MEDICAL RECALL

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HOSPITAL CENTRAL DR. IGNACIO MORONES PRIETO
UASLP Universidad Autónoma de San Luis Potosí | FACULTAD DE MEDICINA

The Polypharmacy Challenge: Addressing Medication Complexity in Geriatric Patients

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INTRODUCTION

Polypharmacy in older adults is an increasingly relevant phenomenon in our society. As the population ages, it is more frequent that they may present several pathologies, such as arterial hypertension, diabetes mellitus, osteoarthritis, among others. These chronic medical conditions require the simultaneous use of multiple drugs. While these drugs may be essential, concomitant use poses significant challenges in terms of safety, effectiveness and quality of life, as they carry potential risks when used in excess or inappropriately. In this context, it is important to understand two things: **1)** the ageing process is accompanied by changes in pharmacokinetics and pharmacodynamics and **2)** most drugs exclude the elderly population from clinical trials. Therefore, the pharmacological appropriateness of various drugs in geriatric and multimorbid patients remains to be determined. Inevitably this lack of evidence has often led to inappropriate drug treatment and consequently to various adverse clinical outcomes.

There are multiple definitions used in the literature to describe polypharmacy. Polypharmacy can be defined as the use of multiple medications by a patient simultaneously, although the precise number of medications used to define "polypharmacy" is variable.

In most literature, it is described numerically as five or more medications prescribed at any one time, including over-the-counter medications or herbal supplements (1).

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PREVALENCE OF POLYPHARMACY

The prevalence of polypharmacy reported in the literature varies widely. It ranges from 4% to 96.5% depending on age, definition, institution and region. The average number of prescriptions taken daily by elderly outpatients ranges from two to nine medications, being more common in women, with prevalence increasing with age (1).

CONSEQUENCES OF POLYPHARMACY: ADVERSE DRUG REACTIONS

Adverse drug reactions (ADRs) are defined as any unintended or unwanted harmful response to a therapeutic agent. They may be expected or unexpected and occur at doses used prophylactically, diagnostically, therapeutically, or to modify physiological function. ADRs do not include accidental or intentional therapeutic failure, poisoning or overdose. Different methods can be used to classify AMR. The classification suggested by Thomson and Rawlings **(Figure 1)** in 1981 is one of the most widely used (2).

Previous studies in the literature have reported that 11-63% of older adults with inappropriate medication have some type of adverse drug reaction and some type of interaction. Thus, in this population, polypharmacy would be responsible for 10% of emergency department visits, 10-17% of hospital admissions and of these admissions, 38% are life-threatening.

Type of reaction	Type of affection	Characteristics	Frequency	Examples	Handling
A	**Enhanced**	• Dose dependent • Low mortality • Predictable	Common	Hypoglycemia due to oral antidiabetics	Reduce dose or discontinue. Consider interactions
B	**Bizarre**	• Not dose-dependent • High mortality • Not predictable	Infrecuent	Hypersensitivity to penicillin	Discontinue treatment and avoid future treatment. Notify as background
C	**Chronic**	• Time dependent • Related to dose accumulation	Infrecuent	Hypothalamic-pituitary-adrenal axis suppression by steroids	Reduce dosage gradually and withdraw
D	**Delayed onset**	• Evident time after treatment	Infrecuent	Teratogenesis	Not treatable
E	**End of treatment**	• Appear when treatment is withdrawn	Infrecuent	Opioid withdrawal syndrome	If possible, reintroduce the treatment and gradually withdraw it
F	**Unexpected failure**	• In relation to pharmaco-logical interactions	Common	Inappropriate dosing of oral contraceptives in coadministration of enzyme inducers	Adjust dose Consider if interaction effect

Figure 1. Classification of adverse drug reactions. Taken from: Zazzara MB. Adverse drug reactions in older adults: a narrative review of the literature.

The most frequent disorders are listed below (3):

- Depression
- Gastrointestinal symptoms
- Pain
- Dyskinesias
- Dryness of mucous membranes
- Endocrine and metabolic disorders
- Genitourinary disorders
- Pressure ulcers
- Pulmonary diseases
- Weight loss
- Hypoglycemia
- Over anticoagulation
- Arterial hypotension
- Renal failure
- Hydroelectric disorders

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- Falls
- Confusion
- Cognitive impairment
- Anxiety
- Delirium

DRUG - DRUG INTERACTIONS

Depending on the text consulted or the author's perspective, multiple definitions of the term "drug-drug interaction" can be found, although the most accepted one refers to the manifestation of a pharmacological effect, either therapeutic or toxic, with a different intensity than expected as a result of the simultaneous administration of other medicines, foods or herbal preparations. In other words, when two or more medicines are administered at the same time and the effect of the first is altered due to the influence of the second.

Sometimes, when we combine medicines, we can increase their therapeutic effects, and this happens so often that we use these combinations intentionally to obtain benefits in treatment. However, the interactions that concern us most are those that do not benefit the patient, but rather harm him or her. These interactions can lead to adverse effects or cause the medicine not to work as expected. They are more likely to occur when multiple medicines are given at the same time.

MECHANISM OF PRODUCTION OF DRUG-DRUG INTERACTIONS

Drug-drug interactions, which occur when a new drug is added to an existing treatment, can have multiple coordinated mechanisms of action, which can be divided into three main categories: pharmaceutical, pharmacokinetic and pharmacodynamic.

- **Pharmaceutical:** these refer to physicochemical incompatibilities, which prevent the mixing of two or more drugs in the same solution.
- **Pharmacokinetic interactions:** these alter the processes of absorption, distribution, metabolism and elimination of a drug due to the simultaneous administration of other drugs.
- **Absorption-related interactions:** these can change the rate or amount of absorption, which is relevant for drugs that need to reach concentrations quickly. There are several mechanisms by which a drug may alter the absorption of other drugs: chelation, changes in gastrointestinal pH, changes in gastrointestinal motility, destruction of bacterial flora, changes in intestinal metabolism.

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- **Distribution-related interactions:** changes in how the drug moves through the body.
- **Metabolism-related interactions:** these are often clinically important and occur when a drug induces or inhibits enzymes responsible for the metabolism of other drugs.
- **Elimination-related interactions:** primarily affect renal excretion, but may also influence biliary elimination.
- **Pharmacodynamic interactions:** occur when one drug affects the concentration-effect relationship of another drug when administered together. This may result in synergistic, antagonistic or potentiating effects on the target organ or system.

AGING-RELATED PHYSIOLOGICAL CHANGES AFFECTING DRUG PHARMACOKINETICS

These are due to changes in absorption, which may **1)** decrease intestinal motility, **2)** increase gastric pH, **3)** decrease splanchnic flow, and **4)** decrease active intestinal transport of substances such as iron or vitamin B12. Changes in distribution are caused by decreased total body water (in conjunction with decreased thirst stimulation), reduced lean body mass and reduced total protein, which affects protein-linked transport. In terms of excretion, reduced glomerular filtration rate and tubular secretion modify drug distribution (4).

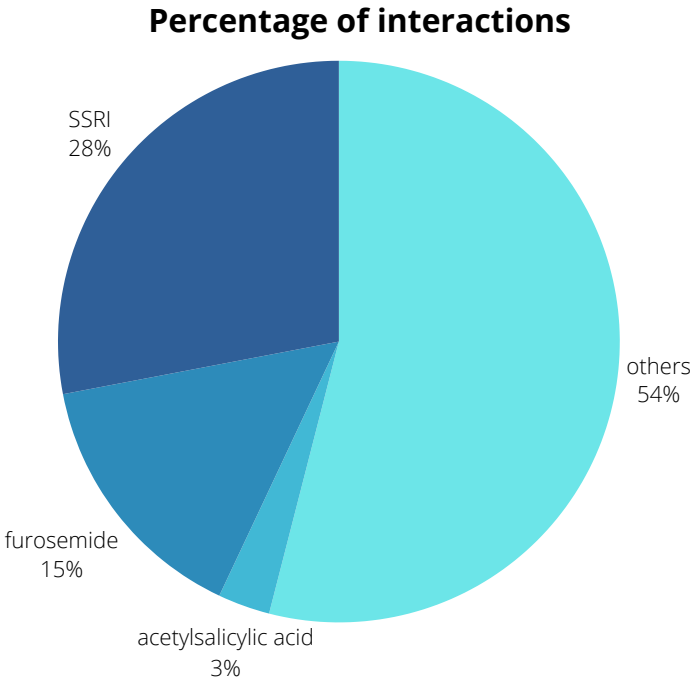

Figure 2. Percentage of the most common interactions Taken from: Petrini E. Risk of drug interactions and prescription appropriateness in elderly patients.

PRESCRIBING CASCADES

Prescribing cascades occur when an additional medicine is prescribed to treat symptoms that are caused by an adverse effect of another medicine that the patient is already taking, but which may not have been identified as related to the previous treatment. As a result, the patient is at risk of experiencing more adverse effects due to the additional drugs that are prescribed in connection with the new therapy (6).
Imagine an older adult who starts taking a β-blocker to treat a heart condition, the patient develops side effects such as a persistent cough, which are not immediately related to the β-blocker. The doctor not recognising the cause of the cough prescribes a cough suppressant;

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this causes constipation in the patient. To address the constipation, the physician prescribes a third drug, a laxative, which can cause electrolyte imbalances. The cascade could continue as each new drug may generate its own side effects, leading to the prescription of more drugs.

NON-ADHERENCE TO MEDICAL TREATMENT

Complex medication regimens and polypharmacy lead to poor adherence to medical treatment. This lack of adherence to treatment is associated with poor health outcomes, disease progression, treatment failure and hospitalisations. Paradoxically, it also leads to an increase in the number of drugs prescribed.
This is true in the case of a patient who is hypertensive, diabetic and currently has data compatible with COPD. According to the clinical practice guidelines, the physician should monitor HbA1c levels/AT levels in order to prescribe pharmacological treatment. It may be managed with lifestyle changes and metformin, in addition to the necessary treatment for hypertension and probable dyslipidemia (statins, ACE inhibitors, etc).

If we do not achieve adequate adherence to treatment, the patient may experience adverse reactions such as hypoglycaemia and dyspepsia due to inadequate intake or overmedication. The patient may decide not to take any more medication and eventually suffer severe metabolic decompensation and/or present acute coronary syndrome as a major complication.

These will require management in a hospital unit, in which we may be faced with two possible scenarios: stabilization and discharge or complication and death. In the first case, given the previous conditions, we can predict that the patient will suffer multiple hospital readmissions due to the new prescription of drugs added to his or her basic scheme, derived from poor pharmacological adherence or the prescription cascade (6).

NON-PHARMACOLOGICAL FACTORS

The success of a treatment depends not only on pharmacological aspects, but also on the patient's individual characteristics, family background, cultural context and economic capacity. These aspects help us to personalise medication management for the patient and to assess their adherence to treatment and expected response.

Considering factors such as the social support network is of great importance when initiating treatment. We often find that, despite diagnostic and therapeutic efforts, we sometimes fail to consider seemingly simple aspects, such as whether the patient has the financial resources to buy the medicines, whether they understand the therapy, whether they can read and understand the instructions, or whether they have someone who can help with the administration of the treatment if they are unable to do so themselves. It is essential to know if the patient has cognitive impairment, which can make it difficult to take medication.

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This is further complicated in those who refuse medication due to behavioural disorders. Therefore, primary care physicians should receive ongoing training to identify early disorders and diseases such as depression, anxiety, Parkinson's dementia, among others, that may affect adherence to treatment. It is also crucial to assess possible fine motor problems that lead to limiting access to and taking more complex medications (4). The success of a treatment depends not only on pharmacological aspects, but also on the patient's individual characteristics, family background, cultural context and economic capacity. These aspects help us to personalise medication management for the patient and to assess their adherence to treatment and expected response.

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Therefore, primary care physicians should receive ongoing training to identify early disorders and diseases such as depression, anxiety, Parkinson's dementia, among others, that may affect adherence to treatment. It is also crucial to assess possible fine motor problems that lead to limiting access to and taking more complex medications (4).

SAFE PRESCRIBING IN GERIATRIC PATIENTS

As we have observed, the patient with polypharmacy must be managed with extreme caution, as the slightest mistake can cause adverse reactions or recoverable drug interactions, as well as conditions that, due to lack of adherence, can generate a cascade of unnecessary prescribing, leading to a greater risk of major adverse effects or death of the patient.
The following are recommendations to help mitigate the presence of the entities described above:

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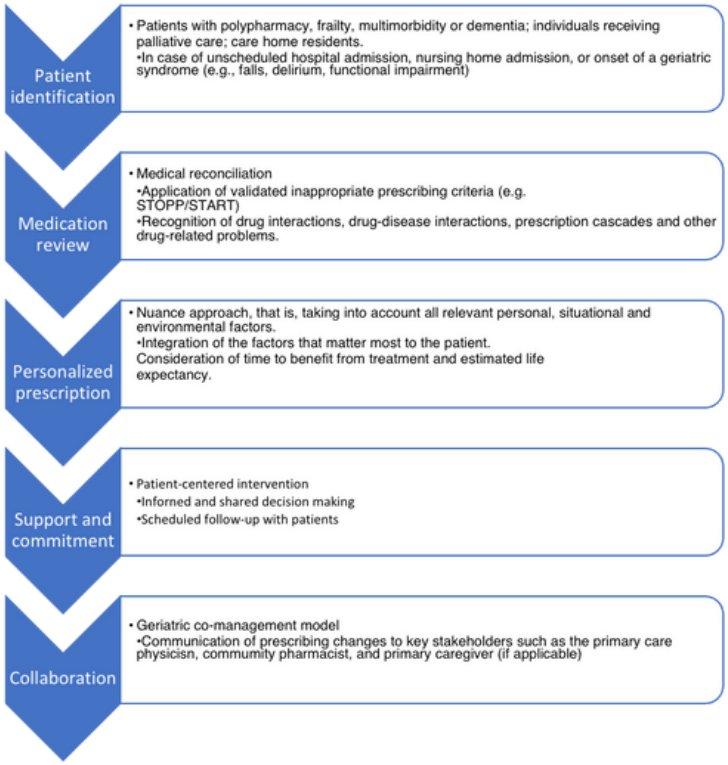

Figure 3. Schematic representation of the stages of the polypharmacy management model. Taken from: Daunt R. Polypharmacy stewardship: a novel approach to tackle a major public health crisis.

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