Postprint of a Meta-Analysis on Medication Adherence and Its Influencing Factors in Older Adults with Polypharmacy

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Date: 2023-07-27T00:00:00+00:00

Abstract

Background Polypharmacy among older adults has become increasingly prevalent. Medication adherence in polypharmacy is closely related to treatment efficacy and safety; therefore, early understanding of medication adherence and its influencing factors in older adults with polypharmacy is of great significance. However, current research findings show considerable variation, and there is no clear and unified standard.

Objective To systematically evaluate the current status of medication adherence and its influencing factors in older adults with polypharmacy, providing a reference for improving medication adherence, reducing adverse drug reactions, and further developing personalized intervention strategies.

Methods A computerized search was conducted in PubMed, Embase, Web of Science, Cochrane Library, Scopus, Ovid, Chinese Biomedical Literature Database, CNKI, Wanfang Data Knowledge Service Platform, and VIP Database for observational studies (cohort studies, case-control studies, cross-sectional studies) on influencing factors of medication adherence in older adults with polypharmacy (age $ $60 years, $ $5 medications). The search timeframe was from database inception to July 2023. Two researchers independently conducted literature screening, quality assessment, and data extraction according to inclusion and exclusion criteria. Meta-analysis was performed using Stata 17.0 and RevMan 5.3 software.

Results A total of 19 articles were included, with a total sample size of 130,047 cases, among which 50,852 had good medication adherence. Meta-analysis results showed that the medication adherence rate for older adults with polypharmacy was 41% [95%CI (0.34, 0.47)]. Medication adherence in polypharmacy was associated with age [OR=2.62, 95%CI (1.60, 4.78),

P<0.0001], gender [OR=1.70, 95%CI (1.30, 2.23), P=0.0001], education level [OR=1.73, 95%CI (1.38, 2.16), P<0.00001], living arrangement [OR=2.85, 95%CI (2.18, 3.72), P<0.00001], medication knowledge level [OR=1.14, 95%CI (1.04, 1.25), P=0.005], medication beliefs [OR=2.06, 95%CI (1.44, 2.93), P<0.0001], depression [OR=2.52, 95%CI (1.96, 3.24), P<0.00001], activities of daily living (ADL) [OR=2.39, 95%CI (1.68, 3.38), P<0.00001], history of falls [OR=3.51, 95%CI (2.03, 6.06), P<0.00001], professional guidance [OR=3.75, 95%CI (1.92, 7.33), P=0.0001], number of medications [OR=2.58, 95%CI (1.96, 3.41), P<0.0001], adverse drug reactions [OR=3.08, 95%CI (2.17, 4.38), P<0.0001], medication regimen complexity [OR=1.08, 95%CI (1.03, 1.14), P=0.004], medication management [OR=1.92, 95%CI (1.34, 2.75), P=0.0003], and medication costs [OR=2.60, 95%CI (1.30, 5.17), P=0.0007]. Sensitivity analysis indicated that the Meta-analysis results were relatively stable. Begg' s test (P=0.441) and Egger' s test (P=0.674) suggested a low risk of publication bias in the included literature.

Conclusion The medication adherence rate for older adults with polypharmacy is 41%. Current evidence indicates that general factors (age, gender, education level, living arrangement), psychosocial factors (depression, ADL, history of falls, medication knowledge level, medication beliefs, professional guidance), and medication-related factors (medication management, medication costs, medication regimen complexity, number of medications, adverse drug reactions) are influencing factors of medication adherence in older adults with polypharmacy. Healthcare professionals should develop personalized intervention measures based on these influencing factors to optimize disease management in older adults with polypharmacy.

Full Text

Preamble

Current Status of Polypharmacy in the Elderly and Its Influencing Factors: A Meta-analysis

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Abstract

Background: Polypharmacy is increasingly prevalent among the elderly population. Medication adherence in the context of polypharmacy is closely related to therapeutic efficacy and safety, making it crucial to understand the current

status of adherence and its influencing factors. However, existing studies report widely divergent conclusions, and no clear, unified standards have been established.

Objective: To systematically evaluate the current status of medication adherence and its influencing factors among elderly patients with polypharmacy, providing evidence for improving adherence, reducing adverse drug reactions, and developing personalized intervention strategies.

Methods: We systematically searched PubMed, Embase, Web of Science, Cochrane Library, Scopus, Ovid, CBM, CNKI, Wanfang Data, and VIP for observational studies (cohort, case-control, and cross-sectional studies) examining factors influencing medication adherence in elderly patients with polypharmacy (age $\geq$ 60 years, $\geq$ 5 medications). The search period extended from database inception to July 2023. Two researchers independently screened literature, assessed quality, and extracted data according to inclusion and exclusion criteria. Meta-analysis was performed using Stata 17.0 and RevMan 5.3 software.

Results: Nineteen studies with a total sample size of 130,047 participants were included, of whom 50,852 exhibited good medication adherence. The pooled medication adherence rate for elderly patients with polypharmacy was 41% [95%CI (0.34, 0.47)]. Adherence was significantly associated with age [OR=2.62, 95%CI (1.60, 4.78), P<0.0001], gender [OR=1.70, 95%CI (1.30, 2.23), P=0.0001], education level [OR=1.73, 95%CI (1.38, 2.16), P<0.00001], living arrangement [OR=2.85, 95%CI (2.18, 3.72), P<0.00001], medication knowledge [OR=1.14, 95%CI (1.04, 1.25), P=0.005], medication beliefs [OR=2.06, 95%CI (1.44, 2.93), P<0.0001], depression [OR=2.52, 95%CI (1.96, 3.24), P<0.00001], activities of daily living (ADL) [OR=2.39, 95%CI (1.68, 3.38), P<0.00001], history of falls [OR=3.51, 95%CI (2.03, 6.06), P<0.00001], professional guidance [OR=3.75, 95%CI (1.92, 7.33), P=0.0001], number of medications [OR=2.58, 95%CI (1.96, 3.41), P<0.0001], adverse drug reactions [OR=3.08, 95%CI (2.17, 4.38), P<0.0001], medication regimen complexity [OR=1.08, 95%CI (1.03, 1.14), P=0.004], medication management [OR=1.92, 95%CI (1.34, 2.75), P=0.0003], and medication cost [OR=2.60, 95%CI (1.30, 5.17), P=0.0007]. Sensitivity analyses indicated stable results. Begg' s test (P=0.441) and Egger' s test (P=0.674) suggested low risk of publication bias.

Conclusion: The medication adherence rate among elderly patients with polypharmacy is 41%. Current evidence indicates that general factors (age, gender, education level, living arrangement), psychosocial factors (depression, ADL, fall history, medication knowledge, medication beliefs, professional guidance), and medication-related factors (medication management, cost, regimen complexity, number of medications, adverse drug reactions) significantly influence adherence. Healthcare professionals should develop individualized interventions and optimize disease management for elderly patients with polypharmacy based on these identified factors.

Keywords: Polypharmacy; Aged; Medication adherence; Root cause analysis; Meta-analysis

Introduction

With accelerated population aging, the prevalence of multimorbidity ($ $2 chronic conditions) among older adults has reached 66.1%, making it a common characteristic of this population [1-2]. Elderly patients with multimorbidity often require multiple medications to manage their conditions. Reports indicate that approximately half of adults over 60 years take five or more medications daily, with an average of eight medications and a maximum of up to 23 [3-4], leading to polypharmacy [5-6]. Most studies define polypharmacy as the concurrent use of five or more medications daily [7-9].

Polypharmacy carries substantial risks, including overuse, inappropriate use, potential adverse clinical consequences, increased drug-related problems, and poor medication adherence [10-12]. Research shows that elderly patients taking more than three medications daily have increased likelihood of non-adherence, which escalates with the number and dosage of medications [13]. Furthermore, more complex treatment regimens correlate with poorer adherence [14]. Poor adherence compromises treatment efficacy and prevents patients from deriving therapeutic benefits. Non-adherence is associated with disease progression, treatment failure, hospitalization, and adverse drug reactions, all of which may affect prognosis and even endanger lives [4,15-16]. Therefore, understanding medication adherence and its influencing factors is critical for improving outcomes and reducing adverse events.

However, current evidence on adherence rates and influencing factors varies considerably. For instance, one study reported a 70.0% adherence rate among elderly patients with polypharmacy [17], while another found only 37.5% [18]. Similarly, age was identified as an influencing factor in some studies [7] but not others [19], and gender effects have been inconsistent across studies [18,20]. This meta-analysis aims to quantitatively synthesize existing evidence to clarify factors influencing medication adherence in elderly patients with polypharmacy, providing an evidence base for future intervention studies and optimization of disease management.

Methods

1.1 Literature Search Strategy

We systematically searched PubMed, Embase, Web of Science, Cochrane Library, Scopus, Ovid, CBM, CNKI, Wanfang Data, and VIP for observational studies (cohort, case-control, and cross-sectional studies) examining factors influencing medication adherence in elderly patients with polypharmacy. The search period extended from database inception to July 2023. We employed

a combination of MeSH terms and free-text keywords. Chinese search terms included: "polypharmacy / multiple medication therapy," "medication adherence / compliance," and "influencing factors / related factors / predictive factors."English search terms included: "polypharmacy/multiple medicine*/multiple medication*/multiple drug*/Polymedication," "medication adherence/adherence, medication/drug adherence/Medication Nonadherence," and "aged/elderly/old people/old adult/senior." To ensure comprehensiveness, we manually searched reference lists of included studies. The specific PubMed search strategy is detailed in Table 1 .

1.2 Inclusion and Exclusion Criteria

Inclusion criteria: (1) Study population: elderly patients with polypharmacy (age $ $60 years, $ $5 medications); (2) Study design: cohort, case-control, or cross-sectional studies; (3) Content: factors influencing, predicting, or correlating with medication adherence; (4) Outcome measures: studies providing or convertible to OR values, 95%CI, and standard errors; (5) Publications in Chinese or English.

Exclusion criteria: (1) Conference abstracts, reviews, or systematic reviews; (2) Studies with missing or non-extractable data; (3) Duplicate publications; (4) Studies with unavailable full text.

1.3 Literature Screening and Data Extraction

Two researchers independently conducted literature screening, data extraction, and cross-checking according to the search strategy and inclusion/exclusion criteria. Disagreements were resolved by a third reviewer. Screening involved initial title and abstract review, followed by full-text assessment. Extracted data included: first author, publication year, country/region, number of adherent patients, total sample size, sample source, study design, adherence assessment tool, influencing factors in multivariate analysis, and outcome indicators.

1.4 Quality Assessment

For cross-sectional studies, we used the Agency for Healthcare Research and Quality (AHRQ) scale [21], which comprises 11 items scored as 1 ("yes") or 0 ("no/unclear"), with total scores of 0-3 indicating low quality, 4-7 moderate quality, and 8-11 high quality. For cohort studies, we used the Newcastle-Ottawa Scale (NOS) [22], which evaluates three domains with a total score of 9 points (0-3: low quality; 4-6: moderate quality; 7-9: high quality). Two trained reviewers independently assessed study quality, with disagreements resolved through discussion or by a third reviewer.

1.5 Statistical Analysis

We used Stata 17.0 to calculate pooled adherence rates and 95%CIs, with subgroup analyses performed when necessary. RevMan 5.3 was used to analyze pooled OR values and 95%CIs for influencing factors. Heterogeneity was assessed using ^{2} tests (α=0.05) and I^2 statistics. I^2<50% with P>0.10 indicated low heterogeneity, warranting fixed-effects models; $I^2$$ 50 $0.10 indicated substantial heterogeneity, requiring random-effects models. For clinical heterogeneity, we conducted subgroup analyses, sensitivity analyses, or meta-regression to identify sources. When fewer than two studies examined a factor or data could not be pooled, we performed descriptive analysis. For factors examined in $ $10 studies, we assessed publication bias using funnel plots, Begg' s test, and Egger' s test in Stata 17.0, with P>0.05 indicating low bias [23].

Results

2.1 Literature Search Results

The initial search yielded 4,542 records. After removing duplicates and screening titles/abstracts, 3,014 records were excluded. Full-text review of 191 articles led to exclusion of 172, resulting in 19 included studies [7,17-20,24-36]. The detailed screening process is illustrated in Figure 1 [Figure 1: see original paper].

2.2 Characteristics of Included Studies

The 19 studies included 130,047 participants, with 50,852 exhibiting good medication adherence (complete adherence to prescribed regimens). Quality assessment revealed 17 studies [7,18-20,24-28,30-36] scored $ $8 points (high quality), and 2 studies [17,29] scored 7 points (moderate quality). We extracted 15 influencing factors that appeared in $ $2 studies, categorized as: general factors (age, gender, education level, living arrangement), psychosocial factors (depression, ADL, fall history, medication knowledge, medication beliefs, professional guidance), and medication-related factors (medication management, cost, regimen complexity, number of medications, adverse drug reactions). Table 2 presents detailed characteristics and quality assessment results.

2.3 Meta-Analysis Results

2.3.1 Pooled Medication Adherence Rate Meta-analysis of 19 studies (n=130,047) revealed significant heterogeneity (I^2=98.37%, P<0.01). Using a random-effects model, the pooled medication adherence rate was 41% [95%CI (34%, 47%)], as shown in Figure 2 [Figure 2: see original paper].

2.3.2 Pooled Effects of Influencing Factors We extracted and analyzed 15 influencing factors from the 19 studies. Age, gender, education level, living arrangement, depression, ADL, fall history, professional guidance, and regimen complexity showed acceptable heterogeneity, warranting fixed-effects mod-

els. Other factors exhibited substantial heterogeneity, requiring random-effects models. Table 3 presents detailed heterogeneity tests and meta-analysis results.

2.4 Sensitivity Analysis

2.4.1 Medication Adherence Rate Excluding each study sequentially did not substantially change the pooled effect size, indicating stable results.

2.4.2 Influencing Factors Alternative Effect Models: We compared fixed-effects and random-effects models for all factors. Except for medication management, results were consistent across models, confirming robustness (Table 4).

Sequential Study Exclusion: For factors with high heterogeneity, we performed sequential exclusion analyses. Excluding specific studies reduced heterogeneity for medication cost, number of medications, and adverse drug reactions, yielding consistent results with fixed-effects models (Table 5).

2.5 Meta-Regression Analysis

Using effect size as the dependent variable and year, country/region, measurement tool, number of medications, and study design as independent variables, meta-regression revealed that number of medications and country/region significantly affected effect sizes, indicating they were sources of heterogeneity (Table 6).

2.6 Subgroup Analysis

2.6.1 Medication Adherence Rate Subgroup analyses identified sources of heterogeneity. Inpatients showed the highest adherence rates, followed by residents of nursing/healthcare centers and outpatients, while community-dwelling elderly had the lowest rates ($P<0.05$). Domestic studies reported higher adherence than international studies ($P<0.05$). Visual Analogue Scale (VAS) assessments yielded higher adherence rates than other tools ($P<0.05$) (Table 7).

2.6.2 Influencing Factors Subgroup analysis of factors with $I^2>50\%$ revealed that heterogeneity decreased in subgroups with $ $5 medications, economically developed regions, community settings, and self-designed assessment tools, identifying these as heterogeneity sources (Table 8).

2.7 Publication Bias

Begg' s test ($P=0.441$) and Egger' s test ($P=0.674$) for the 19 studies indicated low risk of publication bias for adherence rates (Figure 3 [Figure 3: see original paper]). As each influencing factor was examined in fewer than 10 studies, publication bias was not assessed for individual factors.

Discussion

3.1 Current Status of Medication Adherence in Elderly Patients with Polypharmacy

Poor medication adherence represents a major global challenge. According to a 2013 WHO report, only 50% of elderly patients with chronic diseases follow treatment recommendations [37]. Our meta-analysis found a 41% adherence rate, consistent with reports from MIYAZAKI et al. (43.7%) [38], ABEGAZ et al. (45%) [39], and CHANG et al. (39.4%) [40]. Subgroup analyses revealed that inpatients had the highest adherence rates, followed by nursing/healthcare center residents and outpatients, while community-dwelling elderly had the lowest rates. This suggests that professional settings and guidance enhance adherence, highlighting the need for clinical attention to this issue. Institutional settings should develop tailored medication management strategies to reduce polypharmacy and adverse reactions [29]. For community-dwelling elderly, promoting family physician services may improve healthcare accessibility and emphasize treatment continuity [41]. Domestic studies reported slightly higher adherence than international studies, possibly reflecting China' s improving elderly care policies and support systems. Higher social and family support has been shown to promote adherence [42]. The substantial variation in adherence rates across assessment tools, with most studies using self-designed instruments, indicates a need for standardized, validated tools for elderly populations.

3.2 Influencing Factors

3.2.1 General Factors (Age, Gender, Education Level, Living Arrangement) Age significantly influences adherence, with decreasing adherence observed as age increases. This may result from age-related declines in memory, hearing, and vision [43-44], leading to missed doses. Polypharmacy further compounds these challenges. Low education level also impairs adherence, as these patients face difficulties accessing and understanding medical information, making them more susceptible to external influences [45-46] and prone to self-medication, inappropriate drug use, and reduced safety. Female gender was associated with lower adherence, possibly because women, despite longer life expectancy, often prioritize caregiving responsibilities over self-care, leading to missed medications [35,48]. Elderly living alone showed lower adherence than those living with partners or children, as cohabitants can monitor conditions, reinforce proper medication beliefs, manage daily medications, and provide reminders [30].

3.2.2 Psychosocial Factors (Depression, ADL, Fall History, Medication Knowledge, Medication Beliefs, Professional Guidance) Depression significantly reduces adherence, with depressed patients having 3.6 times higher risk of non-adherence than non-depressed individuals [49]. This underscores the importance of addressing mental health in elderly patients. ADL dependence also impairs adherence, as functional limitations requiring assis-

tance with daily activities compromise medication management. Medication knowledge and beliefs are crucial, showing positive correlations with adherence [50], consistent with the knowledge-attitude-behavior model where knowledge forms the foundation for behavior change and beliefs provide motivation [51]. Poor medication knowledge may lead to incomplete understanding of drug benefits, fear of adverse reactions causing dose reduction or discontinuation, and poor adherence when symptoms fluctuate [52]. Professional guidance improves adherence by correcting subjective non-adherence behaviors (e.g., stopping medications due to perceived symptom improvement or fear of adverse effects) and through education that enhances disease awareness and proper medication use.

3.2.3 Medication-Related Factors (Medication Management, Cost, Regimen Complexity, Number of Medications, Adverse Drug Reactions) Medication cost negatively impacts adherence. Elderly patients with multimorbidity require long-term multiple medications, creating financial burdens that exceed payment capacity and lead to non-adherence. Polypharmacy also complicates medication management, as elderly patients struggle to remember drug information and store medications properly. Our findings demonstrate that more medications and greater regimen complexity correlate with poorer adherence, likely because elderly patients have difficulty mastering different dosing schedules, administration methods, and frequencies, leading to missed, extra, or incorrect doses [53]. Adverse drug reactions also reduce adherence, as elderly patients with chronic conditions taking multiple medications long-term experience more frequent and severe adverse events, including organ damage [54]. This creates fear and reluctance to continue medications, further decreasing adherence.

Limitations

This study has several limitations. First, some influencing factors were examined in few original studies, potentially affecting meta-analysis results. Second, despite a rigorous search strategy, heterogeneity in study designs and sample sources may have influenced findings. Third, as studies examined different sets of influencing factors, some could not be pooled, limiting comprehensiveness. Fourth, the small number of studies for certain factors may have introduced selection bias. Finally, the lack of standardized assessment tools across studies limits comparability.

Conclusion

Current evidence indicates low medication adherence (41%) among elderly patients with polypharmacy. Age, gender, education level, living arrangement, depression, ADL, fall history, medication knowledge, medication beliefs, professional guidance, medication cost, medication management, regimen complexity, number of medications, and adverse drug reactions are significant influencing factors. Healthcare professionals should develop individualized interventions

based on these factors to optimize disease management in elderly patients with polypharmacy. However, given limitations in the number and quality of included studies, these conclusions require validation through additional high-quality, large-scale research.

Author Contributions: XIE Xuemei contributed to study conception, literature collection, and manuscript writing; GAO Jing contributed to manuscript revision, quality control, and overall supervision; BAI Dingxi contributed to supervision and manuscript revision; LU Xianying and HE Jiali contributed to data collection, analysis, and interpretation; LI Yue contributed to table preparation.

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

Funding: Sichuan Provincial Social Science Planning Project (SC22B150)

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Received: April 14, 2023; Revised: July 6, 2023

(Edited by JIA Mengmeng)

Note: Figure translations are in progress. See original paper for figures.