

The Polypharmacy Paradox

Navigating the Fine Line Between Treatment and Toxicity

Esther Mizrachi, MD

Emergency Medicine Physician

Silvercare Founder

About Me



**Board Certified Emergency
Medicine Physician**



**Prior Academic and Corporate
Geriatric Roles**



Silvercare Founder

Denver's only Subscription Emergency
Physician Home Visit Service.



meaning more than 5

many

PolyPharmacy

medications

Includes prescriptions, over-the-counter (OTC) drugs, vitamins, and supplements.



contrary

ParaDox

belief

The Core Contradiction

Medications are designed to restore health, yet excessive use creates a clinical paradox where therapeutic intent causes functional decline.

Intended Outcome

Every prescription is an intervention aimed at symptom relief, disease management, or longevity.

The Reality of Excess

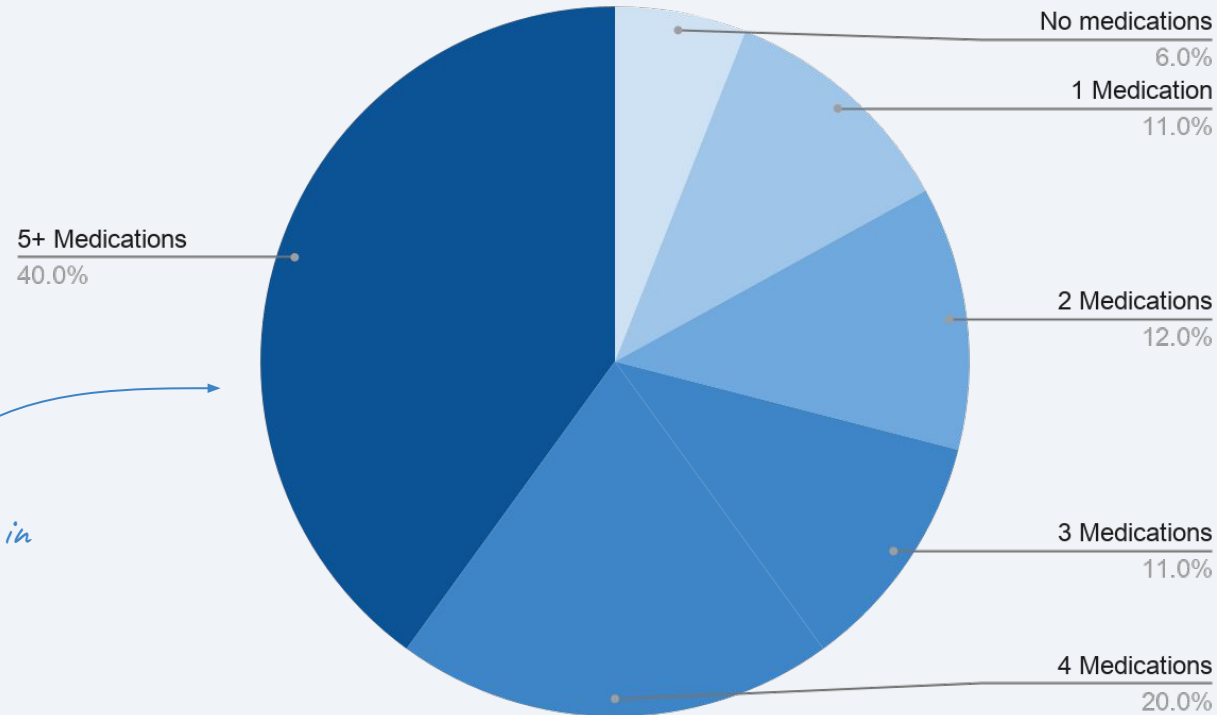
When medications accumulate, the cumulative risk of side effects and drug interactions often outweighs the original benefit.



"I take one pill for my heart, one for my joints, and three just to try and remember where I put the first two."

← Unexpectedly, the cure becomes the complication.

Geriatric Polypharmacy by the Numbers



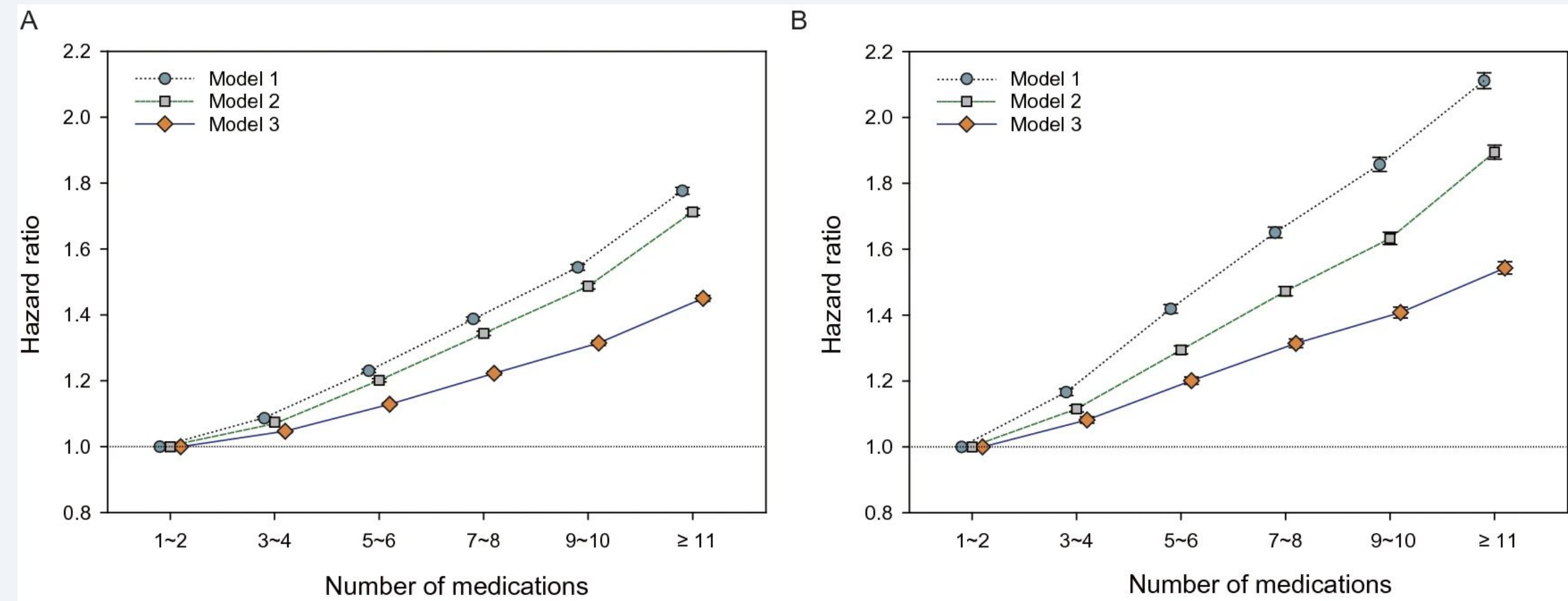
Adverse Drug Events cause over 100,000 hospitalizations annually in older patients.

Sources: Centers for Disease Control and Prevention. Therapeutic Drug Use. National Center for Health Statistics. Accessed June 18, 2026

PMC12778210, Ye et al. (2024), Merck Manuals

Kaiser Family Foundation. Public Opinion on Prescription Drugs and Their Prices. KFF. Published August 21, 2023.

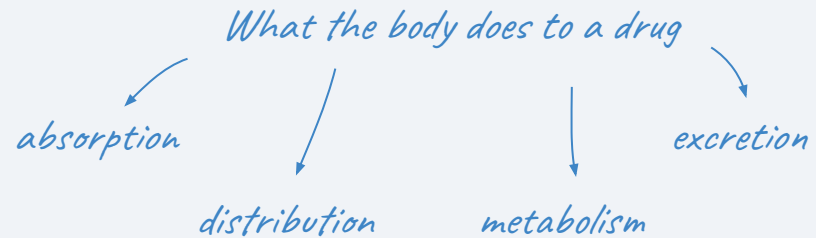
Associations between the number of daily prescribed medications with the risk of **(A)** hospitalization and **(B)** mortality. All models were adjusted for age, sex, residential area, and Charlson comorbidity index score.



medication

Pharmacokinetics

motion



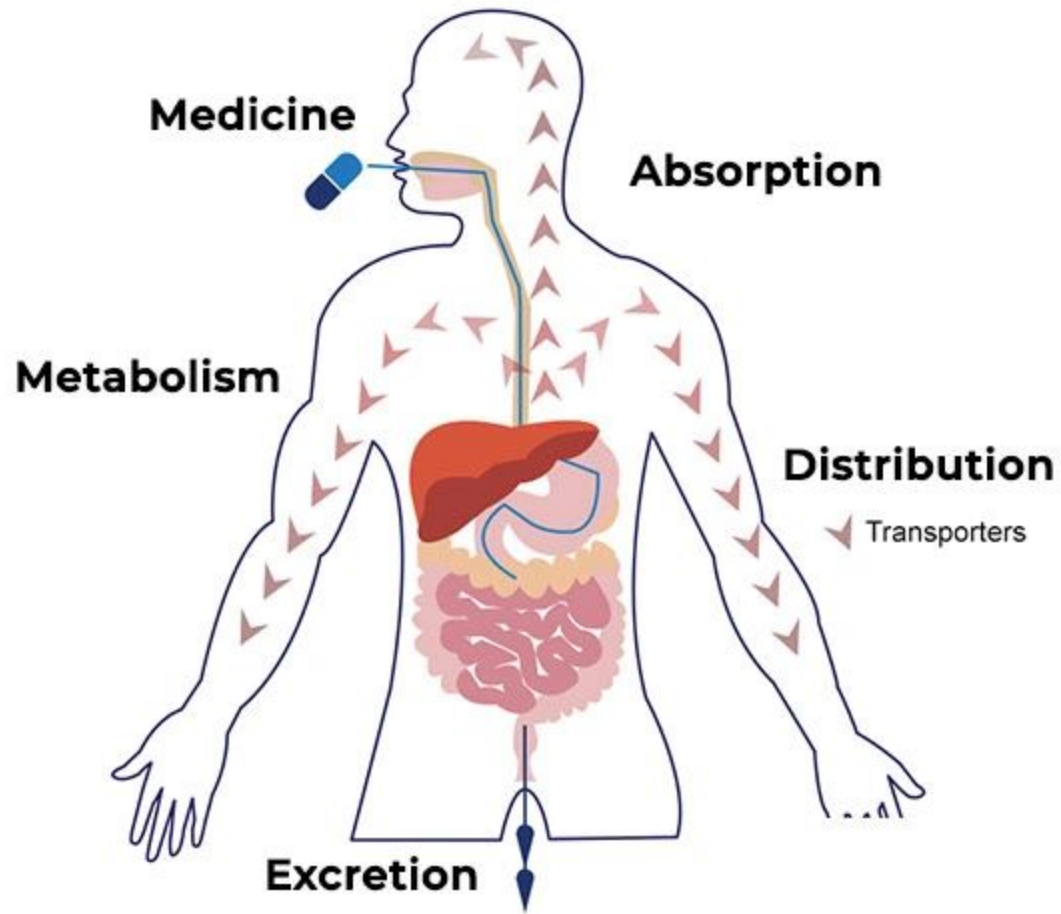
medication

PharmacoDynamics

What a drug does to the body

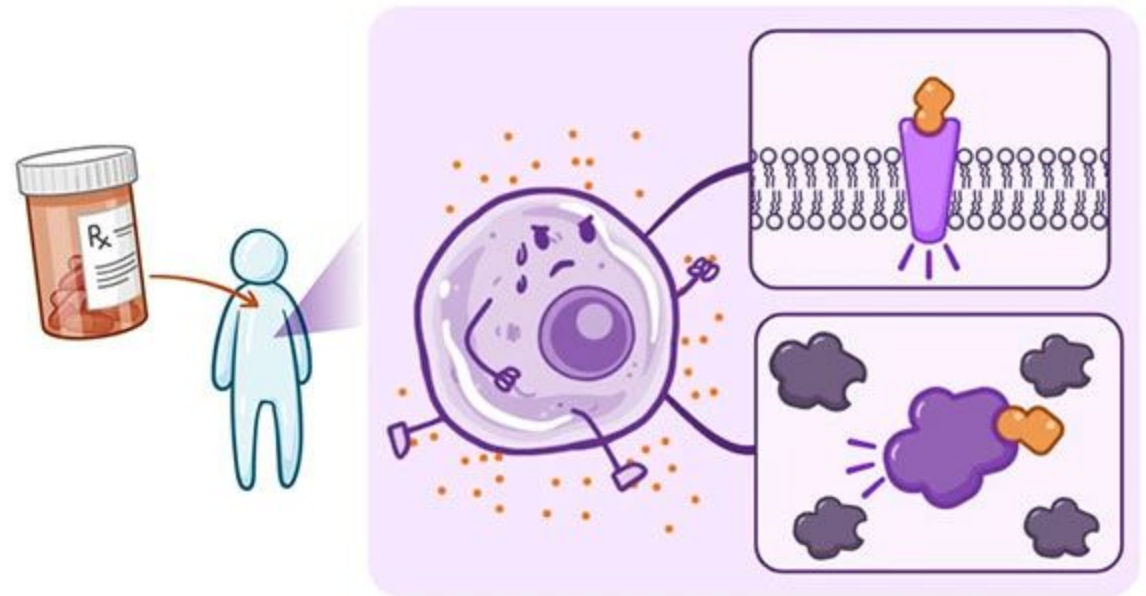
power/ability

Pharmacokinetics



What the body does to the drug.

Pharmacodynamics



What the drug does to the body

Age-Related Pharmacokinetic Changes



Absorption

Weakening of the blood brain barrier, decreased stomach acid production leading to decreased intestinal absorption



Distribution

Significant changes due to shifts in body composition (water vs. fat).



Metabolism & Excretion

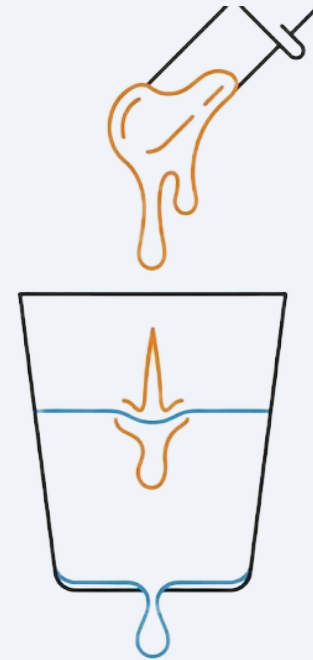
Liver and kidney function decline over time, meaning drugs stick around longer.

Body Composition Shifts

As we age, two major things happen to our body composition:

- **Total Body Water Decreases:** By about 10–15%. We quite literally dry out a bit.
- **Total Body Fat Increases:** Lean muscle mass is replaced by adipose (fat) tissue.

These seemingly simple changes profoundly impact how drugs distribute in the body.



Hydrophilic vs. Lipophilic



Hydrophilic (Water-Loving)

Because older adults have less total body water, these drugs have a **smaller** volume of distribution.

Result: Higher concentration in the blood. (e.g., Digoxin, Lithium)



Volume of Distribution (V_D)

$$V_D = \frac{\text{Total amount of the drug in the body}}{\text{Drug concentration in the blood}}$$



Lipophilic (Fat-Loving)

Because older adults have more body fat, these drugs have a **larger** volume of distribution.

Result: Drug gets trapped in fat, leading to a prolonged half-life. (e.g., Diazepam, Fentanyl)

Adverse Drug Reactions

The risk jumps to ~50% when taking 5+ meds.



Drug-Drug Interactions

Medicines interact adversely with each other.



Falls and Confusion

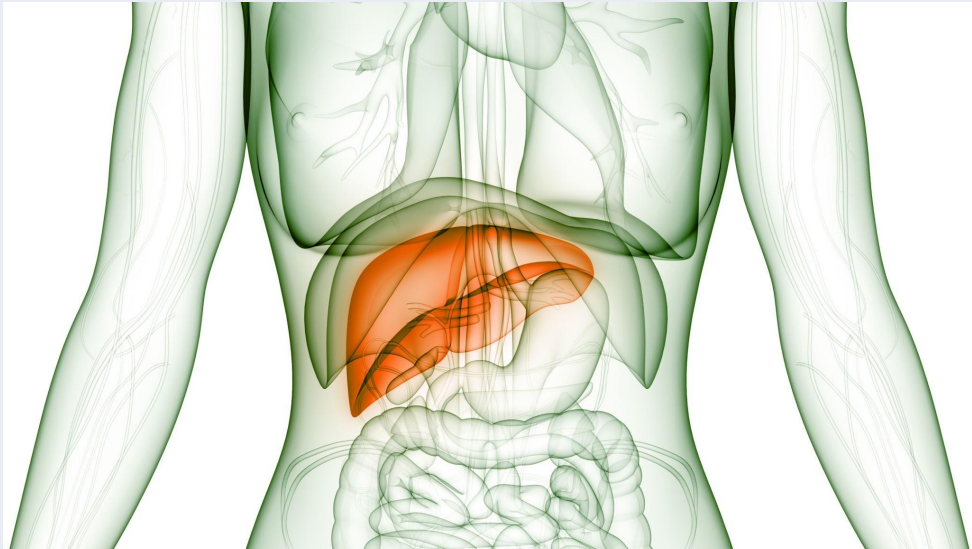
Especially with medications affecting the central nervous system.



The Prescribing Cascade

Treating a side effect of Drug A with Drug B, then treating Drug B's side effect with Drug C, etc.

Cytochrome: The Liver's Metabolic Engine



What is the CYP System?

The **Cytochrome P450 (CYP)** system is a family of enzymes responsible for metabolizing the vast majority of medications.

These enzymes act as "biological gatekeepers," breaking down drugs so they can be eliminated from the body.



The Source of Interactions

Inhibitors: Block enzymes, causing Drug A to build up to toxic levels because it isn't being broken down.

Inducers: Rev up enzymes, causing Drug A to be cleared too quickly, making the treatment ineffective.

Why Medications Increase Fall Risk & Confusion



CNS Sensitivity, Leaky Blood-Brain Barrier

Aging brains are more sensitive to drugs that cross the blood-brain barrier, leading to dizziness and disorientation.



Orthostatic Hypotension

Many meds cause blood pressure to drop suddenly upon standing, leading to "head rushes" and immediate falls.



Sedation & Slowed Reflexes

Anticholinergics and sedatives impair the "righting reflex," making it more difficult to catch oneself during a trip.

The "Prescribing Cascade" (Domino Effect)



The Loop

A drug is prescribed → Side effect occurs →
Misinterpreted as a NEW medical condition →
New drug prescribed for the side effect.

Classic Example

NSAID (for pain) → **Htn** (side effect) →
Amlodipine (new Rx) → **Edema** (side effect) →
Furosemide (new Rx).

Common Prescribing Cascade Examples

- Ibuprofen → hypertension → antihypertensive
- Metoclopramide → parkinsonism → levodopa/carbidopa
- Risperidone → parkinsonism → benztropine
- Amlodipine → edema → furosemide
- Gabapentin → edema → furosemide
- Ciprofloxacin → delirium → risperidone
- Lithium → tremor → propranolol
- Bupropion → insomnia → mirtazapine
- Donepezil → urinary incontinence → oxybutynin
- Amiodarone → tremor → lithium
- Venlafaxine → tremor → diazepam
- Meperidine → delirium → risperidone
- Beta-blocker → depression → antidepressant
- Amitriptyline → decreased cognition → donepezil
- Narcotic → constipation → sennosides
- Sennosides → diarrhea → loperamide
- Lorazepam → morning drowsiness → caffeine
- Enalapril → cough → dextromethorphan
- Furosemide → hypokalemia → potassium supplement
- Nonsteroidal anti-inflammatory drug → heartburn → H₂-antagonist or proton pump inhibitor
- Omeprazole → low B12 → B12 supplement

The Delicate Balance



We must constantly weigh the **benefit** of a medication against its potential for **harm**.

What was appropriate at age 50 might be toxic at age 80 due to **changing pharmacokinetics and pharmacodynamics**.

Deprescribing Strategy

The systematic process of identifying and discontinuing drugs where harms outweigh benefits.



Practical Tips for Safer Medication Management

Taking Control of Your Health

Actionable Steps



Maintain a Master List

Keep an updated list of ALL medications, including OTCs, vitamins, and supplements. Bring it to every appointment.



Communicate

Don't be afraid to ask: "Do I still need this?" or "Could this new symptom be a side effect?"



Consolidate

Try to use a single pharmacy so they can screen for interactions across all your prescriptions.

When You're a Hammer...



The Law of the Instrument

"If the only tool you have is a hammer, it is tempting to treat everything as if it were a nail."

In clinical settings, this cognitive bias leads to **over-prescription**—where medication becomes the default response to every symptom, regardless of the underlying cause.

Overcoming this requires expanding our toolkit beyond the prescription pad.

Deprescribing: The Strategic "Exit Plan"



RECONCILE

List every med (OTC, Herbals too).



RECOGNIZE

Identify PIMs (Potentially Inappropriate Meds).



RE-EVALUATE

Ask: Is there a current diagnosis for this?



REDUCE

Taper slowly; monitor for symptoms.

The Clinical Trial Paradox



Who are we studying?

Most drugs are studied in healthy **25–45 year olds** with zero comorbidities.

Only ~8% of clinical trials specifically enroll patients over age 80.

"We take data from the young and healthy and apply it to patients with heart failure, renal decline, and 12 other medications."

This is the root of the paradox.

Summary

Take Home Points

01

As we age, we often require more medications.

02

As our bodies age, our response to medications is augmented and we become more susceptible to adverse events.

03

Going over medications frequently with your doctor and being aware of the purpose as well as the side effects will help you avoid adverse events.

04

More research is needed to optimize medication use in older adults.

Questions?

Contact Information

Esther Mizrachi, MD

✉ silvercarecolorado@gmail.com

🌐 silvercarecolorado.org

Thank You!