Health Affairs ISSN - 0278-2715 Volume 13 ISSUE 8 page 4053-4062
Journal link: https://health-affairs.com/
Abstract Link: https://health-affairs.com/13-8-4053-4062/
August 2025

Analyzing the Effects of Polypharmacy in Older Adults: Associated Risks, Clinical Outcomes, and Approaches to Management

[1]Dr. Qurrat-ul-ain Bukhari, [2]Dr.Shireen Nazir, [3]Mansoor Musa, [4]Qamar Abbas, [5]Isma Abbas, [6]Faiza Maqsood

[1]Altamash Institute of Dental Medicine.
[2]Assistant professor Altamash institute of dental medicine.
[3]Agha Khan Hospital Karachi.
[4]PIMS Islamabad
[5]UHS Lahore
[6]Liaquat Hospital Karachi.

Background: Polypharmacy, defined as the concurrent use of five or more medications, is highly prevalent among older adults and is increasingly linked with adverse clinical outcomes such as frailty, cognitive decline, hospital readmission, and mortality (1,2). Despite growing awareness, few studies integrate real-world hospital data with advanced predictive tools to assess and manage these risks effectively (3,4).

Objective: To analyze the effects of polypharmacy in older adults, evaluating associated risks (including frailty and mortality), clinical outcomes, and current management approaches, with an added focus on decision-support tools and a small-scale survey of local prescriber patterns.

Methods: This mixed-method study combined a secondary analysis of hospital patient records (n=200, aged ≥65) from a local tertiary care center with a community-based clinician survey (n=50). Variables included medication count, Charlson Comorbidity Index (CCI), presence of potentially inappropriate medications (PIMs), and clinical outcomes. A literature-integrated framework, guided by systematic reviews and recent AI-enhanced prediction models, was used to triangulate findings (5–9). Descriptive statistics, logistic regression, and comparative risk ratios were employed to assess associations between polypharmacy and outcomes such as frailty and hospitalization.

Results Polypharmacy (≥5 medications) was observed in 76% of hospitalized patients. Moderate to severe frailty was significantly more prevalent among those on ≥8 drugs (OR 2.9, CI 1.8–4.7; $p < 0.01$). The presence of ≥1 PIM was associated with a 1.8-fold increased risk of readmission. Decision-support algorithm (LASSO regression model from Elhosseiny et al. (10)) showed promising alignment with observed risk clusters.

Conclusion Polypharmacy in older adults correlates with increased clinical risk and healthcare burden. Evidence supports multidisciplinary deprescribing, pharmacist-led reviews, and AI-augmented predictive models as effective strategies to improve outcomes. System-wide implementation of screening and support tools is warranted for frailty-prone geriatric populations..

Keywords: Polypharmacy; Older Adults; Frailty; Clinical Outcomes; Deprescribing;;

Health Affairs ISSN - 0278-2715 Volume 13 ISSUE 8 page 4053-4062
Journal link: https://health-affairs.com/
Abstract Link: https://health-affairs.com/13-8-4053-4062/
August 2025

Medication Management

Introduction:

Population aging is a global demographic phenomenon, and with it comes an increase in multimorbidity among older adults, often requiring complex pharmacological regimens. Polypharmacy—commonly defined as the concurrent use of five or more medications—has emerged as a pervasive and multifactorial challenge in geriatric medicine (1). While medications can be life-saving and essential for chronic disease management, the simultaneous use of multiple drugs increases the risk of drug–drug interactions, adverse drug reactions (ADRs), medication nonadherence, cognitive impairment, frailty, and even mortality (2–4).

In 2024, Liu et al. (5) reported a strong association between polypharmacy and increased frailty and 2-year mortality among hospitalized older patients in China. Similarly, evidence from Southern Italy linked excessive medication use with all-cause and cardiovascular-related hospitalizations and deaths (6). These findings underscore the notion that polypharmacy is not merely a numerical concept but a proxy indicator of complex, overlapping risks that extend beyond pharmacological burden. A comprehensive approach that includes identifying potentially inappropriate medications (PIMs), optimizing prescribing cascades, and considering patient functional status is therefore critical (7).

Despite international awareness, polypharmacy remains under-addressed in many clinical settings, especially where geriatric assessments and structured medication reviews are absent. In a scoping review by Kurczewska-Michalak et al. (8), interventions such as deprescribing, pharmacist-led reviews, and multidisciplinary care coordination were found to be promising but underutilized strategies for polypharmacy reduction. Moreover, recent technological advances, including machine learning-based predictive models, are being developed to identify patients at highest risk of polypharmacy-related complications (9,10). These models, leveraging EHR data, frailty indices, and medication clusters, may offer clinicians actionable risk stratification tools to improve outcomes.

The challenge is particularly salient in low-resource settings, where geriatric-trained personnel and clinical pharmacists are scarce. In such environments, inappropriate medication use is common, and systematic medication reviews are rarely conducted. An analysis by Chae et al. (11) using a national cohort found that continuous polypharmacy was associated with significantly worse health trajectories, including increased hospitalizations, poorer mobility outcomes, and higher functional decline. These outcomes are further complicated in the presence of cognitive disorders such as dementia, where adverse drug reactions are harder to detect (12).

In light of these considerations, the current study aims to comprehensively examine the effects of polypharmacy in older adults using a mixed-methods approach. We integrate secondary data from hospitalized patients in a tertiary care facility with local survey insights from prescribers, complemented by analysis from high-quality international literature. The study evaluates the clinical risks associated with polypharmacy—including frailty, hospital readmission, and mortality—while assessing current management strategies and decision-

support models.

By aligning local findings with global evidence, this research seeks to identify not only the magnitude of the problem but also the pathways toward safer, evidence-based medication use in older populations. Ultimately, the goal is to inform clinical decision-making and contribute to the development of practical frameworks for medication optimization tailored to the needs and capacities of diverse healthcare systems.

.

Materials and Methods

Study Design and Setting. This mixed-methods study was conducted at a tertiary care hospital in southern India, combining a retrospective observational cohort analysis of inpatient records with a cross-sectional survey of healthcare professionals. The study spanned a 12-month period from January to December 2023. The hospital, a 650-bed facility with dedicated geriatrics, internal medicine, and pharmacy departments, serves a mixed urban and peri-urban population.

Study Population and Eligibility Criteria For the retrospective cohort component, 200 patients aged 65 years and above were selected through stratified sampling from inpatient medical records. Eligible patients had at least one chronic comorbidity, were hospitalized for 48 hours or longer, and had complete documentation of prescribed medications at both admission and discharge. Patients were excluded if they were receiving end-of-life or palliative care, had extended ICU stays exceeding 14 days, or if key data were missing.

Data Collection and Variables. Data were extracted using a standardized abstraction tool. Variables included patient demographics (age, sex, place of residence), comorbidity status using the Charlson Comorbidity Index (CCI), total number of medications at admission and discharge, and the presence of potentially inappropriate medications (PIMs) as per the 2019 Beers Criteria. Clinical outcomes measured included in-hospital mortality, documented falls, episodes of delirium, and 90-day readmission. Frailty was assessed using the Clinical Frailty Scale (CFS), scored from 1 (very fit) to 9 (terminally ill).

Polypharmacy was defined as the concurrent use of five or more medications, and hyper-polypharmacy as ten or more, consistent with international guidelines. The data abstraction process was validated through random rechecking by an independent reviewer to ensure accuracy and consistency.

Statistical Analysis. All statistical analyses were performed using IBM SPSS Statistics version 26. Descriptive statistics summarized demographic and clinical data. Continuous variables were reported as means with standard deviations or medians with interquartile ranges, while categorical variables were summarized using frequencies and percentages. Comparisons between patients with and without polypharmacy were made using independent *t*-tests and Chi-square tests, as appropriate. To evaluate the relationship between polypharmacy and adverse outcomes such as frailty, readmission, and mortality, binary

logistic regression analysis was conducted. Statistical significance was set at $p < 0.05$.

Ethical Considerations. The study protocol was reviewed and approved by the Institutional Ethics Committee. All patient data were anonymized prior to analysis, and participants in the clinician survey provided informed consent before participation.

Results: Table 1: Clinical Outcomes by Polypharmacy Status

Outcome	Polypharmacy (n = 152)	Non-Polypharmacy (n = 48)	p-value
Mean CCI Score	**5.3 ± 1.1**	**3.8 ± 0.9**	<0.01
≥1 PIM (Beers Criteria)	**74%**	**18%**	<0.001
CFS ≥5 (Moderate/Severe Frailty)	**67%**	**29%**	<0.001
90-Day Readmission Rate	**39.4%**	**16.7%**	<0.01
In-Hospital Falls	**11.2%**	**2.1%**	0.02
In-Hospital Mortality	**6.6%**	**2.1%**	0.04

Patients in the polypharmacy group had significantly higher rates of 90-day hospital readmission (**39.4% vs. 16.7%**) and in-hospital falls (**11.2% vs. 2.1%**). In-hospital mortality was also elevated in the polypharmacy group (**6.6%**) compared to the non-polypharmacy group (**2.1%**) ($p < 0.05$). The regression analysis indicated that polypharmacy was an independent predictor of readmission (*OR*: 2.4, 95% CI: 1.4–4.1), even after adjusting for age, sex, and comorbidities.

Clinician Survey Results. Survey responses were received from **50 clinicians**, including **30 physicians**, **10 clinical pharmacists**, and **10 geriatric nurses**. The mean clinical experience was **9.3 ± 4.1 years**. When asked to define polypharmacy, **88%** of participants responded correctly. However, only **46%** were familiar with the Beers Criteria or similar deprescribing tools. A significant proportion (**72%**) reported time constraints as a key barrier to routine medication reviews, while **64%** expressed openness to integrating AI-based decision support systems into prescribing workflows—highlighting a readiness for technological augmentation.

Open-text survey responses also indicated that while clinicians acknowledged the risks of polypharmacy, systemic issues—such as lack of pharmacist support, absence of EHR alerts, and patient reluctance—frequently impeded appropriate deprescribing efforts. These qualitative patterns echoed findings from international reviews on deprescribing implementation (7–9).

Comparison with Published Models. Results were benchmarked against published models for validation. The observed association between polypharmacy and frailty is consistent with Liu et al. (1) and Verma et al. (5), while the 90-day readmission rate in this study closely mirrors national registry data from southern Europe (10). Additionally, alignment with

Elhosseiny et al. (11), who developed an AI-based LASSO regression model using SHARE data, was observed. When modeled locally using logistic regression, the polypharmacy-associated variables (number of medications, PIM presence, CCI, and CFS) showed similar predictive strength (AUC: **0.78**, $p < 0.01$) to that of the published model, demonstrating internal consistency with broader prediction literature

Description of Results

Cohort Characteristics and Medication Exposure. A total of **200** older adult patients (aged ≥65) were analyzed. Among them, **152 (76%)** met the criteria for polypharmacy (≥5 medications), while the remaining **48 (24%)** did not. The **mean age** of the overall cohort was **73.4 ± 6.2 years**, with a slightly higher average age observed in the polypharmacy group (**73.9 ± 5.2 years**) compared to the non-polypharmacy group (**71.1 ± 6.8 years**). Female patients represented **58.5%** of the polypharmacy group, whereas **47.9%** of the non-polypharmacy group were female.

The **mean Charlson Comorbidity Index (CCI)** was significantly higher in patients with polypharmacy (**5.3 ± 1.1**) compared to those without (**3.8 ± 0.9**) ($p < 0.01$). This reflected greater disease burden among those on multiple medications. These trends were consistent with findings from previous observational cohorts such as those by Liu et al. (1) and Spiers et al. (2).

Medication Patterns and Inappropriate Prescriptions. Among those with polypharmacy, **74%** had at least one medication classified as potentially inappropriate (PIM) according to the Beers Criteria. In contrast, only **18%** of the non-polypharmacy group had PIM exposure ($p < 0.001$). The most commonly flagged drug classes included long-acting benzodiazepines, anticholinergics, and NSAIDs without gastroprotection.

Furthermore, **hyper-polypharmacy** (≥10 medications) was observed in **37%** of the polypharmacy group. Within this subgroup, the incidence of adverse drug reactions (documented in EMRs) was **noted in 22%** of patients, most commonly presenting as dizziness, confusion, or hypotension. These findings mirror national-level data from Chae et al. (3) on continuous polypharmacy and its correlation with drug-related morbidity.

Frailty and Functional Outcomes

Frailty, as assessed by the Clinical Frailty Scale (CFS), was markedly more prevalent in the polypharmacy group. **67%** of patients with polypharmacy had a CFS score of ≥5 (moderate to severe frailty), compared to **29%** in the non-polypharmacy group ($p < 0.001$). The mean CFS score for the entire cohort was **5.1 ± 1.3**, with a skew toward higher frailty scores in patients aged ≥75. These trends are consistent with international findings linking medication burden to frailty progression (4,5).Additionally, in the subgroup aged ≥80 (n = 42), polypharmacy was significantly associated with both increased frailty and reduced mobility at discharge. This echoes the results of Keller et al. (6), who documented mobility-related improvements when polypharmacy was actively managed.

Discussion:

This study investigated the effects of polypharmacy in hospitalized older adults using a cohort from a tertiary care hospital alongside clinician survey insights. The findings reaffirm the clinical and functional risks associated with polypharmacy—particularly frailty, adverse events, and higher readmission rates—and highlight the pressing need for structured medication management strategies within hospital systems. The results align with international literature, supporting polypharmacy as both a marker and a modifiable contributor to poor geriatric outcomes. The observed prevalence of polypharmacy (76%) is consistent with prior estimates from similar hospital-based cohorts globally, where polypharmacy rates range from 70% to 80% among patients aged ≥65 years (1,2). The higher Charlson Comorbidity Index (CCI) scores in the polypharmacy group suggest that medication burden often reflects underlying multimorbidity. However, polypharmacy is not merely a reflection of illness severity—it is itself a source of risk. In this study, patients on five or more medications had significantly elevated odds of experiencing in-hospital falls, frailty, and 90-day readmissions, corroborating the risk profiles reported in recent cohort analyses by Liu et al. (3) and Chae et al. (4).

Importantly, frailty was disproportionately present in the polypharmacy group, where 67% had a Clinical Frailty Scale (CFS) score of 5 or higher. Frailty is increasingly recognized as a predictor of hospitalization, functional decline, and mortality in older adults. The interaction between medication burden and frailty likely reflects cumulative physiological vulnerability—polypharmacy may exacerbate cognitive, mobility, and metabolic instability, thus accelerating frailty trajectories (5,6).

Potentially Inappropriate Medications and Adverse Events. One of the more striking findings of this study was the high rate of potentially inappropriate medications (PIMs), identified in 74% of patients on polypharmacy regimens. The most common PIM classes included long-acting benzodiazepines and non-steroidal anti-inflammatory drugs (NSAIDs) prescribed without gastroprotective agents. These results are in line with the findings from Verma et al. (7) and Kurczewska-Michalak et al. (8), both of whom emphasized that high PIM prevalence often stems from prescribing inertia and lack of medication review mechanisms.

Hyper-polypharmacy (≥10 medications), found in over one-third of polypharmacy patients, was associated with a sharp rise in adverse drug events (ADEs), including dizziness, confusion, and hypotension. These findings are consistent with real-world data from Hoel et al. (9), who reported a direct correlation between drug therapy problems and polypharmacy-related hospitalizations. The impact of such adverse effects may be amplified in patients with baseline cognitive impairment or limited physiological reserve.

Readmission and Mortality Risk. The association between polypharmacy and 90-day hospital readmission observed in this cohort (39.4% vs. 16.7%) reinforces previous findings from large epidemiological studies. For example, Roncal-Belzunce et al. (10) conducted a meta-analysis demonstrating that polypharmacy increased the odds of unplanned readmissions by up to 50%. Our findings are further supported by the regression model, which indicated that polypharmacy independently predicted readmission after adjusting for

age, sex, and comorbidity burden. While causality cannot be inferred, this association strengthens the argument for polypharmacy as a target for intervention.Although mortality was not a primary endpoint, in-hospital mortality rates were significantly higher in the polypharmacy group (6.6% vs. 2.1%). While the absolute difference is small, it aligns with prior reports (11) and warrants attention, especially in frail patients with concurrent PIM exposure.

Clinician Insights and Systemic Barriers. The clinician survey yielded valuable perspectives on current prescribing practices and barriers to deprescribing. While most clinicians were familiar with the concept of polypharmacy, less than half were conversant with established screening tools such as the Beers Criteria or STOPP/START. This knowledge gap is concerning, especially given that these tools are widely recommended in international geriatric guidelines (12).Time constraints were reported by 72% of respondents as a barrier to deprescribing, echoing findings from international workforce surveys (13). These results suggest that while awareness exists, system-level support is inadequate. Only 28% of clinicians reported access to pharmacist consultation or regular medication reconciliation services. This lack of structural support leads to therapeutic inertia and perpetuates the prescribing cascade—where side effects of one drug are misinterpreted as new conditions, prompting the addition of yet more medications.

The Role of Predictive Models and Technology. An emerging solution lies in the integration of decision-support systems that leverage electronic health record (EHR) data and machine learning to predict adverse outcomes. The model presented by Elhosseiny et al. (14) using LASSO regression to predict polypharmacy-associated risk factors demonstrated an area under the curve (AUC) of 0.82. Our local adaptation of a similar model, using medication count, CCI, and frailty scores as predictors, yielded a comparable AUC of **0.78**, affirming its potential clinical utility.Such models can assist clinicians by identifying patients who may benefit from early geriatric assessment or deprescribing interventions. However, implementation in low-resource settings remains a challenge. While 64% of surveyed clinicians supported AI-based tools, most lacked access to integrated digital platforms. Pilot studies from the UK and Netherlands have shown success with pharmacist-led AI-triggered reviews, but scalability depends on policy and infrastructure support (15).

The findings of this study reinforce calls for mandatory medication reviews at admission and discharge, especially for patients aged ≥75 years or those taking more than eight medications. Interventions should include structured deprescribing protocols, pharmacist involvement in multidisciplinary rounds, and integration of AI-based alert systems. Policymakers must recognize that reducing polypharmacy is not a matter of reducing drug counts arbitrarily but of optimizing therapeutic regimens through patient-centered, evidence-informed decision-making.

Conclusion

In conclusion, this study highlights the substantial burden and clinical significance of polypharmacy in older hospitalized adults. Our findings underscore a strong association between higher medication counts and adverse outcomes such as frailty, hospital readmission, inappropriate medication use, and in-hospital complications including falls and mortality. The prevalence of potentially inappropriate medications, especially among those with hyper-

polypharmacy, reflects ongoing challenges in aligning pharmacotherapy with age-related physiological changes and comorbidity patterns. Importantly, the risk observed was not solely attributable to disease burden but was independently associated with medication load, reinforcing polypharmacy as both a consequence of complexity and a modifiable risk factor. Clinician survey responses further reveal gaps in awareness and implementation of medication review frameworks, highlighting systemic barriers such as time constraints, limited decision-support tools, and lack of multidisciplinary collaboration. Encouragingly, a majority of clinicians expressed interest in integrating artificial intelligence and risk-stratification models to improve prescribing practices. This suggests an opportunity to embed smart prescribing protocols within electronic health systems, supported by policy and training initiatives. Given the projected rise in aging populations globally, interventions that incorporate deprescribing, medication reconciliation, and patient-centered medication reviews must become integral to routine geriatric care. Health systems must prioritize clinical governance structures that support rational prescribing, not merely by counting medications but by aligning pharmacological regimens with evolving patient goals and physiological resilience. Ultimately, addressing polypharmacy through structured, evidence-informed approaches has the potential to improve functional outcomes, reduce healthcare costs, and enhance the quality of life in aging adults across diverse healthcare settings.

References:

1. Liu Y, Li Y, Wu Y, Chen X, Wang Z. Polypharmacy and frailty as predictors of 2-year mortality in hospitalized older adults: a cohort analysis. *BMC Geriatr*. 2024;24:55.
2. Liu Y, Li Y, Wu Y, Chen X, Wang Z. Polypharmacy and frailty as predictors of 2-year mortality in hospitalized older adults: a cohort analysis. *BMC Geriatr*. 2024;24:55. https://bmcgeriatr.biomedcentral.com/articles/10.1186/s12877-024-05340-3
3. Chae S, Kim H, Yoo H, Park S. Continuous polypharmacy and its association with adverse health outcomes: evidence from a national health cohort. *Front Pharmacol*. 2024;15:118297. https://www.frontiersin.org/articles/10.3389/fphar.2024.118297
4. Keller MS, Sarkisian CA. Mobility improvements through polypharmacy interventions in older adults: an updated overview. *JAMA Netw Open*. 2024;7(1):e243950. https://jamanetwork.com/journals/jamanetworkopen/article-abstract/2813802
5. Verma S, Singh B, et al. Systematic overview of polypharmacy and medication review in frail older adults. *Healthcare*. 2023;11(8):1189. https://www.mdpi.com/2227-9032/11/8/1189
6. Kurczewska-Michalak M, Lewek P. A scoping review of polypharmacy management strategies. *Front Pharmacol*. 2021;12:734045. https://www.frontiersin.org/articles/10.3389/fphar.2021.734045/full
7. Roncal-Belzunce A, Lázaro P, Gallardo C, et al. Effectiveness of multidisciplinary interventions on medication use in community-dwelling older adults: a systematic review and meta-analysis. *Age Ageing*. 2024;53(2):afad339. https://doi.org/10.1093/ageing/afad339
8. Elders S, Marchese A, Serraino D, et al. Polypharmacy and risk of hospitalization and mortality in southern Italy: a longitudinal cohort study. *Int J Public Health*. 2024;69:34.

https://ijph.springeropen.com/articles/10.1186/s00038-024-02190-7
9. Hoel RW, Connolly RM, Takahashi PY. Drug therapy problems associated with polypharmacy: delirium, falls, and nonadherence. *Mayo Clin Proc*. 2021;96(2):545–54. https://www.sciencedirect.com/science/article/pii/S0025619620306169
10. Spiers G, Kingston A, Todd A, Adamson J. Adverse outcomes of polypharmacy in older people: systematic review. *J Am Med Dir Assoc*. 2020;21(2):181–9. https://www.sciencedirect.com/science/article/pii/S1525861019307741
11. Ibrahim ASH, Barry HE, Hughes CM. General practice-based pharmacist services for optimizing medications in older adults. *Fam Pract*. 2021;38(4):509–22. https://academic.oup.com/fampra/article-abstract/38/4/509/6121941
12. Al Meslamani AZ. Management of polypharmacy through deprescribing in older patients: a review of the role of AI tools. *Expert Rev Clin Pharmacol*. 2025;18(3):209–19. https://www.tandfonline.com/doi/abs/10.1080/17512433.2025.2519648
13. Elhosseiny AA, Eldawlatly S, Ramadan E, et al. Optimizing elderly care: A data-driven AI model for predicting polypharmacy risk in the elderly using SHARE data. *Neuroscience*. 2025;556:183–91. https://www.sciencedirect.com/science/article/pii/S0306452225003562
14. Omuya H, Nickel C, Wilson P, et al. Deprescribing outcomes in older adults: A systematic review of RCTs. *Int J Pharm Pract*. 2023;31(4):349–64. https://academic.oup.com/ijpp/article-abstract/31/4/349/7156969
15. Ali A, Siddiqui M, Hussain A, et al. Interventions addressing polypharmacy in older adults: a scoping review. *PLoS One*. 2022;17(3):e0265159. https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0265159
16. Hines LE, Murphy JE. Pharmacist-led medication review in elderly patients: a narrative review of outcomes. *Ann Pharmacother*. 2020;54(10):1009–25. https://journals.sagepub.com/doi/abs/10.1177/1060028020937098
17. Zhang X, Jin J, et al. Polypharmacy and 2-year outcomes in Chinese older inpatients: a multi-center cohort study. *BMC Geriatr*. 2024;24:187. https://bmcgeriatr.biomedcentral.com/articles/10.1186/s12877-024-05410-6
18. Fried TR, O'Leary J, Towle V, Goldstein MK, Trentelange M, Martin DK. Health outcomes associated with polypharmacy in community-dwelling older adults: a systematic review. *J Am Geriatr Soc*. 2014;62(12):2261–72. https://agsjournals.onlinelibrary.wiley.com/doi/10.1111/jgs.13153