A Review Article on Polypharmacy and Its Consequences in Geriatric Patients.

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ABSTRACT:

The continual prescription of numerous medications to a patient is known as polypharmacy. Polypharmacy is a big worry because of the hazards and even mortality that can result from it, especially in light of the changing demographics and rising number of older patients. This geriatric condition has become more prevalent during the past ten years due to a variety of factors. First of all, there are frequently no recommendations for the management of comorbidities. Second, as the population ages, multi-morbidity is increasing. Third, there aren't many describing techniques, and the outcomes are inconsistent. This concise overview includes the causes, consequences, and practical step-by-step instructions for deprescribing polypharmacy, along with its implications on mortality and morbidity. The study is based on a search of the literature for 2015 English- and German-language randomized control trials and reviews as well as integration of pertinent citations as a result of this search later on in the PubMed database. Better health care availability and treatments for diseases that formerly had no cure have been linked to an increase in life expectancy. But taking numerous medications increases the chance of getting the wrong prescription and having drug-related issues. This study looked into inappropriate drug use and polypharmacy among elderly individuals in India.

Keywords: Deprescribing, frailty, various diseases, and wrong drug.

INTRODUCTION:

Based on an analysis of the patient's most recent data, polypharmacy is the concurrent use of five or more drugs. Due to the physiological and pathological changes brought on by aging, people are more likely to develop multi-morbidity (the presence of two or more chronic health disorders) and be given several prescriptions for medications. In older persons, the cutoff threshold of five medicines is linked to the likelihood of unfavourable outcomes such as falls, frailty, disability, and mortality. One of the crucial components of comprehensive geriatric care is the drug regimen. The main components of polypharmacy therapy in the clinical setting are reviewed in this activity. It covers how members of an interprofessional team can handle the care of patients taking various drugs more successfully.[2]

While some define polypharmacy as the concurrent use of numerous medications by patients, others refer to it as the optimization of pharmaceuticals such that a patient can utilize multiple suitable treatments. The actual number of different medications used to describe "Polypharmacy" typically ranges from five or more acceptable medications, therefore the concept is up for debate. The number of over-the-counter medications and herbal supplements used was not taken into consideration in this study because it is crucial to concentrate on the prescription, appropriate medications when defining polypharmacy.[3]

FIGURE 1. The visual depiction captures the elaborate web of medication regimens, intricately intertwined, reflecting the intricate nature of polypharmacy**.**[1]

A person who is 65 years of age or older is considered to be a geriatric, according to WHO rules. Individuals in the geriatric population require additional medication, since they are more likely than younger individuals to have chronic conditions. Because of greater side effects, non-adherence, financial costs, drug-drug interactions, and morbidity consequences, taking more prescriptions is seen as a risk factor [4]. The average life expectancy in the world is expected to rise by 10 years compared to that in the 2000s as a result of the aging global population, with the number of persons over 65 expected to reach 71 million by 2030, up from 35 million in 2000. This drug indicates that a person will need to take more medications [5]. Better access to healthcare and more effective treatments for numerous diseases have been linked to an increase in life expectancy. As a result, more older patients are receiving prescriptions for multiple regimens to treat various illnesses. 'Polypharmacy' refers to the use of numerous medications (at least five different types of drugs) in a single patient. Although the term "polypharmacy" has several different definitions, the one that is most frequently used is the one that was just [6] Despite mounting evidence that polypharmacy raises the risk of drug-drug and drug-disease interactions and adverse drug responses, it is nonetheless common practice to treat numerous chronic conditions simultaneously with a variety of medications [7]. It is undeniably true that older populations are more susceptible to PIP and drug-drug interactions (DDIs) [8, 9]. When safer alternatives are available, administering drugs that entail more risk than benefit is considered inappropriate [10,11]. It includes prescribing medications with harmful drug-drug and drug-disease interactions as well as the inappropriate usage of dosage, dosage form, or duration [12,13].

TYPES OF POLYPHARMACY:

Although there is no single, accepted definition of polypharmacy, there are three basic types:

1. **Excessive polypharmacy (EPP):** using ten or more medications concurrently.

2. **Polypharmacy (PP):** taking five to nine medications.

3. **No polypharmacy:** Not taking more than four medications, including those who don't take any.[1]

TABLE 1: Associated factors [14]

Individual / factors	Physician factors	Systems- level factors
• Increasing age	• Lack of education	• Different electronic medical system
• Female gender	• High patient work load	• Poor physician- physician communication
• White ethnicity/ race	• Improper medication reconciliation	• Lack of continuity between multiple medical providers
• Lower socioeconomic status	• Poor physician -patient communication	• Ineffective transition of care
• Multiple chronic conditions	• Multiple prescribers	
• Decreased cognitive capacity	• Prescribing habits	
• Self-medication • Use of OTC medications • Borrowing from friends/family	• Adherence to multiple medical guidelines. • Use of potentially inappropriate medications [14]	

ISSUES OF CONCERN IN POLYPHARMACY:

For the reasons listed below, polypharmacy is a particular cause for worry among older adults.

1. Adverse effects (ADE): A drug's harm at recommended dosages is referred to as an injury occurring from usage of the drug. In 5% to 28% of acute geriatric medical admissions, ADEs are the underlying cause. One of the significant effects of incorrect pharmaceutical use in older individuals is preventable adverse drug events (ADEs). Cardiovascular medicines, anticoagulants, hypoglycaemics, diuretics, and NSAIDs are the drug classes most frequently linked to avoidable ADEs. Due to age-related metabolic changes and slower medication clearance, adverse drug effects are more common in older persons. As more medications are used, the danger multiplies [15].
2. Drug interactions: The potential for drug-drug interactions, or the pharmacologic or clinical reaction to the administration of a drug combination that differs from the response expected from the known effects of either of these two agents when given alone, is increased by the use of many drugs. The majority of drug interactions involve cardiovascular medications. The cognitive (delirium), acute renal failure, and hypotension adverse effects that are linked to drug-drug interactions are the most frequent ones [15]. e.g., Anti-inflammatory drugs may worsen renal function and raise blood pressure.[18]
3. [Prescribing Cascades]: When further medications are given to treat the side effects (ADE) of additional medications because the ADE was mistakenly thought to be a brand-new medical ailment
4. Improper therapy, or noncompliance [17]: especially if connected to a decline in cognitive or visual abilities
5. The chance of developing a hip fracture: In some case-control studies, polypharmacy has been identified as an independent risk factor for hip fractures in older adults, even though the quantity

of medications may have been a sign of a higher risk of exposure to certain classes of medications, such as central nervous system (CNS)-active medications linked to falls.[16]

6. Use of OTC and complementary medicines has grown over the past ten years as studies have revealed a high prevalence of these drugs among the senior population. Less than half of people talk to their doctors about using herbal supplements, other goods, or supplementary treatment. There are safety concerns with their use, including about the potential for drug-herb interactions.
7. Care transitions include those between a hospital and a patient's home or a facility like a nursing home. Patients who experience drug errors frequently run the risk of polypharmacy. This is due to the fact that patients frequently start new prescriptions or cease old ones, which can lead to numerous medication errors and unfavourable results.
8. Aging-related changes in drug absorption, distribution, metabolism, and elimination, or pharmacokinetics. Aging-related physiologic changes lead to several modifications in the pharmacokinetics and pharmacodynamics of medications, which raises the likelihood of negative drug responses. The key to delivering the best pharmaceutical care for older patients is to take initial dose adjustment into account, as well as frequent medication reconciliation and study of the prescription list [19].

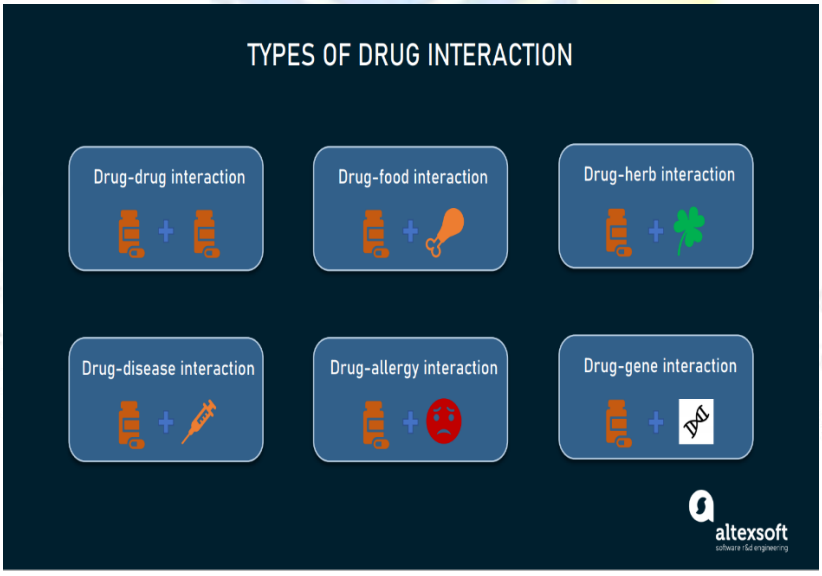
DRUG INTERACTIONS:

When a medicine is taken with certain other medications, meals, or supplements, or when it is taken while you have certain medical conditions, it can alter how the drug behaves in the body.

Examples include:

- Combining two medications, like aspirin and blood thinner.
- Drugs and food interactions, like statins and grapefruit;
- Drugs and dietary supplements, such as gingko and blood thinner.
- Medicines and health issues, such as aspirin and medicine interactions could alter how effective a medicine is, induce side effects, or alter how one or both drugs work [20].

FIGURE 2 Types of drug interaction [21]



DRUG-DRUG INTERACTIONS: It occurs when one medicine interacts with, or interferes with, another. This may change how one or both drugs interact with the body or result in unanticipated side effects.

1. Antibiotic+ Blood thinner - Antagonism (less effect)
2. Codeine+ Paracetamol - Addition (increased analgesic effect)
3. Decongestants + Antihypertensives - Potentiation (high blood pressure)
4. NSAIDS+ COX 2 inhibitors - Synergism (increased bleeding)

TABLE 2: Examples of drug-drug interactions

DDIs severity	Example
Major DDIs	Haloperidol +tizanidine Amiodarone +furosemide
Moderate DDIs	Furosemide +lisinopril Risperidone +atenolol
Minor DDIs	Lansoprazole +aspirin Omeprazole +glimepiride

DRUG -FOOD INTERACTIONS: A drug-food interaction occurs when the substances in the medication you are taking are impacted by the food you are eating, preventing the medication from acting as it should.

1. Bisphosphonates + any drug - reduced effectiveness of the drug
2. Digoxin +oatmeal - decreased the absorption of the drugs
3. Aspirin + milk - upset stomach
4. Acetaminophen+ alcohol - liver damage

DRUG- DISEASE INTERACTION: When a medication aggravates or worsens a pre-existing medical condition, there has been a drug-condition interaction.

1. Nasal decongestants+ hypertension - increased blood pressure
2. Minoxidil + heart failure - fluid retention
3. Nicotine +high blood pressure - increased heart rate
4. Beta blockers + heart failure - worsen asthma [22]

DRUG- HERB INTERACTION: Western medications and herbal products may interact in the body when used combined, causing kinetic and dynamic changes. [23]

Due to the frequent use of herbal medications alongside medicinal treatments, the possibility of herb-drug interactions is increased.

An estimated 5 to 20 percent of people generally use herbal remedies because

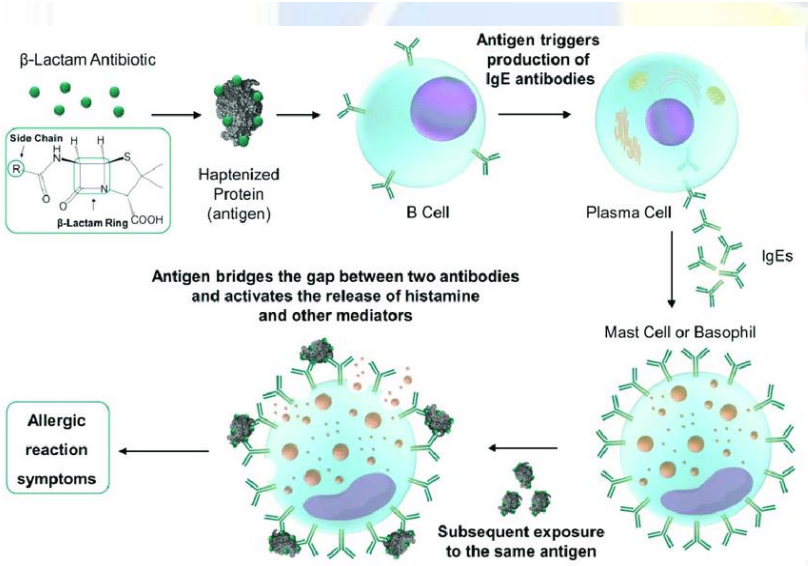
1. Naturally available.
2. Consideration of safe use
3. Readily available

TABLE 3: Herbal and conventional drug interactions.[24]

Herbal	Conventional drug	Interaction
Echinacea	Anabolic steroids, methotrexate	Hepatoxicity
Ginkgo, Ginger, Devils claw	Iron	Decreased absorption.
Tamarind	Acetylsalicylic acid	Increased bleeding
Liquorice	Prednisolone	Enhanced aldosterone effects
St. John's wort	Cyclosporine Midazolam Tacrolimus	Reduced blood levels and decreased area under the curve (transplant rejection with cyclosporine effects)

DRUG- ALLERGY INTERACTION: One unpredictably occurring ADR is drug allergy, which includes a range of immunologically mediated hypersensitivity reactions with various causes and clinical manifestations [25]. It accounts for between 5 and 10 percent of all ADRs [26]. Unpredictable ADRs include pseudo allergic reactions, commonly referred to as pseudo-allergic or non-immune-mediated reactions**.**

FIGURE 3: Schematic representation of drug allergy interaction [27]



These reactions lack immunological specificity but are frequently clinically indistinguishable from actual immunologically mediated allergy reactions.

Symptoms:

- Skin rashes
- Itching
- Swelling
- Anaphylaxis
- Wheezing or other breathing problems [29]

DRUG- GENE INTERACTION: Drug-gene interactions are the actual or implied interactions between drug molecules (ligands) and gene products (targets) discovered by literature mining or database parsing. Numerous of these interactions have details about the different sorts of interactions that describe how medicine interacts with the genes.[28]

ADVERSE DRUG REACTIONS:

According to WHO, an adverse drug reaction (ADR) is 'a response to a drug which is noxious and unintended, and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy or for modification of physiological function.' It is crucial in this statement that the event is harmful (an unanticipated therapeutic response, for instance, may be a side effect but not an unfavourable reaction) and that it relates to the patient's response, in which individual circumstances may play a significant influence.

A serious adverse event is any event that:

- ❖ Is fatal
- ❖ Is life-threatening

TABLE 4: Types of adverse drug reactions [31]

Type	Type of effect	Characteristics	Example
A	Augmented	Dose dependent predicted from the known pharmacology of the drug	Hypoglycaemia-insulin
B	Bizarre	Unpredictable Dose independent Rare, fatal.	Anaphylaxis to penicillin
C	Chronic	Prolong treatment	Analgesic neuropathy
D	Delayed	After years of treatment	Antipsychoti-turdive dyskinesia
E	End of use	Withdrawal effect	GC withdrawal-adrenocortical

- ❖ Is permanently/significantly disabling
- ❖ Requires or prolongs hospitalization
- ❖ Causes a congenital anomaly
- ❖ Requires intervention to prevent permanent impairment or damage [30]

POTENTIAL ADRs DUE TO DRUG- DRUG INTERACTION:

One of the main reasons for mortality and health issues for many people is adverse drug reactions (ADRs). The significance of ADR and the cost to the healthcare system are substantial [32]. According to the findings of numerous research, 2.9% to 5.6% of hospital admissions are the result of ADRs, and up to 35% of patients have an ADR while they are hospitalized.[32,33] Drug-drug interactions (DDI), one of the main causes of ADR, should be noted.[34] According to a recent study, medication interactions were to blame for 25.9% of ADRs.[32] Due to the many study types, populations, frequency measurements, and categorization systems, estimating the incidence of ADR caused by DDI is highly challenging.[35] Patients who take multiple medications are especially vulnerable to these incidents. One of the most frequent and difficult disorders is kidney disease. As kidney function declines, numerous problems occur because of the need for multiple drugs. The same problem also leads to alterations in medication kinetics brought on by renal failure, which opens the door to ADRs and many interactions. Understanding ADR and DDI in this population can therefore enhance

quality of life while lowering expenses, hospitalization, and mortality.[36] To determine the causal relationships between drug administration and adverse effects, the Naranjo algorithm was used.[37]

TABLE 5: Examples of Characteristics of drug interactions leading to adverse drug reactions [38]

DRUG/PAIR	COMPLICATION	NARANJOSCALE	SEVERITY OF DRUG INTERACTION	PATIENT OUTCOME
Prednisone, rituximab	Esophageal candiasis	5	Severe	Partial recovery
Cyclosporine, prednisolone	Dyspepsia	7	severe	Complete recovery
Amiodarone, atorvastatin	↑ ALT, AST	8	moderate	Partial recovery

PRESCRIBING PATTERN IN ELDERLY PATIENTS:

The quality of the prescriptions that are written is a crucial cognitive aspect in assessing the health of the aged population, but the growing need for good prescriptions presents difficulties for primary care doctors.[39] The clinical practice of polypharmacy in the elderly is common since they frequently have multiple concurrent ailments. A higher risk of adverse drug events (ADE), such as myocardial infarction (MI), ventricular re-entry rhythms, etc., might result from inappropriate pharmaceutical prescribing [40,41]. CNS depressants, antipsychotics, tricyclic antidepressants (TCA), and selective serotonin reuptake inhibitors (SSRIs) are a few examples of medications [42]. NSAIDs and anticholinergic medications increase the chance of falling by 50% and are linked to hip fractures, gastrointestinal bleeding, cognitive decline, and functional decline [43]. Therefore, Potentially Inappropriate Prescribing (PIP), which is especially common in the elderly, is a serious problem for patient safety and sane medical care. [44]

The research of medication prescribing trends in healthcare institutions has been aided by a set of drug usage indicators provided by the World Health Organization (WHO) (WHO, 1993). Numerous studies have employed prescribing indicators to highlight issues with global patterns of drug prescriptions. These studies offer information that can be included in future plans to encourage sensitive drug usage. Using WHO prescribing indicators, several studies have evaluated drug usage patterns in the primary healthcare context (Bhavesh KL et al 2012 [45]; Angamo TM [46] et al 2013; T.H. Fereja [47] et al 2013). Examining the drug use situation at healthcare facilities that offer more complicated medical services is nevertheless crucial. Nevertheless, particular signs of this improper use have detrimental effects on both the national health care system's ability to succeed economically and health-wise. More of a global issue than a lack of medical information is the irrational use of pharmaceuticals. In general, irrational drug use affects many people and is complicated, involving the health system, the patient, the physician, the dispenser, and the community.

The average number of medications prescribed per encounter, the proportion of medications prescribed as generics, the proportion of prescriptions containing antibiotics, the proportion of prescriptions containing injections, and the proportion of medications prescribed from the Essential Drug List (EDL), are among the prescribing indicators used, according to the WHO drug use evaluation guidelines.

- To gauge the level of polypharmacy, the average number of medications prescribed per contact was computed. It was calculated by dividing the whole assortment of drugs prescribed by the quantity of observable encounters. Combinations of medications prescribed for a single medical condition are considered as one.
- To determine the prevalence of prescribing by generic name, the percentage of medications prescribed as generics is calculated by multiplying the number of medications prescribed by 100 and dividing the result by the total number of medications dispensed.

- By dividing the number of patient contacts with an antibiotic prescribed by the total number of encounters questioned, multiplied by 100, the percentage of prescriptions with antibiotics was computed. It is estimated to assess the entire consumption of frequently overused and pricey pharmacological therapies.
- By dividing the number of patient encounters involving an injection by the total number of encounters analysed and multiplied by 100, the percentage of prescriptions involving injections was derived. By prescribing from the national essential drug list, it is intended to assess how closely practices adhere to a national drug policy. The study's independent factors included the patients' ages, sexes, educational levels, and diagnoses. Manual data analysis was done on all the data before utilizing Microsoft Excel 2007.The mean, standard deviation, and absolute frequency and percentage were used to express the data.[48]

ROLE OF PHARMACIST:

- Medication reconciliation, a formal procedure for compiling the most thorough and accurate list of a patient's current medications and comparing the list to those in the patient record or medication orders, is the responsibility of pharmacists.[22]
- To prevent medication errors including omissions, duplications, dose mistakes, or drug interactions, reconciliation is performed. Every time new prescriptions are prescribed or present orders are changed, it ought to be done.
- Examining specific limitations (such as poor dexterity, a lack of hand strength, cognitive impairment, or visual loss) to determine the patient's ability to follow a medication schedule.
- Educating patients on how to use certain medications (such as inhalers, transdermal patches, injectable medications, eye or ear drops), as well as how to measure liquid medication dosages. providing medication in patient-accessible forms (e.g., easy-open bottles, unwrapped pills)
- Ensuring that take-home printed materials and medicine labels are in large type and the patient's native tongue.
- teaching patients how to utilize pill crushers, computerized medicine dispensers, commercially available drug boxes, and drug calendar reminders.
- Simplifying and streamlining the entire treatment regimen to remove complexity and duplication.
- Establishing a rapport with a pharmacist and sticking with one pharmacy will help guarantee consistency in care for elderly patients. A pharmacist can aid in avoiding drug-related issues, which are particularly dangerous for elderly people.
- Pharmacists are occasionally the most accessible medical professionals for elderly folks. In addition to administering medications, pharmacists also educate patients and healthcare professionals about medications, keep track of medication use (including adherence), and communicate with patients and doctors to guarantee the best possible pharmaceutical care. [22,49]

CONCLUSION:

In this investigation, polypharmacy in the older group was a problem. Management of ADR and other risk factors will improve with increased knowledge of geriatric medicines and identified disorders. The primary focus of this study was to investigate the relationship between polypharmacy and aging. This study demonstrated a high frequency of polypharmacy, which in turn contributed to a high prevalence of drug-related issues, including potentially inappropriate medications (PIMs), adverse drug reactions (ADR), and prescribing patterns in older individuals. These major health issues need to be avoided or handled carefully.

Patients who are elderly are weaker and more susceptible to drug-related issues. Therefore, a review of the drugs is necessary with a view to description. In addition, there should be evidence-based guidelines for prescribing in this age group. Clinicians should be made aware of patients who may experience drug-related issues by using evidence-based techniques. The results of the current investigation show that comorbidities put geriatric individuals at risk for prescription polypharmacy. The study also discovered a significantly significant predictor for drug-related issues: polypharmacy. In high-risk populations like older patients, rational prescribing and the use of information technology can help to improve pharmaceutical safety. The role of a pharmacist is to enhance the quality of life of geriatric patients.

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