Safety in Polypharmacy Training Course

Session 2

Fundamental Concepts in Drug-Drug Interactions (DDIs)

Written version of the video scripts

In this session

Video #1 — How Drugs Work in Your Body & What Happens When They Collide

Video #2 — The Patient Perspective: PROs, PROMs & Real-World DDI Cases

Original presenters: Rachel Giles, Olga Millán

Original session date: 16 October 2025

Contributors

LeukaNET
Leukemia Advocates Network

Patvocates
PATIENT ENGAGEMENT IS IN OUR DNA

AI Disclaimer

The educational content was created by humans and subsequently edited and summarised with AI assistance.

Funded by the European Union

Funded by the European Union. Views and opinions expressed are however those of the author(s) only and do not necessarily reflect those of the European Union or the European Health and Digital Executive Agency (HADEA). Neither the European Union nor the granting authority can be held responsible for them.

Contents

VIDEO #1 — How Drugs Work in Your Body & What Happens When They Collide 3
1. Introduction 3
2. Main content 3
3. Key takeaways 6
VIDEO #2 — The Patient Perspective: PROs, PROMs & Real-World DDI Cases 8
1. Introduction 8
2. Main content 8
3. Key takeaways 10

VIDEO #1 — How Drugs Work in Your Body & What Happens When They Collide

Estimated Duration: 7–8 minutes
Target Audience: Broad: patients, caregivers, and clinicians

1. Introduction

When you swallow a pill, what actually happens next? Where does it go? How does your body decide what to do with it? And what happens when two drugs meet inside you and start competing for the same spot?

Welcome back to the SafePolyMed series. In Session 1, we defined polypharmacy. Now, in session 2 we are going under the hood. In this video, you will learn how drugs actually travel through your body, how they do their work, and crucially, how they can interfere with each other in ways that are sometimes dangerous, and sometimes surprisingly helpful.

2. Main content

Polypharmacy & The Risk of Drug-Drug Interactions

Let's start with why this matters. As we learned in Session 1, polypharmacy, taking five or more medications, is incredibly common. But here's the critical connection: the more medications you take, the higher your risk of drug-drug interactions, drug-induced side effects, adverse drug reactions, and even simple human errors in managing your medicines.

And DDIs and their side effects can be life-threatening or cause your treatment to fail entirely. To understand why, we need to learn how drugs and our bodies interact.

How Medicines Enter Your Body: Routes of Administration

Medicines can get into your body in lots of different ways. Thought, the most common is orally, like pills, capsules, liquids you swallow, or sublingual. But they can also be injected, intravenously straight into a vein, intramuscularly into a muscle, or subcutaneously just under

the skin. And there are also topical routes like creams, patches, and sprays, as well as suppositories and inhalers.

Now, why does the route matter? ...Because it determines how much of the drug reaches your bloodstream and how quickly.

The First-Pass Effect: Your Liver as a Drug Filter

When you swallow a pill, it has to pass through your stomach and intestines and then go through your liver before reaching the rest of your body. And your liver is a powerful processor, it is the main site of drug metabolism, although your lungs, kidneys, and gastrointestinal tract also play important roles.

This first trip through the liver is called the first-pass metabolism. It is why, for some drugs, the oral dose needs to be much higher than an intravenous dose. The liver simply breaks down a large portion before it ever reaches your bloodstream. Many drugs have what is called heavy first-pass effect, where they are so largely removed by the liver in their first-pass, that taking them orally results in very little of the drug reaching systemic circulation. Therefore, alternative routes need to be used. For example, nitrate medications used for chest pain are broken down so heavily by the liver that they cannot be taken as regular pills, so they have to be given sublingual or through a patch.

To give you a concrete example: if you take 300 milligrams of a drug orally, and only 70% is absorbed from the gut, and then the liver removes 60% of what arrives, your overall available drug is just 28%, and this is what it's called Bioavailability. Out of 300 milligrams, only 84 milligrams reach your body to do their job.

Whereas drugs that are administered by the intravenous route are 100% bioavailable.

Pharmacokinetics (PK): What Your Body Does to a Drug

In this sense, healthcare professionals to describe what the body does to a drug, which is called Pharmacokinetics, they use a helpful framework called ADME, and it stands for Absorption, Distribution, Metabolism, and Elimination.

Absorption is how the drug gets from wherever it was administered into your bloodstream.

Distribution is how it travels to the organs and cells where it is needed.

Metabolism is how the drug is processed and broken down, mainly in the liver by a family of enzymes called cytochrome P450, or CYP450.

And Elimination is how the drug leaves your body: Through urine, faeces, sweat, breast milk, saliva, or even tears.

Each of these four steps is a potential point where another drug can interfere. Two drugs might compete for absorption. They might fight for the same liver enzyme. One might speed up or slow down the elimination of another. So, understanding ADME helps explain how and why drug-drug interactions happen.

Pharmacodynamics: What the Drug Does to Your Body

While pharmacokinetics is what the body does to the drug. Pharmacodynamics is the flip side: it is what the drug does to your body. It is all about the relationship between the dose you take and the effect you get: the dose-response relationship.

And here's a key concept: the therapeutic window. If you take too little of a drug, nothing happens. As you increase the dose, you enter the zone where the drug starts working. But at some point, you hit the maximum effect. Beyond that, adding more drug does not help, it just increases toxicity risk. That sweet spot in the middle is the therapeutic window, and keeping your medication levels within it is the whole balancing act of prescribing.

There are also different dosing strategies commonly used: a flat fixed dose for everyone, a dose adjusted by body size, or a fixed dose per group like adults versus children. Your doctor chooses based on the drug and your individual characteristics.

How Drugs Act on Cells: Receptors, Agonists & Antagonists

Now, at the cellular level, most drugs work by binding to receptors on your cells. An agonist drug activates the receptor and enhances or triggers a response. While an antagonist drug blocks the receptor and prevents signalling.

When two drugs compete for the same receptor, you get a drug-drug interaction at the pharmacodynamic level.

Factors like ageing, ethnicity, liver or kidney disease, genetic mutations, and other conditions all affect pharmacodynamics. Therefore, every person responds slightly differently to a same drug.

Drug-Drug Interactions: When Medicines Collide

Now we can bring it all together. A drug-drug interaction happens when different compounds administered at the same time affect each other's behaviour. Those compounds can be prescription drugs, over-the-counter medicines, natural substances like grapefruit juice, or supplements like St. John's wort or fish oil.

There are more than 2,500 known pairs of interacting drugs, with likely many more undiscovered. And considering what we have learned here, it is important to keep in mind that DDIs are especially dangerous when a drug has a narrow therapeutic window. Therefore, understanding DDIs is key to patient safety.

DDI Case Study 1: When a Heartburn Drug Undermines a Heart Drug

Let's see a couple of real-world examples.

Case one: a 68-year-old woman arrives at the Emergency Room with a heart attack. She takes clopidogrel And Aspirin to prevent clots, plus omeprazole for heartburn. Clopidogrel needs the CYP enzyme to become active, while Omeprazole is a potent inhibitor of the CYP enzyme. Her heartburn drug was silently undermining her clot-prevention drug. Then a heart attack resulted as a consequence.

DDI Case Study 2: Example of how it goes wrong

Let's see case number two, a study of over 11 million people in which patients with psoriasis or rheumatoid arthritis were taking methotrexate alongside NSAIDs a common anti-inflammatory painkiller. Methotrexate is primarily eliminated by the kidneys, while it was found that NSAIDs reduce kidney function, which slowed down methotrexate elimination. The result was a dangerously high methotrexate levels causing bone marrow suppression, Gastrointestinal toxicity, and even kidney failure.

A common painkiller plus a commonly used immunosuppressant, yet the combination can be fatal.

3. Key takeaways

Here some key takeaways. Every drug you take goes on a journey through your body, absorbed, distributed, metabolised, and eliminated. At every step, another drug can interfere.

That's why your healthcare team needs to know everything you're taking, including over-the-counter medicines, supplements, and even grapefruit juice.

In our next video, we will explore why your perspective as a patient is essential in identifying DDIs, and how Patient-Reported Outcomes can make a real difference. See you in the next one!

VIDEO #2 — The Patient Perspective: PROs, PROMs & Real-World DDI Cases

Estimated Duration: 5 minutes
Target Audience: Broad: patients, caregivers, and clinicians

1. Introduction

Have you ever felt different on your medication? More tired, more anxious, a bit off. And just assumed it was normal? What if those changes were not from your disease at all, but from an undetected drug-drug interaction? And what if your own observations could be the key to catching it?

In this video, we will explore why your voice as a patient is one of the most powerful tools for detecting drug-drug interactions, and we will look at real-world cases that show just how common, and how preventable, these problems are.

2. Main content

Why DDIs Matter for You

You might think drug-drug interactions are purely a pharmacist's problem. But patients and caregivers are often the first to notice when something is not right. Research shows that patients on multiple medications face a significantly higher risk of medication-related harm from DDIs, falls, and other adverse events.

DDIs can happen not just from prescribed drugs, but from self-medication ones, an OTC painkiller, a herbal supplement, some foods and drinks like grapefruit juice. And if your healthcare team does not know about them, they cannot support you.

Therefore, understanding how medications affect your quality of life can lead to better care plans, improved shared decision-making, stronger treatment adherence, and discovering previously unknown interactions. Here, your perspective can help fill the gaps.

Patient Reported Outcomes

And this brings us to the Patient Reported Outcomes, or PROs. Unlike standard clinical measures like blood pressure or lab results, PROs capture how you feel. They are questionnaires filled in directly by you, covering health-related quality of life, symptoms, daily functioning, satisfaction with care, and adherence to treatment.

Two patients with the exact same diagnosis and medications may experience their treatment very differently. PROs can capture those differences in ways that standard tests cannot.

PROMs: Measuring What Matters to You

The tools used to collect this data systematically are the PROMs, Patient Reported Outcome Measures. They can track health-related quality of life including physical, social, emotional, and psychological functioning; patient satisfaction with healthcare delivery or treatment; and activities of daily living like mobility, self-care, or work.

So here is the key insight: If PRO data points to a drug-related issue, like new fatigue or rising anxiety after starting a medication, clinicians should consider a drug-drug interaction, not just the effects of a single drug. This data needs to be collected regularly and treated as seriously as any clinical measurement.

Real-World Case 1 - Atorvastatin & Grapefruit Juice

Now let's look at three real-world examples.

Case one: Atorvastatin and grapefruit. Atorvastatin is one of the most common cholesterol medications. It is broken down by certain CYP450 enzymes. While Grapefruit juice blocks those same enzymes. So, if a patient drinks grapefruit juice while taking atorvastatin, the drug builds up or accumulate in the body, which increases significantly the risk of side effects, particularly muscle pain and damage. A DDI caused NOT by another drug, but by a natural substance.

Real-World Case 2 - Hidden DDIs in Cancer Clinical Trials (SWOG Study)

Let's have a look at case two: The Southwest Oncology Group study examined clinical trial participants on oral chemotherapy. Patients were already taking an average of 6.6 medications at enrolment.

Nearly 19% already had an undetected DDI.

Twelve percent had a DDI violating the trial's safety rules.

7,2% has a clinically relevant DDI

And over 83% of the clinically relevant interactions involved acid suppressant drugs taken alongside the cancer drug dasatinib.

A wake-up call about how common hidden drug-drug interactions drug s are.

Real-World Case 3 - When a DDI is Actually Beneficial

And our case three is actually a positive story. A Phase 1 trial studied two diabetes drugs together, dorzagliatin and sitagliptin, in patients with type 2 diabetes and obesity. The combination did not increase side effects but improved blood sugar control far better than either drug alone, without increasing hypoglycemia risk. The interaction was synergistic.

This can show you that not all DDIs are harmful, some can be used to improve outcomes. The key is monitoring!

3. Key takeaways

Our call to action is to remind you that your experience matters. If something feels different after a medication change, write it down. Tell your healthcare team. It could be a drug-drug interaction.

Engage seriously with PRO questionnaires if your clinic uses them. Your answers help your healthcare team make better decisions.

And remember: DDIs are not just about prescription drugs. What you eat, drink, and the supplements you take, all play a role.

You have completed Session 2!

In our next session, we dive into genetics — how your DNA influences how drugs work in your body. See you in Session 3.

Funded by the European Union

Safety in Polypharmacy Training Course

Contributors

LeukaNET
Leukemia Advocates Network

Patvocates
PATIENT ENGAGEMENT IS IN OUR DNA