

Polypharmacy and Potentially Inappropriate Prescriptions: Insights from a Systematic Review of Definitions and Assessment Tools

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Abstract

Background: Polypharmacy is an important and growing challenge for modern clinical practice, attracting interest from clinicians, guideline developers, and policymakers. The variability in definitions and measurement methods across studies complicates direct comparison of results about polypharmacy. A major concern within the context of polypharmacy is the occurrence of Potentially Inappropriate Prescriptions (PIP), medications for which the potential risks outweigh the benefits.

Aims: This study aims to systematically review and synthesize definitions of polypharmacy, PIP and tools for PIP detection in the published literature.

Study design: Systematic review conducted in

accordance with PRISMA guidelines.

Methods: We screened three databases: PubMed, Google Scholar, and Cochrane, including peer-reviewed studies that reported definitions of polypharmacy or PIP, or applied tools to assess them. Eligible studies included observational, interventional, or methodological articles, and relevant systematic reviews focused on adult populations in any care setting, published in English. We extracted the following data and organized results in summary tables: first author, year of publication, study design, main objective, definition of polypharmacy, definition and tools to assess PIP and associated variables (population, age, setting, diagnosis).

Results: A total of 220 records were identified, of

which 70 studies were included. There exists substantial heterogeneity in defining polypharmacy and more specific terms such as excessive polypharmacy, appropriate polypharmacy, and unnecessary polypharmacy. A total of 60 definitions of polypharmacy and associated terms were identified. There were 36 numerical- only definitions (60 % of all definitions), 7 numerical definitions associated with other descriptive terms (11.66 %), and 17 descriptive definitions (28.34 %). The qualitative definitions of polypharmacy reflect a shift from viewing it as a purely numerical concept toward a more clinical and appropriateness-based perspective. The most common definition identified polypharmacy as the concurrent use of 5 or more medications, adopted by 19 studies (52.8 %), followed by other definitions ranging from 4 or more to 15 medications. A clear predominance of explicit criterion-based tools in defining PIP (73.53 %) reflected a standardized approach across studies. In contrast, implicit tools and clinical judgment (8.82 %), risk–benefit conceptual definitions (17.65 %).

Conclusion: This review highlights the need for more standardized yet context-sensitive definitions of polypharmacy and PIP. The integration of validated tools, along with individualized approaches such as deprescribing and shared decision-making, is particularly important in high-risk populations, including older adults and patients with multimorbidity.

Keywords: polypharmacy, potentially inappropriate prescriptions, prescribing, explicit criteria, implicit tools

INTRODUCTION

Polypharmacy is commonly defined as the concurrent use of multiple medications, although no universal definition exists. Most frequently, it is described as the use of five or more medications, particularly in older adults and individuals with multimorbidity (1,2). The prevalence of polypharmacy has increased substantially in recent years, with estimates ranging from 30% to over 60% among older populations and rising trends also observed in younger adults with chronic conditions (3). While polypharmacy may be clinically appropriate in complex cases, it is also associated with increased risks of adverse drug reactions, drug–drug interactions, reduced adherence, and higher healthcare utilization. As a result, attention has increasingly shifted from the number of medications alone to the appropriateness of prescribing (4).

A central concept in this context is Potentially Inappropriate Prescribing (PIP), which refers to situations where the potential risks of a medication outweigh its expected clinical benefits, or when prescribing does not align with evidence-based guidelines (5-10). PIP encompasses three main dimensions of suboptimal prescribing: overprescribing, use of unnecessary or duplicate medications; misprescribing, which refers to incorrect drug, dose, or duration; and underprescribing, also known as *prescribing omission*, which means the failure to prescribe a clinically indicated medication likely to benefit the patient (11-14).

Therefore, PIP represents an overarching construct that includes both the use of potentially inappropriate medications (PIMs) and potential prescribing omissions (PPOs), capturing the full spectrum of inappropriate medication use in clinical practice (15-18).

To identify PIP, both explicit and implicit assessment tools have been developed. Explicit criteria, such as the STOPP/START criteria and Beers Criteria, are standardized, criterion-based tools that allow reproducible and large-scale assessment. The STOPP (Screening Tool of Older Persons' potentially inappropriate Prescriptions) criteria are primarily used to detect overprescribing and misprescribing, while the START (Screening Tool to Alert to Right Treatment) criteria focus on identifying underprescribing or prescribing omissions. The Beers Criteria provide a list of medications that are generally considered inappropriate, particularly in adults aged ≥ 65 years, and are widely used in geriatric practice. In contrast, implicit tools, such as the Medication Appropriateness Index (MAI), rely on clinical judgment to evaluate prescribing in the context of individual patient characteristics, though they are more time-consuming and less standardized (19-21). Each approach has strengths and limitations: explicit tools enable reproducibility and standardisation but may not fully account for individual patient contexts, while implicit tools require clinical expertise and are time-consuming, limiting their application on a large scale (22,23).

Although a substantial proportion of the literature on polypharmacy and potentially inappropriate prescribing focuses on older adults due to their increased vulnerability, these issues are not exclusive to this population. Therefore, this review includes studies involving adult populations (≥ 18 years), while acknowledging the predominance of geriatric-focused evidence. Despite the growing body of research, substantial heterogeneity persists in how polypharmacy and PIP are defined and measured across studies. This variability limits comparability, complicates the interpretation of findings, and hinders the development of standardized clinical and policy approaches. Therefore, this systematic review aims to synthesize existing definitions of polypharmacy and PIP, as well as the tools used for their assessment, in order to clarify current concepts, identify methodological variability, and support more consistent and clinically relevant approaches to medication optimization. Although this review addresses heterogeneous literature, a systematic review was chosen to enable a structured comparison, classification, and synthesis of definitions, rather than simple mapping. This approach allows for quantitative analysis and clinically relevant conclusions, ensuring methodological rigor and reproducibility.

OBJECTIVES

The primary objective of this systematic review is to identify, compare, and synthesize existing definitions of polypharmacy and potentially

inappropriate prescribing (PIP) reported in the literature. The specific objectives are to: Classify the different definitions of polypharmacy (numerical, descriptive, and combined approaches); Characterize the conceptual definitions of PIP, including risk–benefit, explicit, implicit, and multidimensional approaches; Identify and compare the tools used to assess PIP, including explicit criteria (e.g., STOPP/START, Beers) and implicit methods; Evaluate the variability in definitions and assessment methods across different populations and clinical settings; Synthesize the implications of this heterogeneity for clinical practice and research.

Significance of the Study

This study addresses the lack of consistency in how polypharmacy and potentially inappropriate prescribing (PIP) are defined and assessed across the literature, particularly in adult populations with multimorbidity and high medication burden, who are at increased risk of medication-related harm. By systematically identifying and classifying definitions of polypharmacy and PIP, and comparing the tools used to detect inappropriate prescribing (including explicit and implicit criteria), this review highlights key areas of methodological variability. These findings improve the comparability of studies, support the appropriate selection of assessment tools in clinical and research settings, and provide a more consistent foundation for medication optimization strategies.

MATERIALS AND METHODS

Data sources and data strategy

This systematic review was conducted in accordance with the PRISMA 2020 (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [24]. The PRISMA 2020 checklist is provided in Figure 1 at the results. To ensure transparency and reproducibility, the review followed a predefined protocol, including clearly defined eligibility criteria, search strategy, and data extraction procedures.

The literature search was conducted in three databases (PubMed, Google Scholar, and Cochrane Library) to identify relevant studies on polypharmacy definitions, potentially inappropriate prescribing (PIP), and assessment tools. A comprehensive search strategy was developed for each database using predefined keywords and Boolean operators (Appendix 1).

This review was not registered in a prospective database (e.g., PROSPERO), as it focused on the synthesis of definitions and methodological approaches rather than intervention outcomes.

Study selection

Studies were selected based on predefined eligibility criteria to ensure a transparent and reproducible process. Eligible studies included original research (observational studies such as cross-sectional, cohort, and case-control designs, as well as interventional studies), along with systematic reviews and meta-analyses, that provided definitions of polypharmacy and/or

potentially inappropriate prescribing (PIP), or applied tools for their assessment.

Studies involving adult populations (≥ 18 years) were included regardless of gender, disease condition, geographic location, or healthcare setting. Where available, data were considered across age groups (18–65 years and ≥ 65 years), although most studies focused on older adults.

Studies were excluded if they were editorials, conference abstracts, narrative (non-systematic) reviews, or lacked full-text availability.

The search covered studies published between January 2015 and August 2025, and the last search was conducted on 25 August 2025.

Detailed characteristics of excluded studies were not reported, as exclusions were based on predefined eligibility criteria and did not contribute to the synthesis. The selection process and reasons for exclusion are presented in the PRISMA flow diagram.

Data extraction

Data extraction was performed using a structured approach to ensure consistency and reproducibility. Two authors independently screened the studies and extracted data from the included articles, while a third author reviewed the process for accuracy and completeness. Extracted information included: first author, year of publication, study design, main objective, definitions of polypharmacy and PIP, assessment tools, population characteristics (age, setting, and clinical context), and key findings.

Any discrepancies between the two reviewers

were resolved through discussion, and when necessary, consensus was reached with the involvement of the third author. This process ensured the reliability and transparency of data extraction.

Risk of bias assessment

Given the nature of this review, which focuses on definitions and methodological approaches rather than clinical outcomes, a formal risk of bias assessment was not performed. Instead, emphasis was placed on systematically extracting and comparing definitions and tools across studies to ensure methodological consistency and transparency.

RESULTS

The study selection process is presented in Figure 1. A total of 220 records were identified through database searching, of which 196 remained after removal of duplicates. Following screening, 108 records were excluded, and 88 full-text articles were assessed for eligibility. Of these, 18 studies were excluded for reasons including lack of relevant definitions, meeting inclusion criteria, or unavailability of full text. A total of 70 studies were included in the final synthesis.

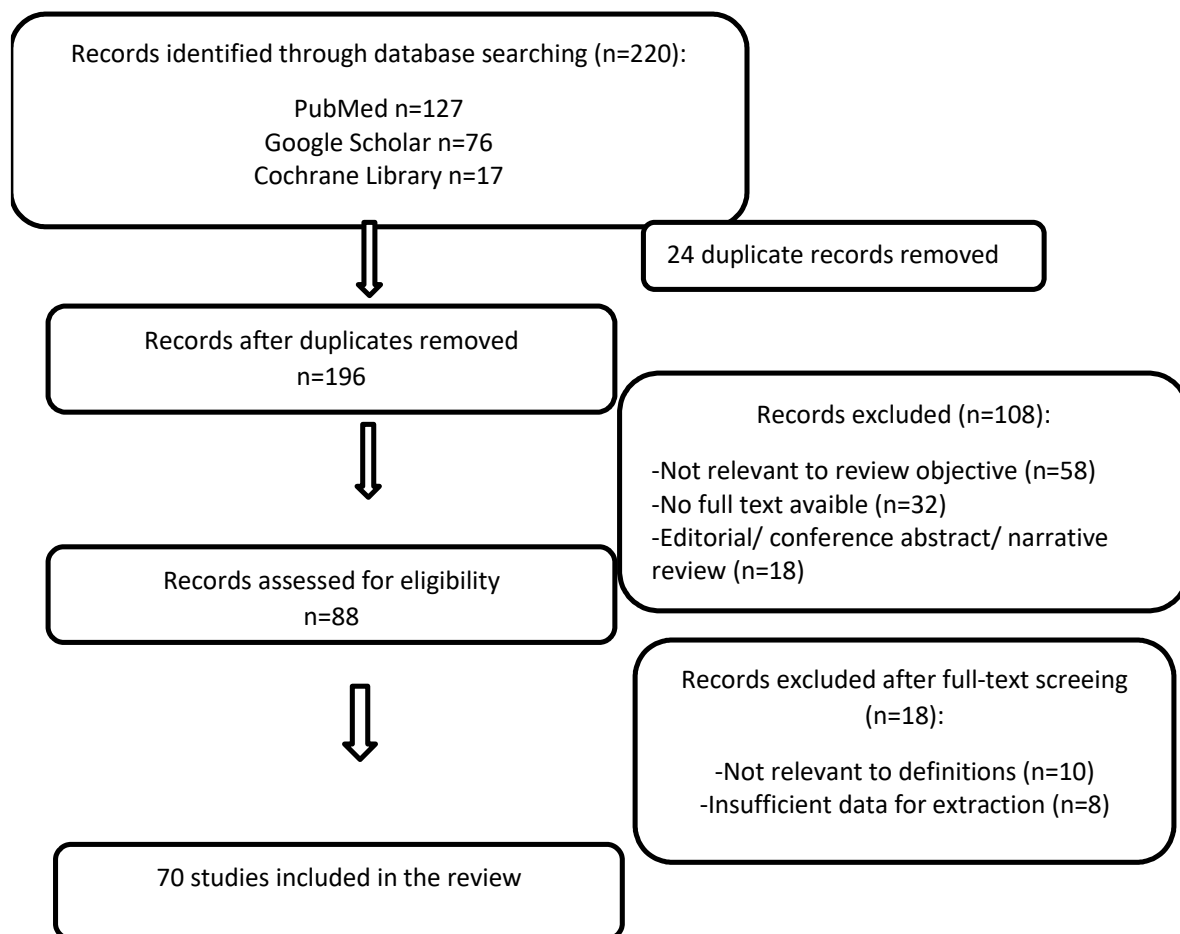


Figure 1. PRISMA 2020 flow diagram of the study selection process

A total of 70 studies were included in the review. However, only 60 provided explicit definitions of polypharmacy and were therefore included in Table 1. The majority 36 definitions (60 %) were numeric-only, specifying a threshold number of medications. 17 definitions (28.34 %) were descriptive, emphasizing the appropriateness or quality of medication use, while 7 definitions (11.66 %) combined numerical criteria with other descriptive terms (a duration of therapy or healthcare setting, diagnosis). These findings are summarized in Table 1, which provides an overview of the main definitions.

The term “Polypharmacy” was the most frequently defined concept (n = 34), predominantly through numeric criteria (n = 26) or in combination with other qualifiers (n = 6). Other frequently reported terms included “Excessive polypharmacy” (n = 7), “Appropriate polypharmacy” (n = 4), and “Unnecessary polypharmacy” (n = 3). Descriptive definitions were primarily used to distinguish between beneficial and harmful forms of polypharmacy (e.g., appropriate, necessary, problematic, or inappropriate).

Table 1. Summary overview of the definitions of Polypharmacy

Definition	Numeric only	Numerical definitions combined with qualitative descriptors	Descriptive	Total number of definitions
Polypharmacy	26	6	2	34
Moderate Polypharmacy	1			1
Hyperpolypharmacy	1	1		2
Excessive Polypharmacy	7			7
Significant Polypharmacy	1			1
Appropriate Polypharmacy			4	4
Necessary Polypharmacy			2	2
Unnecessary Polypharmacy			3	3
Unclear benefit			2	2
Problematic Polypharmacy			2	2
Inappropriate Polypharmacy			2	2
Total number of definitions according to the category of definition	36	7	17	60

Table 2. Numerical definitions of polypharmacy

Definition	Threshold (number of medications)	Number of studies	References
Polypharmacy	≥ 4	1	[25]
	4-6	1	[26]
	≥ 5	19	[2],[27-44]
	5-9	1	[45]
	≥ 8	2	[7], [46]
	≥ 10	2	[47],[48]
Moderate Polypharmacy	5-9	1	[49]
Hyperpolypharmacy	≥ 10	1	[47]
Excessive Polypharmacy	≥ 10	7	[33],[34],[38],[44],[45],[46], [49]
Significant Polypharmacy	≥ 15	1	[50]
Total studies	-	36	-

*Note: Studies were not mutually exclusive and may appear in more than one category. Similar numerical thresholds (e.g., ≥ 10 medications) were described using different terminology across studies.

Table 2 includes 36 studies reporting numerical definitions of polypharmacy, with the majority applying the conventional cutoff of ≥ 5 medications (19 studies, 52.8%). Alternative thresholds were also identified. In addition to the general term polypharmacy, some studies used qualifying terms such as moderate, hyper-, excessive, or significant polypharmacy to describe different levels of medication burden. Studies were not mutually exclusive and may appear in more than one category, as some reported multiple definitions or used different terms for similar numerical thresholds.

Definitions of polypharmacy varied according to the clinical population and treatment context, ranging from >3 to ≥ 9 medications. The lowest threshold (>3 drugs) was applied to older adults with cancer (5) while higher cutoffs were used in chronic or complex conditions such as HIV, chronic kidney disease, and diabetes (51,52). Hospital-based studies tended to use higher thresholds (≥ 9 medications). Hyperpolypharmacy was defined as the use of ≥ 10 medications in patients with chronic kidney disease (4), (53,54). Overall, these findings show that disease-specific definitions of polypharmacy are frequently applied to reflect differences in

medication needs and clinical complexity across patient groups.

Table 3 The qualitative definitions of polypharmacy reflect a shift from viewing it purely as a numerical concept toward a more clinical and appropriateness-based perspective (2). Terms such as appropriate and necessary polypharmacy emphasize therapeutic optimization and the use of evidence-based medications to manage complex or multimorbid

conditions (29,47). Conversely, definitions such as unnecessary, problematic, and inappropriate polypharmacy highlight the negative aspects of medication use, particularly when drugs are prescribed without a clear indication or expected benefit, increasing the risk of adverse outcomes (2,55,56). The inclusion of categories like polypharmacy with unclear benefit suggests awareness of a “grey zone” where the balance between risk and benefit is uncertain (29,47).

Table 3. Descriptive definitions of polypharmacy

Definition	Description	Number of studies	References
Appropriate Polypharmacy	1. “Optimization of medications for patients with complex and/or multiple conditions where medicine usage agrees with best evidence”	2	[2],[29]
	2. ‘Prescribing for an individual for complex or for multiple conditions in circumstances where medicines use has been optimised and the medicines are prescribed according to best evidence’,	1	[48]
	3. "The use of a combination of drugs is optimized"	1	[55]
Necessary Polypharmacy	“Necessary polypharmacy regimens should be considered additional medications that can optimize functional status and prevent disability in older adults.”	2	[2],[47]
Unnecessary Polypharmacy	“Use of medications which are not clinically indicated.”	3	[2],[39] [47]
Polypharmacy	"The concept of 'polypharmacy' is used to describe the multiple, excessive, unnecessary or unindicated consumption of medications"	2	[4],[55]
Unclear benefit	“Polypharmacy with uncertain benefit refers to situations where the balance between risks and benefits is either unclear.”	2	[29],[47]
Problematic Polypharmacy	“Where multiple medications are prescribed inappropriately, or where the intended benefit of the medication is not realized.”	2	[48],[55]
Inappropriate Polypharmacy	“ The use of multiple medications where one or more drugs are unnecessary, not evidence-based, or where the potential risks outweigh the expected clinical benefits.”	2	[55],[56]
Total	-	17	-

*Note. Studies were not mutually exclusive and may appear in multiple categories, as some reported both numerical and descriptive definitions or multiple concepts of polypharmacy.

Table 4. Definitions of PIP by conceptual category

Category	Definition	Nr of studies	References
1.Risk-benefit definitions	Potentially inappropriate medications (PIMs) referred to as medications lacking evidence-based indications, medications with treatment risks that may outweigh their benefits; Medications that are significantly associated with adverse drug reactions, and those that may potentially interact with other medications or other diseases.	6	[5],[6],[7],[8],[9],[10]
2.Explicit tools (criterion-based definitions)	Presence of ≥ 1 potentially inappropriate medication or prescribing omission identified using validated criteria (e.g., STOPP/START, Beers, PRISCUS, TIME)	25	[33–37], [39], [41–42], [44], [46], [49–50], [57–68]
3.Implicit or Clinical Judgment-based definitions	Inappropriate prescribing based on individualized clinical assessment, considering patient-specific factors	3	[15], [69], [70]
Total		34	

Table 4 presents definitions of potentially inappropriate prescribing (PIP), categorized into conceptual (risk–benefit), explicit criteria-based, and implicit (clinical judgment-based) definitions. Only definitional statements were included, while methodological descriptions, interventions, and outcomes were excluded.

Most studies (73.53%) defined PIMs/PIPs using explicit tools such as the Beers or STOPP/START criteria, as shown in Figure 2. Clinical judgment-based definitions represented about 8.82 % of studies, while risk–benefit conceptual definitions accounted for 17.65 %. This indicates a reliance on standardized explicit tools for defining inappropriate prescribing across studies.

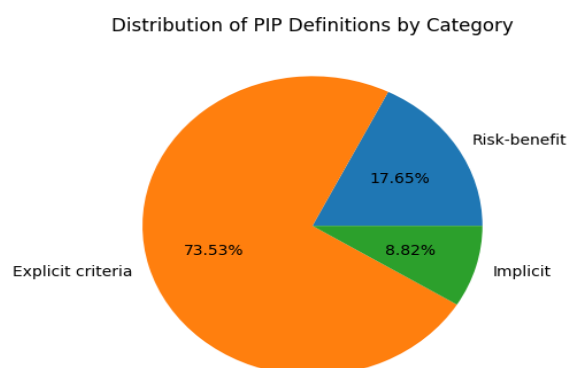


Figure 2. Distribution of definitions

DISCUSSION

This systematic review highlights substantial heterogeneity in the definitions of polypharmacy and potentially inappropriate prescribing (PIP), as well as in the tools used for their assessment. Although the threshold of five or more medications remains the most widely applied numerical definition, considerable variability persists across studies. Importantly, this heterogeneity is not limited to definitions alone but extends to study designs, populations, and outcome measures, which complicates the interpretation and comparability of findings across the literature.

The findings presented in Table 1 demonstrate that polypharmacy is defined using a combination of numerical and descriptive approaches. While numerical definitions remain dominant, the presence of descriptive terms such as appropriate, unnecessary, and problematic polypharmacy reflects an increasing emphasis on the clinical context and appropriateness of prescribing (29,47). This variation supports the view of polypharmacy as a multidimensional concept that cannot be fully captured by a single definition.

Table 2 further highlights the variability in numerical thresholds, ranging from ≥ 4 to ≥ 15 medications. Although the ≥ 5 threshold is the most commonly used, alternative cut-offs are often applied depending on the clinical population or disease context. This lack of standardization may lead to differences in reported prevalence and limit the comparability of studies (3).

The descriptive definitions summarized in Table 3 illustrate a conceptual shift from quantity-based definitions toward a more qualitative assessment of medication use. Terms such as appropriate and necessary polypharmacy emphasize optimized, evidence-based prescribing, whereas terms such as unnecessary and problematic polypharmacy highlight the risks associated with inappropriate medication use. This dual perspective underscores the importance of evaluating both the number and appropriateness of medications in clinical practice (47).

Table 4 demonstrates that definitions of potentially inappropriate prescribing are predominantly based on explicit criteria, such as STOPP/START and Beers criteria, reflecting a preference for standardized and reproducible approaches (19,20). However, these tools may not fully capture patient-specific complexity, while implicit approaches based on clinical judgment remain less frequently used due to their limited reproducibility and greater time requirements (21).

The heterogeneity observed across definitions, tools, study designs, and populations has important implications. It limits comparability between studies, complicates the synthesis of evidence, and may lead to inconsistent conclusions regarding the prevalence and impact of polypharmacy and PIP. Furthermore, differences in populations and outcome measures contribute to variability in findings and reduce the generalizability of results.

This study has several strengths, including a systematic and structured synthesis of definitions and tools across a broad range of studies, allowing identification of key patterns of variability. However, some limitations should be acknowledged. The restriction to English-language publications may introduce language bias, and the heterogeneity of included studies limited the possibility of quantitative synthesis. In addition, a formal risk of bias assessment was not conducted, as the focus of this review was on definitions and methodological approaches rather than clinical outcomes.

Future research should aim to develop standardized yet flexible definitions of polypharmacy and PIP that can be applied across different clinical settings and populations. Achieving greater consensus would improve comparability between studies and support the development of more effective strategies for medication optimization.

CONCLUSIONS

In summary, the findings emphasize several practice-oriented conclusions.

Early identification of polypharmacy and PIP using validated tools, particularly explicit criteria such as STOPP/START and Beers criteria, should be integrated into routine clinical workflows, especially in high-risk populations such as older adults and patients with multimorbidity (19,20).

Pharmacist-led and multidisciplinary interventions, including structured medication

reviews, are effective strategies for reducing medication-related harm and improving prescribing practices (10). Educating both patients and healthcare teams remains essential. Clinical decision support systems and electronic prescribing audits can further facilitate continuous quality improvement in medication use.

Deprescribing should be individualized, regularly reviewed, and embedded within shared decision-making processes with patients to enhance engagement and adherence.

However, the variability in definitions and methodologies across studies should be considered when interpreting these findings and applying them in clinical practice.

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Conflict of Interest Statement: The authors declare that they have no conflict of interest.

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Appendix 1

Detailed list of the screening strategy and keywords for each database.

1. PubMed

Search terms:

- "polypharmacy definition"
- "potentially inappropriate prescribing" OR "PIP"
- "tools to assess inappropriate medications" OR "PIP criteria"
- "STOPP criteria" OR "START criteria" OR "Beers Criteria"

Search strategy:

("polypharmacy definition") AND ("potentially inappropriate prescribing" OR "PIP") AND ("tools to assess inappropriate medications" OR "PIP criteria" OR "STOPP criteria" OR "START criteria" OR "Beers Criteria")

Filters applied:

- Language: English
- Study type: Review, Systematic review, Meta-analysis, Clinical study
- Population: Humans, adults (≥18 years)
- Publication date: January 2015 – August 20

2. Google Scholar

Search terms:

- "polypharmacy definition"
- "potentially inappropriate prescribing" OR "PIP"
- "tools to assess inappropriate medications" OR "PIP criteria"
- "STOPP criteria" OR "START criteria" OR "Beers Criteria"

Search strategy:

("polypharmacy definition") AND ("potentially inappropriate prescribing" OR "PIP") AND ("tools to assess inappropriate medications" OR "PIP criteria" OR "STOPP criteria" OR "START criteria" OR "Beers Criteria")

Filters applied:

- Language: English
- Publication date: 2015–2025

3. Cochrane Library

Search terms:

- "polypharmacy"
- "potentially inappropriate prescribing" OR "PIP"
- "tools to assess inappropriate medications" OR "PIP criteria"
- "STOPP criteria" OR "START criteria" OR "Beers Criteria"

Search strategy:

([mh "Polypharmacy"] OR "polypharmacy") AND ("potentially inappropriate prescribing" OR "PIP") AND ("tools to assess inappropriate medications" OR "PIP criteria" OR "STOPP criteria" OR "START criteria" OR "Beers Criteria")

Filters applied:

- Language: English
- Study type: Review, Systematic review, Meta-analysis, Clinical study
- Population: Adults (≥ 18 years)
- Publication date: January 2015 – August 2025