



Article

Association of Polypharmacy and Health-Related Quality of Life Among US Adults: A Cross-Sectional Analysis of the 2022 MEPS Data

Sreelatha Akkala ^{1,*}, Meesha Iqbal ^{1,†}, Regina Hansen ¹ and Jyothi Akkula ²

¹ School of Public Health, The University of Texas Health Science Center at Houston, Houston, TX 77030, USA; meesha.iqbal@uth.tmc.edu (M.I.); regina.hansen.1@uth.tmc.edu (R.H.)

² Independent Researcher, Hyderabad 500032, India; jyothikiran1429@gmail.com

* Correspondence: sreelatha.akkala@uth.tmc.edu

† These authors contributed equally to this work.

Abstract

Polypharmacy is common among aging populations and is associated with adverse health outcomes. We designed this cross-sectional study to determine the association of polypharmacy with physical and mental health-related quality of life (HRQoL) among the United States (US) adults aged ≥ 50 years. We used the nationally representative Medical Expenditure Panel Survey (MEPS) data, 2022, and conducted the analysis on 5343 adults. Polypharmacy was operationalized as the use of five or more medications simultaneously. HRQoL was assessed via physical and mental component summary scores from the 12-item short form health survey. We applied a multivariate linear regression model to determine the relationship between polypharmacy and HRQoL, after adjusting for sociodemographic factors (age, sex, race/ethnicity, and marital status) and comorbidities (diabetes and cardiovascular disease). Polypharmacy was reported by 70% of participants and was significantly associated with decreased physical (adjusted β : -2.95 , 95% confidence interval [CI]: -3.64 , -2.26 , $R^2 = 0.25$, $p < 0.001$) and mental HRQoL (adjusted β : -0.85 , 95% CI: -1.48 , -0.22 , $R^2 = 0.07$, $p < 0.001$). Other significant predictors of poor HRQoL included female sex, unmarried status, public insurance, lower educational attainment, and higher comorbidity index ($p < 0.001$). In contrast, higher education and private insurance were associated with better HRQoL. Based on the study findings, it is crucial to invest in programs and targeted interventions such as routine medication review and deprescribing strategies to reduce the negative impact of polypharmacy on HRQoL among US adults.

Keywords: polypharmacy; United States; quality of life; HRQoL; health-related quality of life



Academic Editor: Francisco Guillén-Grima

Received: 10 September 2025

Revised: 8 November 2025

Accepted: 13 November 2025

Published: 20 November 2025

Citation: Akkala, S.; Iqbal, M.; Hansen, R.; Akkula, J. Association of Polypharmacy and Health-Related Quality of Life Among US Adults: A Cross-Sectional Analysis of the 2022 MEPS Data. *J. Ageing Longev.* **2025**, *5*, 52. <https://doi.org/10.3390/jal5040052>

Copyright: © 2025 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

1. Introduction

Population aging represents one of the significant demographic shifts worldwide, marked by a rapidly growing elderly population [1]. Global projections indicate that by 2050, more than 2.1 billion people will be aged 60 years and above, accounting for over 21% of the world's population [1]. In the United States (US), the population aged 65 and older is projected to expand from 58 million in 2022 to 82 million by 2050, representing a 47% increase. In the US, advancing age was strongly associated with an increased prevalence of chronic diseases and multimorbidity [2]. More than 70% of individuals aged

≥65 years were affected by two or more chronic conditions, which significantly impacted their health-related quality of life (HRQoL) [3].

Aging is often associated with multimorbidity, defined as the co-occurrence of two or more conditions [4]. Multimorbidity is associated with impaired functioning, decreased HRQoL, intake of multiple medications, as well as higher socioeconomic costs [4]. Although much gerontologic research focuses on adults aged ≥65 years, evidence shows that multimorbidity, prescription complexity, and medication burden are increasing sharply beginning in the fifth decade of life [3,5]. Chronic conditions such as hypertension, diabetes, arthritis, and cardiovascular disease increase significantly from age 50, leading to greater medication use and polypharmacy [5]. Due to the high prevalence of comorbid conditions among older adults, the prescription of multiple medications, commonly referred to as polypharmacy, is increasingly common [4–6]. Although no consensus exists, polypharmacy is commonly defined as the daily use of five or more medications [7]. Recent US studies revealed a substantial rise in polypharmacy among older adults, with prevalence increasing from 24% in 1999–2000 to over 40% by 2017–2020 [8]. Among those aged 65 and older, 65.1% experienced some degree of polypharmacy, and 36.8% were prescribed six or more medications [8]. National data further indicate that polypharmacy prevalence increases between ages 50 and 64 and remains high; adults aged 50–64, often referred to as the “near-elderly”, represent a clinically important population [9]. They experience high medication burden prior to Medicare eligibility, with implications for both healthcare policy and practice [8,10].

Previous studies have shown that polypharmacy negatively impacts physical aspects of HRQoL, though evidence for mental health outcomes is mixed [6,11]. While medications are prescribed to manage symptoms and prevent disease progression, the concurrent use of multiple medications increases the risk of adverse drug reactions, drug–drug interactions, and medication nonadherence, all of which can impair HRQoL of an individual [11]. Prior research has consistently shown that polypharmacy is associated with reduced physical functioning, impaired mobility, increased risk of falls, and increased frailty among older adults [3,6,12]. Moreover, studies demonstrated a strong link between polypharmacy and poorer mental health outcomes, including depression, anxiety, and cognitive decline, further lowering overall HRQoL [11]. In addition to these clinical consequences, the complexity of managing numerous medications contributes to treatment burden, reduced patient satisfaction, and greater financial strain [13]. Evidence strongly suggests that polypharmacy negatively impacts both the physical and psychosocial dimensions of HRQoL, making it a critical public health issue across aging populations [3,6,11,13].

Although previous studies have examined the association between polypharmacy and HRQoL, most of the studies focused on adults aged 65 and older and relied on older datasets, limiting the generalizability of findings to adults ≥ 50 years and to the current US healthcare context [9]. Moreover, few studies have analyzed recent national data to inform deprescribing strategies for aging populations. To address this gap, the present study used the recent Medical Expenditure Panel Survey (MEPS) 2022 data to evaluate the association between polypharmacy and both physical and mental components of HRQoL among US adults aged 50 years and older. By integrating information on prescription medication use, comorbidities, and sociodemographic characteristics, our study provides evidence on the effects of polypharmacy on overall HRQoL. This broader inclusion captures the medication burden from its early rise in midlife through its persistence in older age and highlights a critical stage where prevention and intervention may be most effective. Therefore, the specific purpose of this study was to examine the association between polypharmacy (≥5 medications) and HRQoL among US adults aged ≥50 years.

2. Materials and Methods

2.1. Study Design

We conducted a cross-sectional analysis using 2022 data from the MEPS. MEPS is a nationally representative survey of the US civilian noninstitutionalized population conducted by the Agency for Healthcare Research and Quality. MEPS collects detailed information on healthcare utilization, expenditures, insurance coverage, and health status through its Household Component. For this study, we utilized the 2022 Full Year Consolidated Data File, Prescribed Medicines File, and Medical Conditions File. The 2022 data were collected across multiple overlapping panels corresponding to Rounds 7–9 of Panel 24, Rounds 3–5 of Panel 26, and Rounds 1–3 of Panel 27. Public use files were released between July and August 2024. These files were merged using the unique respondent identifier (DUPERSID) to obtain individual-level data on demographics, prescription medication use, and health status. This study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cross-sectional studies to ensure completeness and transparency in reporting.

2.2. Study Population

The study sample was restricted to adults aged 50 years and older who participated in the 2022 MEPS. Individuals were included if they were aged ≥ 50 years and had complete data available for all the key study variables, including polypharmacy status, HRQoL, and sociodemographic covariates. Participants were excluded if they met the age criterion but had missing information on any of the primary outcome, predictor, or covariates required for analysis. After applying these inclusion criteria and performing data cleaning, the final analytical sample consisted of 5343 individuals.

2.3. Measures

2.3.1. Outcome Variable

The primary outcome was HRQoL, measured using the Physical Component Summary score (PCS) and Mental Component Summary Score (MCS) from the 12-item Short Form Health Survey (SF-12). Scores range from 0 to 100, with higher scores indicating better HRQoL.

2.3.2. Primary Independent Variable

The main predictor was polypharmacy, defined as the concurrent use of more than five prescription medications at any point during the year. Prescription medication use was assessed using variables from the MEPS Prescribed Medicines File, including prescription round (PURCHRD), dispensing year (RXBEGYRX), and dispensing month (RXBEGMM). Medications with overlapping days supplied were counted to identify concurrent use, and individuals were classified as experiencing polypharmacy (yes/no).

2.4. Data Analysis

Descriptive statistics were calculated to summarize the characteristics of the study population. Means and standard deviations were reported for continuous variables, while frequencies and percentages were reported for categorical variables. Scatterplots and correlation matrices were generated to explore relationships between HRQoL and other variables. Multivariate linear regression was performed to examine the association between polypharmacy and HRQoL (PCS and MCS), controlling for key covariates including age, sex (male/female), race/ethnicity (Hispanic, non-Hispanic White, non-Hispanic Black, non-Hispanic Asian/Other), marital status (married, not married), education (no formal education, high school/graduate education development), bachelor's/master's/doctorate),

comorbidities, and insurance status (private, public, uninsured). Comorbidities were assessed using the Charlson Comorbidity Index (CCI), a validated tool that quantifies disease burden by assigning weighted scores to a range of chronic conditions. We identified comorbidities from the MEPS Medical Conditions File using International Classification of Diseases-10 codes and calculated the CCI to generate a summary measure of overall comorbidity burden. All categorical variables were dummy-coded.

Model diagnostics included checks for linearity, normality of residuals (via Q-Q plots), and homoscedasticity (using Breusch–Pagan tests). Multicollinearity was assessed using variance inflation factors (VIFs). Influential observations were examined using leverage values, Cook’s distance, DFFITS, and studentized deleted residuals. Although some observations exceeded conservative thresholds for influence, none were excluded from the analysis due to the robustness provided by the large sample size. All analyses accounted for MEPS’s complex sampling design, incorporating strata (VARSTR), primary sampling units (VARPSU), and person-level weights (PERWT22F). In Statistical Analysis Software (SAS), we used PROC SURVEYREG to obtain design-adjusted estimates. All analyses were conducted using SAS version 9.4. Two-sided p -values < 0.05 were considered statistically significant. Regression coefficients were reported along with their 95% confidence intervals. Adjusted R^2 was used to assess the proportion of variance in PCS and MCS explained by the final model.

3. Results

In the 2022 MEPS dataset, 5343 adults aged 50 years and older met the inclusion criteria and were included in the analysis. Table 1 presents the sociodemographic, clinical, medication, and patient-reported measures of the population. The mean age of the study participants was 68 years, and the majority of the participants were females (57%). Almost 90% were non-Hispanic, and around 87% had received some form of formal education. Half of the study participants were married. Furthermore, 54% and 45% of the sample had private and public healthcare insurance, respectively. Polypharmacy was reported by 70% of the participants. The PCS was 44 ± 12 , while the MCS was relatively higher, at 52 ± 9 . Adults with polypharmacy had significantly lower mean PCS and MCS scores compared to those without polypharmacy.

Table 1. Sociodemographic and clinical characteristics, and patient related outcome measures of the study participants, MEPS 2022.

	Mean (SD) or n (%)	
	N = 5343	
Sociodemographic characteristics		
Age (years), Mean (SD)	67.86	9.6
Sex, n (%)		
<i>Males</i>	2297	42.99
<i>Females</i>	3046	57.01
Race, n (%)		
<i>Hispanic</i>	582	10.89
<i>Non-Hispanic White</i>	3737	69.94
<i>Non-Hispanic Black</i>	740	13.85
<i>Non-Hispanic Asian/Other/Multiracial</i>	284	5.32
Marital Status, n (%)		
<i>Married</i>	2697	50.48
<i>Not married/separated/widowed/divorced</i>	2646	49.52

Table 1. Cont.

	Mean (SD) or n (%)	
	N = 5343	
Education Level, n (%)		
No formal education	687	12.86
High school/GED	2533	47.41
Bachelor's/Master's/Doctorate	2123	39.73
Healthcare insurance, n (%)		
Private insurance	2867	53.66
Public insurance	2383	44.6
Uninsured	93	1.74
Clinical characteristics		
Comorbidity index, Mean (SD)	2.2	1.4
Polypharmacy,n (%)		
Polypharmacy present	3756	70.3
No polypharmacy	1587	29.7
Patient-related outcome measures		
MCS, Mean (SD)	51.7	9.11
PCS, Mean (SD)	44.3	12.06

GED: general education development; MCS: Mental Component Summary Score; MEPS: Medical Expenditure Panel Survey; PCS: Physical Component Summary Score; SD: standard deviation. Values are weighted using MEPS person-level weights. Continuous variables are expressed as mean (SD) and categorical variables as n (%). Rao-Scott chi-squared tests for survey data were done on all categorical variables. All comparisons were statistically significant at $p < 0.001$.

The final multivariable regression model detailing the association of polypharmacy with PCS and MCS is shown in Table 2. R-squared values were found for each model to assess model fit. For the PCS model, the predictors explained about 25% of the variation in physical health. For the MCS model, the predictors explained only 7% of the variation. Adjusted R-squared values for unweighted MCS and PCS models were 0.068 and 0.249, respectively. After adjusting for sociodemographic characteristics and comorbidity index, our model showed a negative association of polypharmacy with HRQoL. Individuals with polypharmacy had, on average, 0.85 points lower MCS ($p = 0.008$) and 2.95 points lower PCS ($p < 0.001$), compared to those without polypharmacy, after adjusting for covariates.

Table 2. Multivariable linear regression models detailing the association of polypharmacy and physical and mental HRQoL.

	Outcome: Mental HRQoL (MCS)				Outcome: Physical HRQoL (PCS)			
	Adjusted β	SE	t-Value	p-Value	Adjusted β	SE	t-Value	p-Value
Polypharmacy present	−0.85 (−1.48, −0.22)	0.32	−2.65	0.008	−2.95 (−3.64, −2.26)	0.35	−8.38	<0.001
Age (years)	0.15 (0.12, 0.19)	0.02	9.76	<0.001	−0.15 (−0.19, −0.11)	0.02	−7.01	<0.001
Sex								
Females	−1.06 (−1.65, −0.48)	0.30	−3.57	<0.001	−1.60 (−2.26, −0.94)	0.33	−4.77	<0.001
Race								
Hispanic	−0.18 (−1.24, 0.89)	0.54	−0.33	0.741	1.19 (−0.19, 2.58)	0.70	1.69	0.091
Non-Hispanic Black	0.84 (−0.07, 1.76)	0.46	1.81	0.071	−0.35 (−1.47, 0.77)	0.57	−0.61	0.540

Table 2. Cont.

	Outcome: Mental HRQoL (MCS)				Outcome: Physical HRQoL (PCS)			
	Adjusted β	SE	t-Value	p-Value	Adjusted β	SE	t-Value	p-Value
<i>Non-Hispanic Asian/Other/ Multiracial</i>	−0.39 (−1.94, 1.17)	0.79	−0.49	0.625	−1.37 (−2.90, 0.16)	0.78	−1.76	0.079
Insurance Category								
<i>Public Insurance</i>	−1.82 (−2.48, −1.16)	0.34	−5.44	<0.001	−2.69 (−3.45, −1.93)	0.39	−6.94	<0.001
<i>Uninsured</i>	0.47 (−1.73, 2.66)	1.12	0.42	0.676	0.63 (−1.25, 2.51)	0.96	0.66	0.511
Marital Status								
<i>Not married/separated/ widowed/ divorced</i>	−1.50 (−2.09, −0.90)	0.30	−4.97	<0.001	−1.31 (2.03, −0.59)	0.37	−3.58	<0.001
Education Level								
<i>High School/GED</i>	1.74 (0.41, 3.07)	0.67	2.58	0.01	2.65 (1.40, 3.91)	0.64	4.17	<0.001
<i>Bachelor/ Masters/ Doctorate</i>	2.56 (1.28, 3.83)	0.65	3.96	<0.001	6.40 (5.11, 7.68)	0.65	9.82	<0.001
Comorbidity index	−0.75 (−0.98, −0.53)	0.11	−6.58	<0.001	−2.07 (−2.33, −1.81)	0.13	−15.81	<0.001

GED: general education development; HRQoL: health-related quality of life; MCS: Mental Component Summary Score; PCS: Physical Component Summary Score; SE: standard error. Note: Results obtained from multivariate linear regression models using MEPS survey design adjustments. F-statistic for the PCS model was 114.36 with p -value < 0.001, and for the MCS model, it was 24.09 with p -value of <0.001.

Significant associations were also observed between HRQoL and other covariates, including age, sex, insurance status, marital status, education level, and comorbidity index (Table 2). Higher comorbidity burden was consistently associated with lower PCS and MCS scores. Individuals with higher educational attainment reported significantly better HRQoL than those with no formal education. Compared with adults with private insurance, those with public insurance reported significantly lower PCS and MCS scores. Women had significantly lower HRQoL scores than men, and unmarried adults reported lower scores than married adults.

4. Discussion

In this nationally representative study of US adults aged 50 years and older, we found that polypharmacy was highly prevalent, affecting approximately 70% of the study population. Consistent with prior literature, our findings demonstrated that polypharmacy was significantly associated with lower HRQoL (PCS and MCS scores) [11,14]. After controlling for sociodemographic and clinical factors, adults with polypharmacy reported an average 2.95 points lower PCS and 0.85 points lower MCS scores than those without polypharmacy, suggesting that medication burden is associated with poor HRQoL.

Our findings align with previous studies that have reported polypharmacy's negative impact on physical health and functioning among older adults [5–7,11,14,15]. Importantly, our study extends this evidence by using recent (2022) nationally representative MEPS data and by focusing on adults ≥ 50 years, an age group particularly vulnera-

ble to multimorbidity and medication burden. The observed reduction in PCS scores is consistent with prior studies showing that polypharmacy is associated with poor functional outcomes, higher risks of falls, frailty, and disability. For instance, a cross-sectional study that analyzed the impact of polypharmacy on HRQoL among patients with chronic disease demonstrated that polypharmacy negatively influenced the physical domain of HRQoL (SF-12 PCS [$\beta = -0.15$; $p = 0.002$]), while its effect on the mental domain was less pronounced [11]. Another community-based rehabilitation study by Cemali et al. further supports our results by showing that polypharmacy was associated with lower quality of life and greater frailty [16]. Importantly, they demonstrated that frailty mediated the relationship between polypharmacy and HRQoL, suggesting that the functional vulnerability induced by multiple medications results in a decline in quality of life [16]. These findings complement our work by highlighting frailty as a potential explanatory mechanism, though frailty was not directly assessed in our analysis.

Similarly, a study by Nivatti et al. among Coronavirus Disease-2019 survivors reported extremely high rates of polypharmacy (94%) and hyperpolypharmacy (46%), with a significant decline in HRQoL [17]. The study also identified poor medication adherence as a critical consequence of high pill burden [17]. Together, these findings underscore that beyond functional impairment, adherence difficulties represent an important mediator of reduced HRQoL in individuals with polypharmacy. Although our study and prior research align on the physical consequences of polypharmacy, mental health findings remain inconsistent. Some evidence suggests little to no association, while a few studies reported significant associations between polypharmacy and mental health [11,14,17]. Our study's small but significant reduction in MCS scores may reflect the cumulative psychological burden of managing complex regimens, or the indirect consequences of functional decline and comorbidity burden. Discrepancies in findings across studies may be explained by differences in study design, population characteristics, and measurement tools.

Although the observed reduction in MCS (0.85) represents a small difference, such changes can be clinically meaningful at the population level, reflecting a decline in overall HRQoL. This discrepancy highlights the need for further longitudinal studies to determine whether polypharmacy directly impacts mental health or whether observed effects are mediated through medication adherence, functional status, or comorbid disease severity.

Several mechanisms may account for the observed associations between polypharmacy and lower HRQoL. First, the physiological burden of multiple medications increases the risk of adverse drug reactions, drug–drug interactions, and higher anticholinergic or sedative load, which can directly impair physical functioning [12,14,15,18,19]. Second, polypharmacy often reflects underlying multimorbidity, which independently contributes to functional decline, disability, and poor quality of life [5,6,15]. Although our models adjusted for comorbidity burden, residual confounding is likely, as disease severity and functional limitations are not fully captured by summary indices. Third, the complexity of managing multiple prescriptions may itself reduce quality of life by increasing treatment fatigue, medication nonadherence, and psychological stress, which can indirectly contribute to both physical and mental health [5,6,15]. Finally, prior studies suggest that frailty and poor adherence may act as mediators between polypharmacy and reduced HRQoL, supporting the consequences of medication burden that could extend beyond physiological effects alone [16,17].

Our study also identified several sociodemographic and clinical factors that are independently associated with HRQoL. Women and unmarried individuals reported lower PCS and MCS scores than men and married individuals, consistent with prior literature [20,21]. Similarly, adults with public insurance coverage reported significantly lower HRQoL than those with private insurance, highlighting persistent inequities in access to resources and

healthcare quality [22]. Education level demonstrated a positive association with both PCS and MCS, reflecting the role of higher education in promoting health literacy, adherence, and access to care [23]. These findings emphasize that the burden of polypharmacy does not occur in isolation but interacts with broader social and structural determinants of health [24].

Our study has important implications for clinical practice and policy. The high prevalence of polypharmacy in adults aged 50 years and older underscores the need for systematic medication reviews as part of routine care [10]. Interventions such as pharmacist-led deprescribing, shared decision-making to prioritize essential treatments, and the use of simplified dosing regimens can prevent the adverse effects of medication burden on HRQoL [25]. At the policy level, improving access to comprehensive care management programs, especially for socioeconomically disadvantaged populations, may help reduce disparities in outcomes linked to both multimorbidity and polypharmacy [3,26].

Limitations

The evaluation and interpretation of the findings should be considered with the following limitations. We could not establish causality in this study as the cross-sectional nature of the data limits the ability to make causal inferences between polypharmacy and HRQoL. Furthermore, HRQoL measures were self-reported and subject to recall or reporting biases. In addition, polypharmacy was operationalized based on overlapping days' supply of prescriptions, which may not fully reflect appropriateness, adherence, or regimen complexity. Finally, because MEPS excludes institutionalized populations such as those in nursing homes, our findings may not be generalizable to individuals in long-term care, where polypharmacy is often more severe. In addition, there is a potential for medication indication bias, as individuals with poor baseline health status are prescribed multiple medications, which may confound the association between polypharmacy and HRQoL, even after adjusting for covariates. Despite these limitations, the study makes a significant contribution by providing nationally representative evidence from the recent MEPS data, demonstrating that polypharmacy is highly prevalent and independently associated with poorer HRQoL.

5. Conclusions

In this nationally representative study of US adults aged 50 years and older, we found that polypharmacy was significantly associated with lower physical and mental HRQoL. Our findings highlight the need for integrated strategies that address both multimorbidity and medication burden in order to improve the well-being of aging populations. From a clinical and public health perspective, these results highlight the need to integrate routine medication reviews, deprescribing strategies, and shared decision-making into clinical care to optimize medications, minimize adverse effects, and improve HRQoL among aging populations. Future research should consider longitudinal and interventional designs to examine causal pathways, explore mediating roles of frailty, adherence, and functional impairment, and evaluate the effectiveness of deprescribing interventions in enhancing both physical and mental domains of HRQoL.

Author Contributions: Conceptualization, S.A. and M.I.; methodology, S.A. and M.I.; software, R.H.; validation, S.A., M.I., R.H., and J.A.; formal analysis, S.A., M.I., and R.H.; writing—original draft preparation, S.A., M.I., R.H., and J.A.; writing—review and editing, S.A., M.I., R.H., and J.A.; supervision, S.A. and M.I. All authors have read and agreed to the published version of the manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: This study used publicly available data.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

CCI	Charlson Comorbidity Index
CI	Confidence Interval
HRQoL	Health-Related Quality of Life
MEPS	Medical Expenditure Panel Survey
MCS	Mental Component Score
PCS	Physical Component Score
SAS	Statistical Analysis Software
SF-12	12-Item Short Form Health Survey
US	United States

References

1. WHO. Ageing and Health. 2022. Available online: <https://www.who.int/news-room/fact-sheets/detail/ageing-and-health> (accessed on 1 January 2025).
2. Jones, C.H.; Dolsten, M. Healthcare on the brink: Navigating the challenges of an aging society in the United States. *npj Aging* **2024**, *10*, 22. [\[CrossRef\]](#)
3. 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. [\[CrossRef\]](#) [\[PubMed\]](#)
4. Dorr, D.A.; Markwardt, S.; Bobo, M.; Allore, H.G.; Botosaneanu, A.; Newsom, J.T.; Nagel, C.; Quiñones, A.R. The extent and burden of high multimorbidity on older adults in the US: A descriptive analysis of Medicare beneficiaries. *BMC Geriatr.* **2024**, *24*, 777. [\[CrossRef\]](#)
5. Aggarwal, P.; Woolford, S.J.; Patel, H.P. Multi-Morbidity and Polypharmacy in Older People: Challenges and Opportunities for Clinical Practice. *Geriatrics* **2020**, *5*, 85. [\[CrossRef\]](#)
6. Butterly, E.W.; Hanlon, P.; Shah, A.S.V.; Hannigan, L.J.; McIntosh, E.; Lewsey, J.; Wild, S.H.; Guthrie, B.; Mair, F.S.; Kent, D.M.; et al. Comorbidity and health-related quality of life in people with a chronic medical condition in randomised clinical trials: An individual participant data meta-analysis. *PLoS Med.* **2023**, *20*, e1004154. [\[CrossRef\]](#)
7. Masnoon, N.; Shakib, S.; Kalisch-Ellett, L.; Caughey, G.E. What is polypharmacy? A systematic review of definitions. *BMC Geriatr.* **2017**, *17*, 230. [\[CrossRef\]](#)
8. Wang, X.; Liu, K.; Shirai, K.; Tang, C.; Hu, Y.; Wang, Y.; Hao, Y.; Dong, J.-Y. Prevalence and trends of polypharmacy in U.S. adults, 1999–2018. *Glob. Health Res. Policy* **2023**, *8*, 25. [\[CrossRef\]](#)
9. Pazan, F.; Wehling, M. Polypharmacy in older adults: A narrative review of definitions, epidemiology and consequences. *Eur. Geriatr. Med.* **2021**, *12*, 443–452. [\[CrossRef\]](#) [\[PubMed\]](#)
10. Delara, M.; Murray, L.; Jafari, B.; Bahji, A.; Goodarzi, Z.; Kirkham, J.; Chowdhury, M.; Seitz, D.P. Prevalence and factors associated with polypharmacy: A systematic review and Meta-analysis. *BMC Geriatr.* **2022**, *22*, 601. [\[CrossRef\]](#)
11. Van Wilder, L.; Devleeschauwer, B.; Clays, E.; Pype, P.; Vandepitte, S.; De Smedt, D. Polypharmacy and Health-Related Quality of Life/Psychological Distress Among Patients With Chronic Disease. *Prev. Chronic Dis.* **2022**, *19*, E50. [\[CrossRef\]](#) [\[PubMed\]](#)
12. Xue, L.; Boudreau, R.M.; Donohue, J.M.; Zgibor, J.C.; Marcum, Z.A.; Costacou, T.; Newman, A.B.; Waters, T.M.; Strotmeyer, E.S. Persistent polypharmacy and fall injury risk: The Health, Aging and Body Composition Study. *BMC Geriatr.* **2021**, *21*, 710. [\[CrossRef\]](#) [\[PubMed\]](#)
13. Gurung, A.; Ogden, E.; Chen, W.S. Experience of the Burden of Using Multiple Medicines and the Associated Impact on Health-Related Quality of Life. *J. Patient Exp.* **2025**, *12*, 23743735251330353. [\[CrossRef\]](#) [\[PubMed\]](#)
14. Meraya, A.M.; Dwibedi, N.; Sambamoorthi, U. Polypharmacy and Health-Related Quality of Life Among US Adults With Arthritis, Medical Expenditure Panel Survey, 2010–2012. *Prev. Chronic Dis.* **2016**, *13*, E132. [\[CrossRef\]](#)
15. Mohamed, M.R.; Mohile, S.G.; Juba, K.M.; Awad, H.; Wells, M.; Loh, K.P.; Flannery, M.; Culakova, E.; Tylock, R.G.; Ramsdale, E.E. Association of polypharmacy and potential drug-drug interactions with adverse treatment outcomes in older adults with advanced cancer. *Cancer* **2023**, *129*, 1096–1104. [\[CrossRef\]](#)

16. Cemali, M.; Kanlica, A.; Yilmaz, S.; Yilmaz, I.; Elmas, O.; Karaduman, A.A. Examining the Effect of Polypharmacy on Quality of Life and Frailty in Older Adults from the Perspective of Community-Based Rehabilitation. *Healthcare* **2025**, *13*, 1531. [[CrossRef](#)]
17. Nivatti, J.; Halder, S.; Goel, A.; Gupta, R.; Wason, R. Elderly Population Has Higher Prevalence of Polypharmacy Associated with Poor Quality of Life and Low Compliance after Recovery from COVID-19. *J. Midlife Health* **2022**, *13*, 288–293. [[CrossRef](#)] [[PubMed](#)]
18. Sanders, L.M.J.; Hortobagyi, T.; van Staveren, G.; Taxis, K.; Boersma, F.; Klein, H.C.; Bossers, W.J.R.; Blankevoort, C.G.; Scherder, E.J.A.; Van der Zee, E.A.; et al. Relationship between drug burden and physical and cognitive functions in a sample of nursing home patients with dementia. *Eur. J. Clin. Pharmacol.* **2017**, *73*, 1633–1642. [[CrossRef](#)]
19. Tran, T.; Mach, J.; Gemikonakli, G.; Wu, H.; Allore, H.; Howlett, S.E.; Little, C.B.; Hilmer, S.N. Diurnal effects of polypharmacy with high drug burden index on physical activities over 23 h differ with age and sex. *Sci. Rep.* **2022**, *12*, 2168. [[CrossRef](#)]
20. Cherepanov, D.; Palta, M.; Fryback, D.G.; Robert, S.A. Gender differences in health-related quality-of-life are partly explained by sociodemographic and socioeconomic variation between adult men and women in the US: Evidence from four US nationally representative data sets. *Qual. Life Res.* **2010**, *19*, 1115–1124. [[CrossRef](#)]
21. Venturini, C.D.; Engroff, P.; Ely, L.S.; Zago, L.F.; Schroeter, G.; Gomes, I.; De Carli, G.A.; Morrone, F.B. Gender differences, polypharmacy, and potential pharmacological interactions in the elderly. *Clinics* **2011**, *66*, 1867–1872. [[CrossRef](#)]
22. Lee, D.; Kim, S.; Dugan, J.A. The effect of prescription drug insurance on the incidence of potentially inappropriate prescribing: Evidence from Medicare Part D. *Health Econ.* **2024**, *33*, 137–152. [[CrossRef](#)]
23. Miller, T.A. Health literacy and adherence to medical treatment in chronic and acute illness: A meta-analysis. *Patient Educ. Couns.* **2016**, *99*, 1079–1086. [[CrossRef](#)]
24. Iqbal, A.; Richardson, C.; Iqbal, Z.; O’Keefe, H.; Hanratty, B.; Matthews, F.E.; Todd, A. Are there socioeconomic inequalities in polypharmacy among older people? A systematic review and meta-analysis. *BMC Geriatr.* **2023**, *23*, 149. [[CrossRef](#)] [[PubMed](#)]
25. Alaa Eddine, N.; Schreiber, J.; El-Yazbi, A.F.; Shmaytilli, H.; Amin, M.E.K. A pharmacist-led medication review service with a deprescribing focus guided by implementation science. *Front. Pharmacol.* **2023**, *14*, 1097238. [[CrossRef](#)] [[PubMed](#)]
26. Alrawiai, S. Deprescribing, shared decision-making, and older people: Perspectives in primary care. *J. Pharm. Policy Pract.* **2023**, *16*, 153. [[CrossRef](#)] [[PubMed](#)]

Disclaimer/Publisher’s Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.