Safety in Polypharmacy Training Course

Session 4

Patient Vulnerability Factors

Written version of the video scripts

In this session

Video #1 — Clinical Risk Factors in Polymedication: Why Some Patients Are More Vulnerable

Video #2 — Health Equity and the Hidden Drivers of Vulnerability

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VIDEO #1 — Clinical Risk Factors in Polymedication: Why Some Patients Are More Vulnerable

Estimated Duration: 9–10 minutes

Target Audience: Broad: patients, caregivers, and clinicians

1. Introduction

Two patients take the exact same medications. One manages just fine. The other ends up in the emergency room. Same drugs, same doses, so what made the difference? The answer often comes down to vulnerability: the individual, social, and system-level factors that shape how safely someone can navigate polypharmacy.

In this video, we are going to unpack what makes a patient "vulnerable" and walk through the layers of clinical risk that every healthcare provider and every patient should know about.

2. Main content

What Do We Mean by "Vulnerability"?

Let's start with the definition of vulnerability.

Vulnerability in healthcare refers to an increased risk of poor health outcomes due to individual, social, or systemic factors. This can include age, chronic illness, disability, language barriers, poverty, lack of access, or discrimination.

When we talk about vulnerable populations, it often includes older adults, children and adolescents, pregnant women, underserved groups such as minorities, people without a fixed address, or people with low education levels, and those living with chronic illnesses, among many others.

At its core, vulnerability highlights a person's susceptibility to harm or adverse effects, and that matters enormously when we talk about taking multiple medications.

Adherence: More Than Just Following Orders

Now, a word you will hear a lot: Adherence. It refers to the extent to which a person's behaviour, like taking a medication, following a diet, or making lifestyle changes, matches the recommendations agreed with a healthcare provider.

Notice here the word "agreed." That's what separates adherence from simple compliance, so it is important to separate and differentiate them. While compliance refers to the passive following of a physician's orders without active input or full understanding; adherence requires the patient's agreement.

Patients should be active partners with their healthcare professionals in their own care, and that only works with a good two-way communication. Without that solid communication, patients may not actually be taking the medications, in the same way, that were originally prescribed.

What Increases the Risk of Drug-Drug Interactions?

Several factors make drug-drug interactions more likely.

Age plays a big role: Older adults and children have different pharmacodynamics and pharmacokinetics, different metabolisms, and older adults in particular carry a higher risk of having multiple conditions, which means more medications stacking up at once.

Then, sex and gender matter too. Women tend to experience more adverse drug events than men, and are less likely to have a caretaker supervising their regimen, partly because women themselves often are the caretaker. Meanwhile, older men are more likely to be prescribed harsher treatments.

And then there is simple math: the more medications someone takes at the same time, the greater the risk of interactions. And that risk does not stop at prescriptions, either. Food, health supplements, herbal products, they all count!

On top of that, a person's genome and epigenome can affect how their body processes medications, and certain preexisting diseases, especially cardiovascular and central nervous system conditions, are commonly involved in serious DDIs.

The Three Layers of Clinical Risk

So how do we make sense of all these different risk factors? It helps to think of them in three interconnected layers: Individual factors, social and contextual factors, and systemic factors. Picture these as three gears turning together: When one shifts, it affects the others. Individual factors can drive social and contextual pressures, which in turn are reflected in systemic issues within the healthcare system itself. Understanding which "gear" needs attention is often the key to getting polypharmacy right for a given patient.

Individual Factors

Let's start with the innermost layer: Individual factors.

Beyond these general factors, every one of us is biologically unique. Differences such as race and ethnicity, age, weight, mental health, and genetics can all impact how a drug is metabolised, and therefore how safe it is for that particular person. These are the traits that make each patient's response to medication genuinely unique. And it is sometimes called inter-individual variability or inter-individual differences. This is a reminder that there is no single "standard" patient.

Social and Contextual Factors

Moving to the next layer: Social and contextual factors.

Let's talk about who tends to carry the highest polypharmacy risk.

First, the intersection of age and sex: like older women. Older adults, in general, clear drugs more slowly, leading to higher drug concentrations in their bodies. Add to that the fact that women are generally at greater risk for adverse drug events, something researchers call the "drug dose gender gap."

Older patients are also routinely excluded from clinical trials, often because of multiple existing health conditions; and then drug safety data is rarely broken down by sex and age. That has real consequences. One striking counter-example: a Phase III CAR-T cell trial presented at the American Society of Haematology in 2023 did a subgroup analysis by age and found that patients over 70 actually had better outcomes on that treatment. This is a reminder that when trials do include older patients, we sometimes learn something we would not have expected.

Beyond older women specifically, other groups carry higher polypharmacy risk too: Older adults in general, due to more chronic conditions; people seeing multiple specialists or without a primary care physician to keep oversight; younger adults and children with chronic conditions or developmental disabilities, who often juggle complex, multi-modal treatments; and patients with mental health conditions, whose psychotropic medications carry a high rate of adverse drug reactions, and sometimes require even more medications just to manage the side effects.

Biological Sex-related Differences

Let's dig a little deeper into sex and gender differences, because the gap here is larger than many people realise.

And here is a fact that tends to surprise people: Women were not legally required to be included in clinical trials until 1992. Not the 1970s, 1992! That means a huge amount of the drug data we still rely on today was generated almost exclusively in men.

We now know women may be more susceptible to drug interactions because of differences in body composition, a larger surface-area-to-mass ratio, longer QT intervals on the heart's electrical rhythm, higher fat content, and hormonal factors. Interestingly, elderly male patients who experience drug-drug interactions tend to be exposed to more polypharmacy than elderly female patients with DDIs.

Heart failure is a great example of how differently sex can shape disease. A cardiovascular measurement called ejection fraction, is the percentage of blood pumped out of your heart's main squeezing chamber (the left ventricle) with each heartbeat. And it is known that women more often have heart failure with a preserved ejection fraction, while men more often have it with a reduced ejection fraction.

So, the pathophysiology, the risk factors, even the outcomes differ: women report lower quality of life despite valuing it more, yet tend to survive longer. And, historically, women have been underrepresented in heart failure trials, a disease long thought of as a "male" condition.

Systemic Factors

Now, let's have a look at the outermost layer: Systemic factors, the risks built into the healthcare system itself.

Poor medical record keeping is a major one, such as discontinued medications that are never removed from a patient's file, then are automatically refilled.

Poor transitions of care are another, whether that is the move from paediatric to adult care, a hospital discharge, or migrants arriving with poorly documented medical histories, often worsened by low health literacy and language barriers.

There is also the risk of prescribing purely to meet disease-specific quality metrics. Imagine a patient with chronic lymphocytic leukaemia - CLL, where the real standard of care might be active monitoring rather than a bone marrow transplant, even though that transplant is technically a "cure." That cure can bring life-changing complications like graft-versus-host disease. But, whether it is "worth it" depends entirely on what matters to that patient, not just the clinical metrics.

And then when specialists only look at their own area of expertise, a cardiologist focused purely on cardiac numbers, for instance, whole parts of a patient's wellbeing, psychological or renal, for example, can simply be missed.

3. Key takeaways

So, here's what you can take away: Vulnerability is not just about one factor, clinical risk in polypharmacy rarely comes from just one place. It is about how individual, social, and systemic layers interact. All three factors keep turning together like interlocking gears. You cannot really separate them.

If you are a patient or caregiver, keep good records and speak up about what matters to you. If you are a healthcare provider, take a moment to ask which of these "gears" might be turning for the person in front of you.

In the next video, we will dive into health equity and the hidden systemic drivers behind so much of this vulnerability. See you there!

VIDEO #2 — Health Equity and the Hidden Drivers of Vulnerability

Estimated Duration: 9–10 minutes

Target Audience: Broad: patients, caregivers, and clinicians

1. Introduction

Two people are diagnosed with the same chronic condition. One attends every follow-up appointment. The other misses several visits. It's easy to label that as non-compliance. But what if every appointment requires two buses, childcare arrangements, and time away from work? Health outcomes are shaped by more than biology. They are shaped by the systems people must navigate every day.

In this video, we are exploring the systemic barriers that shape who get safe, appropriate care, and who gets left behind.

2. Main content

Vulnerable vs. Underserved: Same Ballpark, Different Meaning

Let's start by untangling two terms that often get used interchangeably, but they mean different things, and the distinction really matters: Vulnerable and Underserved.

"Vulnerable" points to internal or individual factors: older adults, children, pregnant women, people with disabilities. It is a category that requires extra care and justify additional support and resources.

"Underserved," on the other hand, points to external and systemic barriers: ethnic minorities, rural residents, LGBTQIA+ groups. Crucially, this was never a choice. Nobody opts into being underserved. It is the system failing to reach them equally, and it is on the system, not the individual, to close that gap.

Why does this distinction matter? Because the way you see the problem shapes the solution. Calling someone "underserved" highlights failures in the system, not flaws in the person, and

that opens the door to strategies that address root causes rather than simply labelling individuals. At the same time, we need to be careful with the word "vulnerable" itself: used carelessly, it can increase stigma, or make people feel they are not capable of making their own decisions about their care. The goal of naming vulnerability is to guide support and resources, never to diminish someone's independence.

The Global Safety Picture

So, let's ground this in numbers. Globally, one in every ten patients is harmed in healthcare. More than three million deaths occur every year due to unsafe care. In low- to middle-income countries, as many as four in one hundred people die from unsafe care. And 1 in 20 patients are exposed to preventable harm in medical care, with roughly half of that harm attributed to medications.

And here's the part that should stay with you: most of this harm is preventable!

Why Does Health Inequity Happen in Healthcare?

So, why does health inequity happen in healthcare? Why do these differences exist in the first place?

There are a few recurring reasons behind this. First, wider societal and environmental determinants: think of someone living high up a mountain in Nepal, far from any city. Access to safe, reliable healthcare simply is not guaranteed the way it might be for someone in a capital city with internet access.

Second, data and measurement gaps. We tend to treat what we can see as "normal," and we rarely measure the people who live outside our everyday view. But just because we don't see something, does not mean it doesn't exist, and without data on a group's needs and preferences, we simply cannot plan for them.

Third, structural and institutional bias. This one takes real honesty. Even well-meaning healthcare professionals carry biases they may not notice. Someone in the live session shared a personal experience: Early in her career as a physician, a patient came in who had not showered in days and had a strong smell from long-term homelessness. Her first reaction was to ask her supervisor if she really had to treat him. Her supervisor's response stuck with her: He said, think of him as a whole person, someone who did not choose this situation; he is in that situation, not out of a choice, not out of a personal preference; he is there because things

happened; and he should be not feeling sorry for him; you should be accepting of the situation; you should be empathising! She expressed that, that was the case for her that day, that held her. That was her bias and was one of her things to work on herself. So, that is the essence of structural bias, and then we also have the structural racism and discrimination; and recognising it, is the first step to changing it.

Fourth, access barriers: geography, affordability, digital exclusion, and language. If two people do not speak the same language, and no translation service is available, how can one properly receive care from the other?

And fifth, heterogeneity in treatment effect and safety. Clinical trials still tend to enrol a narrow slice of the population, often white, and largely male, which means we simply do not have strong safety data for everyone else.

Diversity, Equity, and What It Means to Be Inclusive?

Now let's go over diversity, equity, and what it means to be inclusive?

Diversity has many dimensions: age, biological sex, race, ethnicity, migration status, gender, sexual orientation, disability, socioeconomic status, rural versus urban living, access to technology, neurodiversity, marital status, and more. Some of these dimensions make us unique. Some make us vulnerable. Some make us part of an underserved population. Keeping those distinctions clear is what matters.

Now, equity versus equality: imagine a diverse group of people, a person using a wheelchair, a small child, a very tall adult, and you hand every single one of them the exact same tool to reach an apple. That is equality, same tool, for everyone. Equity means looking at each person's actual needs and giving them what they specifically need to reach what they need. When equity is missing, the result is worse health outcomes, poorer quality of life, and in the most serious cases, preventable harm.

So, what does it actually mean to be inclusive? It is an intentional, ongoing effort, not a one-time box to tick.

It means active participation: creating environments where people feel safe contributing.

It means diversity in clinical trials and research, so that treatments are tested on the people who will actually use them.

It means equity in access to medications and healthcare systems.

It means empowered contribution: making sure no one voice counts for more than another.

It means removing barriers: identifying and dismantling the practices that keep marginalised groups from fully participating, in research, in care, in decision-making.

And it means training and educating healthcare professionals to recognise cultural differences, biases, and systemic issues.

Without a diversity, equity, and inclusion lens, prescribing and safety practices risk causing more harm and producing less reliable research. What is needed is representative evidence and prescribing guidelines that genuinely account for variation in metabolism, physiology, and risk across different groups, not just in theory, but in real implementation and training.

Respectful, inclusive patient-provider communication has to be part of that picture too, and it starts with a simple, achievable step: cultural humility. You don't need to have all the answers, you just need to be willing to be more respectful, and more curious, with everyone you work with. And on the institutional side, healthcare staff need to feel safe enough within their own organisations to actually take that first step towards a more inclusive, diverse practice.

The cycle that drives health inequity

So, here's how these pieces reinforce each other.

When inclusive practices are not built into healthcare and research, underrepresented people fall through the cracks, even though they may carry a disproportionately high burden of disease. Adverse healthcare experiences and resulting mistrust, discourage people from seeking care. Fewer contact points with trusted healthcare mean they are less likely to participate in research studies, even when they are a crucial part of the population being studied. Less representative data leads to knowledge gaps about the disease and unmet health needs, which increases health inequities even further. It is a self-reinforcing cycle, and breaking it requires intervening at more than one point.

Determinants of Health: Why Context Matters

This brings us to the determinants of health. You know! Health does not happen in an empty space. As the World Health Organization puts it "The context of people's lives determines their health, so blaming individuals for having poor health or crediting them for good health is

inappropriate. Individuals are unlikely to be able to directly control many of the determinants of health"

So, these determinants can be our social and economic environment, our physical environment, or our individual characteristics and behaviours. The context of people's lives determines their health.

Here is a vivid way to picture it: Imagine a group of people in excellent health who board a sailboat to cross into a war zone to deliver aid. For the weeks of that journey, they voluntarily leave behind stable housing, their usual social support, and easy access to health services. Temporarily, their health determinants shift towards risk, even though they started from a position of privilege. This is a useful reminder that determinants of health can change for anyone, while the diversity, equity, and inclusion conversation is really about people living in a permanent state of vulnerability or being underserved, not a temporary state.

Social, Cultural, and Institutional Risk Factors

There are several specific social, cultural and institutional factors that increase risk in polymedication.

So, let's talk about something surprisingly everyday: Herbs! Across the Mediterranean, Greece, Spain, Italy, Portugal, herbal teas and remedies are part of daily life. But many people do not realise that herb-drug interactions are real, and combining herbal remedies with conventional medicines can trigger a hypertensive crisis or dangerous swings in blood glucose, sometimes landing someone in the emergency room without them ever understanding why.

Low income then adds another layer. In many regions, financially limited households rely heavily on canned and processed foods, which tend to be very high in salt and sugar, quietly working against conditions like diabetes or high blood pressure, without the person realising the food itself is a risk factor.

Then there is health literacy. When people do not fully understand the name of their medication, what it is for, or its correct dose; the risk of double-dosing or mixing up medicines goes up, and this is not just an issue for older adults, it affects parents managing medication for their children too, for instance.

Also, gender plays a role in adherence: Older women, who are so often the ones supervising medication for others, tend to be less supervised themselves, and may become more forgetful about their own regimen as a result.

Add in rural residence, where access to healthcare and monitoring is limited.

And the use of non-prescribed medications, mixing herbs, over-the-counter medicines and prescriptions without fully understanding any of them.

All this is what one presenter in the live sessions accurately called "A prescription for disaster."

3. Key takeaways

Understanding these factors, who is vulnerable, who is underserved, and why; is the first step towards mitigating the risks they create.

So, here's our invitation: notice your own biases, they are normal, and the moment you become aware of them is the moment you can start to change how you act. And next time you think about a patient's care, ask yourself: is there a barrier here that has nothing to do with what they chose, and everything to do with how the system was built?

Just before we close with this session, we are going deep into real examples and the ethical considerations that come with patient vulnerability.

Real Drug Examples: When Metabolism Differs

Imagine a patient walks into their doctor's office and the doctor asks, "how's your Bucindolol doing?" The patient has no idea what that word even means, they just know their heart still does not feel right. That small communication gap can be the difference between safe treatment and real harm.

Let's view the setting of communication as a barrier when physicians and patients speak a different language, and I'm not referring to English, or Portuguese, I mean when physicians speak medical and patients speak patient. So, here we have three real examples that do have some safety risks due to sex, genetics, weight, etc. but let's see them from the communication perspective.

First, Bucindolol, a beta blocker first studied for treating hypertension and being used for conditions like arrhythmias and essential tremor. Genetic and ethnic differences affect how

well people respond to it, with differences between men and women and people of colour. But here's the everyday complication: most patients do not know the name of their own medication, let alone its drug class. So, when the physician asks, using clinical shorthand, how a patient's Bucindolol is doing, the patient may only be able to answer in "patient language", something like, "I still don't feel well". That mismatch in language is exactly where safety risks can slip through.

Second, Vancomycin, an antibiotic where dosing depends heavily on body weight. Sounds simple, until you consider that many patients genuinely do not know their current weight, they haven't stepped on a scale in months. Getting the dose right depends on information the patient may simply not have on hand, and that is a shared responsibility to solve, not a patient failing. Therefore, it requires good monitoring.

Third, Warfarin, a common blood thinner. Older adults are more sensitive to it, which is why they are typically prescribed lower doses and monitored closely. Without a family member or carer helping to supervise, doses can be missed, doubled, or mixed up, especially when pills of different colours and strengths start to blur together. This is exactly why we describe this group as vulnerable, not because of any personal failing, but because a bit more support could prevent real harm.

Some patients are more vulnerable than others, and how vulnerable someone is, depends heavily on their specific context, their culture, their circumstances, their history with the healthcare system. The good news is that thoughtful, well-designed tools and approaches can protect vulnerable patients and help ensure they are not excluded from care or research simply because they are considered vulnerable.

Ethical and Cultural Considerations in Practice

So how do we act on all of this? A few concrete practices can make a real difference.

In clinical research, enabling tools can protect the vulnerable instead of simply excluding them: like interpreters for migrants who don't speak the local language, or honest and no-false-hope conversations for people managing obesity or chronic disease. The goal is inclusion without compromising honesty.

Informed consent in multicultural settings means adapting language, communication style, and materials so that consent forms use plain, layman's terms, and so that diverse populations are

involved from the start. This may help ensure that the patient actually understands the information, alternatives, risks and implications and has a genuine opportunity to ask questions and make a voluntary decision.

End-of-life care intersects deeply with religious belief. Even when we do not share, or fully understand, someone else's belief system, the answer is always the same: Cultural humility. Being respectful enough to support someone's practices, without needing to agree with or even fully grasp them.

And for pregnant or lactating women, decisions about preventive medication involve four factors that all deserve attention: ethical, clinical and practical, sociocultural, and evidence-based considerations. The goal is not to agree with every choice a patient makes, it is to make sure all four factors are respectfully and thoroughly addressed.

4. Closing

Then again! When we understand what makes a patient vulnerable and why, we can then mitigate the risks and improve outcomes. And awareness is the first step. Once we notice the risk factors, the biases, and the barriers we have covered across this whole session, we can actually start to change them and improve outcomes for the patients.

Also, healthcare organisations need concrete mechanisms for accessible communication, interpreters, medication reconciliation, representative research, patient involvement and monitoring of inequities, in order to translate awareness into action.

> **You have now completed Session 4!**

In our next session, we will turn to side effects and adverse drug reactions, and how patient-reported outcomes help capture what really matters to the people living with multiple conditions and treatments. See you in session 5.

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