SAFEPOLYMED

Safety in Polypharmacy Training Course

Session 5

Fundamental Concepts in Reporting Treatment Side Effects

Written version of the video scripts

In this session

Video #1 — Understanding Adverse Events, Side Effects & Adverse Drug Reactions

Video #2 — Reporting ADRs, Grading Systems & Patient Preferences

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PATIENT ENGAGEMENT IS IN OUR DNA

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VIDEO #1 — Understanding Adverse Events, Side Effects, and Adverse Drug Reactions

Estimated Duration: 10–12 minutes
Target Audience: Broad: patients, caregivers, and clinicians

1. Introduction

Have you ever taken a medicine and felt something unexpected happen afterward, and wondered, was that just something that happens sometimes, or was it actually caused by my medication? Well, the answer matters more than you might think.

In this video, we are going to untangle three terms that get used interchangeably but mean different things: adverse events, side effects, and adverse drug reactions. Getting this right is the first step toward reporting them properly and making medications safer for everyone.

2. Main content

Three Terms, Three Meanings: AE, Side Effect, and ADR

Let's start broad.

An adverse event or AE is any unwanted event or symptom that may or may not be related to a treatment you are taking. It can be any sign or symptom that comes up, and here's the tricky part: because this is often studied in a very controlled research setting, we usually only know about the adverse events linked to the specific medication being studied, not necessarily how it behaves once it is combined with everything else you might be taking. Researchers make an assumption, that a patient experienced an adverse event, and then it is often up to the investigator to decide whether it is actually related to the medicine. So, by definition, an adverse event may not necessarily be caused by that medicine at all.

Next in this continuum comes the side effect. Side effects are unintended effects that occur alongside the effect you actually want from a medication. For example, a pain medication might relieve your discomfort but also make you drowsy. Some well-known examples: paracetamol (also known as Tylenol) can affect the liver, while ibuprofen can affect the

kidneys; and that is tied to how these medications work in the body. Side effects can be positive or negative, even though we tend to assume they are always negative.

Now, an adverse drug reaction or ADR. This is a specifically harmful response that happens even at a standard, normal dose of a medication, essentially, a more severe, unintended effect that we relate directly to the medicine and the treatment itself. An example would be someone developing a severe rash after taking an antibiotic.

It is also worth knowing that medicines are sometimes used off-label, meaning the drug has not been officially studied for that particular use, even though it is approved for something else. Gabapentin is a good example: it is approved in the EU for seizures and nerve pain, but it is sometimes prescribed off-label for restless leg syndrome or anxiety. So, when a medicine is used off-label, side effects like drowsiness or the potential for abuse can be overlooked and under-reported, which means we may actually be underestimating how often ADRs happen. And here's the key message: whether you think you have experienced a full adverse drug reaction, a typical side effect, or just an adverse event, all of these are worth reporting.

Why do ADRs Matter?

Adverse drug reactions are one of the leading causes of illness and death in healthcare. Research from the UK's Yellow Card scheme found that ADRs are linked to 1 out of every 16 hospital admissions, that 10 to 20% of hospitalised patients are thought to have experienced an ADR, and that over 2% of patients who had an ADR died as a result.

Beyond the numbers, ADRs can change a patient's health status and quality of life, which can lead to what is often labelled "non-compliance" with treatment, and this is sometimes overlooked. The key message here is that ADRs matter to patients, and it is okay to speak up. Do not just assume that what you are experiencing is simply "what to expect" from a medication.

Types of ADRs

ADRs can be classified in more than one way. One is by how predictable they are: predictable ADRs, like an excessive effect of a drug or a known secondary side effect, versus unpredictable ones, like an allergic reaction or an idiosyncratic response nobody saw coming.

There is also an alphabetical classification, describing six types: Type A, for Augmented: dose-related reactions, like an insulin overdose causing hypoglycaemia; Type B, for Bizarre: reactions

unrelated to dose, like an allergic or anaphylactic reaction; Type C, for Chronic: reactions that persist over a long time, like adrenal suppression from corticosteroids; Type D, for Delayed: reactions that show up well after the dose, like dyskinesia from antipsychotic medications; Type E, for End of use: withdrawal reactions, like seizures after suddenly stopping phenobarbital; and Type F, for Failure: an unexpected failure of the therapy itself, like antibiotics becoming less effective due to resistance.

Beyond these categories, ADRs can overlap in tricky ways, and this is exactly why education matters: even though we tend to think of ADRs as unpredictable and severe, many are actually predictable as a direct result of the combinations of medicines we take.

Serious vs. Severe: A Critical Distinction

Taking this further, it is worth distinguishing an adverse drug reaction or ADR, from an adverse drug event or ADE. They are related but different terms. An ADE is harm caused by either an appropriate or inappropriate use of a drug, is a broad category. ADRs are actually a subgroup of ADEs, specifically where the harm happens under appropriate use, at the normal prescribed dose.

Also, there are two words that sound similar but mean different things: serious and severe. A serious adverse reaction is one that results in death, is life-threatening, requires hospitalisation or prolongs an existing hospital stay, causes persistent or significant disability, or results in a birth defect. "Severe," on the other hand, is a broader term that includes serious reactions plus other reactions that don't necessarily lead to long-term problems. Important to consider is that both, severe and serious reactions must be reported.

Why Reporting ADRs Matters

Here's why this all matters: If patients and healthcare providers don't report these reactions, we simply don't have the information needed to keep marketed drugs as safe and effective as possible. Reporting can lead to changes in drug development, market withdrawal of a drug, new research directions, dose adjustments, updated drug label warnings, or restricted use in certain populations. And patient reports specifically add real value here: Compared to reports from healthcare providers, patient reports often provide new information, more detailed descriptions, and can refer to a wider range of drug categories and responses.

Real-world reporting can make a genuine difference. In the 1990s, a popular weight-loss medication known as Fen-Phen (fenfluramine and phentermine) hit the market. Once people started taking it, doctors began noticing patients developing high blood pressure, both regular high blood pressure, but also in their lungs, and then damage to their heart valves. Thanks to that reporting, the medication was withdrawn from the market later on due to these significant risks. This is a powerful reminder that a lot can go undetected in short clinical trial settings, and that real-world reporting is what can eventually lead to new warnings, restrictions, or even a drug being pulled from the market altogether.

Who Reports ADRs, and How?

So, who is actually responsible for reporting ADRs? There is a whole chain of people who can report: doctors, pharmacists, nurses and midwives, paramedics, laboratory technicians, medical assistants, and patients themselves. In many countries, these reports flow through to a central authority, sometimes called an ORMP, or Office for Registration of Medicinal Products, Medical devices and Biocidal products.

But it is everyone's responsibility! Including yours, as a patient.

There are two main ways ADRs get reported. Spontaneous reports, which are voluntary, unsolicited notifications by a patient, a health professional, or anyone else, alerting medicine regulators about a possible adverse drug reaction.

And solicited reports, which come from organised data collection systems, like clinical trials, non-interventional studies, registries, and health institutions. Whenever an ADR is suspected in these settings, a causality assessment is done, and if there is a strong link between the reaction and the drug, a solicited report gets prepared.

Looking at real reporting data, for example, from Poland's Office for Registration of Medicinal Products between 2017 and 2019 we can see reporting trends shifting over time, including a gradual increase in reports coming directly from patients and their representatives, alongside those from pharmacies and healthcare institutions.

Grading Adverse Events: The CTCAE System

Since we are on the topic of reporting, let's talk a bit about adverse events, or adverse drug reactions, reported by pharmaceutical companies, since they are required to report these. When they do, they also need to indicate a grade, which is essentially an assessment of the

severity of the event. There have been efforts to standardise this grading. For example, in clinical trials, adverse events are commonly graded using the Common Terminology Criteria for Adverse Events, or CTCAE, sometimes referred to as the "common toxicity criteria".

It grades adverse events on a scale from 1 to 5: Grade 1 is mild, with only clinical or diagnostic observation needed; Grade 2 is moderate, requiring minimal, local, or non-invasive intervention; Grade 3 is severe or medically significant, often requiring hospitalisation; Grade 4 is life-threatening, requiring urgent intervention; and Grade 5 means the adverse event was fatal.

CTCAE has real strengths: It is internationally accepted, organised by organ system, and widely used across clinical trials and cancer therapy. But there are weaknesses too. It may underrepresent patients' own perspectives on their adverse events and how they affect their daily life. Many clinicians consider only Grade 3 and above to be truly "severe" yet even a Grade 2 side effect, like diarrhoea that limits your ability to leave the house, can have a real impact on someone's daily life, and that is not always reflected in how the grading gets used or discussed. Ultimately, deciding what is tolerable is something only the patient themselves can weigh, based on their own risk-benefit analysis.

A scale built for and used only in the context of clinical trials may not translate to the real world nor may it capture the true Adverse Events in the context of polypharmacy.

ADRs in the Context of Polypharmacy

And this is where polypharmacy comes back into the picture. A 2020 meta-analysis by Chang and colleagues found that taking five or more prescribed drugs was associated with a 31% higher mortality risk. That is a striking number. More broadly, the risk of potential drug-drug interactions grows proportionally with the number of drugs a person takes, and up to 14% of ADRs in hospital settings have been caused by DDIs specifically.

Here's a very real, very common example: a patient taking ibuprofen alongside two blood pressure medications. Individually, each of these drugs might be considered safe, and the risk might even be predictable if you know what to look for. But combined, they can cause the kidneys to fail completely. This is especially common in elderly patients who may already have underlying kidney issues. This is a sobering reminder that polypharmacy is not just about counting pills, it is about understanding how they interact once they are all in the same body at the same time.

3. Key takeaways

So, here's what to take away from this video:

You now know the difference, and whether it is an adverse event, a side effect, or an adverse drug reaction; if something feels off after starting a medication, it is always worth mentioning, whether to your clinician or, as we will explore next, by reporting it yourself.

Reporting them, however minor they seem, genuinely helps make medications safer for everyone, and patient reports in particular fill in details clinicians might miss.

In our next video, we are going to explore how patients' own experiences, their reported outcomes and their preferences, are captured, measured, and used to shape real healthcare decisions. See you in the next one!

VIDEO #2 — Reporting ADRs, Grading Systems & Patient Preferences

Estimated Duration: 6–7 minutes
Target Audience: Broad: patients, caregivers, and clinicians

1. Introduction

Imagine two treatment options. One is aggressive and might extend your life but comes with severe side effects. The other is gentler, with fewer side effects, but a shorter life expectancy. Which would you choose? There is no universally "right" answer, because it depends entirely on what matters most to you.

In this video, we are going to explore how patients' own reported outcomes and preferences are captured, and why they are just as important as any clinical measurement.

2. Main content

What Is a Patient-Reported Outcome (PRO)?

A patient-reported outcome, or PRO, is any outcome directly evaluated by the patient and reported based on their own perception of a disease and its treatment. It is an umbrella term covering a lot of ground: subjectively perceived health state, unobservable symptoms like pain intensity, physical, mental, and social functioning, health-related quality of life, and other patient-perspective details, like reporting a new onset of nausea, or satisfaction with treatment.

What makes PROs distinct is that they are reported directly by the patient, without a clinician or anyone else interpreting or filtering the information first. That makes them a genuinely quantitative source of evidence, not as an anecdotal colour, but real data.

PROMs: The Tools Behind PROs

PROs are measured using what is called PROMs or patient-reported outcome measures. These are the actual tools and instruments, like questionnaires, that patients use to report their outcomes.

PROMs have real strengths: they offer a patient-centred perspective with direct, holistic insight; they improve engagement and empowerment because patients actively participate; they provide comprehensive data on how well a treatment is really working; and they can influence regulatory approvals and health policy decisions. But they come with weaknesses too: the information is inherently subjective, which can introduce variability and bias between individuals; validating and standardising PROMs is genuinely challenging; healthcare providers need proper training before integrating them into clinical practice; getting a high, consistent patient response rate over time is not that easy; and they are not specific enough to capture side effects related to polypharmacy.

Importantly, like the CTCAE grading, none of these tools were designed to ask about the other medications someone is taking, so on their own, they still don't capture the polypharmacy picture.

Patient Preferences: What Matters Most to You

Beyond reporting how they feel, patients also have preferences; the specific desires, values, and priorities they hold about their healthcare choices. These reflect what matters most to a person in their own healthcare experience, and they vary enormously from one person to the next.

Let's go back to that opening scenario: An aggressive treatment that could extend life but comes with severe side effects, versus a less aggressive option with fewer side effects but a shorter life expectancy. Some patients will choose to fight for more time, whatever the cost. Others will prioritise quality of life and independence over length of life. Neither choice is right or wrong, they simply reflect different values. And that is exactly why capturing patient preferences matters so much in real healthcare decisions.

Patient Preference Studies (PPS)

So, this brings us to patient preference studies. Because every patient is unique, researchers have developed patient preference studies, that are structured research that captures

patients' preferences regarding treatment attributes, benefits, and risks, and importantly, what trade-offs patients are willing to accept

These studies can be conducted by patient groups, researchers, healthcare providers, or public and private partners, and they take various forms: health-preference assessments, stated-preference health surveys, broader health preference research, and patient-centred research more generally.

While individual preferences on treatment will naturally vary, patient preference studies can still reveal real commonalities across a patient population, or patterns that are useful when designing treatments and communicating about them. And this is what makes them so useful.

How Patient Preference Data Gets Used

So, what happens with all this preference data? Who actually uses this data? Regulators, HTA bodies and payers, academics, physicians, industry, and patients themselves all draw on patient preference data to inform decision-making in drug development and commercialisation across every stage, from discovery and preclinical development, through clinical development and market authorisation, to reimbursement and post-commercialisation.

That might mean shaping which treatment attributes get prioritised in a new drug's design, informing how risks and benefits are communicated to patients, or even influencing regulatory conversations about whether a treatment's benefit-risk profile truly aligns with what patients actually want.

In short: patient preferences are not just a "nice to have" They are becoming a genuine input into how medicines are developed and brought to market.

3. Key takeaways

So, here is what we would like you to take away from this session: Don't stay quiet about ADRs, however small they might seem, report them, whether through your healthcare provider, directly to regulators, or both.

And remember that your preferences and priorities matter just as much as the clinical data. Your experience, how you feel, what side effects you are living with, and what trade-offs matter to you; this is real data and they can genuinely shape how future treatments are developed and delivered.

We are not going to eliminate side effects from medication use altogether, but through education, reporting, and patient-informed research, we can keep improving how safely and thoughtfully these medications are used.

If your clinic offers patient-reported outcome questionnaires, take them seriously and fill them in consistently. And don't be afraid to talk openly with your healthcare team about what matters most to you in your treatment choices.

You have completed Session 5!

In our next session, we will look at safety signal reporting and the digital health tools that are making it easier than ever for patients to report side effects directly.

See you in session 6!

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