ORIGINAL RESEARCH

The Relationship Between Polypharmacy and Geropsychiatric Assessment Scales in Geriatric Outpatients

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Abstract

Objective: The aim of the study was to investigate the association between geropsychiatric assessment scales and polypharmacy.

Materials and Methods: A cross-sectional study was conducted that included patients ≥65 years, who applied to geriatric outpatients in a university hospital. Functionality was assessed by instrumental activities of daily living (IADL) and activities of daily living (ADL). The clinical frailty scale (CFS) was used for frailty screening. Multidimensional scale of perceived social support (MSPSS), mini-nutritional assessment-short form (MNA-SF), quality of life scale in older people (CASP-19), mini-mental state examination, loneliness scale for elderly, generalized anxiety disorder-7, geriatric depression scale (GDS), templer death anxiety scale, and cumulative illness rating scale for geriatrics (CIRS-G) were performed. Polypharmacy was defined as taking five or more medications.

Results: The study included 136 patients with a median (interlique range) age of 72.2 (68.1-76.3). The prevalence of polypharmacy was 52.2%. Age, IADL, GDS, CFS, MSPSS, CASP-19, and CIRS-G scores significantly differed between the polypharmacy and non-polypharmacy groups (p<0.05). There were inverse correlations between the number of medications and ADL, IADL, MNA-SF, MSPSS, and CASP-19. GDS had a weak and positive correlation (p<0.001, r=0.322) whereas, CFS (p<0.001, r=0.463) and CIRS-G (p<0.001, r=0.530) had moderate and positive correlations. In multivariable analysis, age [odds ratio (OR), 1.087; 95% confidence interval (CI), 1.005-1.176], CFS (OR, 1.602; 95% CI, 1.048-2.448), and CIRS-G (OR, 1.273; 95% CI, 1.090-1.486) were independent variables.

Conclusion: Age, CIRS-G, and frailty score by using CFS are independent variables of polypharmacy. The relationship between polypharmacy and functional dependency, depression, social support, and life quality should be supported by future large and comprehensive studies.

Keywords: Geriatric psychiatry, frailty, polypharmacy, geriatrics, geriatric psychology

Introduction

Polypharmacy is described as the concurrent use of multiple medications. It is an important geriatric syndrome and a global health problem (1). Although there are so many definitions of it, polypharmacy is usually described as taking five or more medications, routinely (2). The prevalence of polypharmacy ranges between 10% and 90% (3). As the number of medications is higher, related problems emerge like adverse reactions, drug-drug interactions, and compliance with drugs (4). The clinical consequences of polypharmacy, reviewed mostly in the literature, are frailty, falls, cognitive dysfunction, physical impairment, hospitalization, and death (2). On the other hand, the occurrence of geriatric syndromes causes the increment of polypharmacy (5). Mainly, the bidirectional interaction between frailty and polypharmacy is a crucial concern. It is emphasized that reducing polypharmacy may reverse or delay frailty (6). There are emerging strategies for deprescribing strategies as a

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global health problem (1,7,8). It is recommended to screen and manage the medications of older patients, regularly. Besides, potentially inappropriate prescribing tools are present to help with this problem including TIME criteria, and Beers criteria (9,10). Comprehensive geriatric assessment is the cornerstone of polypharmacy management. Multidimensional studies are needed to find out the effects of possible other factors for medication care.

The aim of the study was to investigate the relationship between geropsychiatric assessment scales and polypharmacy. We evaluated the effect of functionality, frailty, cognitive function, nutritional status, depression, anxiety, fear of death, loneliness, social support, life quality and multimorbidity by using related, reliable and validated tools.

Materials and Methods

Study Design

A cross-sectional study was conducted in a university hospital. Patients, who were 65 years and older, and who applied to the geriatric outpatient clinic between October 2020 and October 2021 were included. Subjects with malignancy, acute infections, acute diseases, severe cognitive impairment, and psychiatric diseases that may cause communication problems were excluded. Baseline characteristics including age, sex, living conditions, educational status, and medications were recorded. Polypharmacy was defined as the daily taking of five or more medications (2). Comprehensive geriatric assessment and psychiatric scales were performed. The burden of chronic disease was assessed by the cumulative illness rating scale for geriatrics (CIRS-G) (11).

Comprehensive Geriatric Assessment

The comprehensive geriatric assessment included standardized and validated tools. Functionality was assessed by using the Lawton-Brody instrumental activities of daily living (IADL), and Katz activities of daily living (ADL) scale (12,13). ADL was ranged between 0-6, and IADL was ranged between 0-8. The higher score indicated more independency. Mini nutritional assessment short-form (MNA-SF) was used for malnutrition screening. The score ranged from 1 to 14 (14). The mini-mental state examination (MMSE) was performed for cognitive status assessment. The score ranged between 0-30 (15). Frailty was measured by the clinical frailty scale (CFS). CFS was scored between 1 to 9 (16). A 15-item Yesevage geriatric depression scale (GDS) was measured to screen depression. Higher scores were about the severity of depression (17,18). Points 5-8, 9-11, and 12-15 showed mild, moderate, and severe depression respectively.

Psychiatric Scales

Social support was measured by the multidimensional scale of perceived social support (MSPSS), which consists of questions about family, friends, and significant other (19). The total score is between 12-84. A higher score indicates higher social support. Life quality was examined by the quality of life scale (CASP-19). The scale includes 19 items and four factors (autonomy, self-realization, control, and pleasure). The higher score is related to higher life quality (20). Anxiety was assessed by 7-item generalized anxiety disorder (GAD-7) test. The score ranges between 0 and 21. It is categorized as follows; mild (0-4), moderate (5-9), high (10-14), and severe anxiety (15-21) (21). The level of loneliness was measured by the loneliness scale for the elderly (LSE) which consists of 11 items. The total score was between 0 and 22. Higher scores are associated with a higher level of loneliness (22). The Templer death anxiety scale including 15-item was used to define death anxiety. The total score ranged from 0 to 15. The higher scores were related to higher fear and death (23).

Statistics

Statistical Package of Social Science 25.0 (SPSS) was used for statistical analysis. The normality of variables was examined by using visual and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk's test). Descriptive variables were presented as mean $\pm$ standard deviation or median (25th-75th percentile) according to their distribution. Categorical variables were summarized in terms of counts and percentages. Patients were divided into two groups polypharmacy and non-polypharmacy groups. The comparison between groups was performed by using the Mann-Whitney U test, independent t-test, and the chi-squared test where appropriate. The Spearman rank correlation coefficient was used for correlation analyses. The association of variables with the existence of polypharmacy was investigated by using binary logistic regression analyses with odds ratio [odds ratio (OR), 95% confidence interval (CI)]. A Hosmer-Lemeshow test (p>0.05) was used for the model fit. The statistically different variables identified with univariate analyses were put into the multivariable logistic regression analysis. The significance level of p was set to 0.05.

Ethical Approval

The study was approved by the Hacettepe University Department of Medicine Clinical Research Ethics Committee, and commissions with the Declaration of Helsinki (decision number: 2020/313, date: 15/12/2020). Written informed consent was present for all participants.

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Results

One-hundred and thirty-six patients who applied to the geriatric outpatient and who were eligible for the study were enrolled to the study. The median (IQR) age of 136 patients was 72.2 (68.1-76.3). The rates of robust, pre-frail and frail patients were 72.1% (n=98), 17.6% (n=24) and 10.3% (n=14) respectively. The 42.9% of robust, 70.8% of pre-frail, and 85.7% of frail patients had polypharmacy.

Patients were divided into two groups as polypharmacy and non-polypharmacy group. The polypharmacy rate was 52.2% (n=71). Baseline characteristic of two groups were given in Table 1 in comparison. The median age was 74 (65-89) in polypharmacy group and 70 (65-90) in non-polypharmacy group (p=0.015). IADL, GDS, CFS, MSPSS, CASP-19 and CIRS-G scores were significantly different between two groups (p<0.05).

Correlation analysis of variables with numbers of medications was given in Table 2. There were inverse correlations between the numbers of medications and ADL, IADL, MNA-SF, MSPSS, and CASP-19. GDS had weak and positive correlation (p<0.001, r=0.322) whereas, CFS (p<0.001, r=0.463) and CIRS-G (p<0.001, r=0.530) had moderate and positive correlations.

Binary logistic regression analysis of variables associated with polypharmacy was given at Table 3. Age, IADL, CFS, GDS, MSPSS, CASP-19 and CIRS-G was significantly associated with polypharmacy in univariable analysis (p<0.05). In multivariable analysis only age (OR, 1.087; 95% CI, 1.005-1.176; p=0.038), CFS score (OR, 1.602; 95% CI, 1.048-2.448; p=0.030) and CIRS-G (OR, 1.273; 95% CI, 1.090-1.486; p=0.002) were independent variables.

Discussion

This study assessed the polypharmacy with multidimensional approach including comprehensive geriatric assessment. Therefore, the effects of other important factors like loneliness, anxiety, fear of death, social support and life quality were investigated. Polypharmacy management in a holistic approach is a critical and trending issue worldwide. On the light of these issues, this study provided important data, and will set light to future studies.

The rate of polypharmacy was 52.2% in our study. We used the widely accepted definition of polypharmacy as the routine intake of five or more medications (2). The prevalence of polypharmacy range between 10% and 90% in the literature (3). DO-HEALTH study, included community-dwelling adults age 70 and older from seven European countries, reveled the rate of polypharmacy as 27.2% from 16.4% in Geneva to 60.8% in Coimbra (24). SHELTER study, including nursing home (NH) residents from 50 European and 7 Israeli NH facilities, reported the polypharmacy as 49.8% (25). These wide range of rates may be effected by the different definition of polypharmacy, used in the studies.

Table 1. Comparison of polypharmacy and non-polypharmacy groups

	Non-polypharmacy n=65 (47.8)	Polypharmacy n=71 (52.2)	p
Age, years	70 (65-90)	74 (65-89)	**0.015**
Sex, female	39 (60.0)	45 (63.4)	0.685
Education, illiterate	9 (13.8)	16 (22.5)	0.191
Living alone	14 (21.5)	19 (26.8)	0.478
ADL	6 (6-6)	6 (6-6)	0.246
IADL	8 (8-8)	8 (7-8)	**0.003**
MMSE	29 (26-30)	28 (26-30)	0.575
MNA-SF	13 (12-14)	12 (11-14)	0.061
Geriatric depression scale	2 (1-4)	4 (2-7)	**<0.001**
Clinical frailty scale	2.0 (1.5-3.0)	3.0 (2.0-4.0)	**<0.001**
MSPSS	76.0 (60.5-84.0)	71.0 (57.0-82.0)	**0.032**
CASP-19	31.0 (24.5-35.0)	24.0 (15.0-31.0)	**0.001**
Generalized anxiety disorder-7	2.0 (0-5.5)	3.0 (0-7.0)	0.329
Loneliness scale for elderly	6 (2-11)	8 (2-14)	0.160
Death anxiety scale	4 (1-8)	4 (2-8)	0.420
CIRS-G	4 (2-6)	6 (5-9)	**<0.001**

ADL: Activities of daily living, CASP-19: Quality of life scale in older people, CIRS-G: Cumulative illness rating scale for geriatrics, IADL: Instrumental activities of daily living, MMSE: Mini-mental state examination, MNA-SF: Mini-nutritional assessment-short form, MSPSS: Multidimensional scale of perceived social support, Variables were presented as median (25p-75p) or n (%)

Table 2. Correlation analysis of variables with numbers of medications

Number of medication	rho	
ADL	-0.204	**0.017**
IADL	-0.295	**<0.001**
MMSE	0.015	0.866
MNA-SF	-0.247	**0.004**
Geriatric depression scale	0.322	**<0.001**
Clinical frailty scale	0.463	**<0.001**
MSPSS	-0.245	**0.004**
CASP-19	-0.321	**<0.001**
Generalized anxiety disorder-7	0.070	0.420
Loneliness scale for elderly	0.153	0.076
Death anxiety scale	0.087	0.314
CIRS-G	0.530	**<0.001**

ADL: Activities of daily living, CASP-19: Quality of life scale in older people, CIRS-G: Cumulative illness rating scale for geriatrics, IADL: Instrumental activities of daily living, MMSE: Mini-mental state examination, MNA-SF: Mini-nutritional assessment-short form, MSPSS: Multidimensional scale of perceived social support

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Table 3. Binary logistic regression analysis of variables associated with polypharmacy

	Univariable		Multivariable	
	OR (95% CI)	p	OR (95% CI)	p
Age*	1.080 (1.012-1.152)	**0.020**	1.087 (1.005-1.176)	**0.038**
Sex, female	0.867 (0.434-1.732)	0.685		
Education, illiterate	0.552 (0.225-1.355)	0.195		
Living alone	1.331 (0.603-2.936)	0.479		
ADL*	0.613 (0.335-1.123)	0.113		
IADL*	0.654 (0.463-0.923)	**0.016**	1.225 (0.798-1.881)	0.353
MNA-SF*	0.882 (0.753-1.033)	0.119		
MMSE*	0.970 (0.878-1.071)	0.544		
CFS*	1.990 (1.444-2.742)	**<0.001**	1.602 (1.048-2.448)	**0.030**
GDS*	1.229 (1.091-1.385)	**0.001**	1.114 (0.942-1.317)	0.207
MSPSS*	0.978 (0.959-0.999)	**0.037**	1.003 (0.954-1.076)	0.851
CASP-19*	0.941 (0.906-0.977)	**0.002**	1.013 (0.954-1.076)	0.668
LSE*	1.047 (0.988-1.110)	0.124		
GAD-7*	1.047 (0.979-1.119)	0.178		
DAS*	1.026 (0.975-1.114)	0.541		
CIRS-G*	1.390 (1.202-1.607)	**<0.001**	1.273 (1.090-1.486)	**0.002**

ADL: Activities of daily living, CASP-19: Quality of life scale in older people, CFS: Clinical frailty scale, CIRS-G: Cumulative illness rating scale for geriatrics, DAS: Death anxiety scale, GAD-7: Generalized anxiety disorder-7, GDS: Geriatric depression scale, IADL: Instrumental activities of daily living, LSE: Loneliness scale for elderly, MMSE: Mini-mental state examination, MNA-SF: Mini-nutritional assessment-short form, MSPSS: Multidimensional scale of perceived social support, OR: Odds ratio, CI: Confidence interval, *included as continuous variables

In our study, the median age of polypharmacy group was higher than the non-polypharmacy group. In polypharmacy group IADL and CFS scores were worst. They were more dependent and frail. CIRS-G score and depression score were higher. On the other hand, we observed that MSPSS and CASP-19 scores were lower. That means that perceived social support and life quality of patients were worse in polypharmacy group. Correlation analysis revealed that, polypharmacy had positive moderate correlation with CFS and CIRS-G score, and low correlation with GDS score. Significant inverse correlations between polypharmacy and ADL, IADL, MNA-SF, MSPSS, CASP-19 were striking. Basically, we can say that frailty, multimorbidity, depression, functional dependency, social support and life quality seems to be related with polypharmacy. However, in multivariable analysis, we only found the independent effect of age, CFS and CIRS-G. However, only age, CIRS-G and CFS had independently associated with polypharmacy in multivariable analysis. A one-point increment of CFS score causes 1.6-fold, and one-point increment of CIRS-G score causes 1.27-fold risk of polypharmacy.

The relationship between age, multimorbidity and polypharmacy is a known fact. As we are getting aged, the rate of chronical diseases rises and the number of used medication get higher. Besides the changes on pharmacokinetics and pharmacodynamics of drugs; the risk of adverse drug reactions and drug-drug interactions rise. On the other hand, geriatrics syndromes, including falls, delirium, depression, cognitive impairment, malnutrition, orthostatic hypotension, incontinence, and chronic pain, may decrease the potential benefit of medications, increase the not only risk of adverse reactions, but also the rate of inappropriate prescriptions (5).

In DO-HEALTH study, polypharmacy was related to sex, age, number of comorbidities, and body mass index. This study was designed comprehensively and searched socio-demographic factors and health-related indicators with polypharmacy. They assessed frailty with Fried criteria and cognitive function with Montreal cognitive assessment (MOCA). However, frailty and cognitive functions were related to polypharmacy only in unadjusted model (24). Age and comorbidities are independent variables of polypharmacy in our study, too. We assessed frailty with CFS, and analyzed it as a continuous variable. We showed the effect of one-point increment in CFS on polypharmacy.

There are studies, investigating the mechanism and association between frailty and polypharmacy and supporting our study. In a systematic review and meta-analysis, polypharmacy was shown to be a major trigger of frailty, and future studies were called to confirm the effect of deprescribing in the development, reversion or delay of frailty (6). In another systematic review and meta-analysis concluded that, older adults living with frailty and polypharmacy were less likely to improve frailty states, and were prone to adverse hospital-related outcomes and mortality. They emphasized the requirement of further researches evaluating outcomes associated with polypharmacy in the frail population (26).

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Wastesson et al. (27) reported the factors associated with chronic polypharmacy as higher age, female sex, multimorbidity, multidose dispensing, and living in an institution. We presented the independent effect of age, multimorbidity and frailty. On the other hand, we highlighted the perceived social support, life quality, depression, frailty, functional dependency and disease burden on geriatric outpatients. Wastesson et al. (27) found living in an institution as a factor. We may anticipate that patients living in an institution can have less social support, depression, functional dependency, and they can perceive their life quality as low. This issue varies from an institution to institution. These associations should be investigated in future studies.

Makovski et al. (28) conducted an interesting study, evaluating the role of functional, clinical and social factors in multimorbidity and quality of life. They showed symptoms, polypharmacy, loneliness and ADL/IADL to be significant, after all factors of interest were introduced in the base model (adjusted for age, sex, employment, household income, living alone, and education) separately. They suggested to consider these factors to estimate the impact of multimorbidity and life quality for improving patient care (28). This study is important as it highlighted the relationship between polypharmacy and loneliness, functionality, multimorbidity and life quality.

Study Limitations

This is the first study investigating the factors related to polypharmacy by using validated and reliable tools. Besides socio-demographic factors, we evaluated functionality, nutritional status, cognitive function, frailty, anxiety, depression, loneliness, social support, and life quality. Polypharmacy management requires multi-dimensional approaches, and all factors influencing it should be clarified and confirmed with future, longitudinal and comprehensive studies. Our study highlights to this issue (4). On the other hand, performing all screening tests were long lasting and needed great effort.

The cross-sectional design of our study is a weak limitation. Firstly, we could not assess the chronic polypharmacy and its long-term effects. However, our primary aim was to draw attention to social, cognitive, functional and psychiatric factors. Because not only for health professionals but also health care systems have been trying to prevent polypharmacy and related outcomes. Secondly, it was a single center experience.

Conclusion

Age, CIRS-G and frailty score by using CFS are independent variables of polypharmacy. The relationship between polypharmacy and functional dependency, depression, social support, life quality should be supported by future large and comprehensive studies.

References

1. Pereira A, Veríssimo M. Deprescribing in older adults: time has come. Eur Geriatr Med 2023;1:1-3.

2. Pazan F, Wehling M. Polypharmacy in older adults: a narrative review of definitions, epidemiology and consequences. Eur Geriatr Med 2021;12:443-452.

3. Khezrian M, McNeil CJ, Murray AD, Myint PK. An overview of prevalence, determinants and health outcomes of polypharmacy. Ther Adv Drug Saf 2020;11:2042098620933741.

4. Gutiérrez-Valencia M, Martínez-Velilla N, Vilches-Moraga A. Polypharmacy in older people: time to take action. Eur Geriatr Med 2019;10:1-3.

5. Zazzara MB, Palmer K, Vetrano DL, Carfì A, Onder G. Adverse drug reactions in older adults: a narrative review of the literature. Eur Geriatr Med 2021;12:463-473.

6. Gutiérrez-Valencia M, Izquierdo M, Cesari M, Casas-Herrero Á, Inzitari M, Martínez-Velilla N. The relationship between frailty and polypharmacy in older people: A systematic review. Br J Clin Pharmacol 2018;84:1432-1444.

7. Ulley J, Harrop D, Ali A, Alton S, Fowler Davis S. Deprescribing interventions and their impact on medication adherence in community-dwelling older adults with polypharmacy: a systematic review. BMC Geriatr 2019;19:15.

8. Onder G, Vetrano DL, Palmer K, Trevisan C, Amato L, Berti F, Campomori A, Catalano L, Corsonello A, Kruger P, Medea G, Nobili A, Trifirò G, Vecchi S, Veronese N, Marengoni A. Italian guidelines on management of persons with multimorbidity and polypharmacy. Aging Clin Exp Res 2022;34:989-996.

9. Bahat G, Ilhan B, Erdogan T, Halil M, Savas S, Ulger Z, Akyuz F, Bilge AK, Cakir S, Demirkan K, Erelel M, Guler K, Hanagasi H, Izgi B, Kadioglu A, Karan A, Kulaksizoglu IB, Mert A, Ozturk S, Satman I, Sever MS, Tukek T, Uresin Y, Yalcin O, Yesilot N, Oren MM, Karan MA. Turkish inappropriate medication use in the elderly (TIME) criteria to improve prescribing in older adults: TIME-to-STOP/TIME-to-START. Eur Geriatr Med 2020;11:491-498.

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10. By the 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc 2019;67:674-694.

11. Miller MD, Paradis CF, Houck PR, Mazumdar S, Stack JA, Rifai AH, Mulsant B, Reynolds CF 3rd. Rating chronic medical illness burden in geropsychiatric practice and research: application of the Cumulative Illness Rating Scale. Psychiatry Res 1992;41:237-248.

12. Katz S, Ford AB, Moskowitz RW, Jackson BA, Jaffe MW. Studies of illness in the aged. The index of adl: a standardized measure of biological and psychosocial function. JAMA 1963;185:914-919.

13. Lawton MP, Brody EM. Assessment of older people: self-maintaining and instrumental activities of daily living. Gerontologist 1969;9:179-186.

14. Rubenstein LZ, Harker JO, Salvà A, Guigoz Y, Vellas B. Screening for undernutrition in geriatric practice: developing the short-form mini-nutritional assessment (MNA-SF). J Gerontol A Biol Sci Med Sci 2001;56:M366-M372.

15. Folstein MF, Folstein SE, McHugh PR. "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-198.

16. Rockwood K, Song X, MacKnight C, Bergman H, Hogan DB, McDowell I, Mitnitski A. A global clinical measure of fitness and frailty in elderly people. CMAJ 2005;173:489-495.

17. Almeida OP, Almeida SA. Short versions of the geriatric depression scale: a study of their validity for the diagnosis of a major depressive episode according to ICD-10 and DSM-IV. Int J Geriatr Psychiatry 1999;14:858-865.

18. Yesavage JA, Brink TL, Rose TL, Lum O, Huang V, Adey M, Leirer VO. Development and validation of a geriatric depression screening scale: a preliminary report. J Psychiatr Res 1982-1983;17:37-49.

19. Zimet GD, Powell SS, Farley GK, Werkman S, Berkoff KA. Psychometric characteristics of the Multidimensional Scale of Perceived Social Support. J Pers Assess 1990;55:610-617.

20. Hyde M, Wiggins RD, Higgs P, Blane DB. A measure of quality of life in early old age: the theory, development and properties of a needs satisfaction model (CASP-19). Aging Ment Health 2003;7:186-194.

21. Spitzer RL, Kroenke K, Williams JB, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. Arch Intern Med 2006;166:1092-1097.

22. De Jong-Gierveld J, Kamphuls F. The development of a Rasch-type loneliness scale. Applied psychological measurement 1985;9:289-299.

23. Templer DI. The construction and validation of a Death Anxiety Scale. J Gen Psychol 1970;82:165-177.

24. de Godoi Rezende Costa Molino C, Chocano-Bedoya PO, Sadlon A, Theiler R, Orav JE, Vellas B, Rizzoli R, Kressig RW, Kanis JA, Guyonnet S, Lang W, Egli A, Bischoff-Ferrari HA; DO-HEALTH Research Group. 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:e051881.

25. Zazzara MB, Villani ER, Palmer K, Fialova D, Corsonello A, Soraci L, Fusco D, Cipriani MC, Denkinger M, Onder G, Liperoti R. Frailty modifies the effect of polypharmacy and multimorbidity on the risk of death among nursing home residents: Results from the SHELTER study. Front Med (Lausanne) 2023;10:1091246.

26. Toh JJY, Zhang H, Soh YY, Zhang Z, Wu XV. Prevalence and health outcomes of polypharmacy and hyperpolypharmacy in older adults with frailty: A systematic review and meta-analysis. Ageing Res Rev 2023;83:101811.

27. Wastesson JW, Morin L, Laroche ML, Johnell K. How Chronic Is Polypharmacy in Old Age? A Longitudinal Nationwide Cohort Study. J Am Geriatr Soc 2019;67:455-462.

28. Makovski TT, Le Coroller G, Putrik P, Choi YH, Zeegers MP, Stranges S, Ruiz Castell M, Huiart L, van den Akker M. Role of clinical, functional and social factors in the association between multimorbidity and quality of life: Findings from the Survey of Health, Ageing and Retirement in Europe (SHARE). PLoS One 2020;15:e0240024.