Ageing Research Reviews 117 (2026) 103060

Contents lists available at ScienceDirect

Ageing Research Reviews

journal homepage: www.elsevier.com/locate/arr

Review article

Quality and recommendations of guidelines for multimorbidity and polypharmacy in older adults: A systematic review

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ARTICLE INFO

Keywords:
Older adults
Multimorbidity
Polypharmacy
Guidelines
Systematic review

ABSTRACT

Background: Global population aging exacerbates the challenges of multimorbidity and polypharmacy in older adults. Clinical practice guidelines are essential for addressing these issues. This systematic review aims to evaluate the quality of existing guidelines and synthesize their recommendations based on the Ariadne principles, to inform future guideline development and clinical practice.

Methods: We searched nine databases and five guideline repositories (e.g., PubMed, Web of Science, Cochrane Library, CNKI, WHO) up to August 2025. Guidelines and consensus documents focusing on multimorbidity or polypharmacy in older adults, published in English or Chinese, were included. Each guideline was evaluated using four validated tools: AGREE II (methodological quality), RIGHT (reporting completeness), AGREE-REX (recommendation credibility and applicability), and GLIA (implementation feasibility). Recommendations were categorized and synthesized according to the Ariadne principles, with independent screening and data extraction and consensus resolution of discrepancies.

Results: The multidimensional appraisal of the 21 included guidelines revealed consistent weaknesses. According to AGREE II, the domains of Scope and Purpose (81.9 %) and Clarity of Presentation (61.1 %) demonstrated the highest median scores, whereas Rigor of Development (16.7 %) and Applicability (8.3 %) scored the lowest. Based on the RIGHT checklist, overall reporting completeness was 43.2 %, with the Evidence (0.0 %) and Quality Assurance (0.0 %) domains being particularly underreported. AGREE-REX evaluation indicated limited implementability at the individual recommendation level (12.5 %), and GLIA, while suggesting moderate implementability at the guideline level (65.4 %), identified frequent barriers in the domains of Measurable Outcomes (100.0 %) and Innovation Requirements (66.7 %). Thematically, most guidelines addressed interaction assessment (n = 15, 71.4 %), but far fewer incorporated patient preferences (n = 9, 42.9 %) or monitoring strategies (n = 9, 42.9 %). Only three guidelines (14.3 %) fully adhered to all five steps of Ariadne principles.

Conclusion: Current guidelines for older adults with multimorbidity or polypharmacy exhibit substantial weaknesses in methodological rigor, reporting completeness, and implementation feasibility. Synthesis based on the Ariadne principles revealed an imbalanced pattern of recommendations, with a predominant focus on medication safety rather than patient-centered and longitudinal care management. Future guideline development should strengthen methodological processes, systematically integrate patient perspectives, and co-design practical implementation strategies to better support personalized care for an aging population.

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https://doi.org/10.1016/j.arr.2026.103060
Received 13 November 2025; Received in revised form 8 January 2026; Accepted 8 February 2026
Available online 10 February 2026

1. Introduction

Accelerating global population aging and rising prevalence of chronic diseases have intensified multimorbidity and polypharmacy among older adults (United Nations Population Division, 2024; Nicholson et al., 2024; Hu et al., 2024). Currently, individuals aged ≥ 65 years constitute 9.8 % of the global population (800 million), a proportion projected to reach 16.5 % (1.6 billion) by 2050 (United Nations Population Division, 2024). In this group, multimorbidity affects 51 % and polypharmacy 45 % (Chowdhury et al., 2023; Kim et al., 2024), with marked regional variation (Xue et al., 2025; Conderino et al., 2024; Souza et al., 2021). These trends substantially increase inappropriate medication use (Liew et al., 2020), adverse drug reactions (Hart et al., 2025), healthcare costs, (Tran et al., 2022) and mortality (Li et al., 2022), posing a major global health challenge.

Clinical practice guidelines are essential for standardizing care, and their quality directly influences patient outcomes (Chen et al., 2018). Yet most remain rooted in a single-disease framework, lacking systematic assessment of complex drug–drug and drug–disease interactions (Rochon et al., 2021), which heightens risk in patients with multimorbidity. Even guidelines addressing multimorbidity often overlook key complexities in older adults—frailty, falls and cognitive decline—limiting individualized care (Martin et al., 2024). Although several multimorbidity- or polypharmacy-specific guidelines for older adults have emerged, comprehensive quality appraisal and evaluation of implementability are lacking. Furthermore, recommendations remain fragmented and un-synthesized into coherent, actionable clinical pathways.

To date, few reviews have systematically evaluated guidelines addressing multimorbidity or polypharmacy. Wang et al. (Wang et al., 2024) assessed the quality of multimorbidity guidelines but excluded disease-oriented ones and focused solely on methodological and reporting quality, without evaluating implementability or targeting older adults. Lun et al. (Lun et al., 2021) conducted a scoping review on multimorbidity in older adults, yet it was confined to prescribing guidelines, covered literature only up to 2019, and lacked a formal quality appraisal.

Given the frequent coexistence of multimorbidity and polypharmacy in older adults, this review will include guidelines addressing either condition or both, with a scope that encompasses broader care strategies for this population, beyond medication management alone. This systematic review aims to evaluate the quality of guidelines for older adults with multimorbidity and/or polypharmacy, and to categorize and synthesize their recommendations, providing evidence to inform future guideline development and clinical practice.

2. Methods

This systematic review was conducted following the PRISMA statement, (Page et al., 2021) and the protocol was registered on PROSPERO (CRD42023404647).

2.1. Search strategy

We conducted a comprehensive search in PubMed, Web of Science, and the Cochrane Library, as well as on 11 additional databases and guideline platforms, for guidelines related to multimorbidity or polypharmacy in older adults from inception to August 16, 2025. Search terms combining “older adults” “geriatric” “multimorbidity” and “polypharmacy” were applied using Boolean operators (Mancin et al., 2023). Detailed search strategies are provided in Supplementary 1.

2.2. Inclusion and exclusion criteria

Guidelines were included based on the National Academy of Medicine’s definition, (Institute of Medicine., 2011) or documents classified as consensus, providing explicit clinical recommendations on multimorbidity, (National Institute for Health and Care Excellence, 2016) polypharmacy, or both in older adults. Exclusion criteria were: (1) inaccessible full texts, (2) duplicates, (3) superseded versions, (4) publications in languages other than English or Chinese, and (5) documents not focused on older adults (e.g., adult- or pediatric-specific multimorbidity/polypharmacy).

2.3. Guideline selection

Four investigators (JY, HL, QX, and HZ) in two groups screened records and determined eligibility using NoteExpress v4.2.0. Before formal screening, all investigators piloted 50 records and resolved discrepancies through discussion to achieve consensus. Each group independently screened titles and abstracts, followed by full-text review of potentially eligible guidelines on multimorbidity or polypharmacy in older adults. Disagreements were resolved by consensus.

2.4. Data extraction

The same investigator pairs independently extracted data using a standardized form. Extracted information included: (1) Basic characteristics: title, year, country/region, developer type (society, government, international organization, research institute, university, or foundation), publication format (journal or website), definitions of multimorbidity/polypharmacy, target users, and setting, (2) Methodology: systematic search use, consensus process, grading of evidence and recommendations, funding, and conflicts of interest, and (3) Recommendations: categorized into five steps according to the Ariadne principles (Muth et al., 2014, 2019).

2.5. Quality evaluation

Guideline quality was evaluated using a multidimensional framework incorporating four validated tools: the Appraisal of Guidelines for Research and Evaluation II (AGREE II) (Brouwers et al., 2010) for methodological rigor, the Reporting Items for Practice Guidelines in Healthcare (RIGHT) (Chen et al., 2017) for reporting completeness, the AGREE–Recommendations Excellence (AGREE-REX) (AGREE-REX Research Team., 2019, Wang et al., 2021) for applicability and credibility, and the Guideline Implementability Appraisal (GLIA) (Shiffman et al., 2005; van Dijk et al., 2011) for feasibility of implementation. Two investigator pairs independently performed all assessments after standardized training. A pilot test ensured interrater consistency before formal evaluation. Reliability was quantified using the intraclass correlation coefficient (ICC) for AGREE II and AGREE-REX (7-point scales) and Fleiss’ kappa for RIGHT and GLIA (categorical items). Formal assessment proceeded only after achieving predefined thresholds (ICC ≥ 0.75, $\kappa \geq 0.6$) (Li et al., 2023; Koo and Li, 2016). Discrepancies were resolved through consensus meetings, with unresolved cases adjudicated by a senior methodologist. Following best practices, domain-specific scores were emphasized over overall ratings to enhance granularity and reduce interpretive bias. Detailed protocols and scoring structures are available in Supplementary 2.

2.6. Recommendation synthesis

The Ariadne principles, developed by Muth et al. (Muth et al., 2014), provide a structured framework for decision-making in multimorbidity care, encompassing five steps: (1) identifying the target population, (2) assessing interactions, (3) incorporating patient preferences and goals, (4) delivering individualized management, and (5) monitoring and follow-up. Originally designed for primary care consultations, the framework has been validated as a taxonomy for categorizing recommendations in multimorbidity guidelines (Muth et al., 2019). Guided by this framework, we applied the Ariadne principles to classify and

synthesize recommendations from included guidelines. Identical recommendations were consolidated for conciseness, and complementary statements were integrated into coherent clinical guidance.

2.7. Data analysis

Recommendations from the included guidelines were synthesized narratively and organized thematically using the Ariadne principles (Muth et al., 2019). Data organization and computation of key metrics were conducted in Microsoft Excel 2021 following predefined analytical protocols (Supplementary 2). Inter-rater reliability was quantified using intraclass correlation coefficients in SPSS (v26.0). Data visualization was performed using Origin 2024, including heatmaps, to facilitate cross-guideline and cross-domain performance comparisons, and boxplots, to delineate score distributions within individual quality domains.

3. Results

3.1. Search results

The search identified 22,540 records. After removing duplicates and screening titles, abstracts, and full texts (Supplementary 3), 21 publications met inclusion criteria, comprising clinical practice guidelines and expert consensus statements (Fig. 1).

3.2. Characteristics of included guidelines

Included guidelines were published between 2012 and 2025, originated mainly from China (n = 13, 61.9 %), with societies or associations as the most common developers (n = 12, 57.1 %). Eleven (52.4 %) focused on multimorbidity and 10 (47.6 %) on polypharmacy. Thirteen (61.9 %) defined multimorbidity as ≥ 2 chronic conditions. Most targeted the general older adult with multimorbidity or polypharmacy, without specifying disease combinations or care settings (Table 1; Supplementary 4 and 5).

Table 1
Characteristics of included guidelines (n = 21).

Item	Characteristics	No. (%)
Publication year	2012–2019	7 (33.33)
	2020–2025	14 (66.67)
Country/region of developer organization	China	13 (61.9)
	UK	3 (14.3)
	US	3 (14.3)
	Australia	1 (4.8)
	Germany	1 (4.8)
Type of developer organization	Society/association	12 (57.1)
	Hospital	5 (23.8)
	University	3 (14.3)
	Government organization	1 (4.8)
Publication format	Journal article	18 (85.7)
	Website only	3 (14.3)
Primary emphasis	Multimorbidity	11 (52.4)
	Polypharmacy	10 (47.6)
Definition of multimorbidity	≥ 2 chronic conditions	13 (61.9)
	Not applicable[a]	7 (33.3)
	Not reported	1 (4.8)
Definition of polypharmacy	≥ 5 medicines	5 (23.8)
	Not applicable[a]	9 (42.9)
	Minimum number of medicines not clearly defined	7 (33.3)
Target population	General older adults	12 (57.1)
	Specific subgroups of older adults	9 (42.7)
Target users	Health care providers	8 (38.1)
	Health care providers and others[b]	6 (28.6)
	Not reported	7 (33.3)

[a] Guidelines exclusively addressing multimorbidity need not define polypharmacy, and conversely.
[b] Includes, such as patients, policymakers, and public health professionals.

The guidelines contained a median of 7 recommendations (IQR, 4–14), spanned 10 pages (IQR, 8–21), and cited 52 references (IQR,

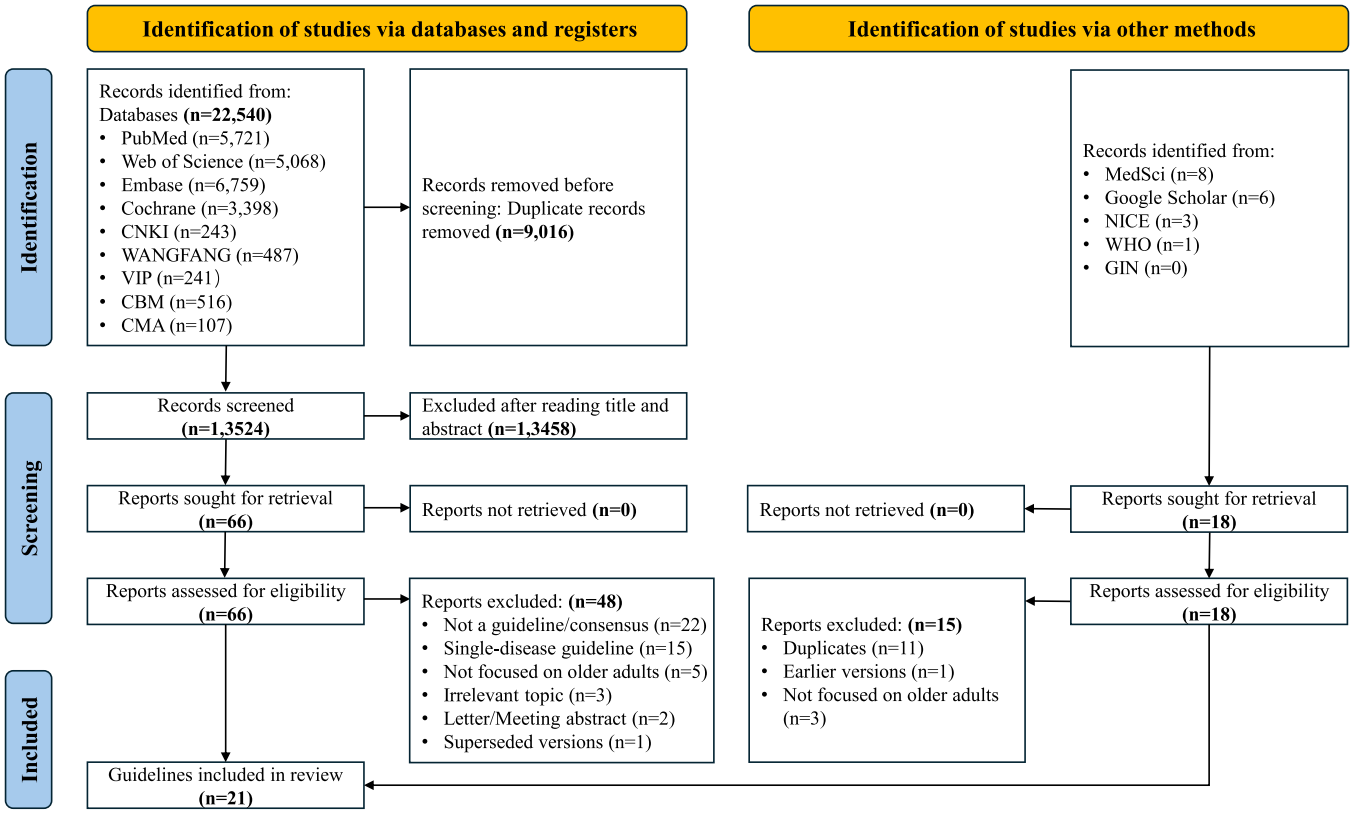

Fig. 1. Flow diagram for the included guidelines.

37–124). Development panels had a median of 5 (IQR, 3–14) writers and 24 (IQR, 19–41) experts for consensus. None reported methodological expert participation. Only two guidelines (Dale et al., 2023; Chinese Society of Clinical Pharmacy of Chinese Medical Association, 2022) used formal grading systems, one (Chinese Society of Clinical Pharmacy of Chinese Medical Association, 2022) was prospectively registered, and four (Endocrinology and Metabolism Branch of Chinese Association of Geriatric Research, 2018; Committee for the Promotion of the Combination of Medical Care and Nursing of the Chinese Geriatric Society, 2022; Hypertension Branch of Chinese Geriatrics Society et al., 2021 ; Zhu et al., 2024) were published in multiple journals.

3.3. Quality evaluation

Interrater reliability among four independent investigators showed excellent agreement across all four appraisal tools (Supplementary 6).

3.3.1. Methodological quality

Application of the AGREE II revealed substantial heterogeneity in methodological quality. Median normalized domain scores (NDS) across six domains ranged from 8.3 % to 81.9 % (Supplementary 7.1). As shown in Fig. 2.A, Scope and Purpose (median 81.9 %, IQR: 72.2, 86.1) and Clarity of Presentation (median 61.1 %, IQR: 44.4, 70.8) scored highest, reflecting clearly defined objectives and recommendations. In contrast, Applicability (median 8.3 %, IQR: 4.2, 29.2) and Rigor of Development (median 16.8 %, IQR: 10.7, 34.1) scored lowest, indicating that while recommendations were generally well presented, they often lacked methodological robustness and practical implementation guidance, limiting their overall credibility and impact.

3.3.2. Reporting quality

Evaluation using the RIGHT checklist showed wide variability, with an overall compliance rate of 43.2 %. Median domain compliance rates (DCR) across seven domains ranged from 0.0 % to 83.3 %

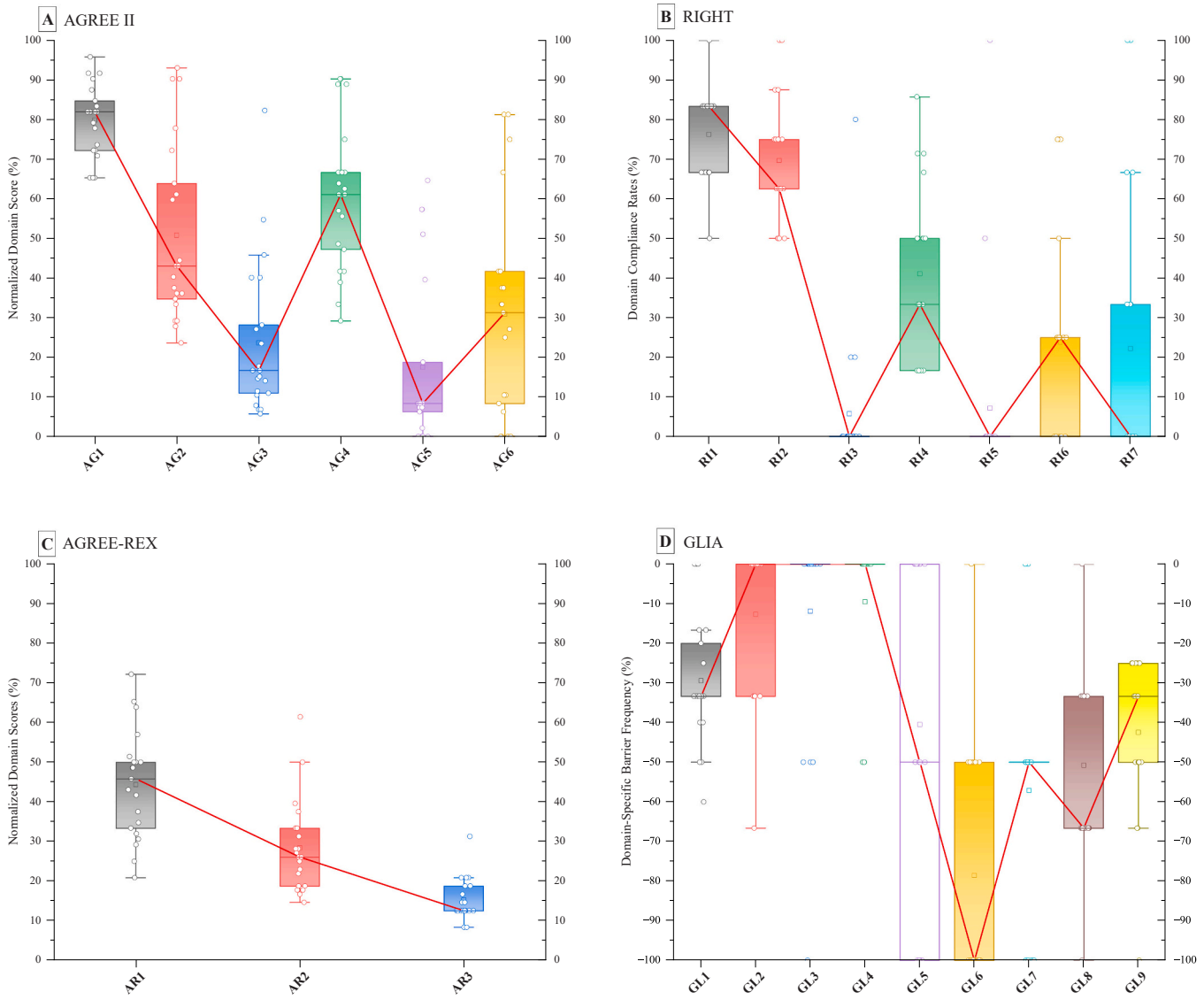

Fig. 2. Box plots of domain scores from four guideline appraisal tools. **A**, Methodological Quality (AGREE II), **B**, Reporting Completeness (RIGHT), **C**, Recommendation Credibility and Applicability (AGREE-REX), **D**, Implementation Feasibility (GLIA). **AGREE II:** AG1, Scope and purpose, AG2, Stakeholder involvement, AG3, Rigor of development, AG4, Clarity of presentation, AG5, Applicability, AG6, Editorial independence. **RIGHT:** RI1, Basic information, RI2, Background, RI3, Evidence, RI4, Recommendations, RI5, Review and quality assurance, RI6, Funding and declaration and management of interests, RI7, Other information. **AGREE-REX:** AR1, Clinical applicability, AR2, Values and preferences, AR3, Implementability. **GLIA:** GL1, Global considerations, GL2, Decidability, GL3, Executability, GL4, Effect on process of care, GL5, Presentation and formatting, GL6, Measurable outcomes, GL7, Apparent validity, GL8, Novelty/innovation, GL9, Flexibility. Note that GL1-GL9 are inverse-scored domains where lower scores indicate better performance.

(Supplementary 7.2). As shown in Fig. 2.B, reporting was most complete for Basic Information (median 83.3 %, IQR: 66.7, 83.3) and Background (median 62.5 %, IQR: 56.3, 81.3), reflecting adequate documentation of essential elements. In contrast, Evidence and Review and Quality Assurance (both median 0.0 %, IQR: 0.0, 0.0) were minimally reported. This pattern highlights major gaps in transparency—although guideline context was generally clear, limited reporting of evidence bases and quality assurance processes undermines assessment of trustworthiness and methodological rigor.

3.3.3. Recommendation credibility and applicability

Findings from the AGREE-REX indicated a marked decline in recommendation quality across its three domains. As illustrated in Fig. 2.C, Clinical Applicability scored highest (median 45.8 %, IQR: 32.6, 50.7), followed by Values and Preferences (median 26.0 %, IQR: 18.8, 33.3), while Implementability was lowest (median 12.5 %, IQR: 12.5, 18.8) (Supplementary 7.3). This gradient indicates that although recommendations demonstrate some clinical relevance, limited integration of stakeholder values and lack of a structured implementation framework reduce their credibility and real-world usability.

3.3.4. Implementation feasibility

Analysis using the GLIA instrument showed a median overall implementability rate of 65.4 % (IQR: 50.0, 76.5). Domain-specific barrier frequency (DBF) analysis revealed wide heterogeneity across nine domains (Fig. 2.D; Supplementary 7.4). Measurable Outcomes (median 100.0 %, IQR: 50.0, 100.0) and Novelty (median 66.7 %, IQR: 33.3, 66.7) showed the highest barrier frequencies, whereas Executability and Effect on Process of Care (both median 0.0 %, IQR: 0.0, 0.0) showed minimal barriers. These findings underscore two major limitations: (1) absence of measurable outcomes impedes evaluation of adherence and effectiveness, and (2) novelty-related barriers—stemming from required new clinician skills or limited patient engagement—further constrain adoption.

3.3.5. Subgroup analysis

Subgroup analyses assessed associations between guideline characteristics (publication year, language, and primary emphasis) and quality scores using median values and the Mann-Whitney *U* test. Differences with $P < 0.05$ and large effect sizes ($|r| \geq 0.50$) were considered significant. Distinct patterns emerged: guidelines published before 2020 scored higher in Stakeholder Involvement (AG2), Applicability (AG5), and Background (RI2). English-language guidelines outperformed others across multiple domains—Scope and Purpose (AG1), Stakeholder Involvement (AG2), Rigor of Development (AG3), Applicability (AG5), Background (RI2), Clinical Applicability (AR1), and Values and Preferences (AR2)—and showed fewer implementation barriers in Global Considerations (GL1). Guidelines emphasizing multimorbidity achieved higher scores in Clarity of Presentation (AG4) and Clinical Applicability (AR1), with lower barriers in Measurable Outcomes (GL6), Novelty (GL8), and Flexibility (GL9), resulting in higher overall implementability (Supplementary 7.5 and 8).

Table 2
Coverage of the Ariadne Principles by Guideline Recommendations. (AGS, 2012); (AWMSG, 2023); (Bergert et al., 2014); (Boyd et al., 2019); (CAGR-AHSSB, 2018); (CAGR-EBM, 2018); (CGS-CMCN, 2021a); CGS-CMCN, 2021b); (CGS-CMCN, 2022); (CGS-HB, 2021); (CSC, 2023); (CSCP, 2022); (Dale et al., 2023); (Holton et al., 2017); (NICE, 2015); (RACGP, 2025); (Shen et al., 2024); (Shi et al., 2023); (Tang et al., 2022); (Zhu et al., 2023); (Zhu et al., 2024).

Study ID	Target	Interact	Preferences	Manage	Monitor
(AGS, 2012)	No	No	Yes	Yes	No
(AWMSG, 2023)	No	Yes	No	No	No
(Bergert et al., 2014)	No	Yes	Yes	No	Yes
(Boyd et al., 2019)	No	No	Yes	No	No
(CAGR-AHSSB, 2018)	Yes	Yes	Yes	Yes	Yes
(CAGR-EBM, 2018)	No	Yes	No	No	No
(CGS-CMCN, 2021a)	No	Yes	No	No	No
CGS-CMCN, 2021b)	Yes	Yes	Yes	Yes	Yes
(CGS-CMCN, 2022)	No	Yes	Yes	Yes	Yes
(CGS-HB, 2021)	Yes	No	No	Yes	Yes
(CSC, 2023)	Yes	No	No	Yes	No
(CSCP, 2022)	No	Yes	No	No	No
(Dale et al., 2023)	No	Yes	No	Yes	No
(Holton et al., 2017)	No	Yes	No	No	No
(NICE, 2015)	Yes	No	Yes	Yes	No
(RACGP, 2025)	Yes	Yes	No	No	No
(Shen et al., 2024)	Yes	Yes	Yes	Yes	Yes
(Shi et al., 2023)	Yes	Yes	No	Yes	Yes
(Tang et al., 2022)	Yes	No	No	No	No
(Zhu et al., 2023)	Yes	Yes	Yes	No	Yes
(Zhu et al., 2024)	Yes	Yes	No	Yes	Yes

Interact, Interaction assessment, Manage, Individualized management, Monitor, Monitoring and follow-up, Preferences, Patients' preferences, prioritization and goal setting, Target, Identification of the target population.
AGS, American Geriatrics Society, AWMSG, All Wales Medicines Strategy Group, CAGR-AHSSB, Aging Health Service and Standardization Branch of Chinese Association of Geriatric Research, CAGR-EMB, Endocrinology and Metabolism Branch of Chinese Association of Geriatric Research, CGS-CMCN, Committee for the Promotion of the Combination of Medical Care and Nursing of the Chinese Geriatric Society, CGS-HB, Hypertension Branch of Chinese Geriatrics Society, CSC, Chinese Society of Cardiology of Chinese Medical Association, CSCP, Chinese Society of Clinical Pharmacy of Chinese Medical Association, NICE, National Institute for Health and Care Excellence, RACGP, Royal Australian College of General Practitioners.

3.4. Recommendation synthesis

Across the 21 guidelines, Interaction Assessment was the most frequently addressed principle (n = 15, 71.4 %), while patient-centered principles—Patients' preferences, prioritization and goal Setting, as well as Monitoring and follow-up—were least represented (each n = 9, 42.9 %). Only three guidelines (14.3 %) (Aging Health Service and Standardization Branch of Chinese Association of Geriatric Research, 2018; Committee for the Promotion of the Combination of Medical Care and Nursing of the Chinese Geriatric Society, 2021b; Shen et al., 2024) incorporated all five steps of the Ariadne framework (Table 2). Recommendations were synthesized into five components corresponding to the Ariadne principles (Panel 1–5).

3.4.1. Identification of the target population

Identification and stratification of the target population are the key initial steps in individualized management for older adults with multimorbidity (Golinelli et al., 2025). This process aims to identify individuals at increased risk of adverse outcomes related to multimorbidity, polypharmacy, functional decline, or frailty who would benefit most from comprehensive interventions (Liu et al., 2024). Current guidelines advocate moving beyond single-disease diagnoses toward a proactive, multidimensional screening approach that integrates risk profiling (e.g., advanced age, polypharmacy, frailty) (Chinese Society of Cardiology of Chinese Medical Association et al., 2023; Royal Australian College of General Practitioners, 2025; Shen et al., 2024), targeted assessment of high-risk subgroups, and consideration of social care needs and standardized definitions (Panel 1) (National Institute for Health and Care Excellence, 2015; Tang et al., 2022; Zhu et al., 2023). This structured framework forms the foundation for subsequent precision assessment and management.

3.4.2. Interaction assessment

Systematic evaluation of complex interactions within multimorbidity and polypharmacy is critical to minimizing risk and supporting evidence-based management. This step moves beyond isolated disease or drug assessments to examine interactions among diseases, drugs, and drug–disease combinations using validated tools and standardized processes (Hoel et al., 2021; Romskaug et al., 2020). Guidelines emphasize a structured, multidimensional clinical approach integrating comprehensive geriatric assessment, specialized risk screening instruments, systematic medication review, and checklist-based management of high-risk domains (Panel 2)(Dale et al., 2023; All Wales Medicines Strategy Group, 2023; Bergert et al., 2014; Shen et al., 2024). This framework enables the comprehensive detection of interaction risks—from global patterns to specific clinical issues—thereby strengthening the evidence base for personalized prescribing and medication optimization.

3.4.3. Patients' preferences, prioritization and goal setting

Integrating patient preferences, treatment priorities, and individual health goals into clinical decision-making is fundamental to patient-centered care (Watson et al., 2024) for older adults with multimorbidity. This step reorients care from a disease-focused model toward a collaborative, goal-directed process ensuring that decisions align with patients' values, life aspirations, and expectations regarding treatment. Management goals should be regularly reassessed and adapted in accordance with disease trajectory and prognosis (Panel 3) (American Geriatrics Society, 2012; Boyd et al., 2019; National Institute for Health and Care Excellence, 2015; Zhu et al., 2023). Such dynamic alignment ensures that care remains responsive to evolving patient needs, enhancing relevance, adherence, and the perceived value of care.

3.4.4. Individualized management

Individualized management represents the implementation phase translating assessment findings into coordinated, feasible care strategies tailored to each patient's complexity and prognosis (World Health Organization, 2024). Guidelines highlight the importance of flexible, adaptive, and patient-centered approaches that combine evidence-based medicine, clinical feasibility, and multidisciplinary collaboration (Panel 4) (American Geriatrics Society, 2012; Aging Health Service and Standardization Branch of Chinese Association of Geriatric Research, 2018; National Institute for Health and Care Excellence, 2015). This integrative framework aims to optimize outcomes, balance therapeutic benefits and burdens, and maintain or improve functional capacity and quality of life.

3.4.5. Monitoring and follow-up

Systematic monitoring and follow-up ensure the sustained safety, effectiveness, and adaptability of management plans for older adults with multimorbidity (Jiao et al., 2025). This phase establishes a proactive, continuous evaluation process in which each encounter serves as an opportunity for comprehensive reassessment rather than a routine review (Friedemann Smith et al., 2022). Guidelines emphasize multidimensional monitoring encompassing clinical outcomes, functional status, medication management, and adherence through standardized intervals, structured tools, and interdisciplinary input (Panel 5) (Bergert et al., 2014; Shen et al., 2024; Shi et al., 2023, Zhu et al., 2023). This ongoing process facilitates early identification of emerging problems, prevention of adverse outcomes, and long-term achievement of individualized management goals.

4. Discussion

4.1. Main findings

This systematic review provides the first comprehensive and multidimensional synthesis of guidelines for older adults with multimorbidity and/or polypharmacy, incorporating evaluations of their methodological rigor, reporting completeness, recommendation applicability, and implementation feasibility. The findings reveal substantial heterogeneity and structural deficiencies across these dimensions. These deficiencies highlight the inadequacy of current guideline development frameworks in addressing the complex and evolving needs of this population.

Overall, the methodological and structural quality of existing guidelines remains insufficient to support safe and effective care for older adults with multimorbidity and polypharmacy. Our multidimensional evaluation identified a fundamental paradox: despite increasing publication of such guidelines, their methodological underpinnings are weak, the recommendation formulation process lacks transparency, and patient-centered values and implementation pathways are often neglected. Consequently, guidelines intended to standardize and enhance clinical decision-making may, paradoxically, impede individualized, high-quality care. A related concern is the lack of conceptual uniformity—particularly in defining polypharmacy—which complicates epidemiologic monitoring and reflects the absence of a mature, shared knowledge framework in this field.

Detailed quality analysis indicates that most guidelines remain constrained by a single-disease paradigm. Their relative strengths lie in foundational domains, such as Scope and Purpose and Background, whereas critical components essential for multimorbidity management—evidence adaptation, integration of patient values, and implementation mechanisms—show consistently poor performance. Assessments using AGREE-REX and GLIA converge on a common conclusion: current recommendations often fail to translate knowledge into action. They frequently lack measurable indicators for evaluating adherence and outcomes, or they are impractical because they require clinicians to acquire new competencies without corresponding structural support. This cascade—from weak methodology and incomplete reporting to limited applicability and failed implementation—illustrates that existing guideline development systems have yet to establish the

methodological and operational capacity required for managing clinical complexity.

From a content perspective, analysis based on the Ariadne principles revealed a conceptual imbalance in recommendation coverage. Most guidelines prioritized interaction assessment, reflecting a predominant focus on safety-oriented medication management, whereas patient-centered components—such as preference integration, goal setting, and monitoring—were often underrepresented. Only a few guidelines addressed all five steps of the Ariadne framework within their recommendations. This imbalance underscores the persistence of a disease-focused paradigm (Ong et al., 2020) and a systemic failure to embed patient values, treatment priorities, and continuous health management into guideline design. Consequently, while these guidelines may help mitigate medication risks, they remain insufficient to support holistic, patient-centered, and longitudinal care.

Multiple interrelated factors contribute to these quality deficits. First, the dual limitations of methodological rigor and evidence availability remain critical barriers. The frequent absence of methodological experts in development panels undermines supervision of evidence retrieval, synthesis, and grading, while the scarcity of high-quality direct evidence impedes the formulation of robust recommendations. Second, a persistent implementation gap exists between guideline development and clinical practice. Insufficient engagement of patients and caregivers prevents recommendations from reflecting end-user needs, and the absence of specific, actionable implementation strategies creates a "last-mile" disconnect between guidance and application. Finally, a lack of consensus on fundamental definitions exacerbates conceptual fragmentation and inconsistency across guidelines and institutions.

4.2. Strengths and limitations

This review provides new insights and methodological advances. First, it establishes an integrated framework that concurrently evaluates four dimensions—methodological quality, reporting completeness, recommendation applicability, and implementation feasibility. This approach not only corroborates existing weaknesses in rigor and reporting but also introduces a "credibility–implementability gap," shifting the focus from identifying deficiencies to understanding why guidelines fail. Second, it synthesizes fragmented recommendations into a coherent clinical pathway—Target, Interact, Preferences, Manage, Monitor—based on the Ariadne principles. By incorporating disease-oriented guidelines for older adults, our synthesis offers more granular, actionable recommendations for complex scenarios, such as cardiovascular comorbidities and integrated medical-nursing care, enhancing clinical applicability compared to previous syntheses of broad principles. Third, subgroup analyses highlight the impact of publication year, language, and primary focus on quality, offering actionable insights for guideline improvement across various contexts.

As with any systematic review, this review has its limitations. Restriction to English and Chinese guidelines may introduce language bias. Additionally, the synthesis process lacked formal input from a broader range of end-users, such as frontline clinicians, patients, and caregivers, which may influence the practical relevance and adoption of the summarized recommendations. The modest number of included guidelines limits statistical power and the ability to explore complex interdomain relationships. Moreover, as this review evaluates documentary quality rather than real-world implementation, its findings cannot directly infer clinical effectiveness or patient outcomes.

4.3. Implications

This review highlights the need to strengthen the methodological rigor, patient-centered orientation, and real-world applicability of guidelines for managing multimorbidity and polypharmacy in older adults. In clinical practice, efforts should focus on developing pragmatic, evidence-informed tools and workflows to translate guideline concepts into routine care, thereby bridging the gap between recommendations and implementation (Cole et al., 2023). Specifically, these efforts should encompass defining criteria for identifying multimorbidity and polypharmacy, integrating assessment and monitoring tools into care (Heen et al., 2021), and enhancing digital decision-support systems and training in primary and long-term care to strengthen clinicians' capacity in managing multimorbidity (Cassidy et al., 2021; Michielsen et al., 2023). At the level of guideline development and policy, (1) initiatives should ensure methodological expertise, leveraging tools such as the STAR (Yang et al., 2023, 2025) and adˆStandarder (STAR Working Group Secretariat,2025) to enhance the rigor of guideline development, and promote structured engagement of patients and caregivers (Hwang et al., 2022). (2) Developers should design scalable implementation strategies, informed by frameworks like the CFGI (Zhong et al., 2025a, 2025b), and supported by digital applications to facilitate real-world adoption (Smith et al., 2025). (3) Strengthening policy support (Chen et al., 2022) and promoting international collaboration led by organizations such as WHO and NICE are crucial for establishing standardized definitions (Khunti et al., 2023) and developing a coherent, globally adaptable framework for guideline development.

5. Conclusion

Guidelines addressing multimorbidity and polypharmacy in older adults have advanced in the clarity of recommendations and the management of pharmacotherapy, however, they remain constrained by limited methodological rigor, incomplete reporting, and suboptimal implementability. Their predominant focus on interaction assessment overshadows patient-centered dimensions, including preference incorporation, goal alignment, and longitudinal follow-up. Future guideline development should reinforce methodological robustness, systematically integrate patient engagement, and refine implementation frameworks to translate recommendations into reliable, applicable, and actionable tools that better meet the complex care needs of an ageing population.

Summary of recommendations structured around the Ariadne principles

Panel 1
Identification of the target population

- **Establish core screening criteria**
- **Define the routine screening population**. Consider adults aged ≥ 65 years—particularly those in primary care and geriatric settings—as the baseline group for multimorbidity and polypharmacy screening (Royal Australian College of General Practitioners, 2025; Shen et al., 2024)
- **Identify key risk indicators**. Prioritize assessment for individuals with: (1) Polypharmacy (concurrent use of ≥ 5 medications), (2) Frailty (positive screening results on the FRAIL scale), (3) Functional decline (limitations in ADLs/IADLs), (4) Recent unplanned hospitalization (Aging Health Service and Standardization Branch of Chinese Association of Geriatric Research, 2018; Chinese Society of Cardiology of Chinese Medical Association et al., 2023, Royal Australian College of General Practitioners, 2025)
- **Targeting specific high-risk disease subgroups**
- Perform routine frailty screening in all older adults with cardiovascular disease (Chinese Society of Cardiology of Chinese Medical Association et al., 2023)
- Conduct cognitive screening (e.g., AD-8, Mini-Cog) for hypertensive patients, particularly those ≥ 75 years or with subjective memory complaints (Hypertension Branch of Chinese Geriatrics Society et al., 2021)
- **Incorporating non-medical dimensions**
- Systematically evaluate social support status and long-term care needs during initial assessments (National Institute for Health and Care Excellence, 2015)
- **Applying unified conceptual standards**
- Adopt consensus-based definitions of "multimorbidity" and "comorbidity" in clinical practice and research to ensure identification accuracy and consistency (Tang et al., 2022; Zhu et al., 2023)

Panel 2

Interaction assessment

- **Implement a comprehensive foundational assessment framework**
- **Central role of geriatric assessment (GA).** Guidelines strongly recommend implementing GA—evaluating functional status, comorbidity, cognition, nutrition, and social support—as a core practice to identify vulnerabilities in patients aged ≥ 65 years receiving chemotherapy (Dale et al., 2023). Polypharmacy evaluation is explicitly positioned as an integral component of GA(Shen et al., 2024)
- **Standardized medication review process.** A structured medication review based on a detailed medication history is recommended for all patients with polypharmacy. Validated instruments such as the Medication Appropriateness Index (MAI) should be used for systematic evaluation (Bergert et al., 2014)
- **Apply diverse specialized assessment and prediction tools**
- **Prognosis and risk prediction tools.** Clinicians may use validated resources such as ePrognosis to estimate life expectancy (Dale et al., 2023)
- **Specific risk screening tools.** Targeted screening is advised for risks including frailty, falls, and anticholinergic drug use (All Wales Medicines Strategy Group, 2023). For alcohol–medication interactions, specialized tools such as the POSAMINO criteria can assist in identification(Holton et al., 2017)
- **Manage frequent and high-risk interactions**
- **Consult disease-specific risk lists.** When managing complex cases, such as cardiovascular disease coexisting with neuropsychiatric disorders(Chinese Society of Clinical Pharmacy of Chinese Medical Association, 2022) or multimorbidity in very old adults,(Committee for the Promotion of the Combination of Medical Care and Nursing of the Chinese Geriatric Society, 2021a) guidelines provide detailed lists of potentially inappropriate medications and risk management strategies to alert clinicians to serious consequences, including bleeding, QT prolongation, and central nervous system depression(Chinese Society of Clinical Pharmacy of Chinese Medical Association, 2022)
- **Focus on drug-drug interactions.** Several guidelines elaborate on potential risks and management strategies for interactions between drug classes from different systems (e.g., hypoglycemics, antihypertensives, psychotropics) (Endocrinology and Metabolism Branch of Chinese Association of Geriatric Research, 2018)
- **Adhere to core principles throughout the management cycle**
- **Dynamic assessment and deprescribing.** Re-evaluation of medication regimens during care transitions (e.g., hospital admission/discharge, change of provider) is emphasized. Deprescribing is highlighted as a continuous core strategy for addressing inappropriate polypharmacy (Bergert et al., 2014; Shen et al., 2024; Zhu et al., 2023)
- **Systemic risk control.** Patients are advised to use a single primary pharmacy to facilitate comprehensive checks for drug–drug interactions and maintain a complete medication record (Bergert et al., 2014)

Panel 3
Patients' preferences, prioritization and goal setting

- **Establish shared decision-making as the cornerstone**
- **Proactively elicit patient preferences.** When making any medical decision for patients with multimorbidity, clinicians should actively solicit and integrate patients' personal preferences, values, and expectations (Dale et al., 2023). This includes reaching a clear agreement on patient needs and expectations regarding drug therapy before initiating prescriptions (Bergert et al., 2014)
- **Position the patient at the center.** Patients should be engaged through shared decision-making throughout the entire process of clinical decision-making and intervention planning (Zhu et al., 2023)
- **Implement dynamic, goal-oriented management**
- **Identify health priorities and trajectory.** A core aspect of clinical practice involves identifying and communicating patients' health priorities and expected health trajectory with them and their caregivers. Care should be initiated, modified, or discontinued based on these priorities, potential benefits versus harms, and the overall trajectory (Boyd et al., 2019)
- **Set stratified and adaptive goals.** Management goals should be differentiated according to the patient's health state (e.g., robust, frail, disabled) and continuously adjusted in response to evolving health status, key problems, and personal preferences (Zhu et al., 2023)
- **Identify and integrate individualized considerations**
- **Assess patient willingness and adherence.** Before developing a multimorbidity management plan, clinicians should evaluate patient willingness. (Aging Health Service and Standardization Branch of Chinese Association of Geriatric Research, 2018) Regularly reviewing medication adherence and addressing related barriers provides a practical foundation for realistic goal setting (All Wales Medicines Strategy Group, 2023)
- **Incorporate social support and care needs.** Care plans must systematically account for patients' social engagement, support systems, and caregiver capacity, and include measures to prevent social isolation by integrating these nonmedical dimensions into individualized goals (National Institute for Health and Care Excellence, 2015)

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- **Ensure goal attainment through communication and education**
- **Provide ongoing information and support.** Patients and caregivers should receive clear, consistent information and support. Ensuring their understanding of treatment goals, medication records, and care plans is critical to promote effective self-management (Bergert et al., 2014; National Institute for Health and Care Excellence, 2015)
- **Reinforce medication education.** Medication education is emphasized as a cornerstone of management. Explaining medication purposes, expected benefits, potential risks, and precautions enhances understanding and adherence, facilitating the achievement of co-created goals (Shen et al., 2024)

Panel 4
Individualized management

- **Establish a core framework for individualized decision-making**
- **Interpret evidence and balance benefits and burdens.** The limitations of applying medical literature to patients with multimorbidity should be acknowledged and carefully interpreted. Clinical decisions must be contextualized within risks, burdens, benefits, and prognosis (e.g., life expectancy, functional status, quality of life). Strategies should aim to optimize benefit, minimize harm, and enhance overall well-being (Dale et al., 2023)
- **Evaluate treatment complexity and feasibility.** The complexity and practicality of therapeutic options should be systematically assessed and prioritized when formulating management plans for older adults with multimorbidity (Dale et al., 2023)
- **Formulate stratified management strategies based on assessment**
- **Develop interventions guided by comprehensive geriatric assessment (CGA).** Conducting CGA is recommended for older adults with cardiovascular disease and frailty, followed by the development of targeted intervention plans based on the results. (Chinese Society of Cardiology of Chinese Medical Association et al., 2023) For patients with multimorbidity, chronic diseases and geriatric syndromes should be managed using CGA within a multidisciplinary framework (Zhu et al., 2023)
- **Implement health state–stratified management.** Management goals and interventions should be tailored according to the patient's health state (e.g., robust, frail, or disabled). The effectiveness of care should be evaluated across multiple dimensions, including clinical outcomes, functional performance, and patient satisfaction (Zhu et al., 2023)
- **Implement individualized clinical decisions in key domains**
- **Personalize antihypertensive therapy.** Blood pressure targets should be individualized for older hypertensive patients based on age (≥65 or ≥80 years), frailty, and cognitive function. A more relaxed control strategy may be appropriate for those with multimorbidity (Hypertension Branch of Chinese Geriatrics Society et al., 2021 ; Chinese Society of Cardiology of Chinese Medical Association et al., 2023)
- **Tailor lipid-lowering and glycemic management.** In patients with atherosclerotic cardiovascular disease and frailty, lipid-lowering therapy should begin with low-dose statins. For those with coexisting cardiocerebrovascular disease and diabetes, glycemic control should follow individualized principles, prioritizing agents with proven cardiovascular benefits and adopting simplified regimens (Chinese Society of Cardiology of Chinese Medical Association et al., 2023; Shi et al., 2023)
- **Exercise caution in revascularization and antithrombotic therapy.** Revascularization decisions should be made judiciously for older patients with coronary artery disease and frailty. Antiplatelet regimens must follow a comprehensive assessment of both ischemic and bleeding risks (Chinese Society of Cardiology of Chinese Medical Association et al., 2023)
- **Utilize multidisciplinary teams and structured processes**
- **Establish multidisciplinary collaboration.** A multidisciplinary care model is recommended to deliver coordinated medical, rehabilitative, and nursing services for older adults with multimorbidity and frailty (Aging Health Service and Standardization Branch of Chinese Association of Geriatric Research, 2018; Chinese Society of Cardiology of Chinese Medical Association et al., 2023; Zhu et al., 2023)
- **Implement structured deprescribing protocols.** Deprescribing is a cornerstone strategy for managing polypharmacy. Medication optimization should be conducted in a patient-centered manner based on CGA, following structured frameworks such as the 5-step method (Shen et al., 2024)
- **Integrate health and social care.** The formulation and implementation of care plans should align medical and social care resources to ensure continuity, coordination, and long-term support (National Institute for Health and Care Excellence, 2015)

Panel 5
Monitoring and follow-up

- **Establish foundational clinical and structured reassessment mechanisms**

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- Standardize monitoring frequency for high-risk medications. Monitoring should follow guideline-recommended intervals to evaluate treatment response and detect adverse drug reactions (Bergert et al., 2014)
- **Conduct periodic medication regimen reviews.** The geriatric multidisciplinary team should perform regular, planned evaluations of the overall medication regimen, focusing on safety and effectiveness (Shen et al., 2024)
- **Define follow-up schedules for pharmacotherapy.** Clear time points should be established after initiating or adjusting treatment. For instance, follow-up within 2 weeks is recommended after starting or changing antihypertensive therapy, extending to every 1–3 months once stabilized (Shi et al., 2023)
- **Enhance medication-specific safety monitoring**
- **Monitor adherence and adverse drug reactions (ADRs).** Patient adherence should be regularly assessed using validated tools, and new symptoms should be actively screened to identify potential ADRs and prevent prescribing cascades (Bergert et al., 2014; Shen et al., 2024)
- **rack risk indicators for specific medications.** For drugs with potential toxicity, such as statins, relevant indicators (e.g., hepatic and renal function, muscle enzyme levels) should be periodically monitored after initiation, typically within the first 3 months (Shi et al., 2023)
- **Implement dynamic and holistic assessment centered on patient status**
- **Ensure continuity of care.** Particularly in home-based or long-term care settings, maintaining uninterrupted medical and support services is essential for effective monitoring[36]
- **Perform dynamic comprehensive geriatric assessments.** Health evaluation in older adults with multimorbidity should be continuous and adaptive. Reassessment should be triggered by disease progression, emergence of new conditions, or shifts in primary health issues to promptly identify changes in status (Zhu et al., 2023)
- **Address specific clinical scenarios and high-risk periods**
- **Strengthen perioperative monitoring.** In older hypertensive patients undergoing surgery, close monitoring of blood pressure fluctuations and anesthetic effects on cognitive function is essential (Hypertension Branch of Chinese Geriatrics Society et al., 2021)
- **Assess blood pressure variability.** Beyond routine office measurements, both short- and long-term variability should be evaluated using 24-hour ambulatory or home blood pressure monitoring to achieve comprehensive control assessment (Hypertension Branch of Chinese Geriatrics Society et al., 2021)

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.arr.2026.103060.

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