

**POLYPHARMACY: - A BRIEF SYSTEMATIC REVIEW**

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**ABSTRACT**

Polypharmacy is a preventable and significant contributor to morbidity and mortality in the geriatric population. To effectively treat polypharmacy and avoid ADE in patients down the road, a multi-pronged strategy based on evidence-based therapies is required. Targeting people, circumstances, and prescribing practices associated with a higher risk of having an adverse drug event is important. Liberalizing clinical aims for elderly patients and incorporating ideas from palliative care can open the door for logically stopping a number of drugs. Interdisciplinary teams and treatment models that have been shown to be successful in reducing polypharmacy use several of these tactics.

**KEYWORDS:** Medications, Adverse Drug Events, Elderly, Drug interactions.

**INTRODUCTION**

From the Greek word "poly," which generally implies "more than one," comes the term "polypharmacy."<sup>[1,2]</sup> Polypharmacy is described by the World Health Organization as "the administration of many drugs at once or the administration of more drugs than are necessary."<sup>[3]</sup> The number of drugs that fall under the criteria of polypharmacy is not stated in this definition, though. According to several studies, polypharmacy can be defined either as descriptive polypharmacy or as a numerical number. Polypharmacy is defined numerically as the use of five or more medications.<sup>[4]</sup> It is a substantial and preventable cause of morbidity and mortality in the elderly population. By 2026, it is estimated that 12.4% of Indians would be beyond the age of 65, and by 2025, the country's life expectancy will have increased to 75 years.<sup>[5]</sup> Furthermore, according to UN estimates, the old population of India would increase

to 21.2% of the total by 2055 (from an anticipated 7.2% in 2005). As they get older, they develop a number of ailments, necessitating the usage of various drugs at once. Many individuals self-medicate since over-the-counter medications that target specific symptoms are widely available and find doctor consultation for minor illnesses unnecessary. For everyday issues like pain, weakness, and constipation, the elderly may also self-prescribe specific medications, dietary supplements, and herbal remedies. There is a culture of prescribing more medications than necessary in order to increase patient satisfaction. As a result, elderly persons frequently meet the criteria for polypharmacy. The likelihood of adverse drug events (ADE) rises when more prescription drugs are taken. It happens frequently that concurrent prescriptions written by doctors treating various conditions are not checked for harmful drug interactions or inappropriate prescriptions. Although polypharmacy is frequently performed, there is no universally accepted definition of the term. Additionally, it is unknown how many medications used concurrently constitute polypharmacy. The assessment of polypharmacy has been done using several thresholds. Some publications assess polypharmacy using criteria of 3, 4, 5, or 10 drugs. This definition is simply based on the number of medications, regardless of the patient's clinical conditions and indications.<sup>[6]</sup> The use of multiple medications, or polypharmacy, may be clinically appropriate in many situations, but it's crucial to spot patients who may be engaging in inappropriate polypharmacy that puts them at an increased risk of adverse events and unfavourable health outcomes. To effectively treat polypharmacy and avoid harm caused to the patients down the road, a multi-pronged strategy based on evidence-based treatment is required. Targeting patients, circumstances, and prescribing practices associated with a higher risk of having an adverse drug event is important.

### CAUSES OF POLYPHARMACY

- ✓ An ageing population with comorbidities that require several medications and the growing accessibility of newer drugs.
- ✓ Patients who self-medicate with over-the-counter drugs and herbal remedies without fully knowing the potential side effects and interactive effects.
- ✓ A "prescribing cascade," which happens when patients take medication, display adverse effects that the doctor interprets as signs of an illness, and prescribes more medication.
- ✓ There is a failure to inform all parties of each other's actions even though the patient sees many doctors and fills prescriptions at various pharmacies.

- ✓ Redundancy occurs as a result of poor coordination and communication amongst healthcare professionals.<sup>[7]</sup>

## **POLYPHARMACY IS A PARTICULAR CONCERN IN OLDER PEOPLE DUE TO THE FOLLOWING REASONS**

1. Adverse effects (ADE): Refers to harm brought on by a medication when taken at the recommended dosage. The risk rises with the number of medications consumed as well.<sup>[8]</sup>
2. Drug interactions: Taking numerous drugs raises the risk of drug interactions. The neuropsychological side effects (delirium), acute renal failure, and hypotension are the most often reported adverse drug interaction events.
3. Prescribing Cascades.
4. Inappropriate therapy, or non-adherence.

## **WHAT IS POLYPHARMACY**

The definitions of polypharmacy and its associated terms, such as mild, moderate, and significant polypharmacy, vary widely. With 46.4% of studies adopting this criteria, polypharmacy is most frequently defined as taking five or more drugs daily.<sup>[9]</sup> Six or more prescription drugs is the second most typical definition of polypharmacy.<sup>[10]</sup> The criteria of polypharmacy pertaining to the length of therapy ranged from the use of five to nine medications used for 90 days or more to the use of two or more medications for more than 240 days (referred to as "long-term usage").<sup>[11]</sup> The use of five or more medications upon hospital discharge and the use of ten or more medications throughout a hospital stay were included in definitions of polypharmacy that took into account the healthcare setting.<sup>[11]</sup> While several research referred to polypharmacy in a different way, they all employed the same definition. For instance, polypharmacy is defined as the use of numerous medications at the same time as well as in some of the definitions "Co-prescribing multiple medications" and "Simultaneous and long-term use of different drugs by the same individual" has also been used. Other research made reference to a different problem about the right or wrong drugs for a specific patient. A concise definition of polypharmacy can be used alone or in conjunction with polypharmacy instruments like the Beers criteria and the Medication Appropriateness Index (MAI).<sup>[12]</sup> "Polypharmacy spans from the use of a large number of medications, medication underuse, duplication, or the usage of potentially inappropriate medications (PIM)," is an example of polypharmacy definition that acknowledges the use of appropriate and inappropriate medications.<sup>[13]</sup>

Examples of PIMs from the literature were used in the study, including drug duplication, drug-drug interactions, drugs taken to address the adverse effects of other medications, and medications that are not required for a certain patient. Appropriate polypharmacy was only defined clearly in one study as "the optimization of drugs for patients with complicated and/or numerous illnesses where medicine use agrees with the best evidence."<sup>[14]</sup> The necessity to discern between appropriate and inappropriate polypharmacy based on the pharmacology of the drugs involved, how they interact with one another or comorbidities for a particular patient was not particularly mentioned in any of the studies.

## **STRATEGIES FOR REDUCING POLYPHARMACY ARE**

### **1. Risk Identification: High-Risk Patients and Situations**

The identification, stratification, and targeting of individual patients who are more likely to experience polypharmacy and ADE is a crucial technique. There are risk variables related to polypharmacy and patients who develop ADE, according to numerous research.<sup>[11]</sup> These patient characteristics can be divided into three categories:

- 1) demographic (increasing age, white race, female gender, higher levels of education)
- 2) health status (general poor health, cardiovascular disease, hypertension, asthma, diabetes)
- 3) access to health care (increased number of health care visits, multiple providers, type of insurance).

Additionally, patients with a prior ADE were more likely to experience subsequent ADE.<sup>[12]</sup> Due to comorbidity and age-related functional decline of the kidney and liver, which affects drug metabolism and clearance, geriatric individuals are especially more susceptible to the consequences of polypharmacy.<sup>[13]</sup> Drug kinetics can also be affected by decreasing lean body mass and total body water with a proportionate rise in total body fat. As a result, drugs used in elderly patients might have a quicker onset, greater bioavailability, and longer duration of action.<sup>[14]</sup> Providers should pay close attention to these variable factors in the elderly which can cause ADE and other issues when administering drugs. Patients receiving care from several different providers is another situation with a high risk.

### **2. Risk Identification: high-risk prescribing practices**

The use of PIMs as a benchmark in older patients enrolled in Medicare and other managed care plans is regarded to be an important indicator of the quality of care linked to clinical outcomes.<sup>[16,17]</sup> To find PIMs in real-world settings, researchers and physicians employ a variety of metrics. The Beers criteria is the oldest and most well-known of them.

The criteria include a list of drugs that patients under the age of 65 should avoid or replace.

Although it is easy to use and may be applied to huge populations, it has a number of drawbacks, including:

- 1) the inclusion of obsolete medications
- 2) A requirement for regular update
- 3) A few debatable contraindications
- 4) failing to mention drug interactions or drug duplications
- 5) failing to notice medication omission mistakes.<sup>[19]</sup>

A non-significant increase in the likelihood of developing an ADE when exposed to a drug on the list was discovered by a study utilising the 2003 Beers criteria.<sup>[20]</sup> Another study used the Beers criteria in conjunction with other explicit criteria (that took into consideration drug-drug interactions and therapeutic duplication) to designate inappropriate drugs and discovered a substantially stronger correlation with ADE.<sup>[21]</sup>

To overcome the shortcomings of the Beers criterion, the Screening Tool of Older Persons Potentially Inappropriate Prescriptions (STOPP) and Screening Tool to Alert Doctors to the Right Treatment (START) criteria were created and validated. STOPP/START criteria are arranged by system, including a list of potential pharmacological interactions to avoid (for instance, thiazide diuretics with a history of gout), and address therapeutic duplication and omission errors.<sup>[22]</sup>

On the other hand, MAI is regarded as an implicit tool due to the inclusion of clinical judgment. Each medication should be subjected to the tool's ten questions, which include: "Is there a medical indication for the drug? Does it work to treat the condition? Is there an unnecessary overlap with other medications? The MAI monitors changes over time and places and gives more emphasis on the patient-drug interaction than just the drug itself. While Beers criteria and the original MAI scoring approach did not significantly predict ADE risk, Lund et al. reported that a modified MAI scoring approach (enabling clinicians to choose which MAI elements were acceptable) did.<sup>[20]</sup>

A basic, straightforward, patient-centered assessment that can be used in both inpatient and outpatient settings would be excellent. While there are flaws in all of the current methods, the explicit tools are simpler to use and can even be added to an electronic medical record

(EMR). The STOPP/START criteria may be more useful in identifying high-risk prescribing in clinical practice, given that the Beers criteria was created as a research tool. When utilised by physicians with the proper training, the MAI, albeit taking more time, is more effective as a prediction tool for ADE.

**3. Comprehensive Geriatric Assessment:** Using an interdisciplinary team, the Comprehensive Geriatric Assessment (CGA) evaluates the medical, psychological, and functional limits of elderly people.<sup>[23,24]</sup>

These teams consist at least of a geriatrician, social worker, and nurse and adhere to the following protocols:

- 1) check for geriatric syndromes like incontinence and falls.
- 2) evaluate functional, cognitive, affective, and nutritional status.
- 3) Evaluate the social and caregiving assistance.
- 4) Create a specific, unique plan for every patient.<sup>[25]</sup>

In order to improve prescription quality and identify and prevent potential ADE<sup>[14]</sup>, the CGA pays particular attention to medication management.

**4. Clinical pharmacists' roles:** In many settings, incorporating pharmacist expertise is necessary to reduce polypharmacy. First off, it has been demonstrated in randomised studies that a clinic pharmacist may both educate patients and healthcare professionals while also reducing the overall number of prescription drugs and PIMs.<sup>[27]</sup> In a recent prospective study, it was shown that patient adherence and clinical outcomes were both significantly improved at six months when a clinic pharmacist reviewed each patient's medication regimen, offered advice, and reported to the healthcare provider. Second, information from various providers can be centralised by pharmacists working in the community and at the managed care level.

The following categories of drugs make up the majority of the PIM prescription for people over 65 years of age:

- Cardiovascular medications (25%).
- Sedatives and hypnotic medications (15%)
- Antiarrhythmics (15% of total)
- Antidepressants (13%)
- Anti-phlogistics/Analgesics (9%)
- Antidepressants (7%)

➤ Anticholinergics (6%).

For people over the age of 65 with statutory health insurance, general practitioners prescribe 86% of the daily doses and an estimated 77% of the PIM.<sup>[28]</sup> In general practice, patients over the age of 70 receive an average of 3.7 prescription medications. Almost 30% of this group takes more than five medications, and 53% take five medications and OTC preparations at the same time.<sup>[29]</sup> On average, residents receiving home care receive six or seven medications. An examination of routinely collected data from 148 German primary care facilities on patients over the age of 65 revealed at least one potential drug-disease interaction in approximately 10% of patients.

### THE PRESENT SCENARIO IN INDIA

The following are the most common causes of polypharmacy in India:

- 1. Multiple prescribers:** Patients with chronic illnesses like diabetes frequently see specialists in addition to their primary care doctors. These patients may also be seen and treated by mid-level prescribers including physician assistants and nurse practitioners. Each of these healthcare professionals give prescriptions, adding more pharmaceuticals to the patient's profile. Patients' medicine lists are much too frequently not routinely checked for potential issues. Drugs are more likely to be added to a patient's regimen than they are to be removed from it. A previously utilised medicine could become obsolete with the addition of new therapies. One of the main causes of the development of polypharmacy is the gradual addition of new medications without routinely reviewing the drug regimen.<sup>[30]</sup>
- 2. An ageing population:** The elderly are particularly affected by polypharmacy because they are more likely to have chronic conditions and have fixed or low incomes, making it difficult for them to pay for the high cost of multiple medications.<sup>[31]</sup>
- 3. Complex medication therapies:** Over the past ten years, there has been a dramatic increase in the range of expert panel recommendations, clinical practice recommendations, and other national standards for medical care. In July 2005, the National Guideline Clearinghouse reported more than 1,650 clinical practice guidelines that were still in use, 386 of which were specifically focused on diabetes. These recommendations frequently overlap and occasionally conflict with one another.<sup>[32]</sup>
- 4. Psychosocial contributions:** Families and patients typically disregard justifications for why drug therapy may not be in their best interests and regularly want medicine. This increases the need for additional treatment among patients or their families. Similarly,



prescription medications which are direct-to-consumer advertising put additional pressure on doctors to provide prescriptions for medications that might not be necessary.<sup>[33]</sup>

**5. Adverse drug reactions that could be mistaken for a new medical condition:** This occurs when a patient takes a drug for the first time and experiences negative side effects that are mistaken for a new condition, leading to the prescription of a new treatment.

## DISCUSSION

This article demonstrates the significant heterogeneity in the terminology used to define polypharmacy, which can range from numerical counts only to numerical counts for a specific duration of therapy or setting, or descriptive terminology like minor, moderate, major, and excessive polypharmacy. It is difficult for healthcare professionals to evaluate and take into account efficacy and safety concerns in the clinical setting because there is no clear, accepted definition of polypharmacy. Numerical only definitions were the most frequently reported category of definitions for polypharmacy and related terms. 46.4% of studies defined polypharmacy, as the use of five or more medications. Numerous number only definitions of polypharmacy were available, ranging from two or more drugs to eleven or more. However, the therapeutic justification for employing a numerical count to identify polypharmacy—for example, five or more medications—and the potential for this to rationalize medication use and improve health outcomes—are not usually explained in studies. Theoretically, although the term "polypharmacy" has changed throughout time, the concept still refers to taking or being given more medications than are clinically necessary in light of a patient's comorbidities.<sup>[37]</sup> According to regular reports, the incidence of adverse drug events and the likelihood of injury increases as the number of prescription medications rises.<sup>[38]</sup> The precise quantity of medications taken, however, does not necessarily indicate how effective the therapy is because all of the medications may be clinically suitable and required for the patient. Elderly individuals frequently use multiple medications. General practitioners in particular frequently face this difficulty. A complex situation with several relations (causal and/or associative) is always present when polypharmacy occurs. Lists, questionnaires, and recommendations have been created for the assessment of polypharmacy in order to deal with this complexity. Whether their use enhances the clinically important objectives is an evident question. Due to a lack of sufficient evidence, no definitive answer can yet be given. Another question is whether worsened clinical endpoints are caused by polypharmacy or by the underlying multimorbidity in patients who take multiple medications. Based on the currently available evidence from systematic reviews and individual studies, these questions cannot be



answered conclusively. Nonetheless, there are implications for both research and practice.<sup>[39,40,41]</sup>

## CONCLUSION

Polypharmacy increases the risk of adverse events, functional decline, and geriatric syndromes in older patients. The above-mentioned strategies, such as the use of a risk stratification tool and the application of palliative care principles, are preliminary steps toward reducing polypharmacy; however, much work remains to be done. Future research should focus on developing and validating risk assessment tools in a variety of elderly populations and settings. Some of these tools may eventually be integrated into an EMR, allowing clinicians to easily identify patients who are at risk. While being on five or more medications is the most commonly used definition of polypharmacy, definitions vary, which can confuse both researchers and clinicians in practice. Polypharmacy numerical definitions do not account for specific comorbidities, making it difficult to assess the safety and appropriateness of therapy in the clinical setting. A globally agreed-upon definition of polypharmacy is required. The findings point to the need for a shift toward the term "appropriate polypharmacy," which employs a holistic approach to assessing medication use in the context of existing comorbidities in order to optimise health outcomes. Future clinical trials, particularly those focusing on the elderly, may also provide information about optimal clinical targets and lenient treatment strategies. Care models based on the comprehensive geriatric assessment approach should become the norm for elderly patients. In these models, pharmacists play an important role in reducing medications and errors, improving patient safety and outcomes. There are evidence-based strategies, but more implementation research in the geriatric population is needed to assess their utility in clinical practice. A small number of drugs in low doses with a simple regimen is ideal for elderly drug therapy. Polypharmacy affects a considerable number of hospitalised geriatric patients. More research is needed to determine the risk of harmful drug effects after multiple drug administrations, as well as particular possible drug-drug interactions. It might be useful to create a country-specific list of medications that are inappropriate for the elderly and include it in national drug formularies in order to limit prescriptions and use in this age group.

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