactions is necessary among the elderly, especially for medications with a narrow therapeutic index.¹⁴ Several guidelines have been published to address polypharmacy and prescription issues in the elderly.^{14–16}

Polypharmacy, commonly defined as the concomitant use of 5 or more medications by one patient, is a consequence of polymorbidity and a major issue in the management of patients with chronic diseases.¹⁷ Older patients are at even higher risk of polypharmacy due to their multimorbidity; decline in physical, physiological, sensory and cognitive functions; and vulnerability to the prescription cascade.¹⁸ Healthcare system and provider factors also potentially contribute to the high prevalence of polypharmacy among the elderly. Factors such as poorly maintained records, automated medication refill and absence of prescription guidelines are linked to a higher risk of polypharmacy.¹⁹

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

Many studies have reported high rates of polypharmacy among old patients. A large cohort study of more than 1.5 million elderly patients calculated the prevalence of polypharmacy at 44.0% and that of excessive polypharmacy at 11.7%.²⁴ In Qatar, polypharmacy was observed in 75.5% of the elderly population. Female sex and the presence of chronic diseases were strong determinants of higher risks of polypharmacy in these studies.²⁵ A study conducted in Saudi Arabia revealed that as high as 55% of the elderly suffered from polypharmacy.²⁶ A large systematic review of 27 studies and more than 9,000 participants found that 49% of old people were on 5 or more medications and 31% were on more than 10 medications.²⁷

The current study aimed to determine the prevalence, characteristics and determinants of polypharmacy among elderly patients attending primary healthcare centres in Bahrain. To the best of the authors' knowledge, no previous studies have assessed the prevalence and characteristics of polypharmacy among elderly patients attending primary healthcare centres in Bahrain.

Methods

This cross-sectional study was conducted among elderly patients attending primary healthcare centres in Bahrain from March to April 2022. There are 27 primary health centres and 5 health regions in Bahrain. Elderly patients attending all health centres were considered eligible for this study.

A total of 15,666 elderly patients visited primary healthcare centres in Bahrain in the period between March and April 2022. Considering the total population of the elderly in Bahrain ($n = 48,053$), as well as a 95% confidence interval, 5% precision level and predicted polypharmacy prevalence of 50%, a sample size of 385 was targeted to determine statistical significance. A computer-based random sample was taken from the pool of patients ($n = 15,666$).

An elderly patient was defined as any patient aged 60 years or above. Polypharmacy was defined as the concomitant use of 5 or more medications at a selected clinical encounter (the first visit in the period between March and April 2022), and excessive polypharmacy was defined as the concomitant use of 10 or more medications at a selected visit within 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 the 10th edition of the International Classification of Diseases.

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

A data collection tool was formulated. The tool consisted of 3 parts. The first part of the tool inquired about the sociodemographic characteristics of the patients, such as age, sex, nationality and marital status; the second part assessed patients' comorbidities, including diabetes mellitus, essential hypertension, hyperlipidaemia, cerebrovascular accident and chronic kidney disease. The third part assessed all the medications available at the primary care centres in Bahrain and included the name and category of the medication according to the Anatomical Therapeutic Chemical classification system.

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 the Chi-squared test. The data were analysed using the Statistical Package for Social Sciences (SPSS), Version 26.0 (IBM Corp., Armonk, New York, USA). A *P* value of less than 0.05 was considered statistically significant.

Research approval was obtained from the Research and Ethics Committees of Primary Healthcare in Bahrain, and informed written consent was obtained from all participants prior to the commencement of the study.

Results

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 ($n = 533$, 54.55%). Majority of the patients were Bahraini (94.37%) and married (74.51%). Essential hypertension, hyperlipidaemia and diabetes mellitus were the most common comorbidities among the participants (61.51%, 57.63% and 53.22%, respectively) [Table 1].

Table 1: Characteristics of the participants (N = 977)

Characteristic	n (%)
Gender	
Male	444 (45.45)
Female	533 (54.55)
Mean age in years \pm SD	67.90 \pm 6.87
Nationality	
Bahraini	922 (94.37)
Non-Bahraini	55 (5.63)
Marital status	
Single	43 (4.40)
Married	728 (74.51)
Divorced	54 (5.53)
Widowed	152 (15.56)
Comorbidities	
Essential hypertension	601 (61.51)
Hyperlipidaemia	563 (57.63)
Diabetes mellitus	520 (53.22)
Hypothyroidism	121 (12.38)
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)

SD = standard deviation

Table 2: Most prescribed medications among elderly patients

Medication	n (%)
Metformin	422 (43.19)
Atorvastatin	296 (30.30)
Perindopril	248 (25.38)
Amlodipine	227 (23.23)
Valsartan	215 (22.01)
Aspirin	215 (22.01)
Gliclazide	181 (18.53)
Simvastatin	151 (15.46)
Pantoprazole	146 (14.94)
Bisoprolol	145 (14.84)
Rabeprazole	126 (12.90)
Hydrochlorothiazide	123 (12.59)
Thyroxine	119 (12.18)
Insulin Glargine	108 (11.05)
Rosuvastatin	105 (10.75)

Metformin was the most commonly used medication among the elderly patients in this study, followed by atorvastatin ($n = 296$, 30.30%) and perindopril ($n = 248$, 25.38%) [Table 2].

Most of the patients ($n = 534$, 54.66%) were taking less than 5 medications, and the average number of medications was 4.36 per patient. Additionally, 45.34% of the participants were on 5 or more medications, and approximately 7% were taking 10 or more medications ($n = 66$, 6.76%) [Table 3].

A univariate analysis showed that patients with advanced age ($P = 0.001$), diabetes mellitus ($P < 0.001$), essential hypertension ($P < 0.001$), hyperlipidaemia ($P < 0.001$), cardiovascular diseases ($P < 0.001$), bronchial asthma ($P < 0.001$) and hypothyroidism ($P = 0.010$) were more likely to suffer from polypharmacy [Table 4].

In contrast, a multivariate analysis showed that patients with diabetes mellitus were 6 times more likely to suffer from polypharmacy than those without diabetes (OR = 5.836, 95% CI: 4.061–8.385; $P < 0.001$).

Table 3: Number of medications used by the participants

Number of medications	Number of patients (%)
<5	534 (54.66)
5–9	377 (38.59)
≥ 10	66 (6.76)
Average number of medications per patient	4.36

Similarly, patients with hypertension were more likely to have polypharmacy than normotensive patients (OR = 6.231, 95% CI: 4.235–9.168; $P < 0.001$). Moreover, the prevalence of polypharmacy was 4 times higher among patients with hyperlipidaemia (OR = 3.999, 95% CI: 2.756–5.802; $P < 0.001$) and cardiovascular diseases (OR = 3.589, 95% CI: 1.787–7.205; $P < 0.001$). Patients' age and the presence of hypothyroidism did not influence polypharmacy status.

Table 4: Associations between participants' baseline characteristics and their polypharmacy status

	n (%)		P value
	Polypharmacy (n = 443)	No polypharmacy (n = 534)	
Sex			0.414
Male	195 (44.02)	249 (46.63)	
Female	248 (55.98)	285 (53.37)	
Mean age ± SD	68.67 ± 6.99	67.26 ± 6.71	0.001
Nationality			0.413
Bahraini	421 (95.03)	501 (93.82)	
Non-Bahraini	22 (4.97)	33 (6.18)	
Marital status			0.024
Single	21 (4.74)	22 (4.12)	
Married	310 (69.98)	418 (78.28)	
Divorced	28 (6.32)	26 (4.87)	
Widowed	84 (18.96)	68 (12.73)	
Diabetes mellitus			<0.001
Yes	358 (80.81)	162 (30.34)	
No	85 (19.19)	372 (69.66)	
Essential hypertension			<0.001
Yes	385 (86.91)	216 (40.45)	
No	58 (13.09)	318 (59.55)	
Hyperlipidaemia			<0.001
Yes	373 (84.20)	190 (35.58)	
No	70 (15.80)	344 (64.42)	
Cardiovascular diseases			<0.001
Yes	64 (14.45)	15 (2.81)	
No	379 (85.55)	519 (97.19)	
Stroke			0.457
Yes	2 (0.45)	1 (0.19)	
No	441 (99.55)	533 (99.81)	
Bronchial asthma			<0.001

Yes	53 (11.96)	27 (5.06)	
No	390 (88.04)	507 (94.94)	
Chronic kidney diseases			0.197
Yes	6 (1.35)	3 (0.56)	
No	437 (98.65)	531 (99.44)	
Psychiatric disorders			0.108
Yes	20 (4.51)	14 (2.62)	
No	423 (95.49)	520 (97.38)	
Hypothyroidism			0.01
Yes	68 (15.35)	53 (9.93)	

SD = standard deviation

Discussion

This study revealed that almost half of the studied cohort suffered from polypharmacy and that polypharmacy was significantly higher among patients with non-communicable diseases, such as diabetes mellitus, hypertension, hyperlipidaemia, cardiovascular disease, bronchial asthma and hypothyroidism.

Similar to the findings of this study, several regional studies have reported high rates of polypharmacy among elderly patients.^{23–25} Internationally, lower rates of polypharmacy have been reported. A cohort study conducted in Iran reported a lower prevalence of polypharmacy (23.1%) among people aged 60 years and above.²⁸ The estimated prevalence of polypharmacy in Brazil was 13.5%.²⁹ A national health survey in the USA determined that the prevalence of polypharmacy among the elderly tripled from 12.8% in 1988 to 39.0% in 2010.³⁰ Furthermore, a large multi-centre study, conducted in primary healthcare centres

Table 5: Logistic regression analysis of polypharmacy determinants

Characteristic	OR (95% CI)	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
Hyperlipidaemia	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

OR = odds ratio; CI = confidence interval

across Europe, reported a polypharmacy prevalence of 27.2% (a range of 16.4% to 60.8%).³¹

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

The high prevalence of polypharmacy observed in this study could be attributed to the high prevalence of non-communicable diseases among the studied subjects. More than half of the participants were suffering from either diabetes mellitus, hypertension or hyperlipidaemia. This finding is in line with the results of the Bahrain National Health Survey 2018, where more than 76% of those aged above 60 years suffered from diabetes and more than 54% were hypertensive.⁵ These conditions have a similar risk profile and tend to occur together, often with increasing age. Most of these conditions require several medications to achieve adequate control. This is supported by 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 among this study's participants is the prescription of medications for prevention. Medications such as statins and aspirin are commonly used for primary and secondary preventive purposes. Furthermore, there are no national or institutional guidelines to encourage deprescription among this group of patients in Bahrain. This might have impacted the rate of polypharmacy in the present study.

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

Although the multivariate analysis in this study showed no association between polypharmacy and patient's age, such finding is reported in the literature.²⁵ This association could be explained by the fact that the prevalence of chronic conditions and their concomitant need for drug treatment usually increase with age. However, no significant differences were found between male and female elderly subjects and the risk of polypharmacy. The studies are inconsistent

regarding the influence of the patient's gender on the risk of polypharmacy. While some studies reported no significant differences between males and females with regard to polypharmacy, some studies reported a higher rate of polypharmacy among elderly females.^{24,30}

Considering the negative consequences of polypharmacy and the increasing number of elderly people in Bahrain, this study emphasises the importance of practicing deprescription and avoiding unnecessary medications in this age group, especially among patients with non-communicable diseases. Since primary healthcare is the first encounter for elderly patients in Bahrain and the optimal setting for prevention, quaternary prevention should always be considered by family physicians while prescribing medications to elderly patients, especially with the implementation of the 'choose your doctor' programme, a new programme that allows each patient to choose a family physician who would provide them with therapeutic and preventive services. This programme will link each patient with one family physician instead of different ones, which could minimise the prescription of unnecessary medications among elderly patients in particular.³² While treating elderly patients, family physicians should periodically review the indication and importance of each medication and discontinue those that are no longer needed. In addition, polypill use can minimise the risk of polypharmacy and simplify management regimens; therefore, polypills should be considered by family physicians when treating elderly patients with chronic conditions.³³

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

Conclusion

This study reveals a high prevalence of polypharmacy among elderly patients attending primary healthcare centres in Bahrain. Polypharmacy was observed to be significantly more common among patients with non-communicable diseases such as diabetes mellitus, essential hypertension, hyperlipidaemia, cardiovascular diseases and bronchial asthma. The

high rate of polypharmacy raises concerns about its impact on patients' outcomes, morbidity and mortality. Considering the high prevalence of polypharmacy, the rising number of the elderly population and their associated polymorbidity and frailty and the consequences of polypharmacy, guidelines on the rational use of medicines and targeted educational programmes for general practitioners and family physicians must be developed. Studies assessing the influence of polypharmacy on the medication-taking behaviour of elderly patients and the control of their medical conditions are needed.

AUTHORS' CONTRIBUTION

MA and FH conceptualised and designed the study. EA, ED and MAB reviewed the literature and prepared the first draft of the study. MA analysed and interpreted the data. All authors drafted the manuscript and read and approved the final version of the manuscript.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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References

1. Frishman WH. Ten secrets to a long life. *Am J Med* 2019; 132:564–6. <https://doi.org/10.1016/j.amjmed.2018.12.020>.
2. Ben-Haim MS, Kanfi Y, Mitchell SJ, Maoz N, Vaughan KL, Amariglio N, et al. Breaking the ceiling of human maximal life span. *J Gerontol A Biol Sci Med Sci* 2018; 73:1465–71. <https://doi.org/10.1093/gerona/glx219>.
3. World Health Organization. Ageing and health. From: <https://www.who.int/news-room/fact-sheets/detail/ageing-and-health> Accessed: Sep 2023.
4. UNHCR. Older persons. From: <https://emergency.unhcr.org/entry/43935/older-persons> Accessed: Sep 2023.
5. Information and eGovernment Authority. Bahrain national health survey 2018. From: <https://www.iga.gov.bh/Media/Agencies/Bahrain%20National%20Health%20Survey%202018%20English.pdf> Accessed: Sep 2023.
6. Sabharwal S, Wilson H, Reilly P, Gupte CM. Heterogeneity of the definition of elderly age in current orthopaedic research. *Springerplus* 2015; 4:516. <https://doi.org/10.1186/s40064-015-1307-x>.
7. Singh S, Bajorek B. Defining 'elderly' in clinical practice guidelines for pharmacotherapy. *Pharm Pract (Granada)* 2014; 12:489. <https://doi.org/10.4321/s1886-36552014000400007>.
8. Borelli WV, Carmona KC, Studart-Neto A, Nitrini R, Caramelli P, da Costa JC. Operationalized definition of older adults with high cognitive performance. *Dement Neuropsychol* 2018; 12:221–7. <https://doi.org/10.1590/1980-57642018dn12-030001>.
9. Mini GK, Thankappan KR. Pattern, correlates and implications of non-communicable disease multimorbidity among older adults in selected Indian states: a cross-sectional study. *BMJ Open* 2017; 7:e013529. <https://doi.org/10.1136/bmjopen-2016-013529>.
10. Jaul E, Barron J. Age-related diseases and clinical and public health implications for the 85 years old and over population. *Front Public Health* 2017; 5:335. <https://doi.org/10.3389/fpubh.2017.00335>.
11. İnci H. Evaluation of multiple drug use in patients with type 2 diabetes mellitus. *Diabetol Int* 2021; 12:399–404. <https://doi.org/10.1007/s13340-021-00495-5>.
12. Gorup EC, Šter MP. Number of medications or number of diseases: What influences underprescribing? *Eur J Clin Pharmacol* 2017; 73:1673–9. <https://doi.org/10.1007/s00228-017-2336-x>.
13. Alvis BD, Hughes CG. Physiology considerations in geriatric patients. *Anesthesiol Clin* 2015; 33:447–56. <https://doi.org/10.1016/j.anclin.2015.05.003>.
14. Milton JC, Hill-Smith I, Jackson SH. Prescribing for older people. *BMJ* 2008; 336:606–9. <https://doi.org/10.1136/bmj.39503.424653.80>.
15. Stewart D, Mair A, Wilson M, Kardas P, Lewek P, Alonso A, et al. Guidance to manage inappropriate polypharmacy in older people: Systematic review and future developments. *Expert Opin Drug Saf* 2017; 16:203–13. <https://doi.org/10.1080/14740338.2017.1265503>.
16. Lun P, Law F, Ho E, Tan KT, Ang W, Munro Y, et al. Optimising prescribing practices in older adults with multimorbidity: A scoping review of guidelines. *BMJ Open* 2021; 11:e049072. <https://doi.org/10.1136/bmjopen-2021-049072>.
17. Masnoon N, Shakib S, Kalisch-Ellett L, Caughey GE. What is polypharmacy? A systematic review of definitions. *BMC Geriatr* 2017; 17:230. <https://doi.org/10.1186/s12877-017-0621-2>.
18. Khezrian M, McNeil CJ, Murray AD, Myint PK. An overview of prevalence, determinants and health outcomes of polypharmacy. *Ther Adv Drug Saf* 2020; 11. <https://doi.org/10.1177/2042098620933741>.
19. Halli-Tierney AD, Scarbrough C, Carroll D. Polypharmacy: Evaluating risks and deprescribing. *Am Fam Physician* 2019; 100:32–8.
20. Chen LJ, Trares K, Laetsch DC, Nguyen TNM, Brenner H, Schöttker B. Systematic review and meta-analysis on the associations of polypharmacy and potentially inappropriate medication with adverse outcomes in older cancer patients. *J Gerontol A Biol Sci Med Sci* 2021; 76:1044–52. <https://doi.org/10.1093/gerona/glaa128>.
21. Leelakanok N, Holcombe AL, Lund BC, Gu X, Schweizer ML. Association between polypharmacy and death: A systematic review and meta-analysis. *J Am Pharm Assoc* 2017; 57:729–38. <https://doi.org/10.1016/j.japh.2017.06.002>.
22. Machado-Duque ME, Castaño-Montoya JB, Medina-Morales DA, Castro-Rodríguez A, González-Montoya A, Machado-Alba JE. Drugs with anticholinergic potential and risk of falls with hip fracture in the elderly patients: A case-control study. *J Geriatr Psychiatry Neurol* 2018; 31:63–9. <https://doi.org/10.1177/0891988718757370>.
23. Davies LE, Spiers G, Kingston A, Todd A, Adamson J, Hanratty B. Adverse outcomes of polypharmacy in older people: Systematic review of reviews. *J Am Med Dir Assoc* 2020; 21:181–7. <https://doi.org/10.1016/j.jamda.2019.10.022>.
24. Morin L, Johnell K, Laroche ML, Fastbom J, Wastesson JW. The epidemiology of polypharmacy in older adults: Register-based prospective cohort study. *Clin Epidemiol* 2018; 10:289–98. <https://doi.org/10.2147/CLEP.S153458>.
25. Al-Dahshan A, Al-Kubiasi N, Al-Zaidan M, Saeed W, Kehyayan V, Bougmiza I. Prevalence of polypharmacy and the association with non-communicable diseases in Qatari elderly patients attending primary healthcare centers: A cross-sectional study. *PLoS One* 2020; 15:e0234386. <https://doi.org/10.1371/journal.pone.0234386>.

26. Alsuwaidan A, Almedlej N, Alsabti S, Daftardar O, Al Deaji E, Al Amri A, et al. Comprehensive overview of polypharmacy in elderly patients in Saudi Arabia. *Geriatrics (Basel)* 2019; 4:36. <https://doi.org/10.3390/geriatrics4020036>.
27. Bhagavathula AS, Vidyasagar K, Chhabra M, Rashid M, Sharma R, Bandari DK, et al. Prevalence of polypharmacy, hyperpolypharmacy and potentially inappropriate medication use in older adults in India: A systematic review and meta-analysis. *Front Pharmacol* 2021; 12. <https://doi.org/10.3389/fphar.2021.685518>.
28. Hosseini SR, Zabihi A, Jafarian Amiri SR, Bijani A. Polypharmacy among the elderly. *J Midlife Health* 2018; 9:97–103. https://doi.org/10.4103/jmh.JMH_87_17.
29. Seixas BV, Freitas GR. Polypharmacy among older Brazilians: Prevalence, factors associated, and sociodemographic disparities (ELSI-Brazil). *Pharm Pract (Granada)* 2021; 19:2168. <https://doi.org/10.18549/PharmPract.2021.1.2168>.
30. Charlesworth CJ, Smit E, Lee DS, Alramadhan F, Odden MC. Polypharmacy among adults aged 65 years and older in the United States: 1988-2010. *J Gerontol A Biol Sci Med Sci* 2015; 70:989–95. <https://doi.org/10.1093/gerona/glv013>.
31. de Godoi Rezende Costa Molino C, Chocano-Bedoya PO, Sadlon A, Theiler R, Orav JE, Vellas B, et al. Prevalence of polypharmacy in community-dwelling older adults from seven centres in five European countries: A cross-sectional study of DO-HEALTH. *BMJ Open* 2022; 12. <https://doi.org/10.1136/bmjopen-2021-051881>.
32. Martins C, Godycki-Cwirko M, Heleno B, Brodersen J. Quaternary prevention: Reviewing the concept. *Eur J Gen Pract* 2018; 24:106–11. <https://doi.org/10.1080/13814788.2017.1422177>.
33. Roy A, Naik N, Srinath Reddy K. Strengths and limitations of using the polypill in cardiovascular prevention. *Curr Cardiol Rep* 2017; 19:45. <https://doi.org/10.1007/s11886-017-0853-y>.